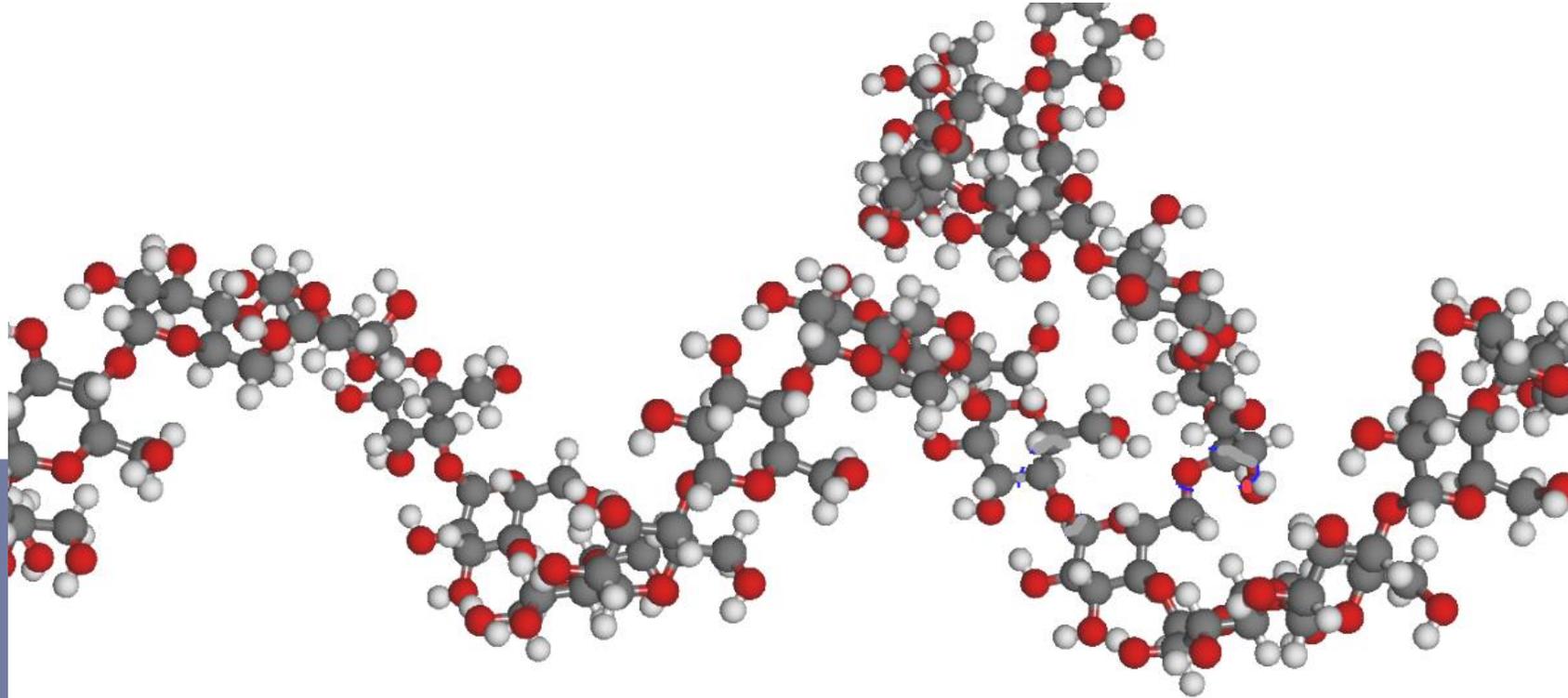


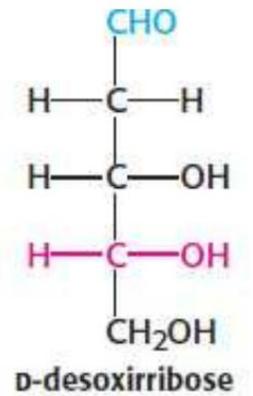
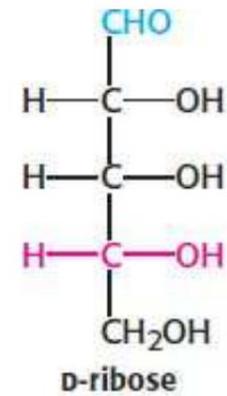
Estrutura e função de carboidratos e glicoconjugados



QBQ0204 Bioquímica
Felipe Jun Fuzita

Contextualização e História

- ▶ Carboidratos são as biomoléculas mais abundantes na Terra (fotossíntese- celulose, amido; chitina em artrópodes).

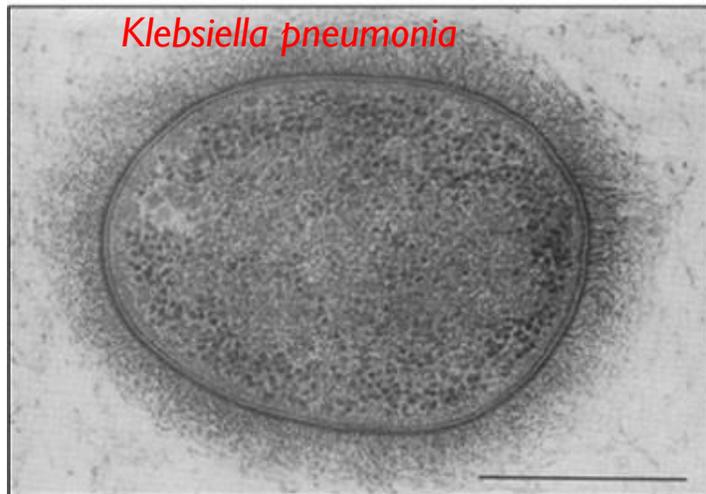
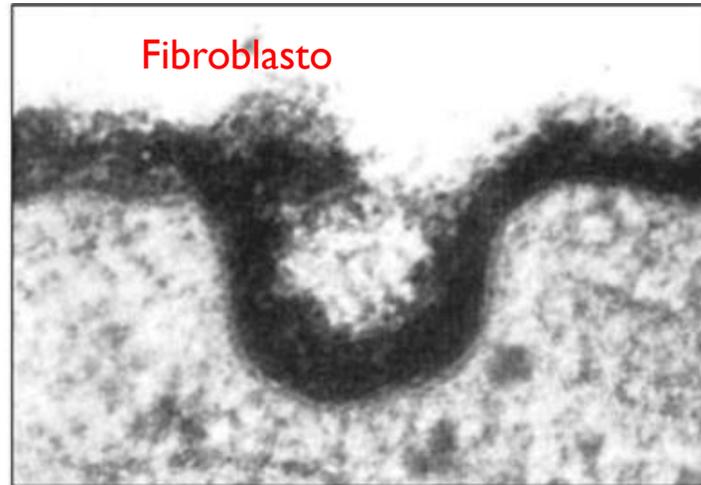
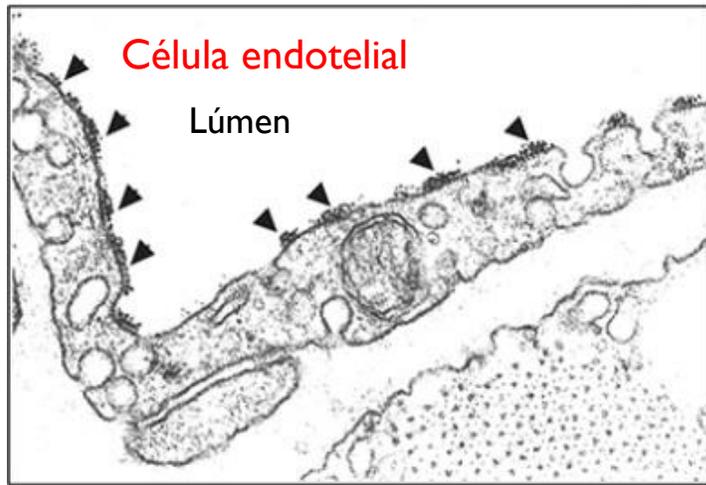


- ▶ Todas as células são recobertas por uma complexa mistura de açúcares.

- ▶ Presentes na estrutura dos ác. nucleicos (pentose), glicolipídeos , glicoproteínas, proteoglicanas ou livres.



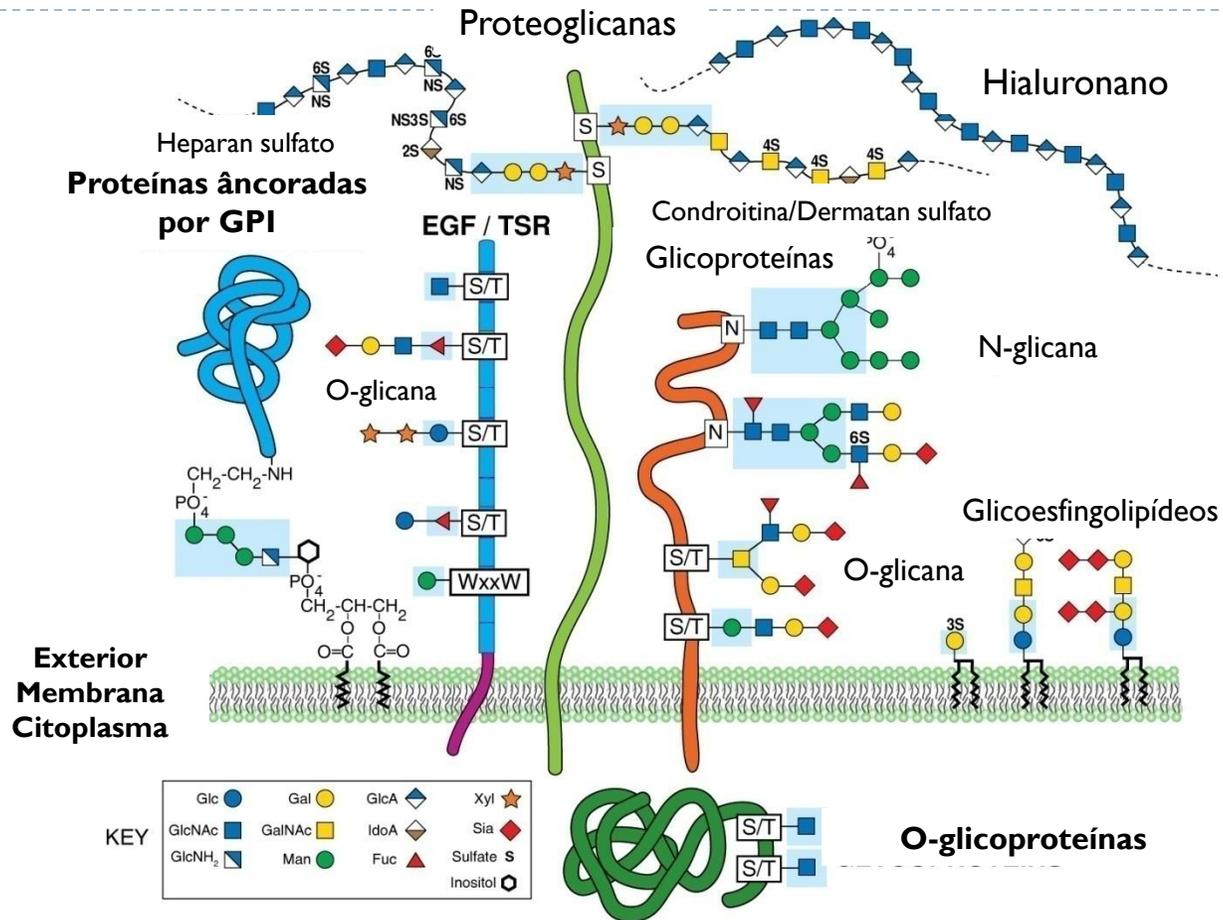
Contextualização e História



Capítulo 1, Figura 4. VARKI et al. (2015) *Essentials of Glycobiology*, 3rd Edition. New York. Cold Spring Harbor Press.



Representação Esquemática da superfície celular



Capítulo 1, Figura 6. *Essentials of Glycobiology*, Third Edition

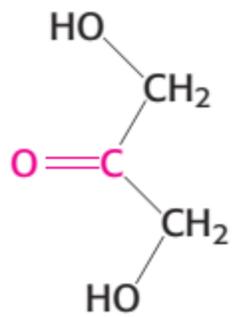


Parte I:
Estrutura

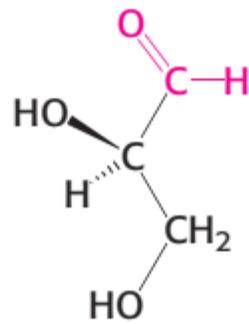


Estrutura e nomenclatura

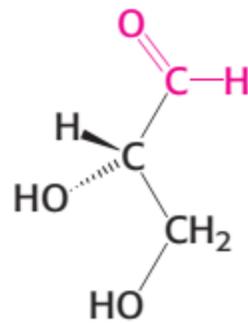
- ▶ Carboidratos = hidratos de carbono $(C.H_2O)_n$, $n \geq 3$.
- ▶ As unidades básicas são os monossacarídeos (não podem ser hidrolisadas em unidades menores).
- ▶ Grupos funcionais: poli-hidroxi aldeídos (aldose) ou poli-hidroxicetonas (cetose), genericamente –oses.



Dihydroxyacetone
(a ketose)



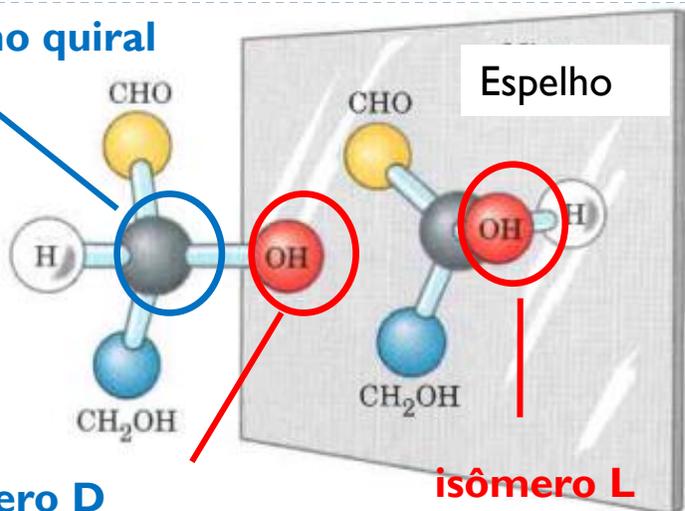
D-Glyceraldehyde
(an aldose)



L-Glyceraldehyde
(an aldose)

Estrutura – Formas de representação

carbono quiral

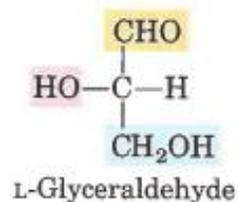
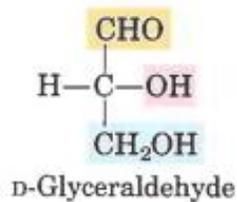


n centros quirais, 2^n estereoisômeros

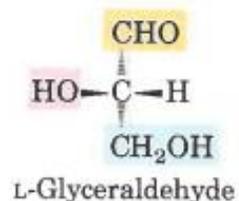
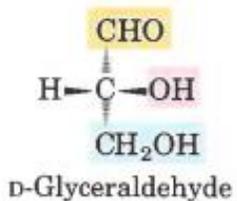
Modelo esfera e bastão

isômero D

isômero L

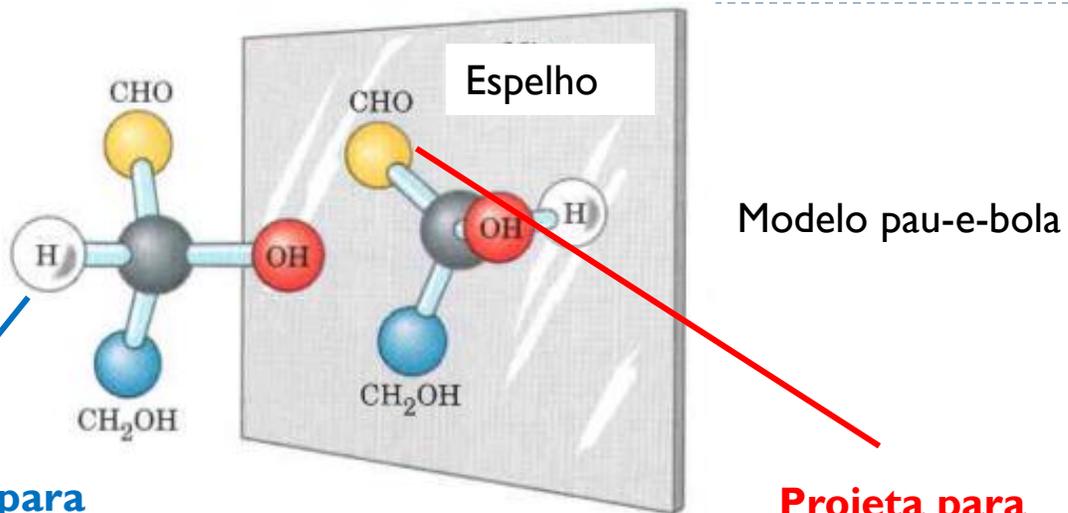


F Projeção de Fischer



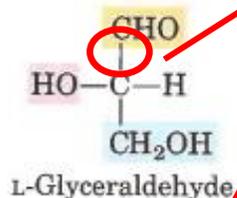
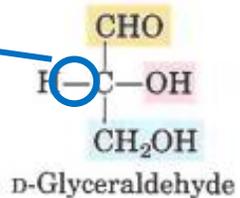
Fórmulas em perspectiva

Estrutura – Formas de representação

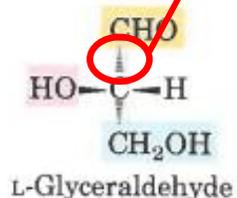
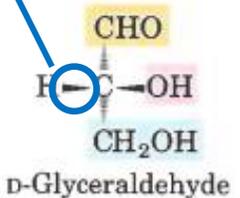


Projeta para
FORA do plano
da folha

Projeta para
DENTRO do
plano da folha



Projeção de Fischer



Fórmulas em perspectiva

Estrutura e isomeria

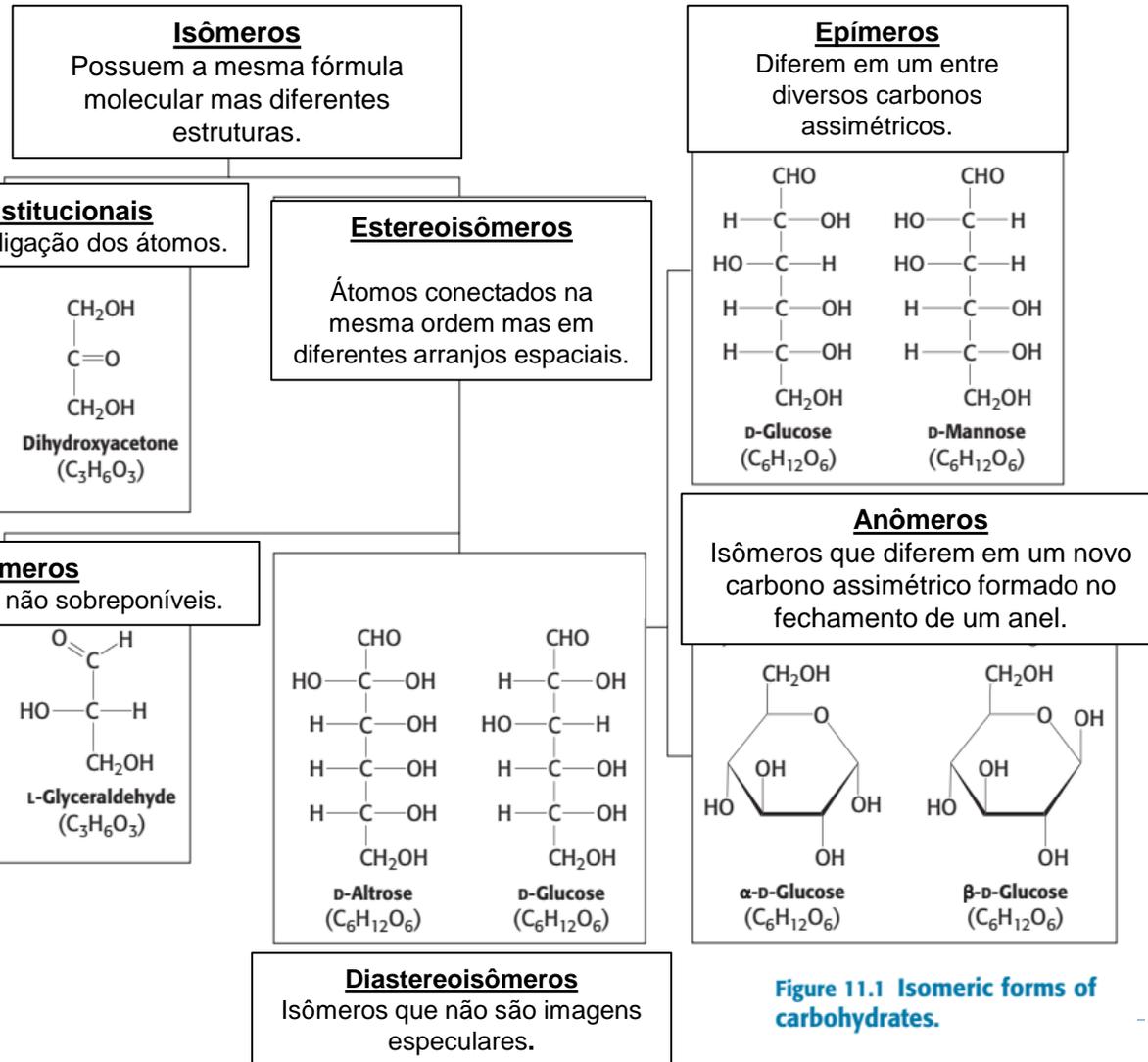


Figure 11.1 Isomeric forms of carbohydrates.

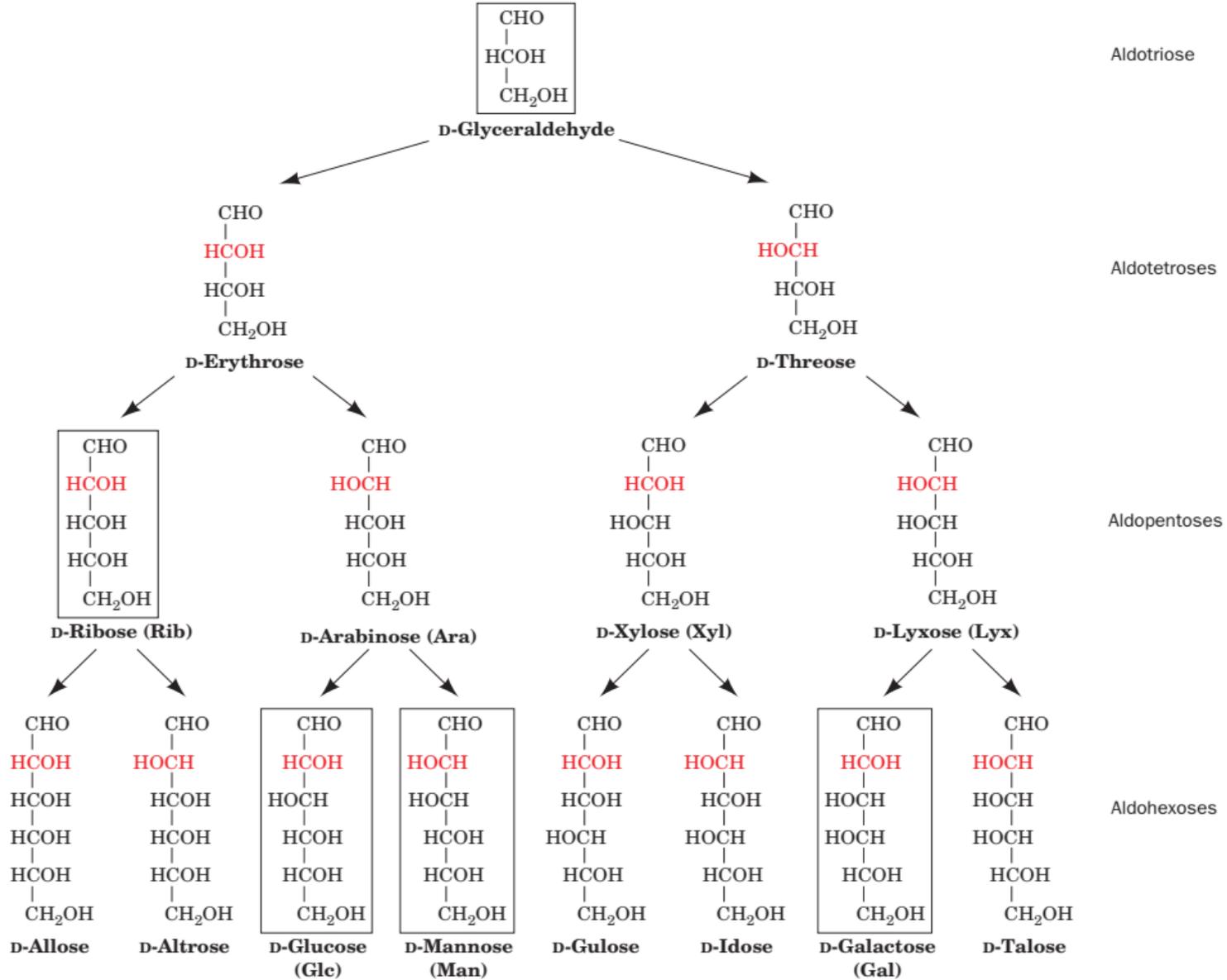


Figure 11-1 The stereochemical relationships, shown in Fischer projection, among the D-aldoses with three to six carbon atoms. The arrows indicate stereochemical relationships (not biosynthetic reactions). The configuration about C2 (red)

distinguishes the members of each pair. The L- counterparts of these 15 sugars are their mirror images. The biologically most common aldoses are boxed.

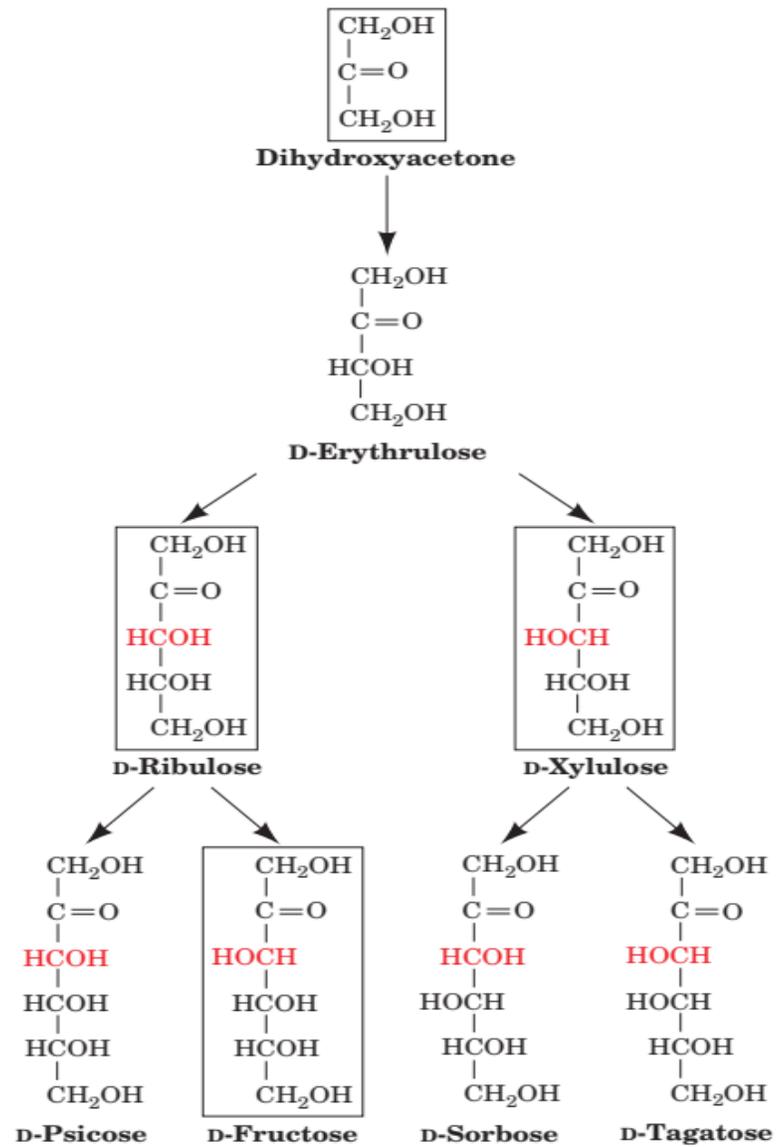
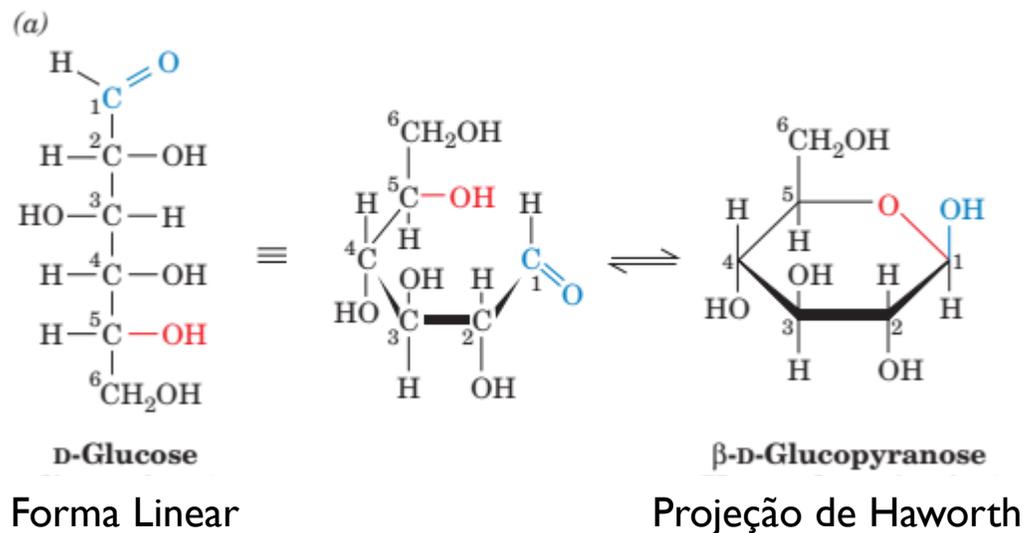
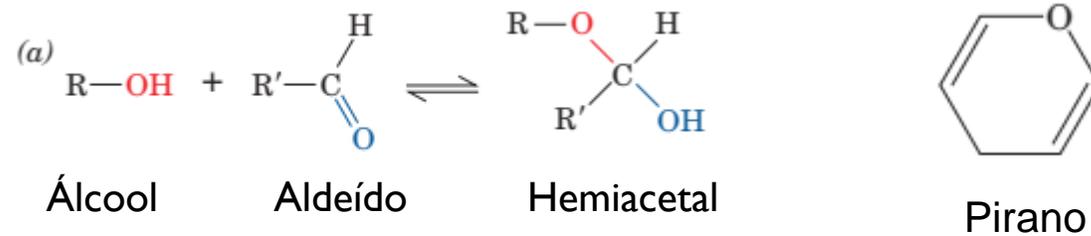
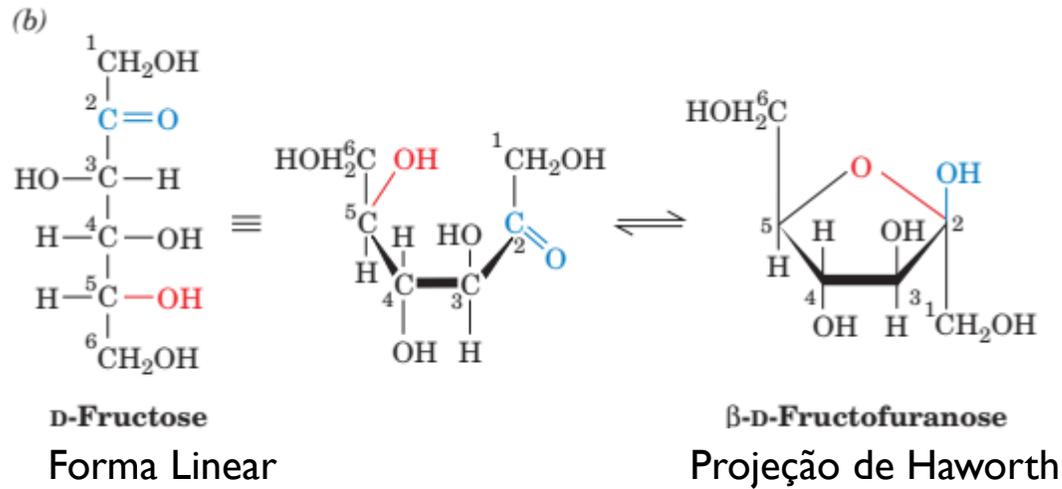
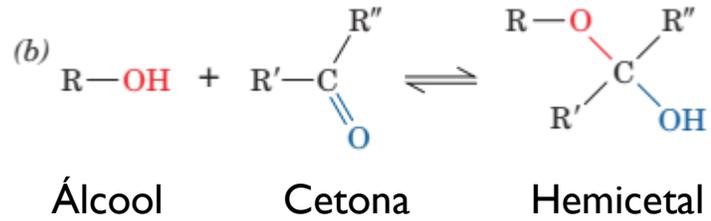


Figure 11-2 The stereochemical relationships among the **D-ketoses with three to six carbon atoms**. The configuration about C3 (*red*) distinguishes the members of each pair. The biologically most common ketoses are boxed.

Ciclização de monossacarídeos- Piranose



Ciclização de monossacarídeos- Furanose



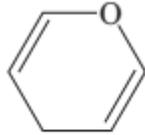
Furano



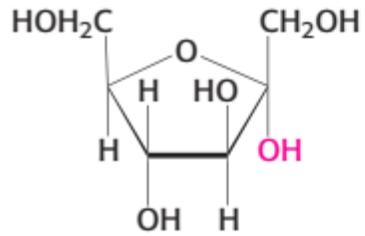
Furanose vs Piranose



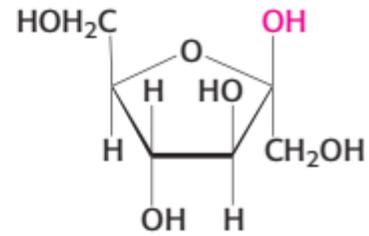
Furan



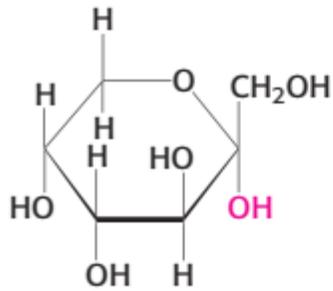
Pyran



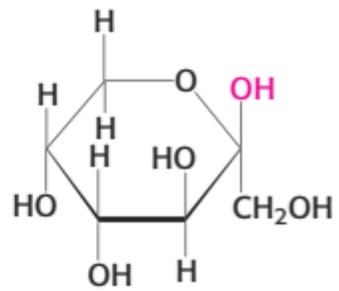
α -D-Fructofuranose



β -D-Fructofuranose



α -D-Fructopyranose



β -D-Fructopyranose



Anomeria

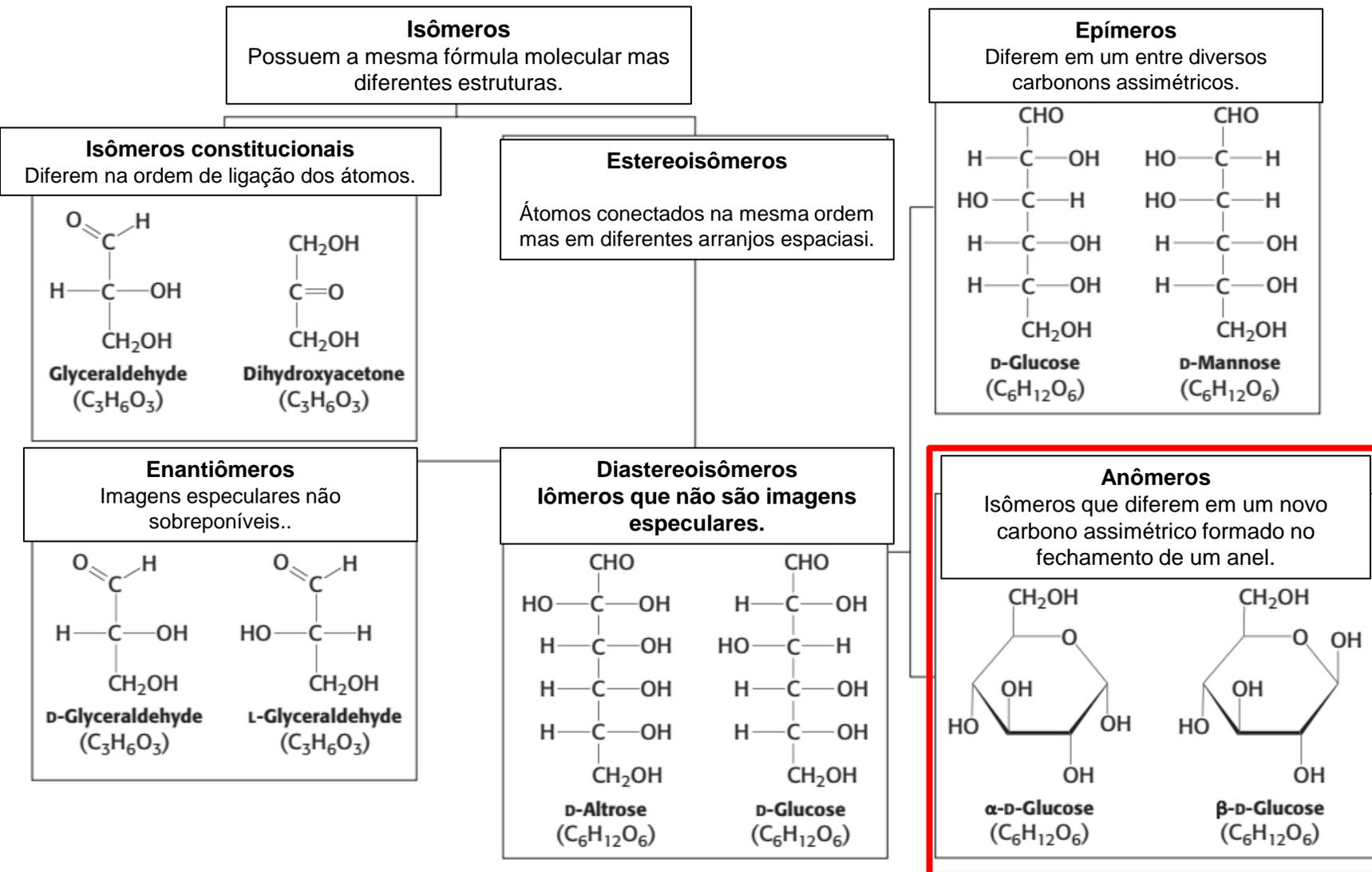
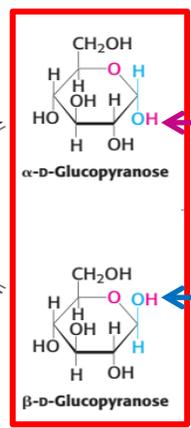
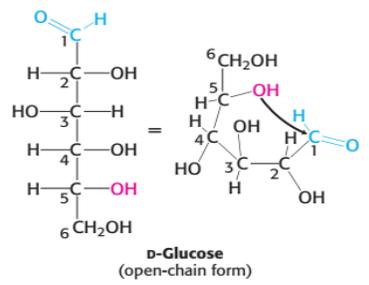


Fig. 11.1

Figure 11.1 Isomeric forms of carbohydrates.

<1% na forma linear

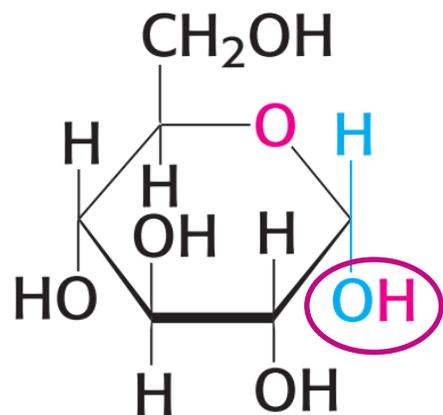


Alfa

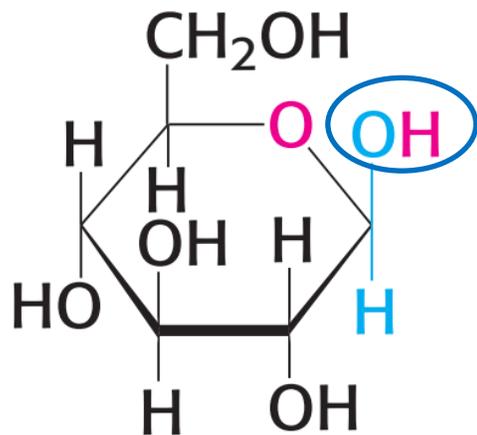
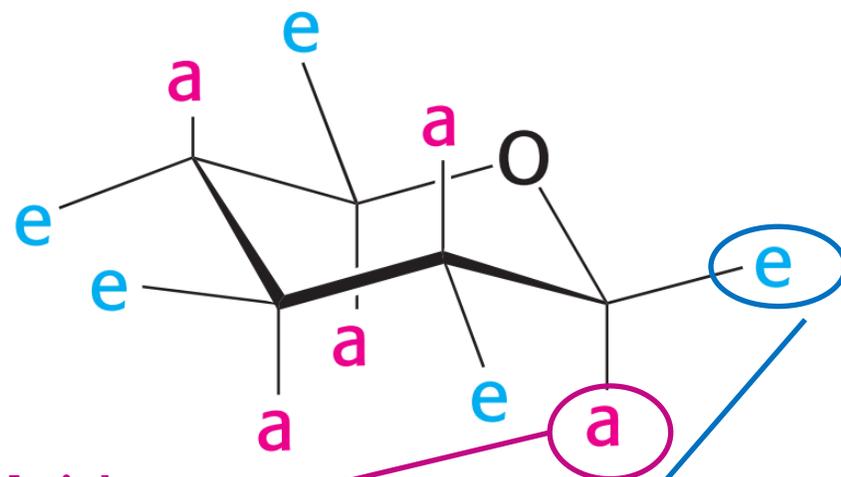
Beta



Anomeria



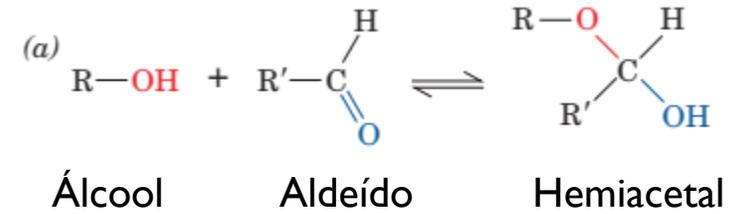
Alfa - Axial
"para baixo"



Beta - Equatorial
"para cima"



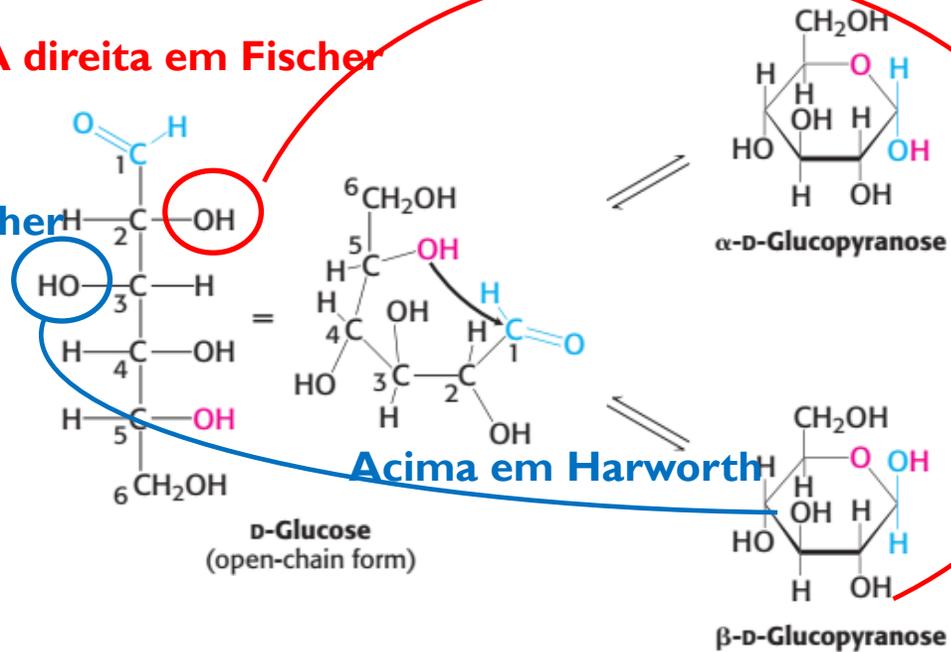
Projeção de Haworth



À direita em Fischer

Abaixo em Haworth

À esquerda em Fischer



Projeção de Haworth



Anomeria

<1% na forma linear

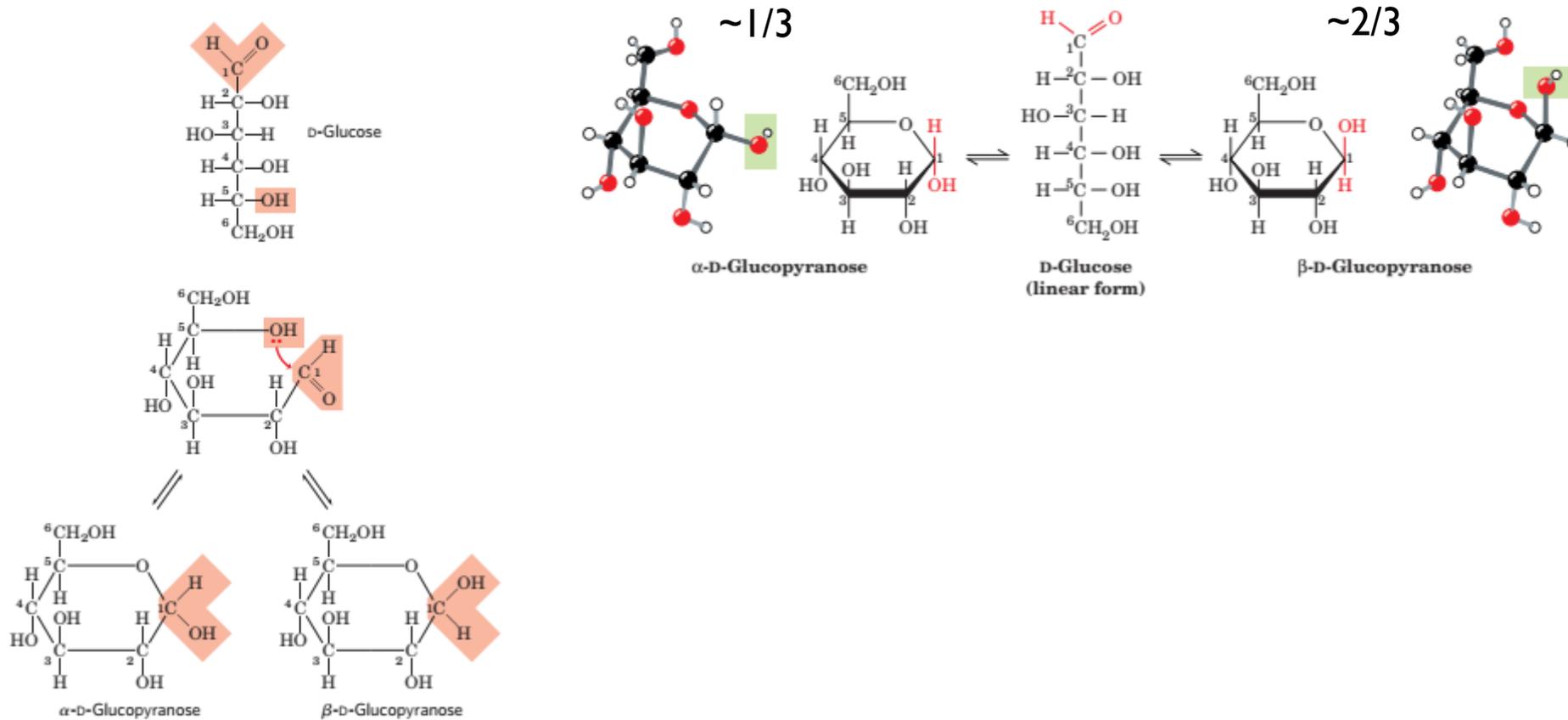
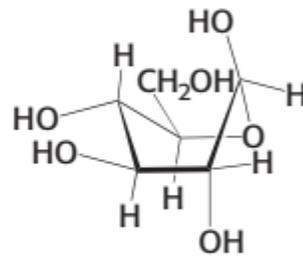
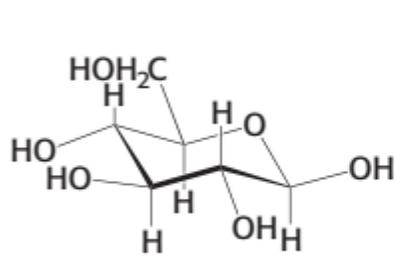
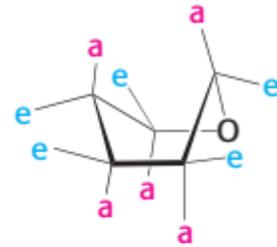
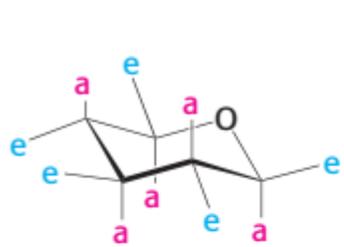
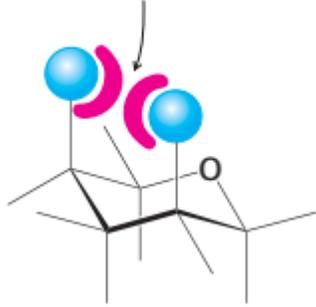


Fig. 7.6
LEHNINGER, A. L., NELSON, D.
L., & COX, M. M. (2014).
Lehninger principles of biochemistry.
New York, Worth Publishers.

Conformações das formas cíclicas

Steric hindrance



Formato cadeira

Formato barco

Fig. 11.7
BERG, J. M., TYMOCZKO, J.
L., STRYER, L., & STRYER, L.
(2012). *Biochemistry*. New
York, W.H. Freeman.



Ligação N-Glicosídica

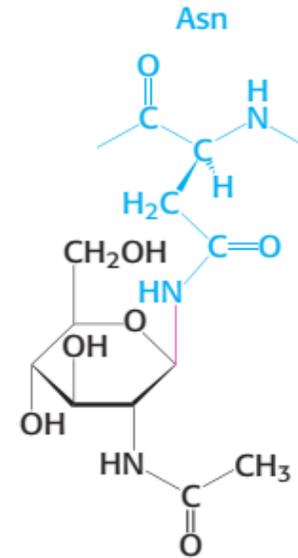
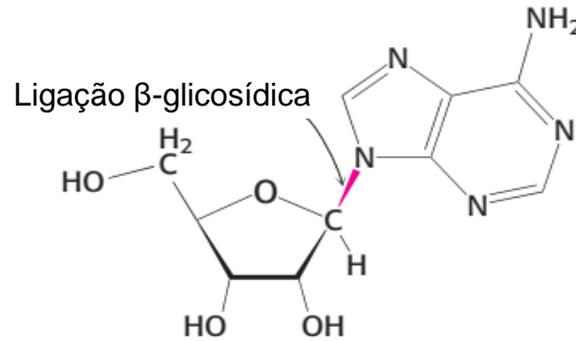
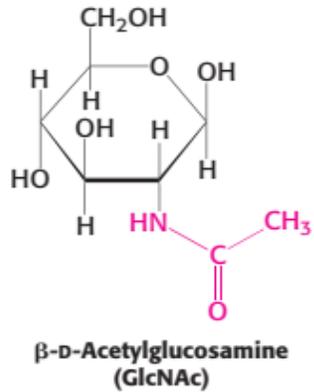
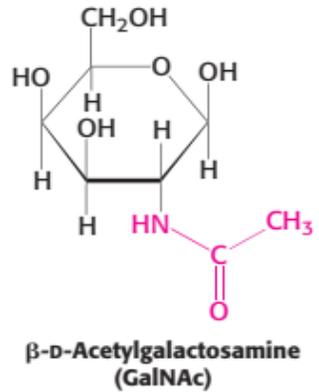


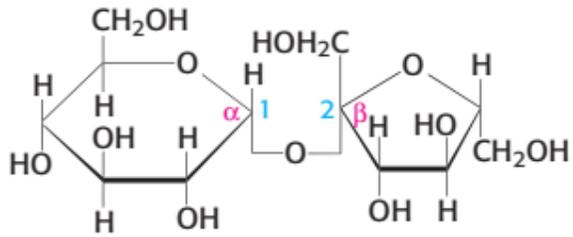
Figura 11.9 – Monossacarídeos modificados **Figura 4.5** – Ligação β -glicosídica em nucleosídeo.

Figure 11.15

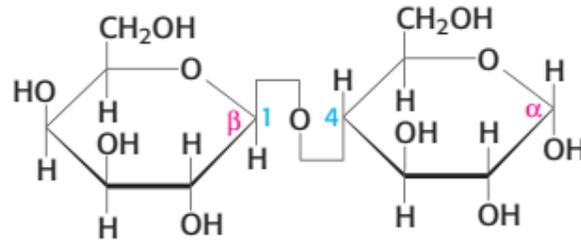
Ligação do carbono anomérico ao átomo de Nitrogênio de uma amina



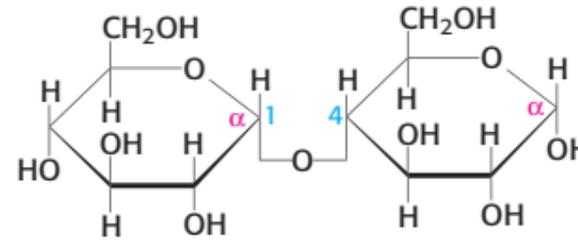
Ligação O-Glicosídica



Sacarose
Ligação α -1,2-glicosídica

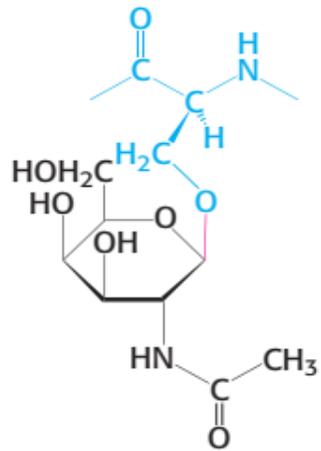


Lactose
Ligação β -1,2-glicosídica



Maltose
Ligação α -1,4-glicosídica

Ser



Ligação O-glicosídica GalNAc a hidroxila da cadeia lateral de Ser.

Ligação do carbono anomérico ao átomo de oxigênio de uma hidroxila.

Homopolissacarídeos - Amido e Celulose

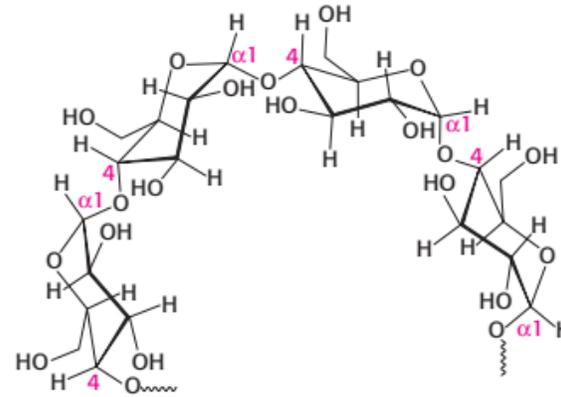
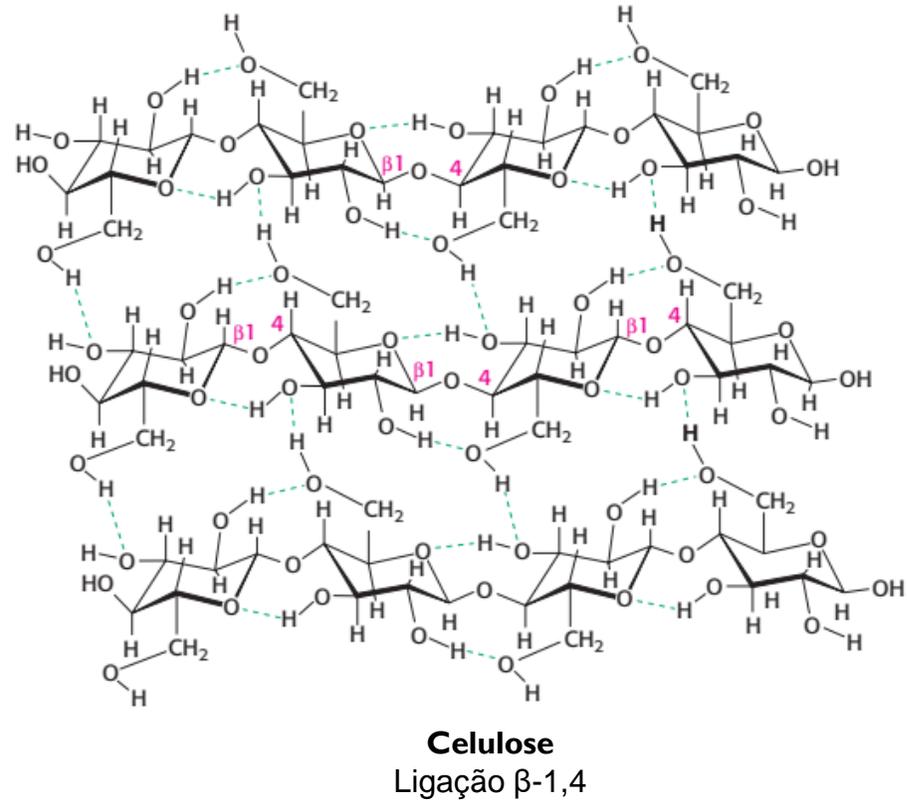
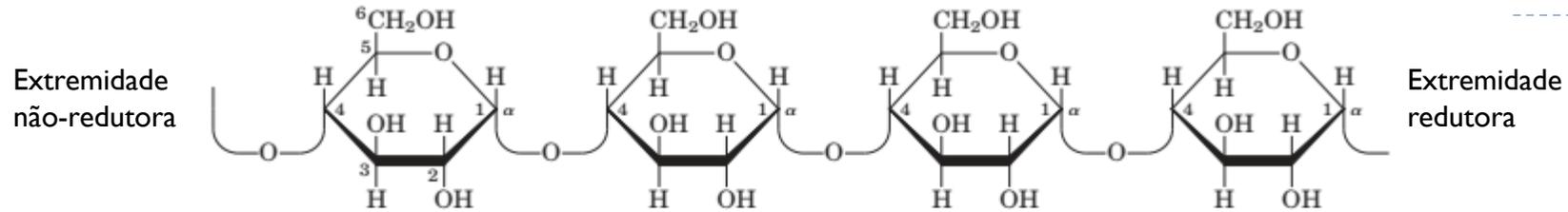
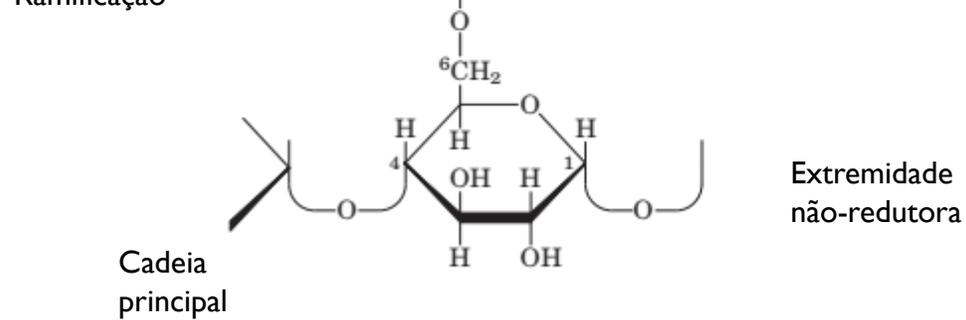
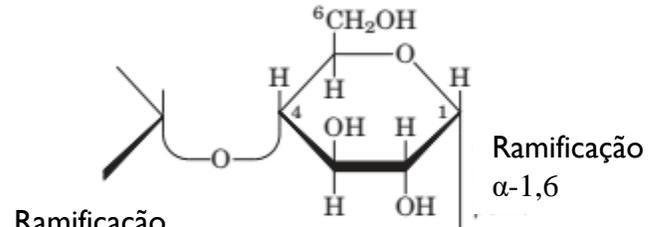


Figura 11.14 – As ligações glicosídicas determinam a estrutura do polissacarídeo.

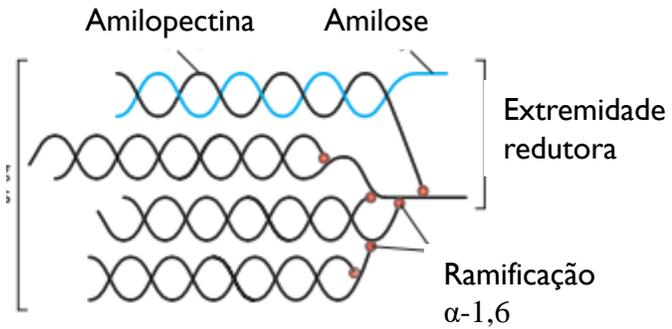
Amido



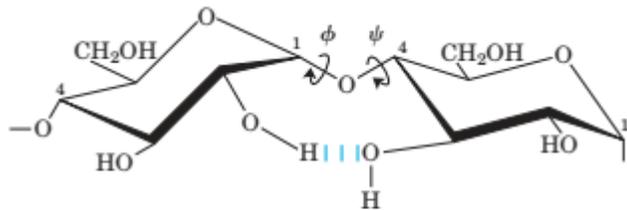
Amilose



(b)



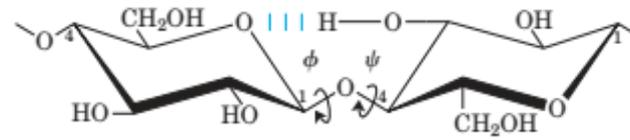
(c)



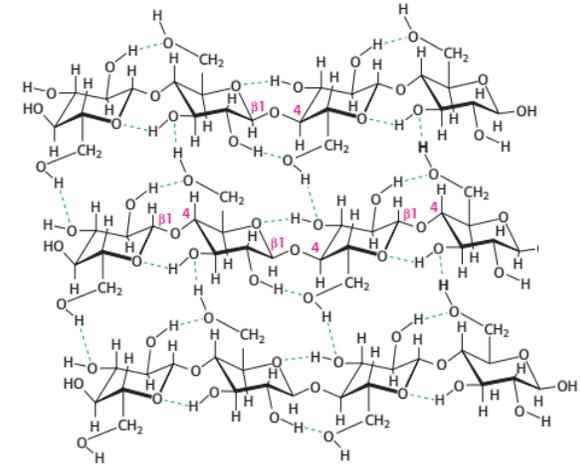
(α 1- Amilose



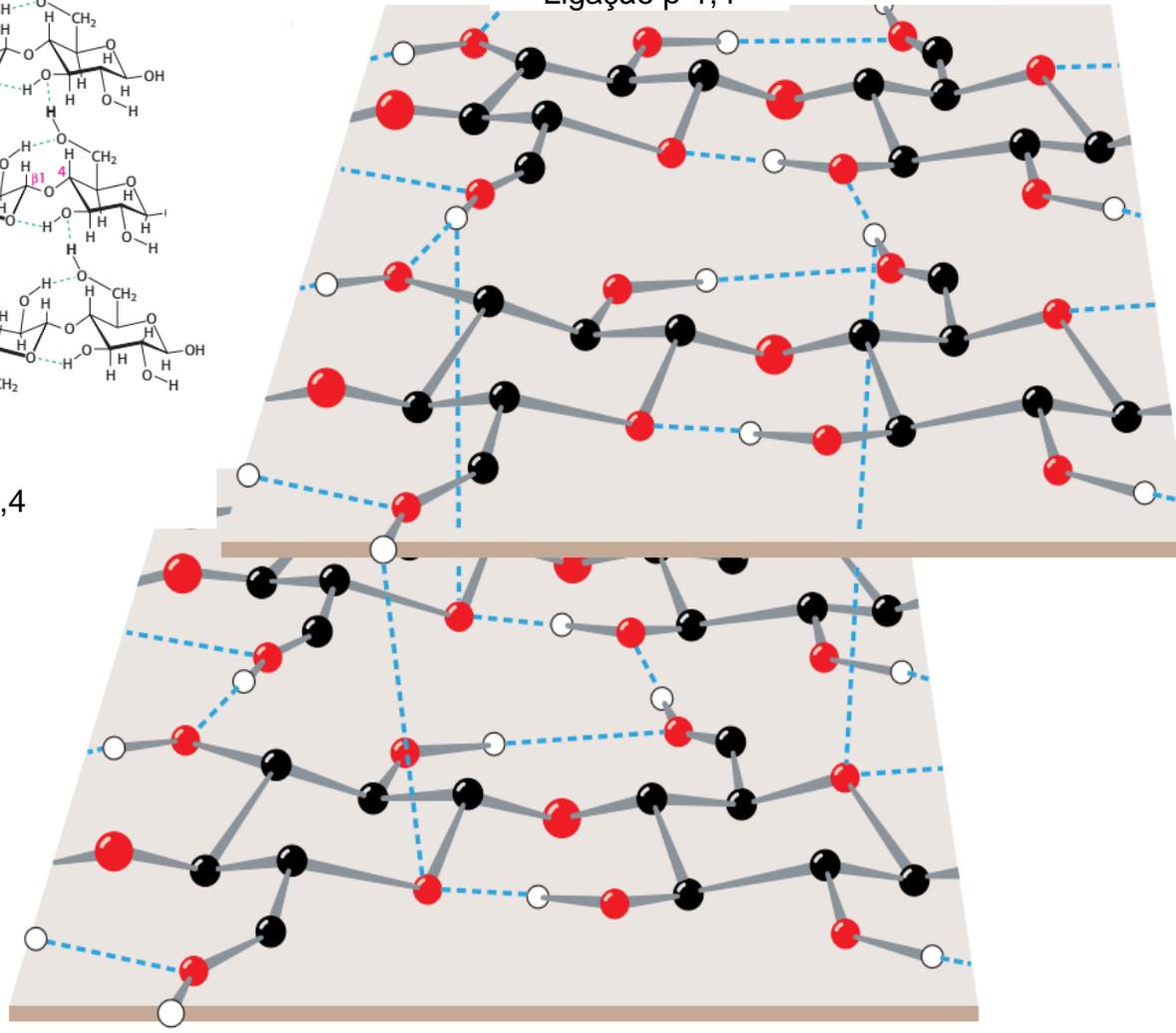
Celulose



Celulose
Ligação β -1,4

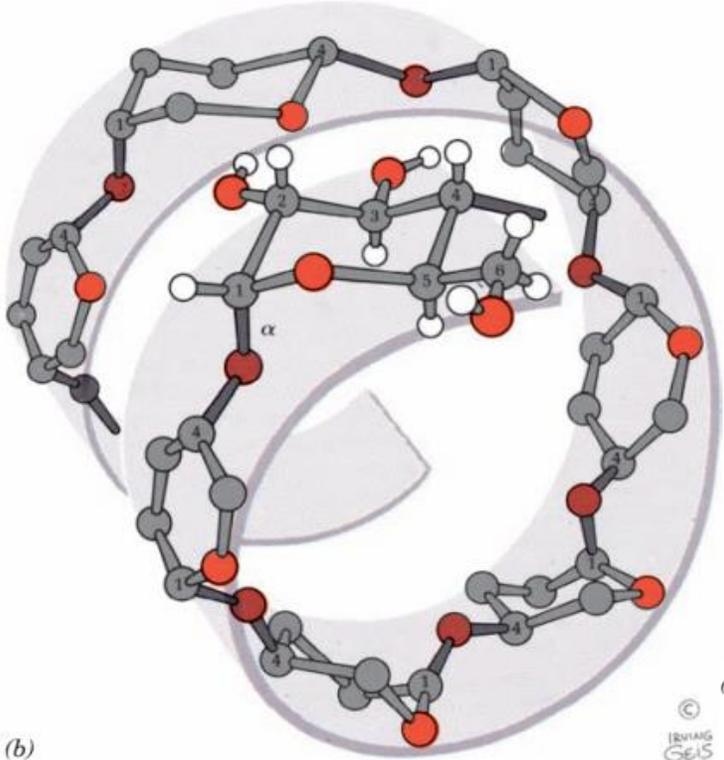


Celulose
Ligação β -1,4



(a)

Amilose



(b)

Fig. 11;18 – Amilose, ligação α -1,4

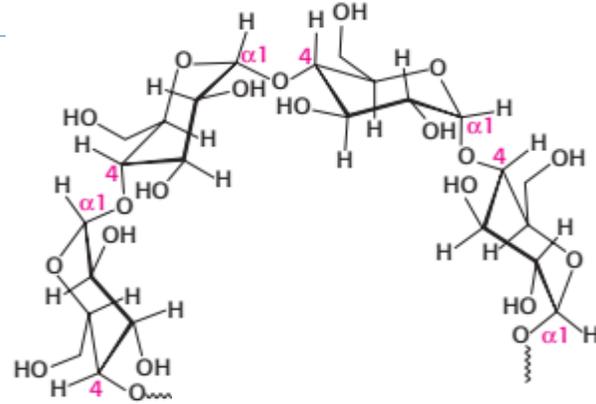


Fig. 11;14
Amido e
glicogênio
Ligação α -1,4

(b)
© IUNING
GEIS

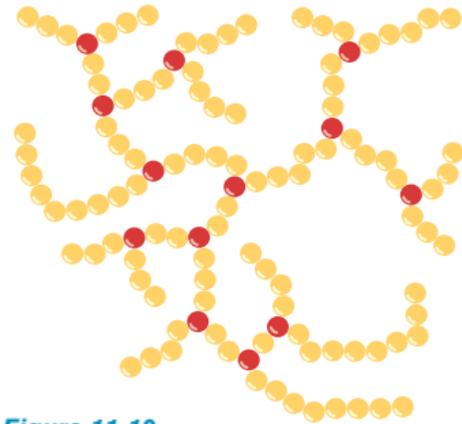


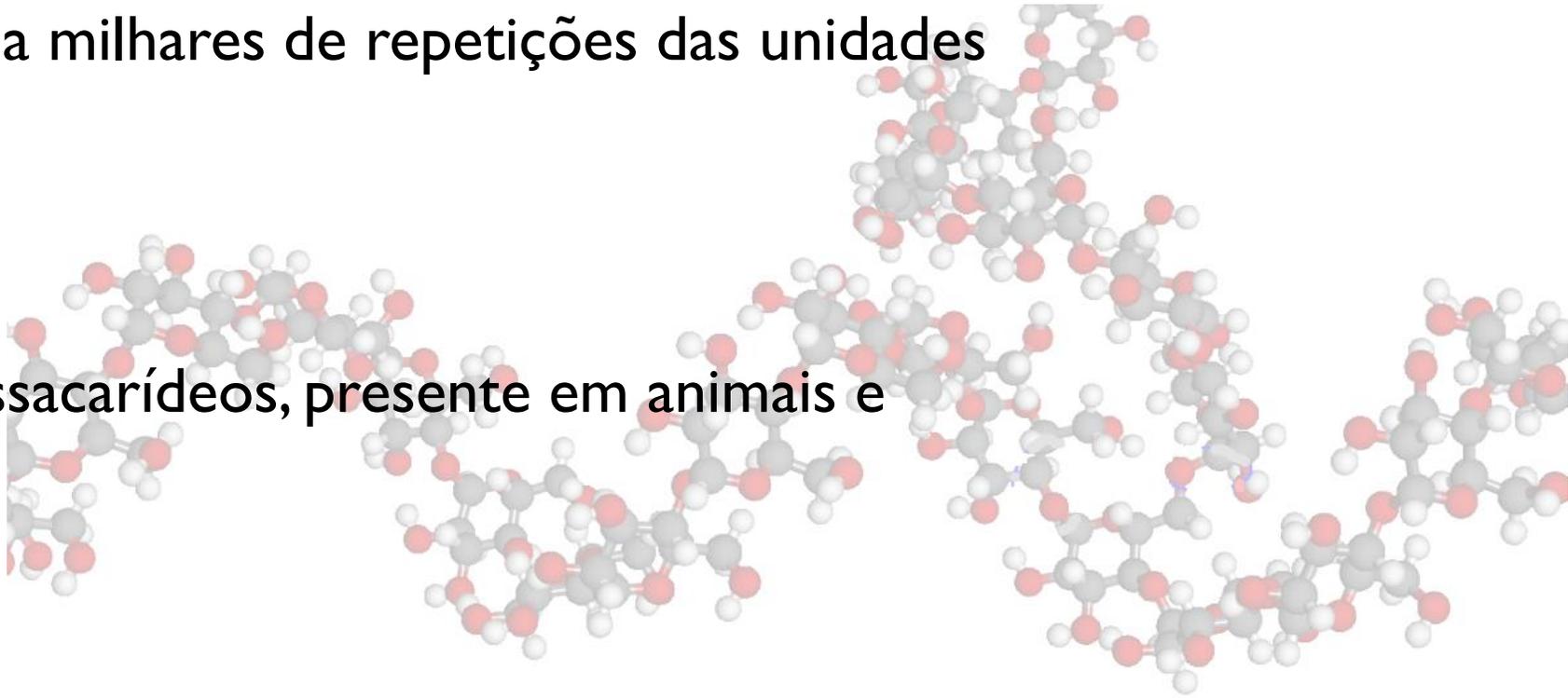
Figure 11-19

Heteropolissacarídeos

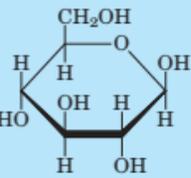
▶ Centenas a milhares de repetições das unidades básicas.

▶ Mucopolissacarídeos, presente em animais e bactérias.

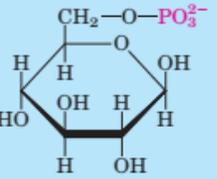
▶ Ácido hialurônico (absorção de impacto, lubrificação)
– matriz extracelular, líquido sinovial.



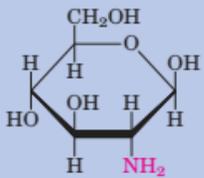
Glucose family



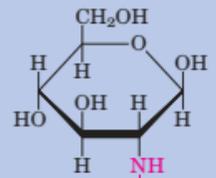
β-D-Glucose



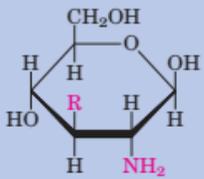
β-D-Glucose 6-phosphate



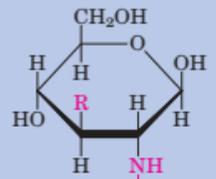
β-D-Glucosamine



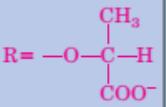
N-Acetyl-*β*-D-glucosamine



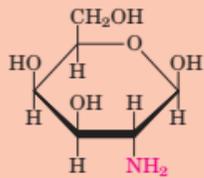
Muramic acid



N-Acetylmuramic acid



Amino sugars

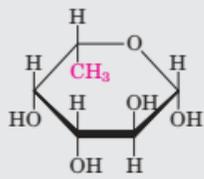


β-D-Galactosamine

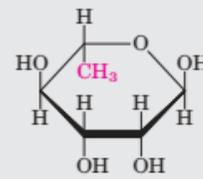


β-D-Mannosamine

Deoxy sugars

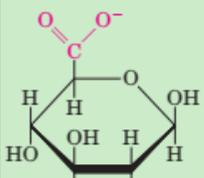


β-L-Fucose

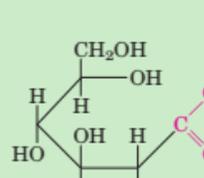


α-L-Rhamnose

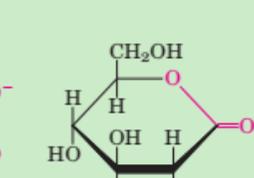
Acidic sugars



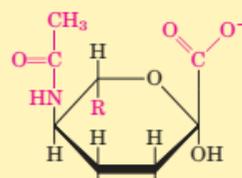
β-D-Glucuronate



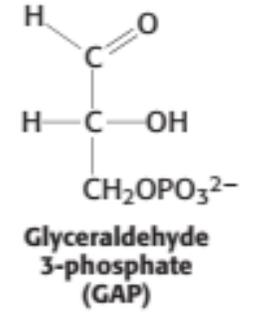
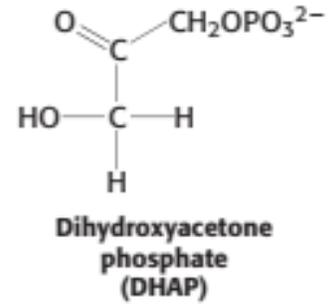
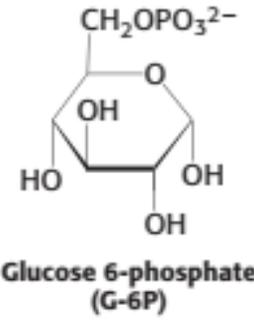
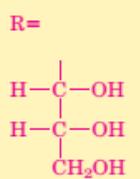
D-Gluconate



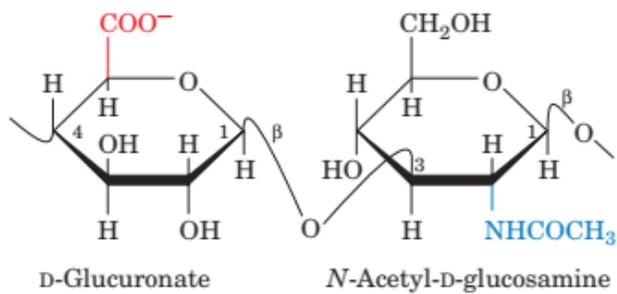
D-Glucono- δ -lactone



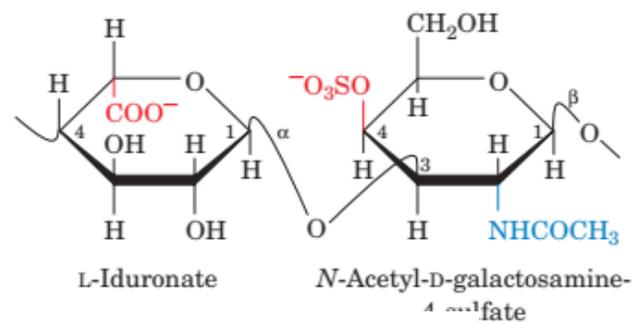
N-Acetylneuraminic acid (a sialic acid)



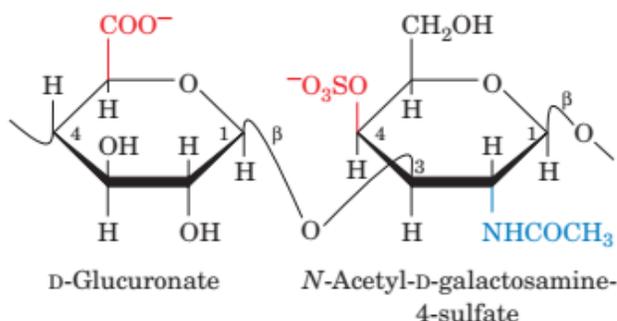
Heteropolissacarídeos - Glicosaminoglicanas (GAG)



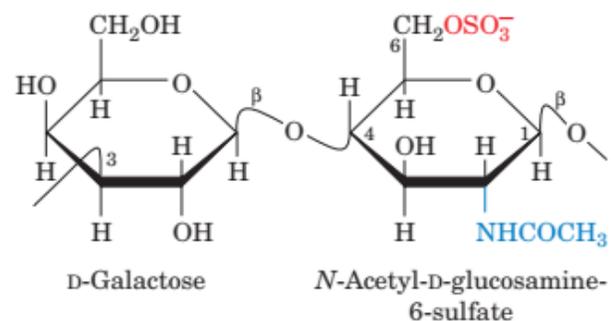
Hialuronato



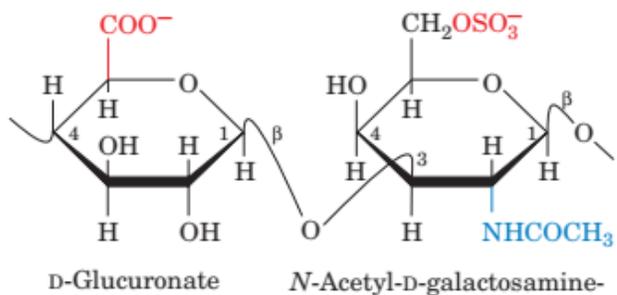
Dermatan sulfato



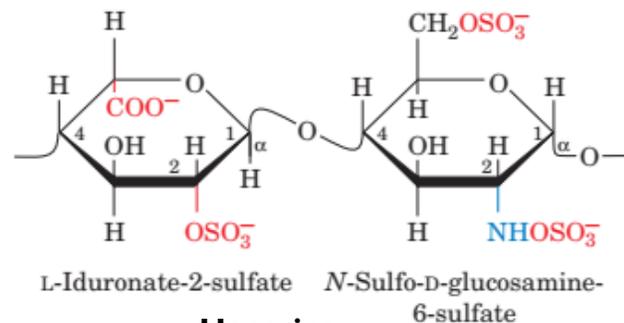
Condroitina-4-sulfato



Queratan-sulfato

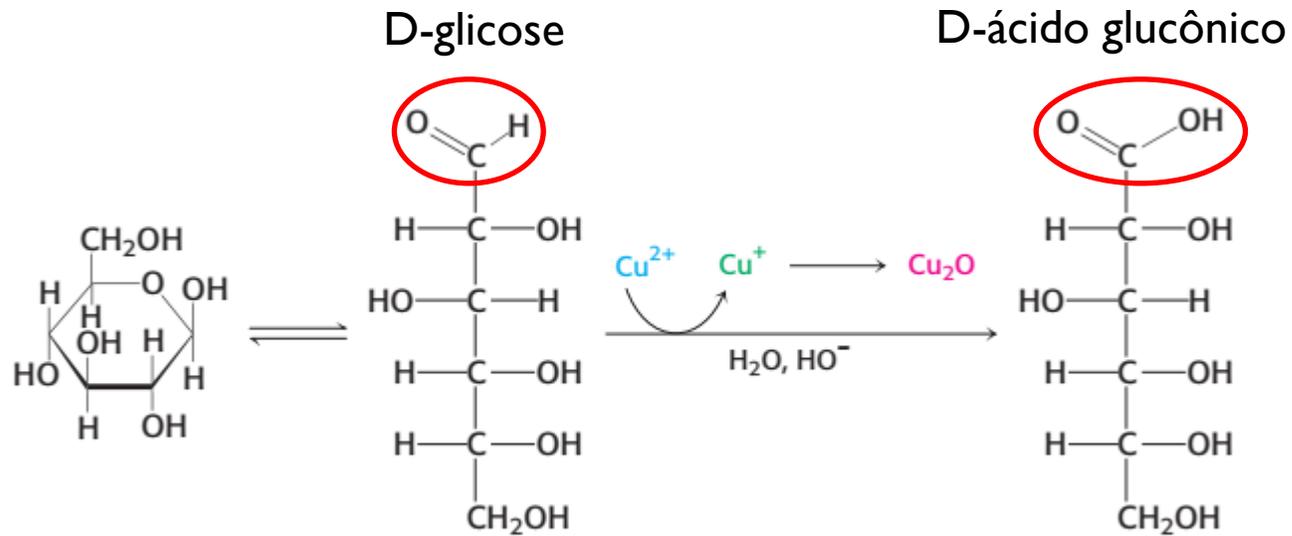


Condroitina-6-sulfato

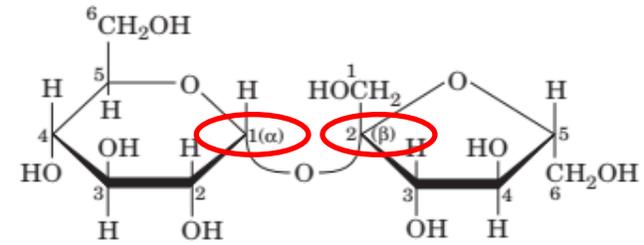


Heparina

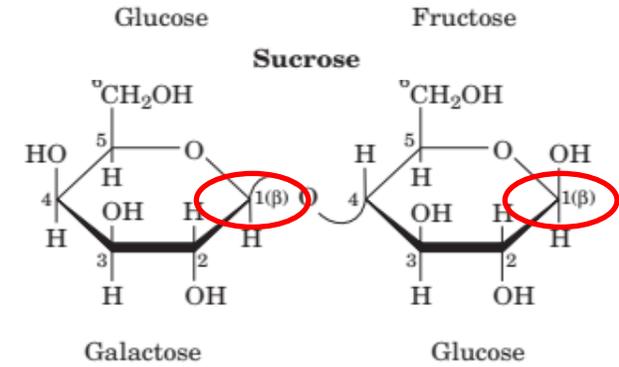
Açúcares são redutores



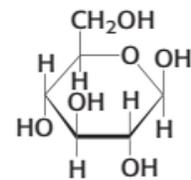
Açúcares são redutores



Sacarose não tem extremidades redutoras livres

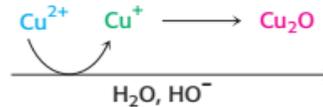
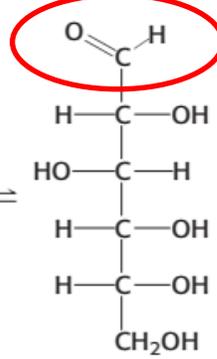


Lactose

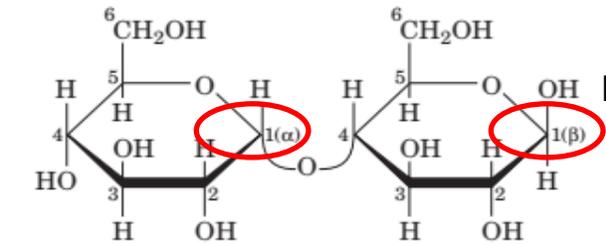
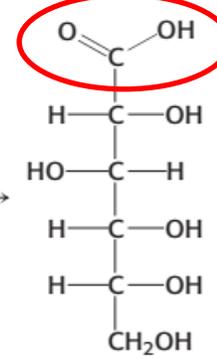


Glicose

Aldeído



Ác. Carboxílico



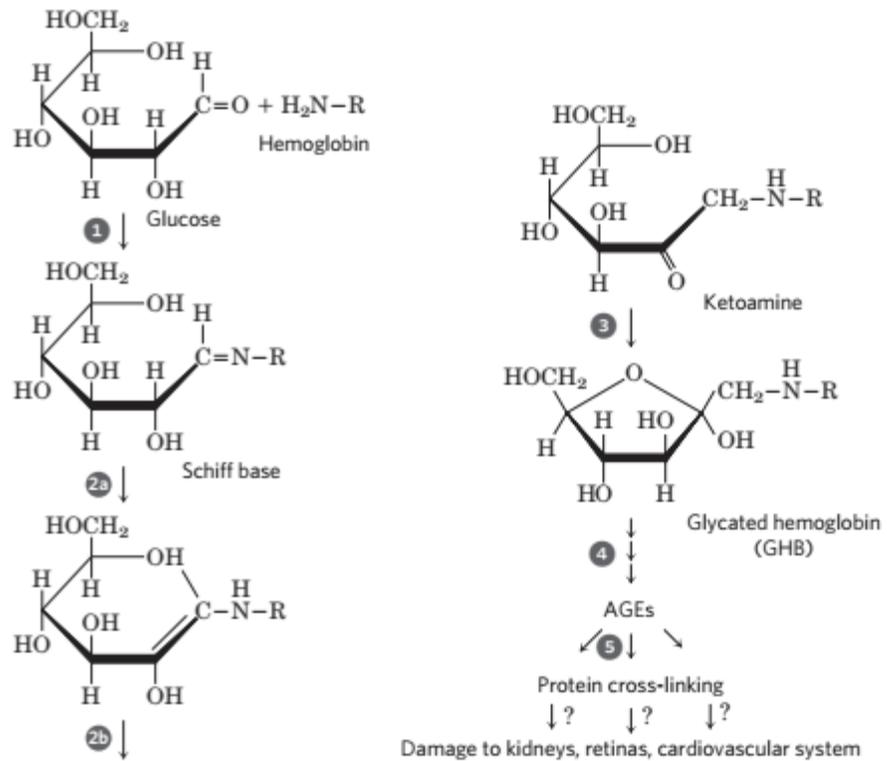
Lactose e maltose possuem extremidades redutoras livres

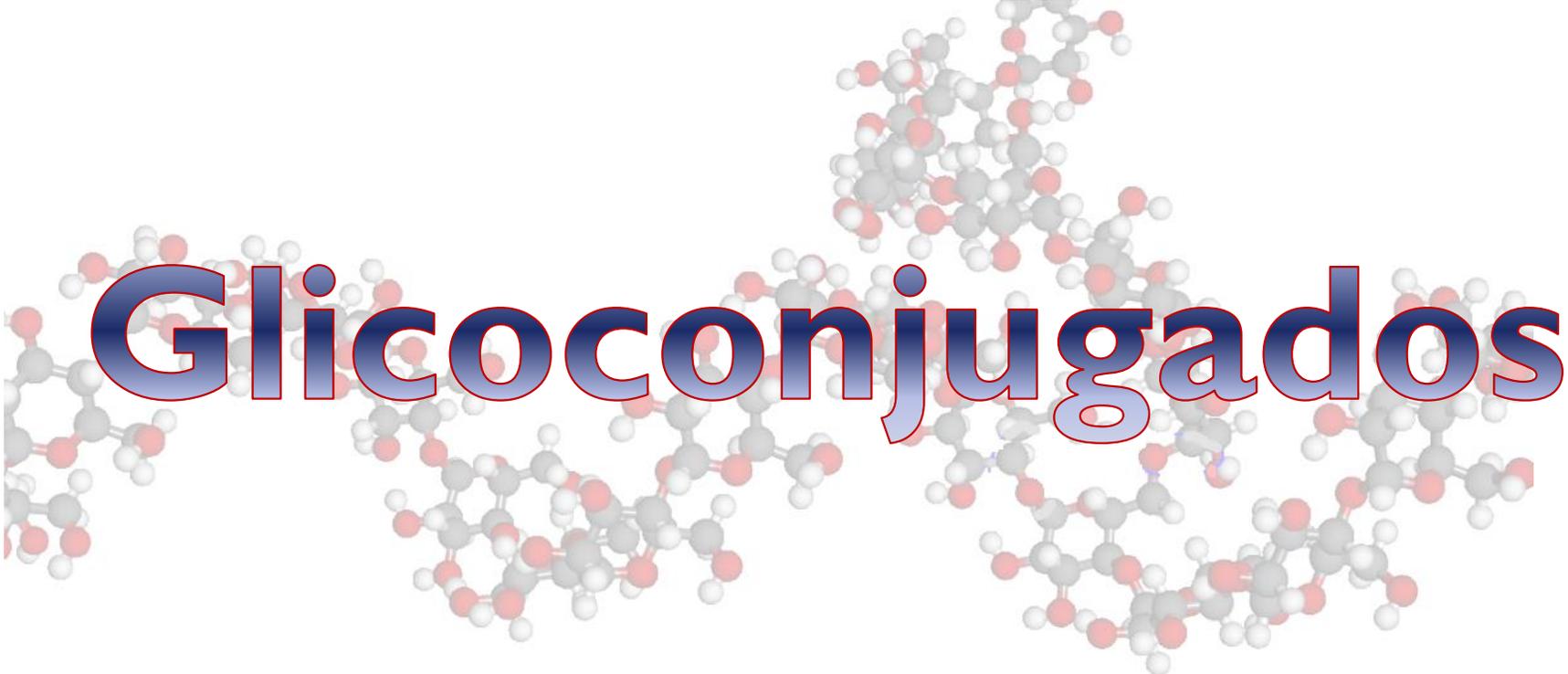
Maltose



Açúcares são redutores

- ▶ Glicosilação da hemoglobina em diabetes.



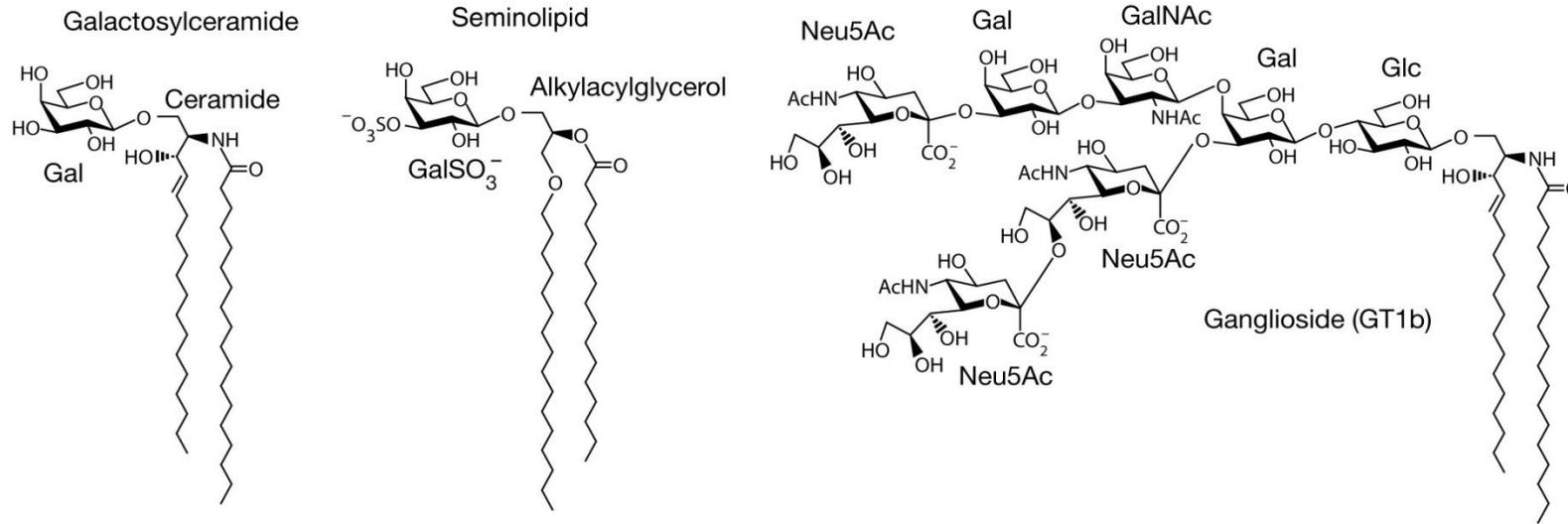


Glicoconjugados

A ball-and-stick molecular model of a glycoconjugate is shown in the background. The model consists of a complex, branched structure of atoms represented by spheres: carbon (grey), oxygen (red), and hydrogen (white). The structure is intricate, with various functional groups and a highly branched, tree-like appearance, characteristic of a carbohydrate chain attached to a protein or lipid.



Glicolipídeos

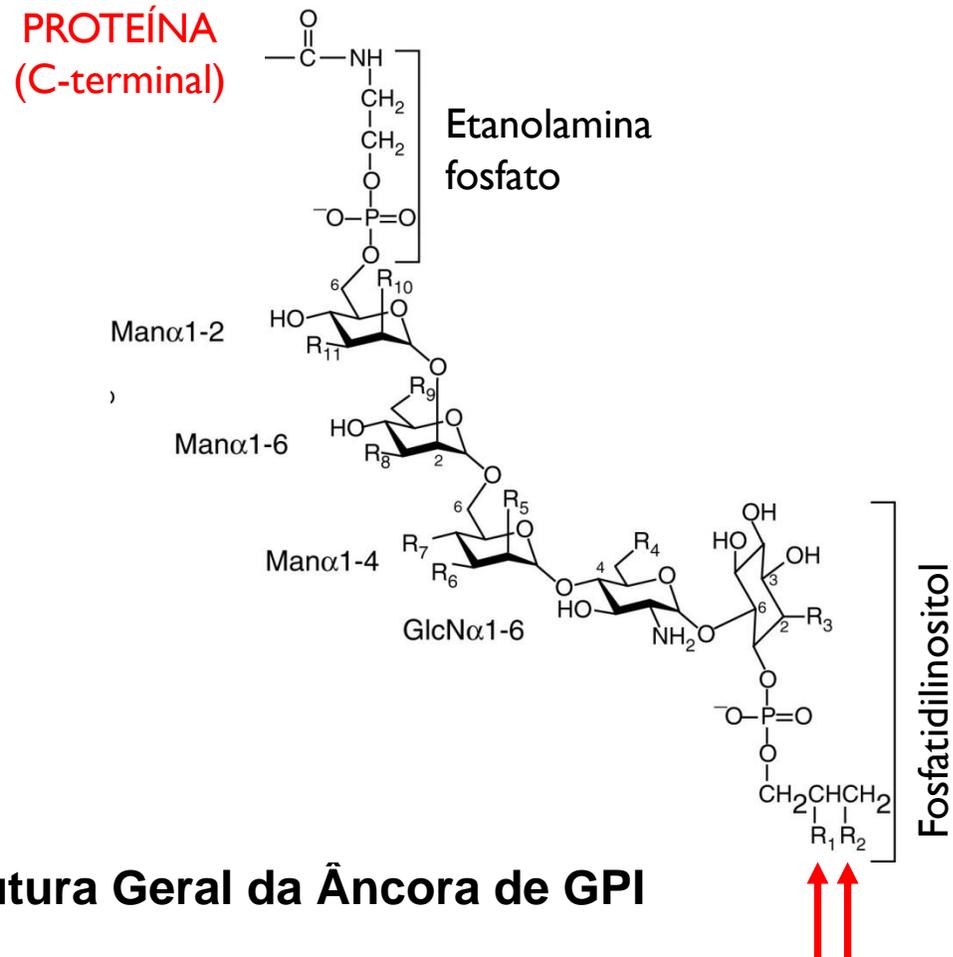


Estruturas representativas de Glicosfingolipídeos e Gliceroglicolipídeos

Capítulo 11, Figura 1. *Essentials of Glycobiology*, Third Edition



Glicolipídeos – Âncora de GPI

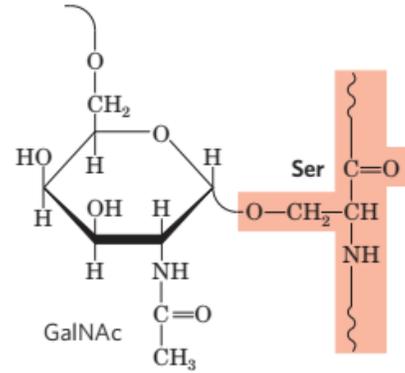
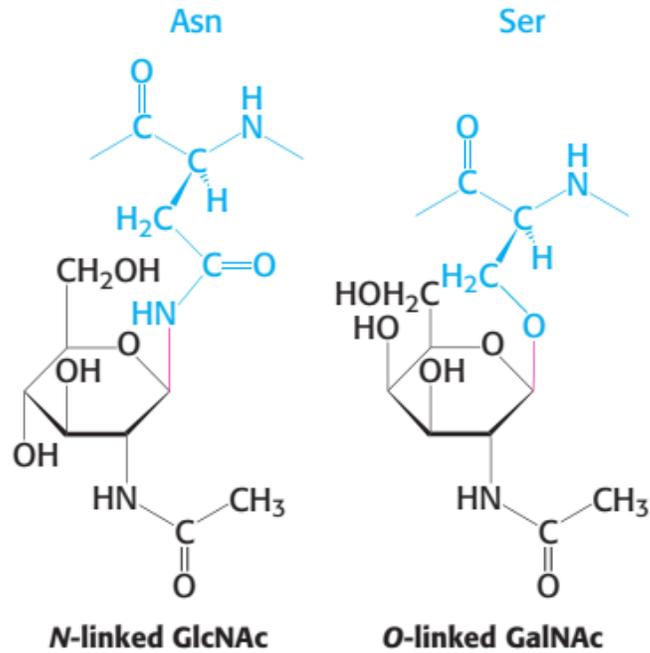


Capítulo 12, Figura 1. *Essentials of Glycobiology*, Third Edition

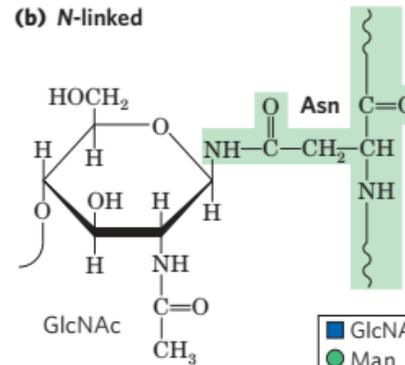
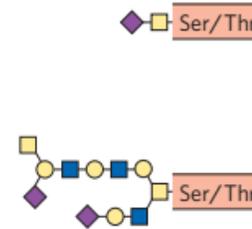
Lipídeos inseridos na membrana plasmática

Glicoproteínas e proteoglicanas

- ▶ Ligação N-glicosídica (Asparagina)- sequon **Asn-X** (a) O-linked
- ▶ Ligação O-glicosídica (serina, treonina).



Examples:



Examples:

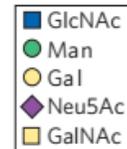
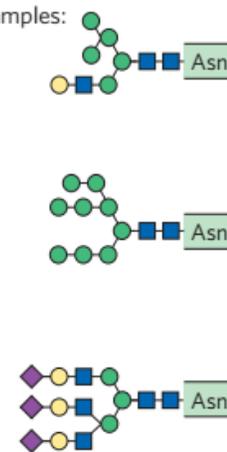


Figura 11.15. Ligação glicosídica entre açúcares e proteínas

BERG, J. M., TYMOCZKO, J. L., STRYER, L., & STRYER, L. (2012). *Biochemistry*. New York, W.H. Freeman.

LEHNINGER, A. L., NELSON, D. L., & COX, M. M. (2014). *Lehninger principles of biochemistry*. New York, Worth Publishers.

Glicoproteína

É majoritariamente uma proteína, mas com açúcares ligados.



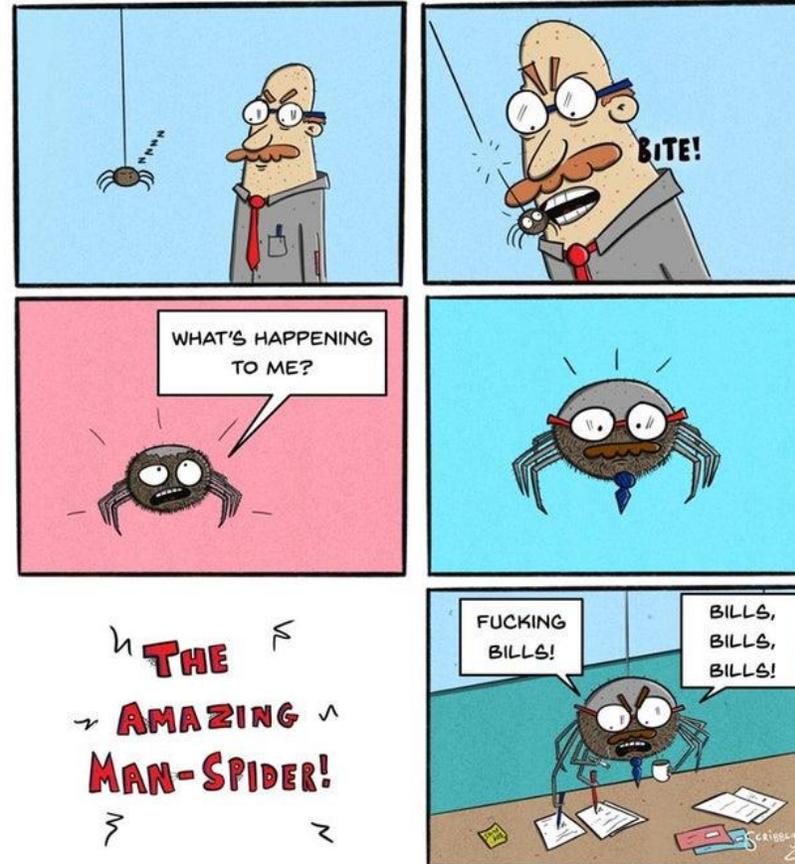
<https://www.amazon.com/Spider-Man-Classic-John-Rhett-Thomas/dp/0785157506>

Spider-man

É um ser humano, mas com características de aranha.

Proteoglicana

É majoritariamente um açúcar, mas ligado a uma proteína.



THE
AMAZING
MAN-SPIDER!

Man-spider

É uma aranha, mas com características de humano.

Glicoproteínas

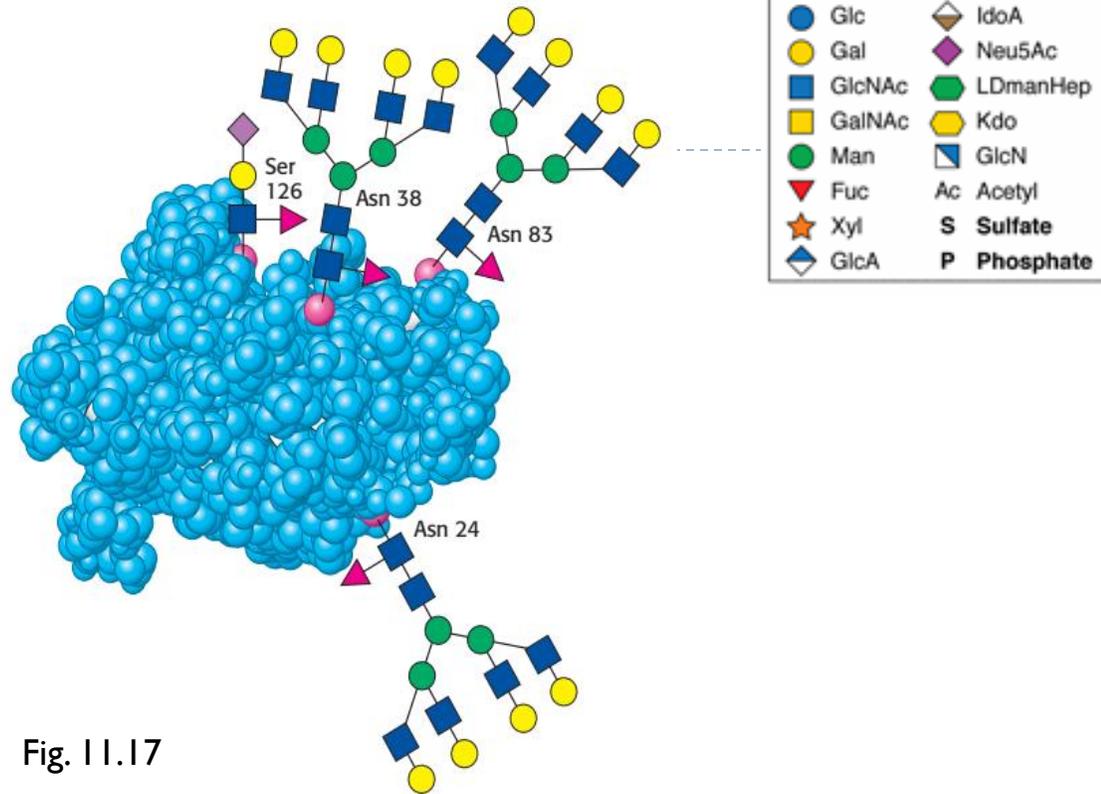
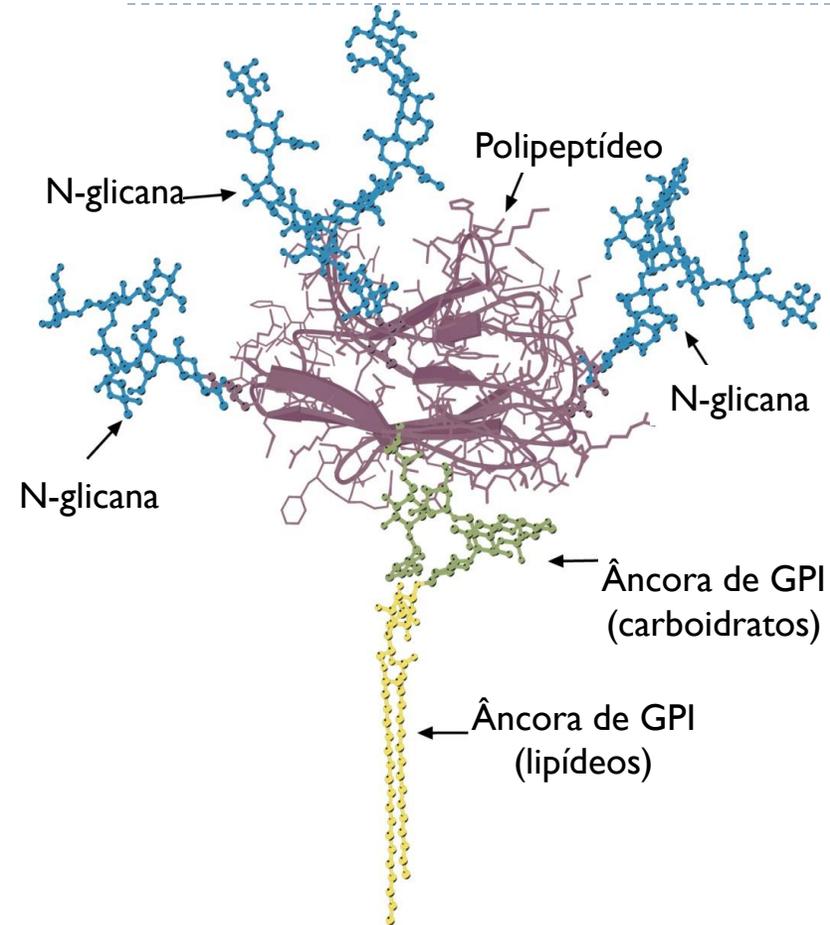


Fig. 11.17

Glicofoma- Proteínas que compartilham exatamente a mesma sequência de aminoácidos, mas carregam diferentes glicanas nos sítios de glicosilação.

Proteoglicanas

Uma ou mais glicosaminoglicanas ligadas a uma proteína núcleo.
O-glicosilação.

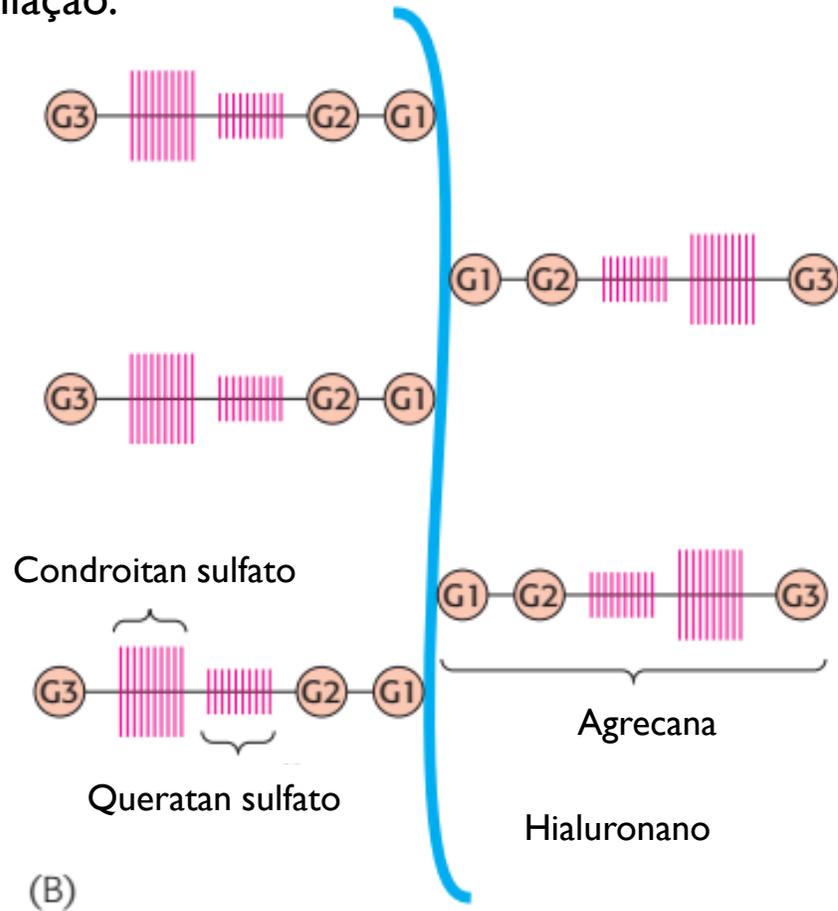


Fig. 11.20. Estrutura de proteoglicana da cartilagem.

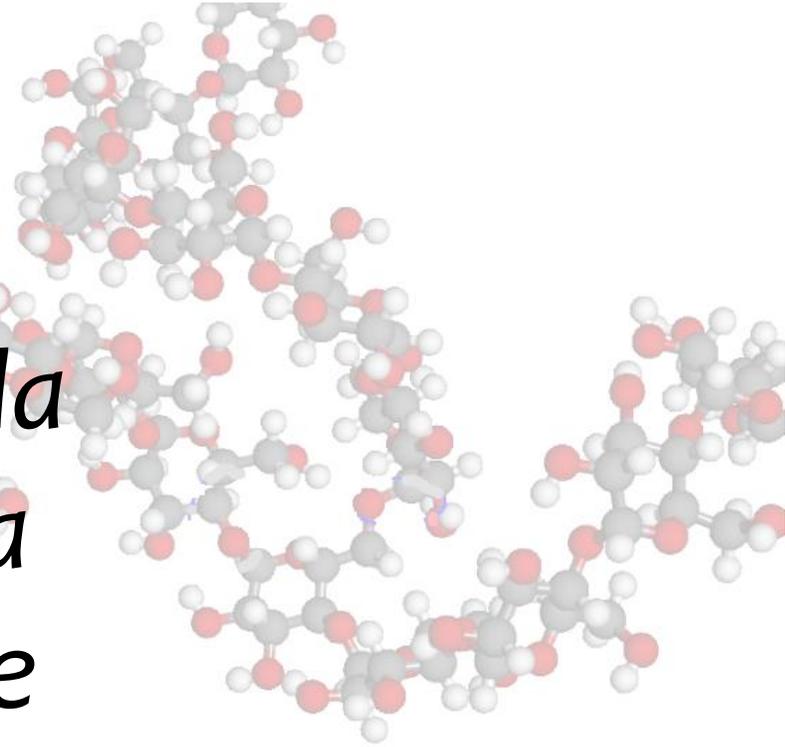


Parte 2:
Função biológica

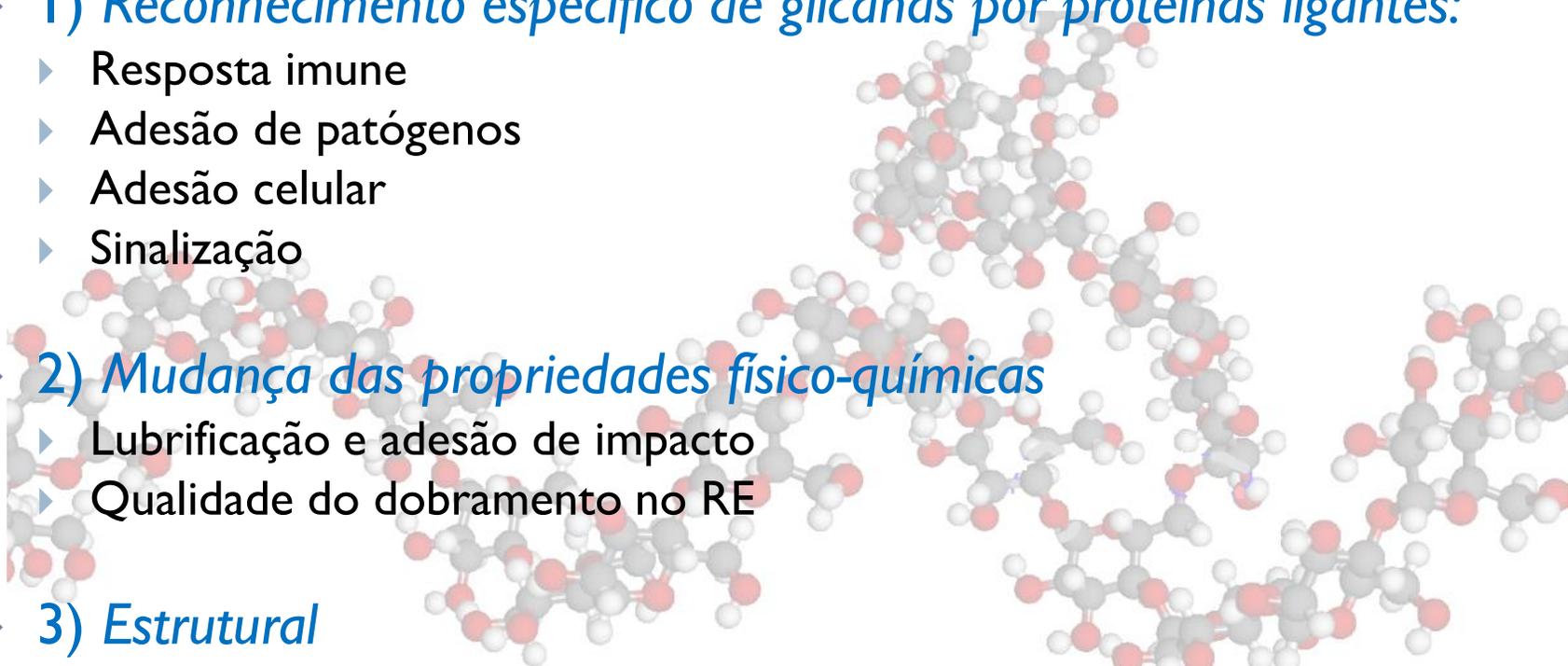


Princípios Gerais

A distribuição das glicofomas tecido-específicas que cada célula sintetiza lhe proporciona um diferente espectro de características.

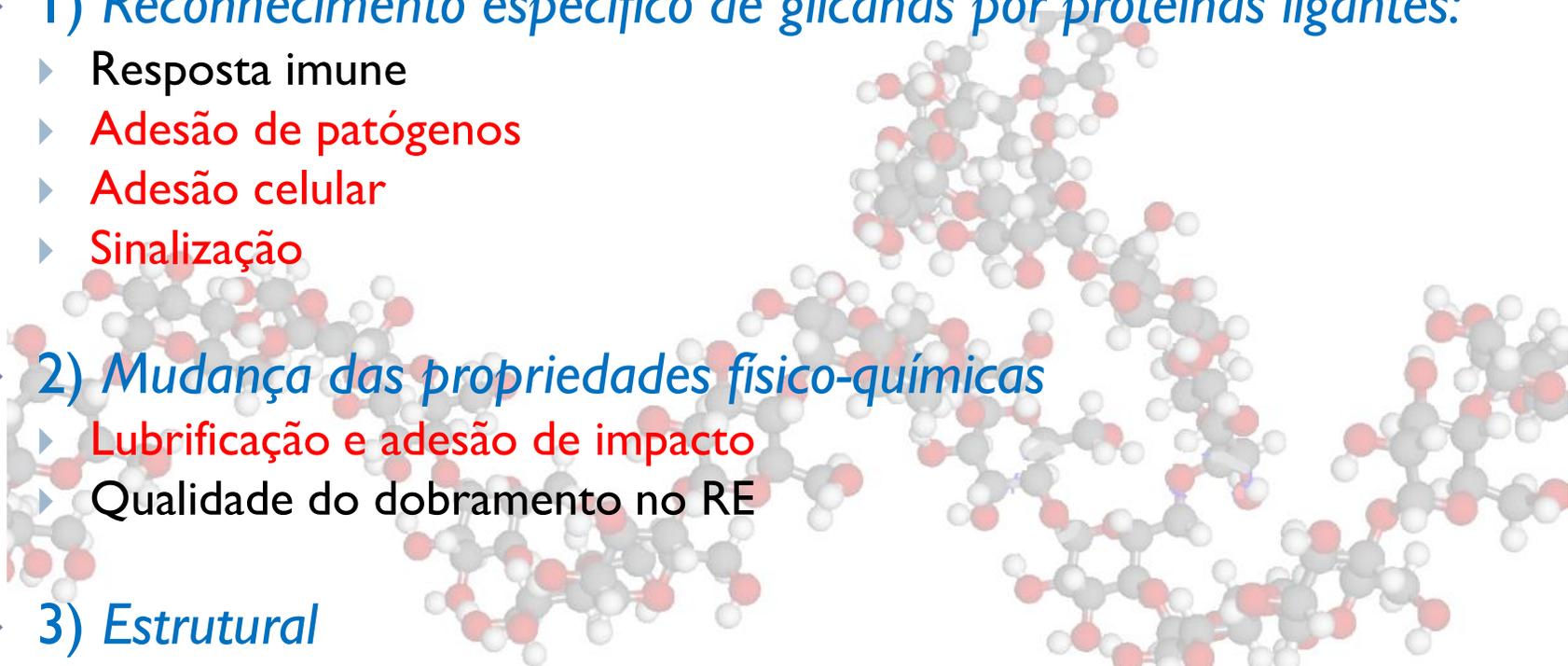


Função

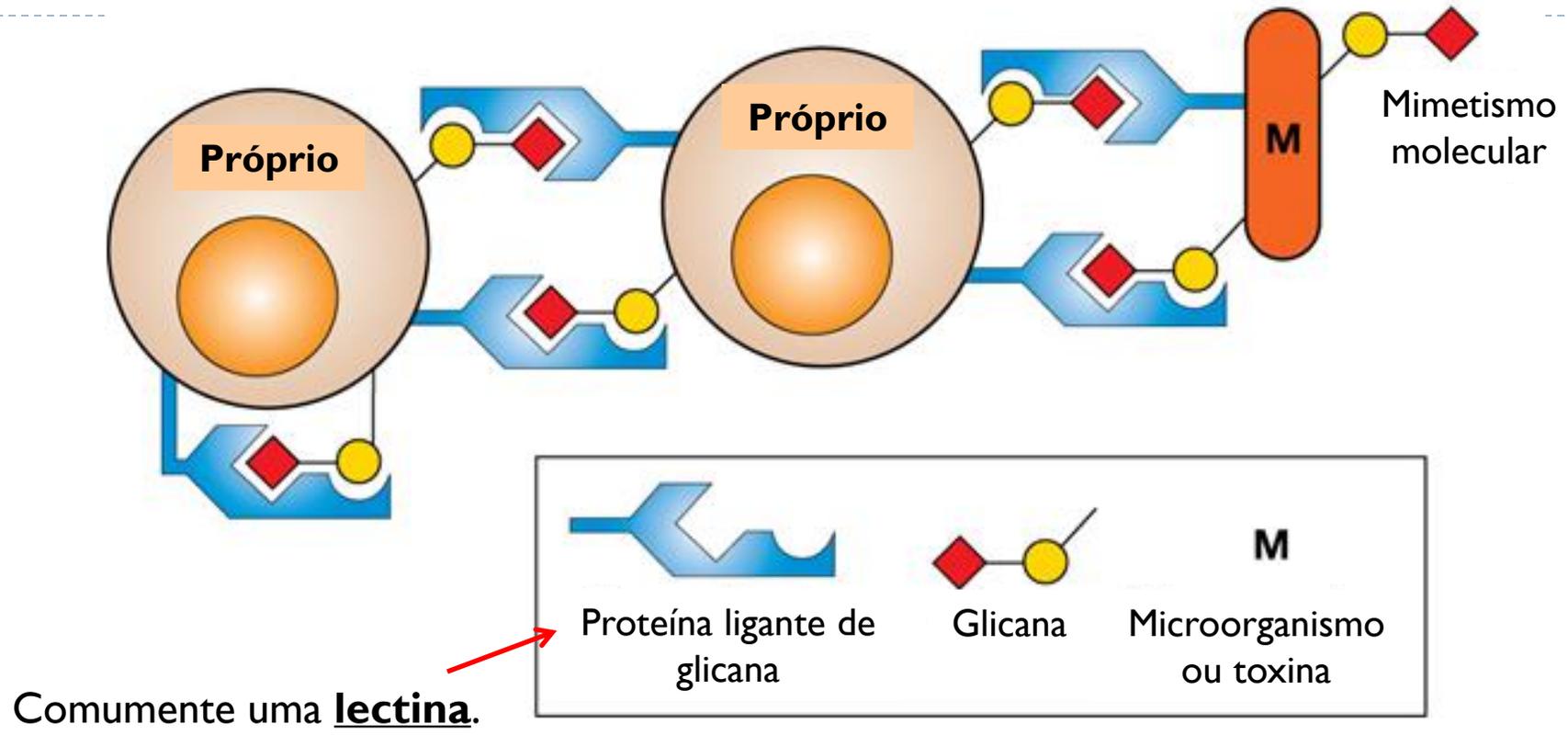
- ▶ 1) *Reconhecimento específico de glicanas por proteínas ligantes:*
 - ▶ Resposta imune
 - ▶ Adesão de patógenos
 - ▶ Adesão celular
 - ▶ Sinalização
 - ▶ 2) *Mudança das propriedades físico-químicas*
 - ▶ Lubrificação e adesão de impacto
 - ▶ Qualidade do dobramento no RE
 - ▶ 3) *Estrutural*
 - ▶ Parede bacteriana
 - ▶ Celulose
 - ▶ Sustentação da matriz extracelular
 - ▶ 4) *Energética*
- 



Função

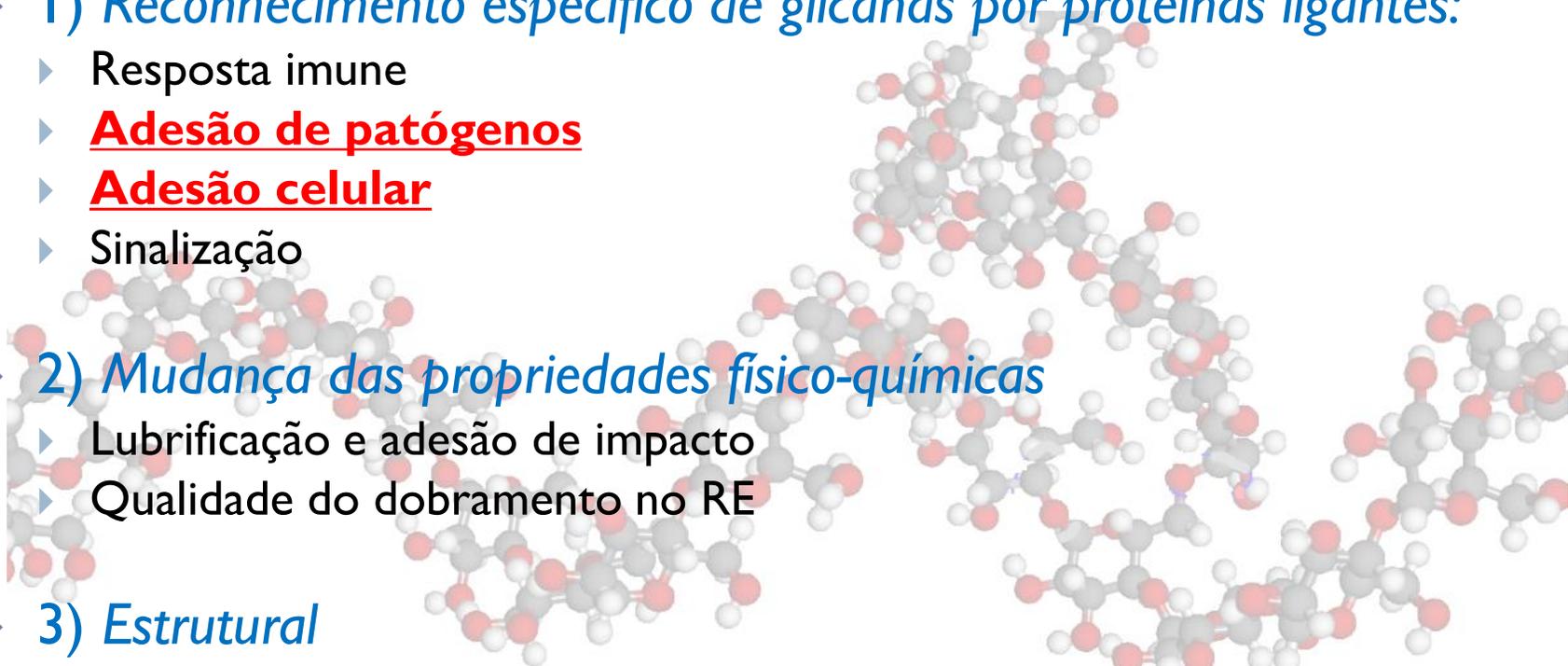
- ▶ 1) *Reconhecimento específico de glicanas por proteínas ligantes:*
 - ▶ Resposta imune
 - ▶ Adesão de patógenos
 - ▶ Adesão celular
 - ▶ Sinalização
 - ▶ 2) *Mudança das propriedades físico-químicas*
 - ▶ Lubrificação e adesão de impacto
 - ▶ Qualidade do dobramento no RE
 - ▶ 3) *Estrutural*
 - ▶ Parede bacteriana
 - ▶ Celulose
 - ▶ Sustentação da matriz extracelular
 - ▶ 4) *Energética*
- 





Capítulo 7, Figura 1. *Essentials of Glycobiology*, Third Edition

Função

- ▶ 1) *Reconhecimento específico de glicanas por proteínas ligantes:*
 - ▶ Resposta imune
 - ▶ **Adesão de patógenos**
 - ▶ **Adesão celular**
 - ▶ Sinalização
 - ▶ 2) *Mudança das propriedades físico-químicas*
 - ▶ Lubrificação e adesão de impacto
 - ▶ Qualidade do dobramento no RE
 - ▶ 3) *Estrutural*
 - ▶ Parede bacteriana
 - ▶ Celulose
 - ▶ Sustentação da matriz extracelular
 - ▶ 4) *Energética*
- 



Adesão de patógenos

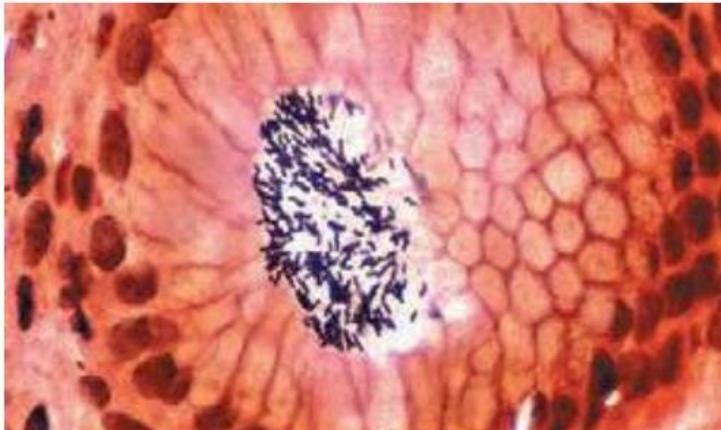


Fig. 7.34 *Helicobacter pylori* aderindo à superfície gástrica.

LEHNINGER, A. L., NELSON, D. L., & COX, M. M. (2014). *Lehninger principles of biochemistry*. New York, Worth Publishers.

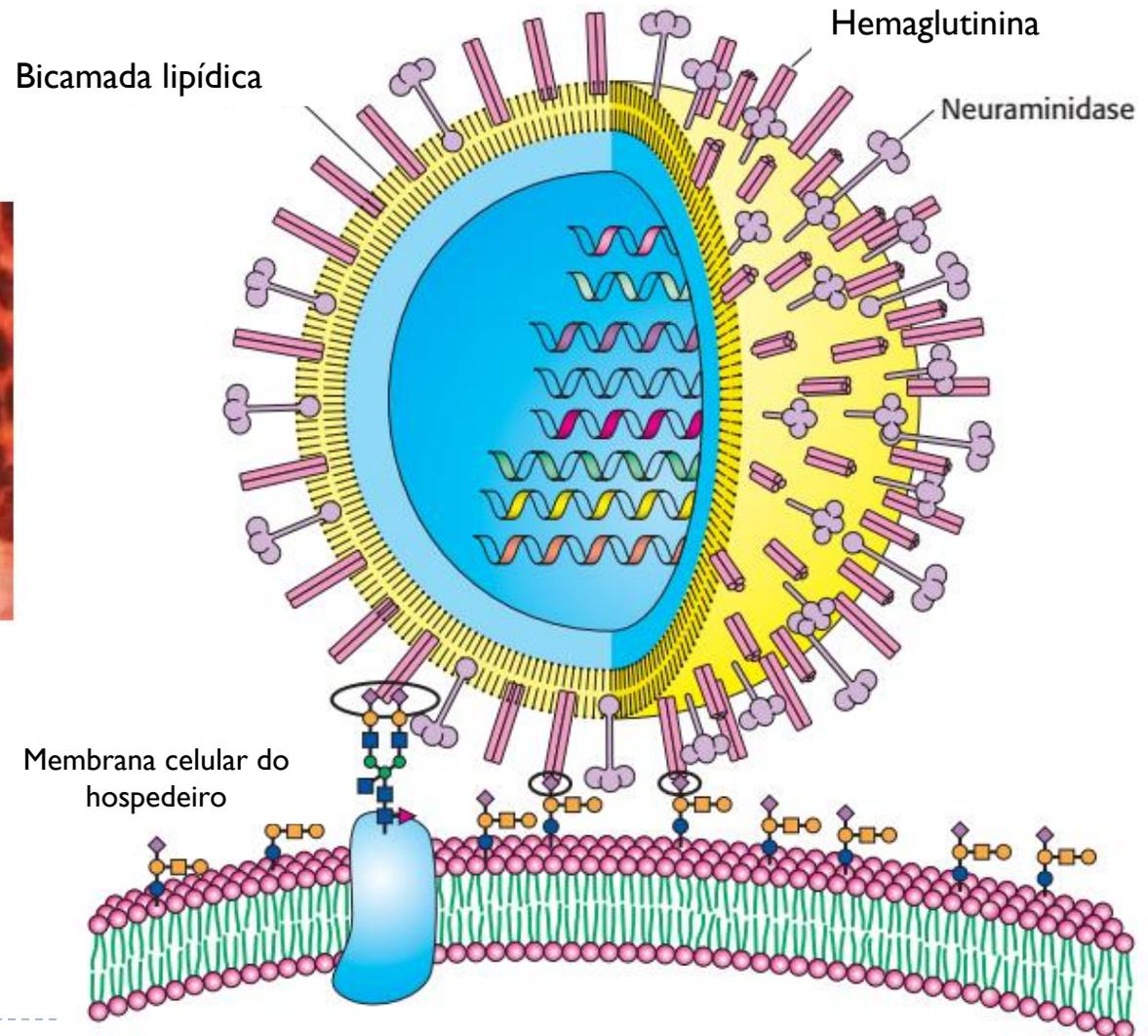


Fig. 11.31. BERG, J. M., TYMOCZKO, J. L., STRYER, L., & STRYER, L. (2012). *Biochemistry*. New York, W.H. Freeman.

Adesão celular

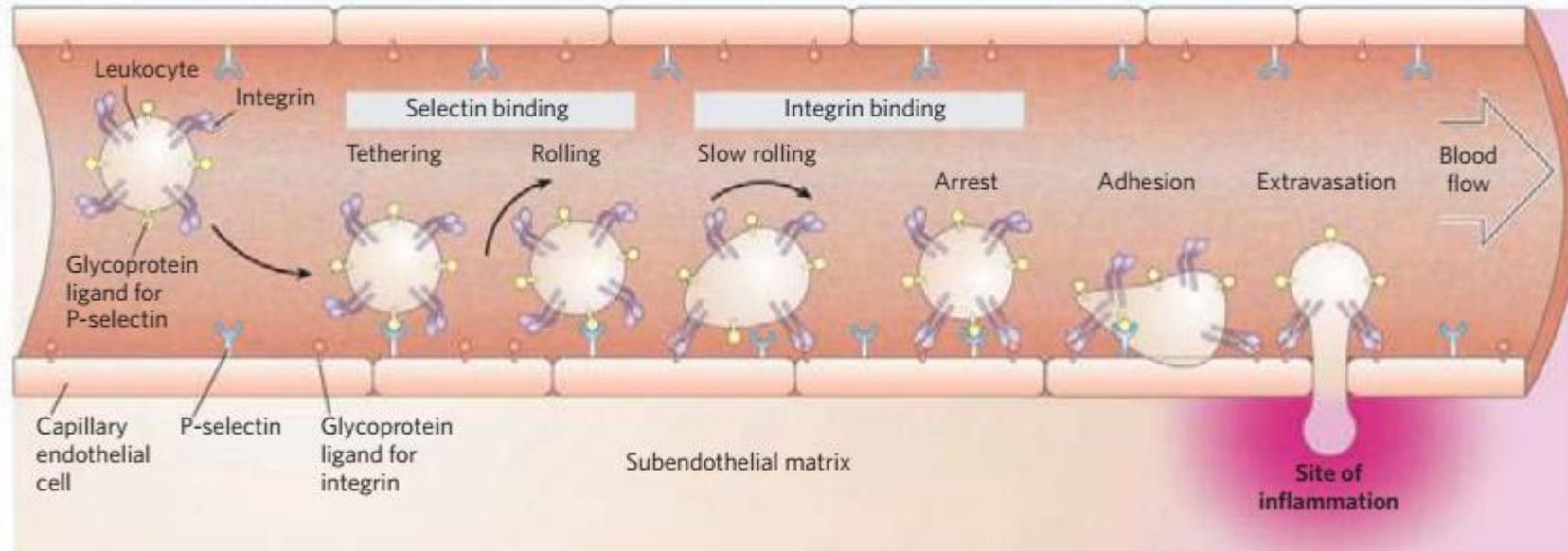
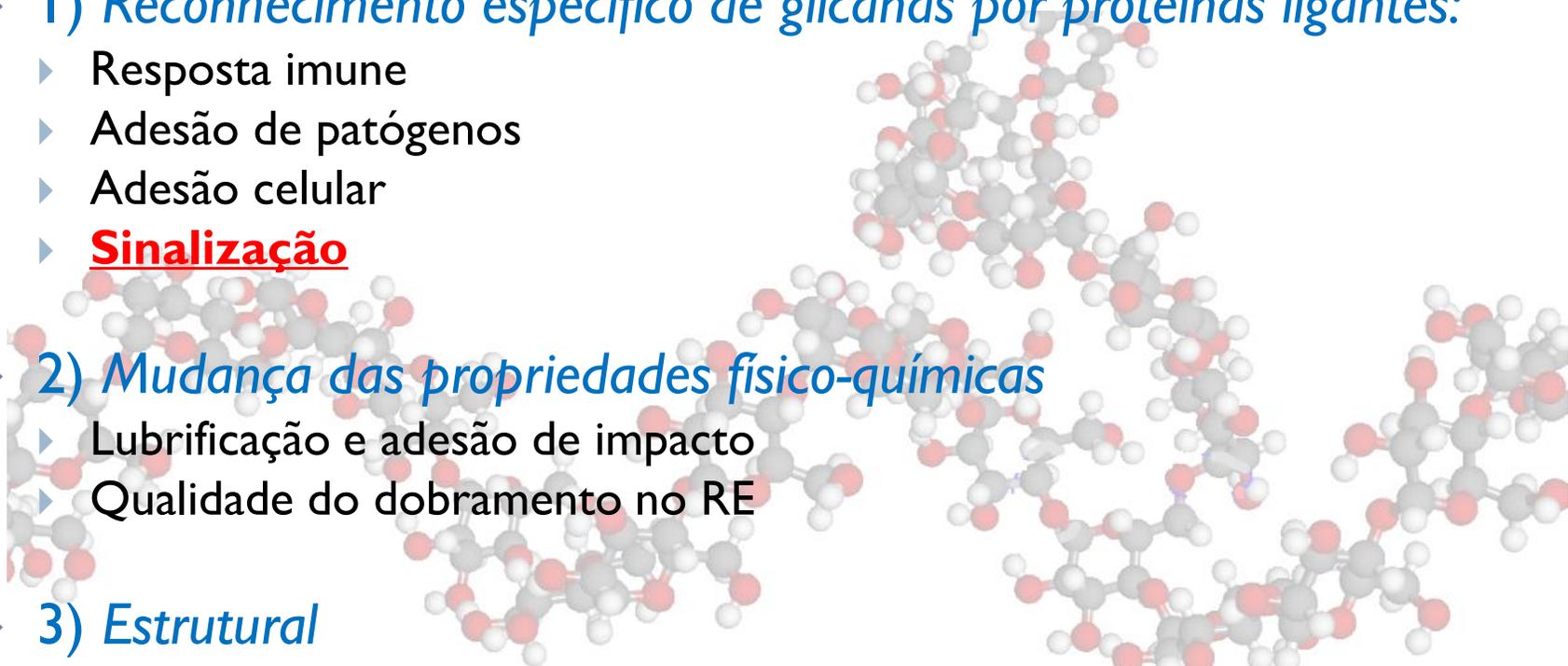


FIGURE 7-32 Role of lectin-ligand interactions in leukocyte movement to the site of an infection or injury. A leukocyte circulating through a

Função

- ▶ 1) *Reconhecimento específico de glicanas por proteínas ligantes:*
 - ▶ Resposta imune
 - ▶ Adesão de patógenos
 - ▶ Adesão celular
 - ▶ **Sinalização**
 - ▶ 2) *Mudança das propriedades físico-químicas*
 - ▶ Lubrificação e adesão de impacto
 - ▶ Qualidade do dobramento no RE
 - ▶ 3) *Estrutural*
 - ▶ Parede bacteriana
 - ▶ Celulose
 - ▶ Sustentação da matriz extracelular
 - ▶ 4) *Energética*
- 



Sinalização – Heparan sulfato

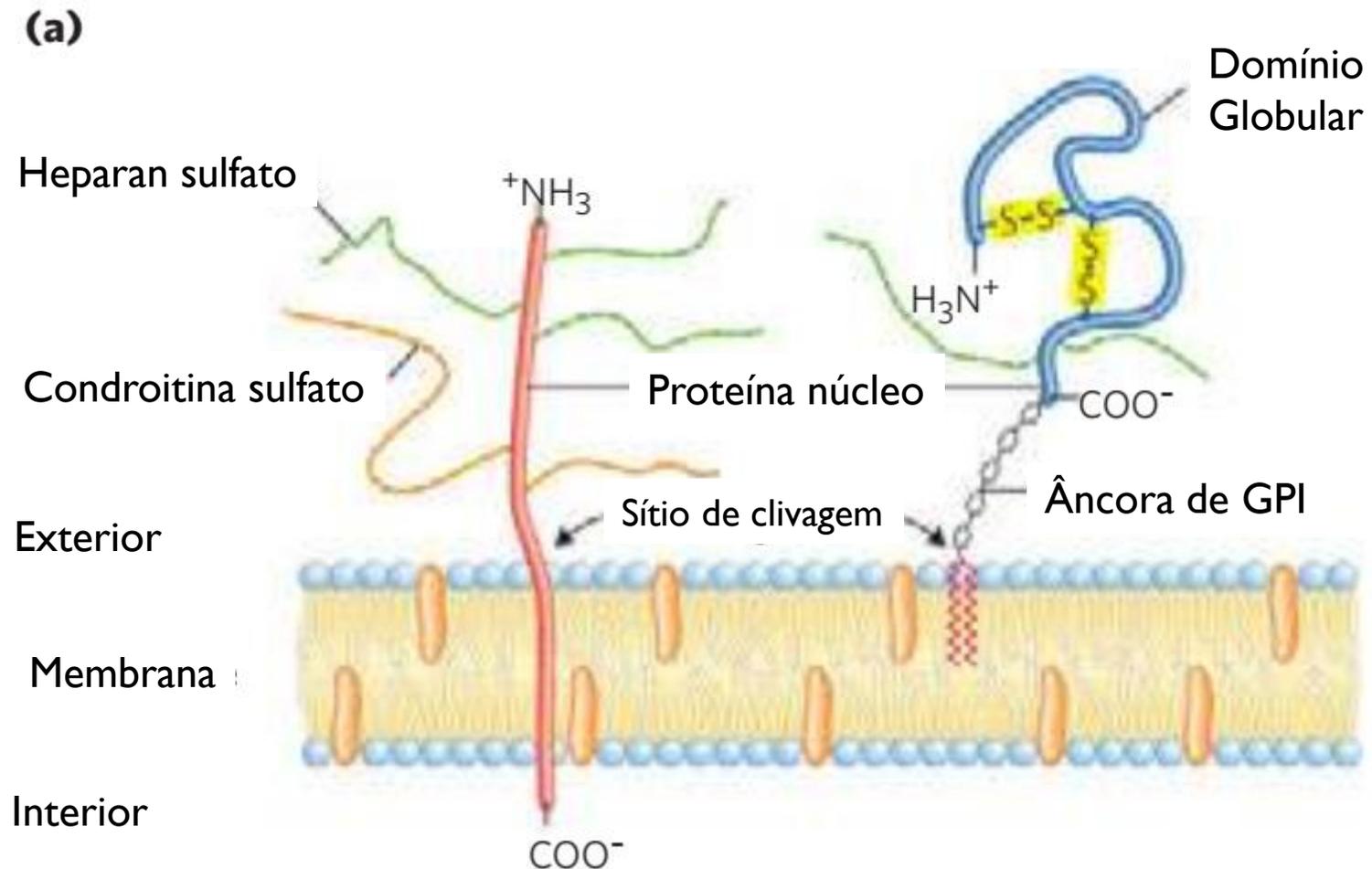
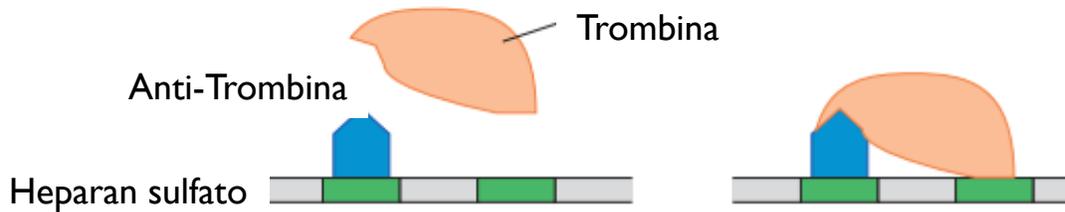


Fig. 7.26

LEHNINGER, A. L., NELSON, D. L., & COX, M. M. (2014).
Lehninger principles of biochemistry. New York, Worth Publishers.

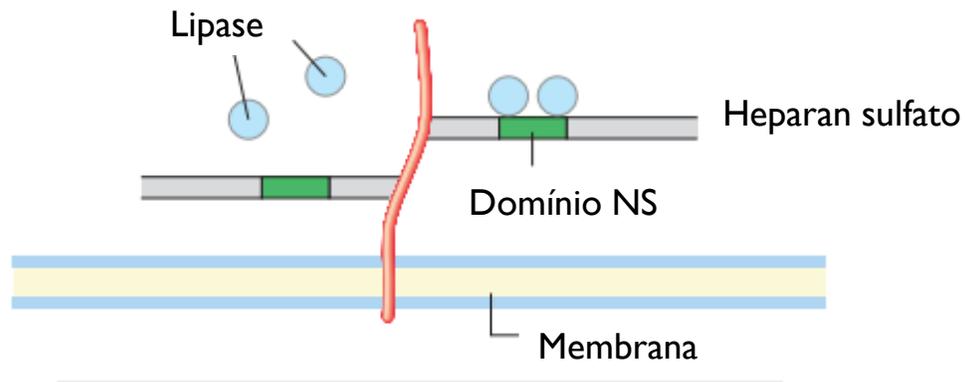
Sinalização – Heparan sulfato

(b) Interação proteína-proteína melhorada



Ligação de Anti-Trombina e trombina a 2 domínios adjacentes de heparan sulfato aproxima as proteínas favorecendo sua interação e inibe a coagulação sanguínea

(d) Concentração na superfície celular



A alta densidade de cargas negativas no heparan sulfato atrai as moléculas de lipase que são carregadas positivamente, segurando-as através de interações eletrostáticas e sequência-específicas com o domínio NS

Função

▶ 1) Reconhecimento específico de glicanas por proteínas ligantes:

- ▶ Resposta imune
- ▶ Adesão de patógenos
- ▶ Adesão celular
- ▶ Sinalização

▶ 2) Mudança das propriedades físico-químicas

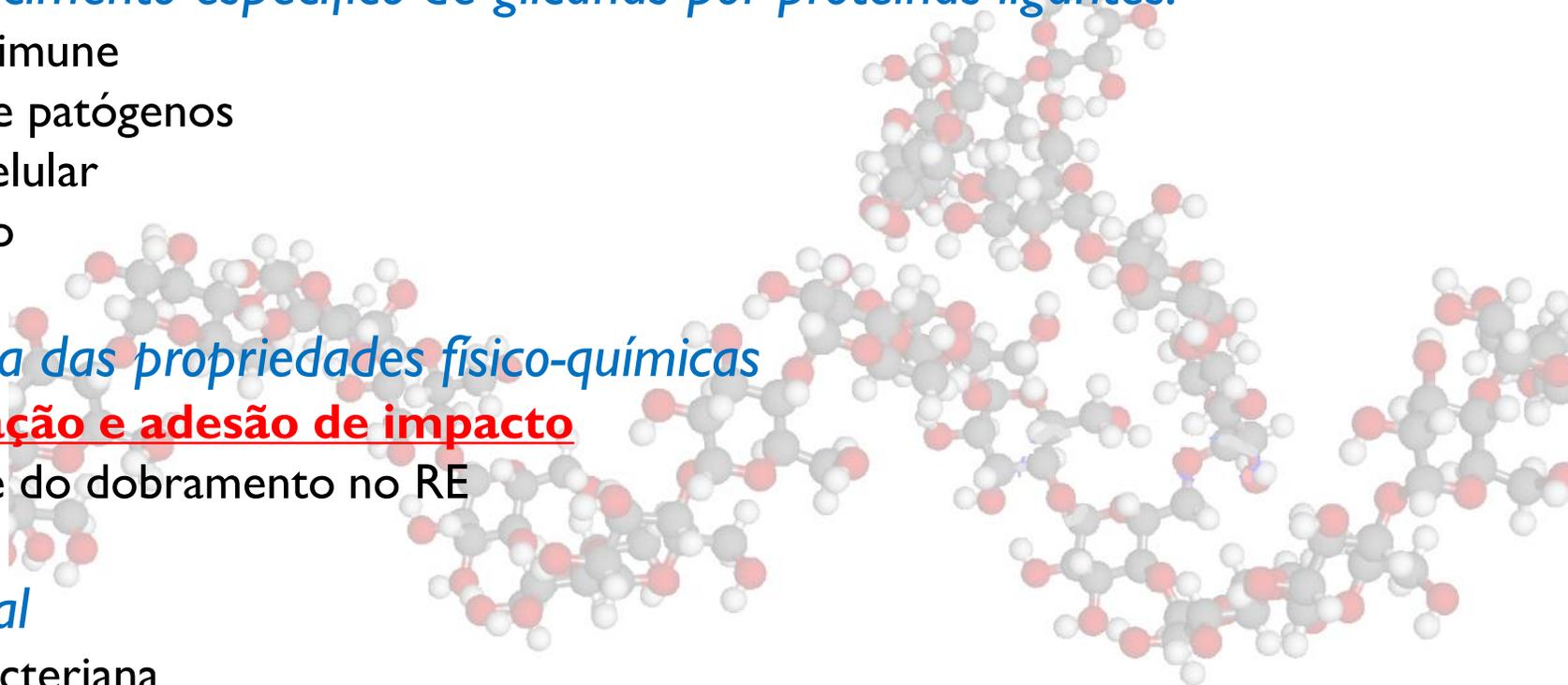
▶ Lubrificação e adesão de impacto

- ▶ Qualidade do dobramento no RE

▶ 3) Estrutural

- ▶ Parede bacteriana
- ▶ Celulose
- ▶ Sustentação da matriz extracelular

▶ 4) Energética



Viscosidade e absorção de impactos

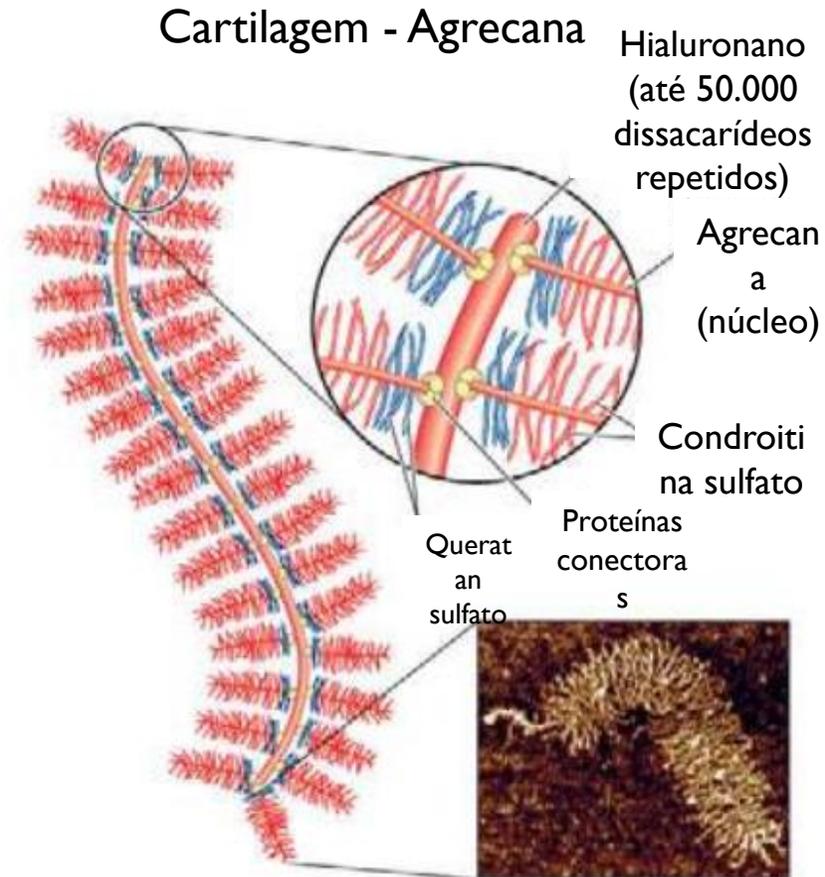
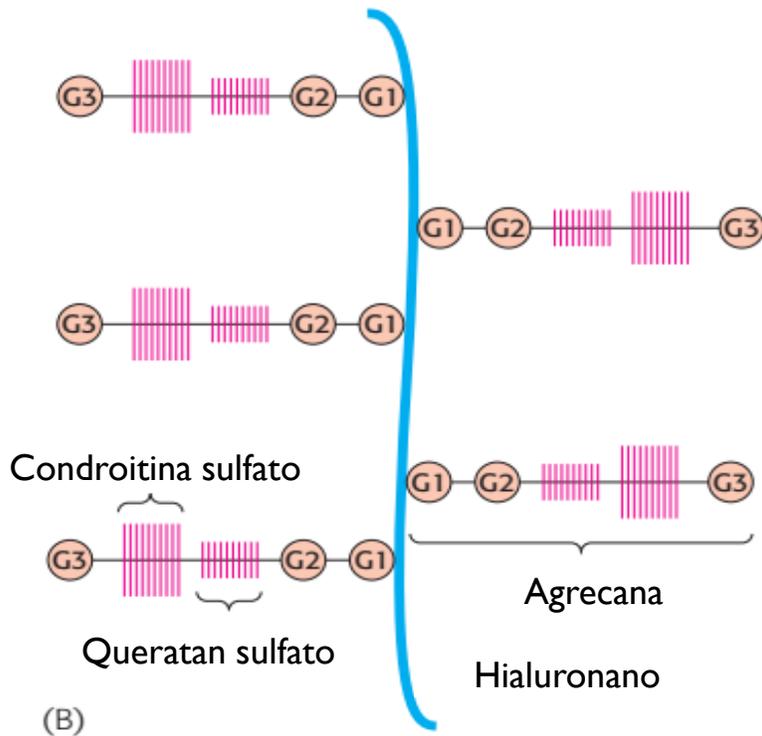


Fig. 11.20. Estrutura de proteoglicana da cartilagem.

Função

▶ 1) Reconhecimento específico de glicanas por proteínas ligantes:

- ▶ **Resposta imune**
- ▶ Adesão de patógenos
- ▶ Adesão celular
- ▶ Sinalização

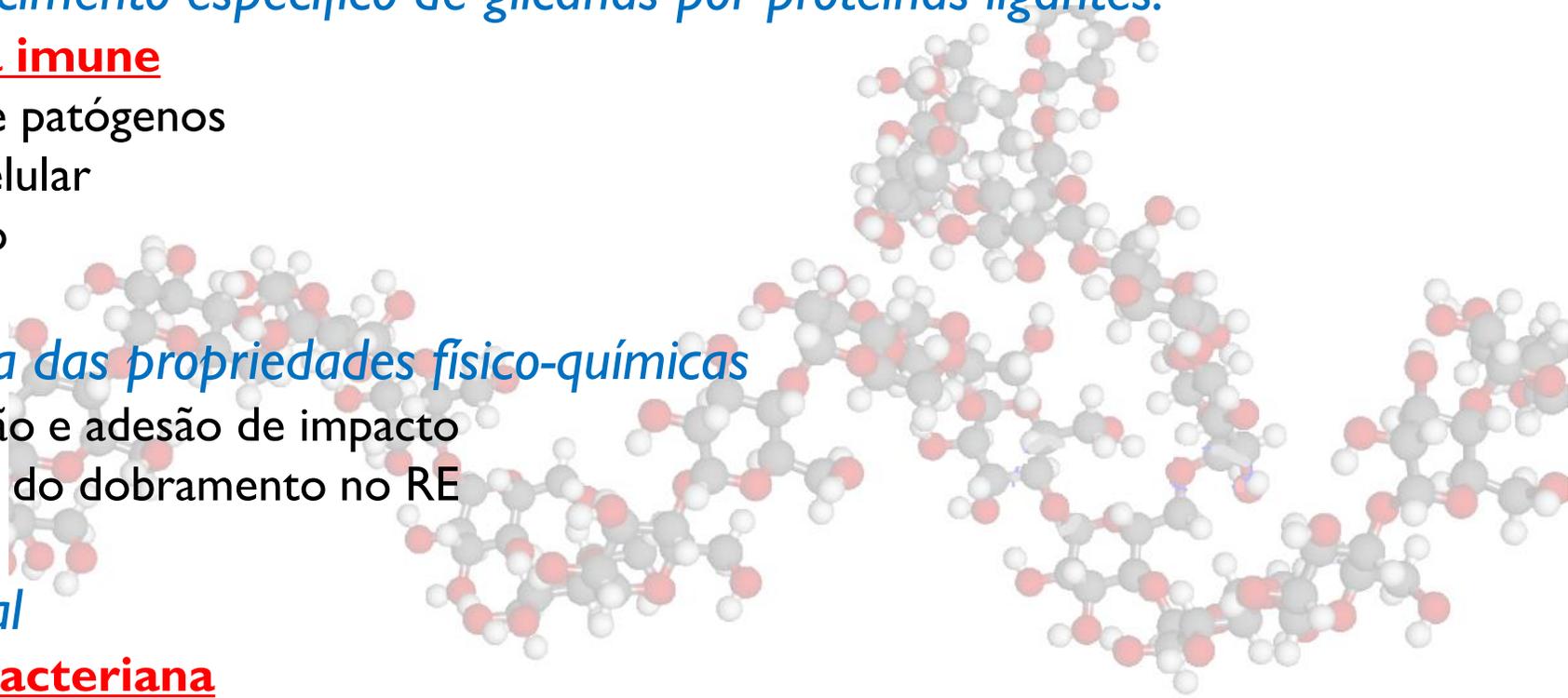
▶ 2) Mudança das propriedades físico-químicas

- ▶ Lubrificação e adesão de impacto
- ▶ Qualidade do dobramento no RE

▶ 3) Estrutural

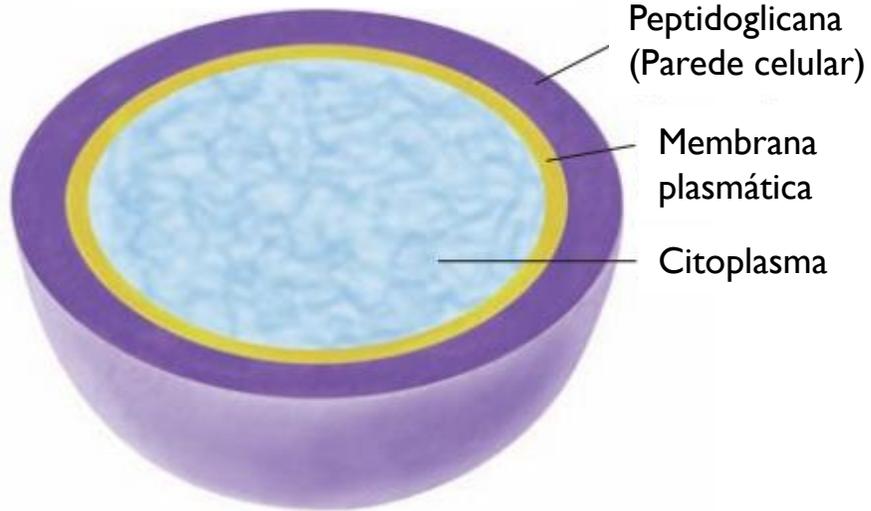
- ▶ **Parede bacteriana**
- ▶ Celulose
- ▶ Sustentação da matriz extracelular

▶ 4) Energética

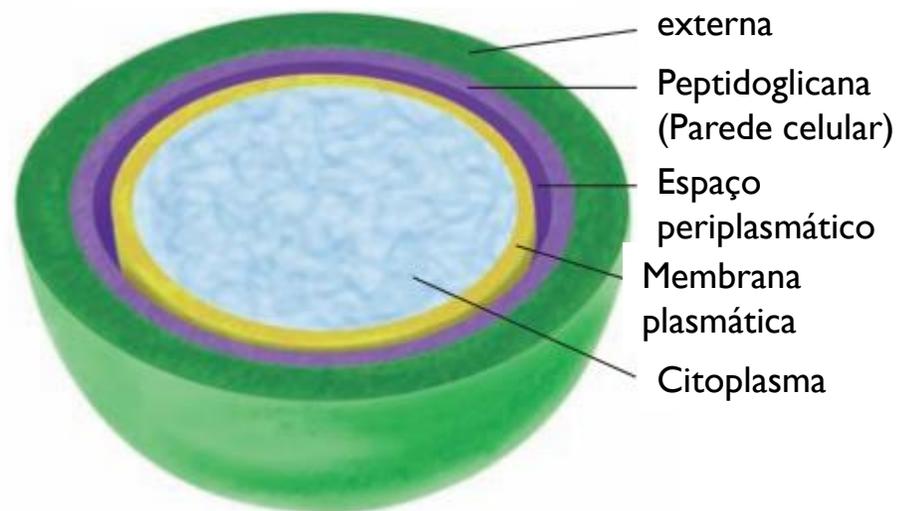


Peptidoglicanas- bactérias

(a) Bactéria gram-positiva



(b) Bactéria gram-negativa



Penicilina

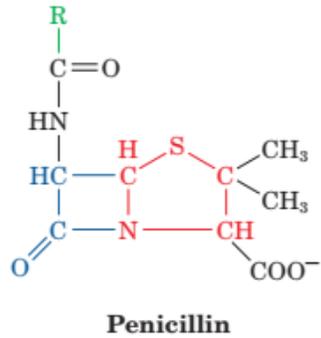


Figure 11-28 Structure of penicillin. Penicillin contains a thiazolidine ring (*red*) fused to a β -lactam ring (*blue*). A variable R group is bonded to the β -lactam ring via a peptide linkage. In benzyl penicillin (penicillin G), one of several naturally occurring derivatives that are clinically effective, R is the benzyl group ($-\text{CH}_2\phi$). In **ampicillin**, a semisynthetic derivative, R is the aminobenzyl group [$-\text{CH}(\text{NH}_2)\phi$].

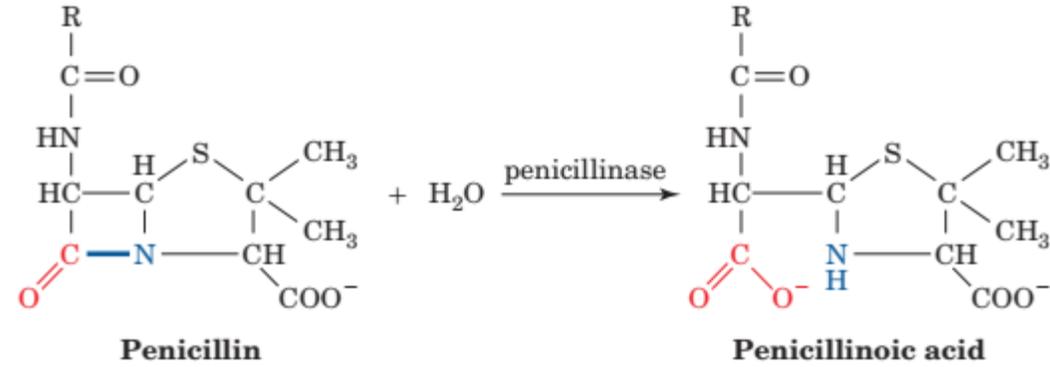


Figure 11-29 Enzymatic inactivation of penicillin. Penicillinase inactivates penicillin by catalyzing the hydrolysis of its β -lactam ring to form **penicillinoic acid**.

Antígenos

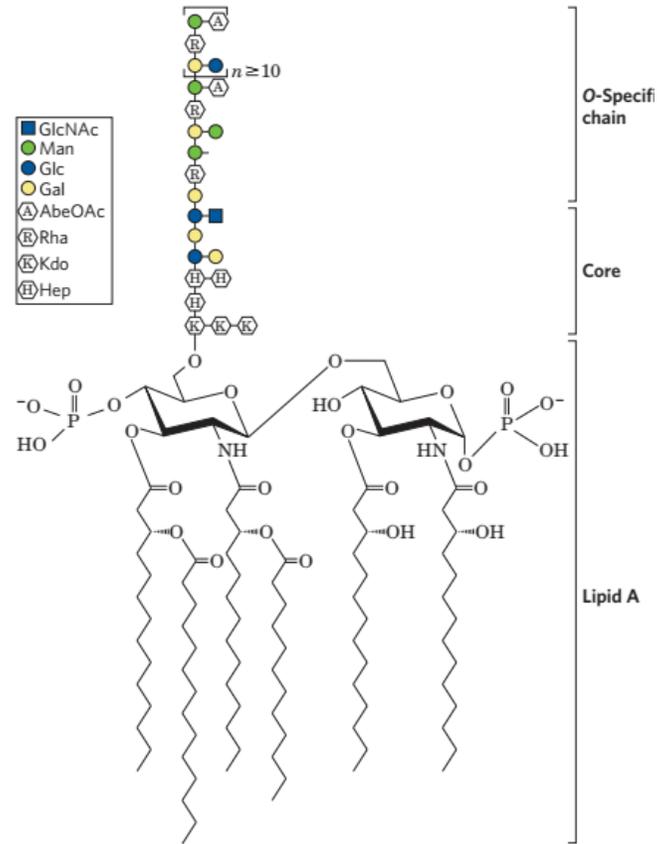
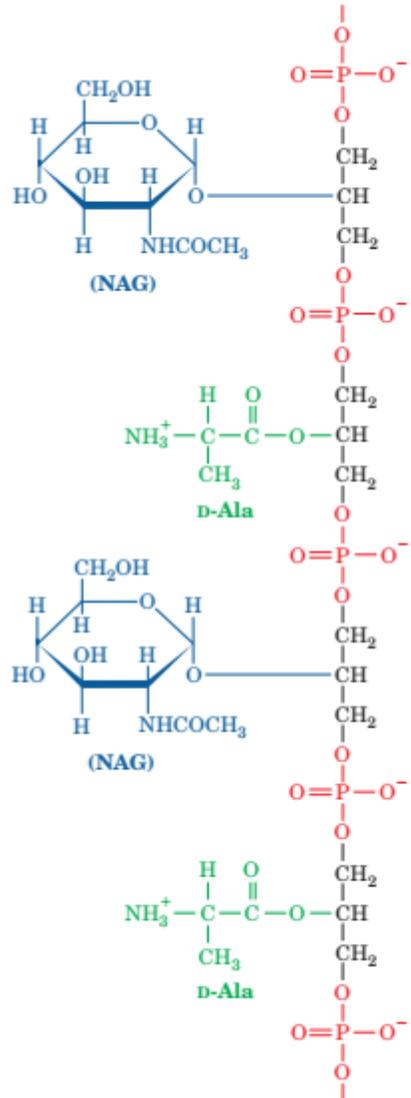


FIGURE 7-31 Bacterial lipopolysaccharides. Schematic diagram of the

Antígenos- sistema ABO

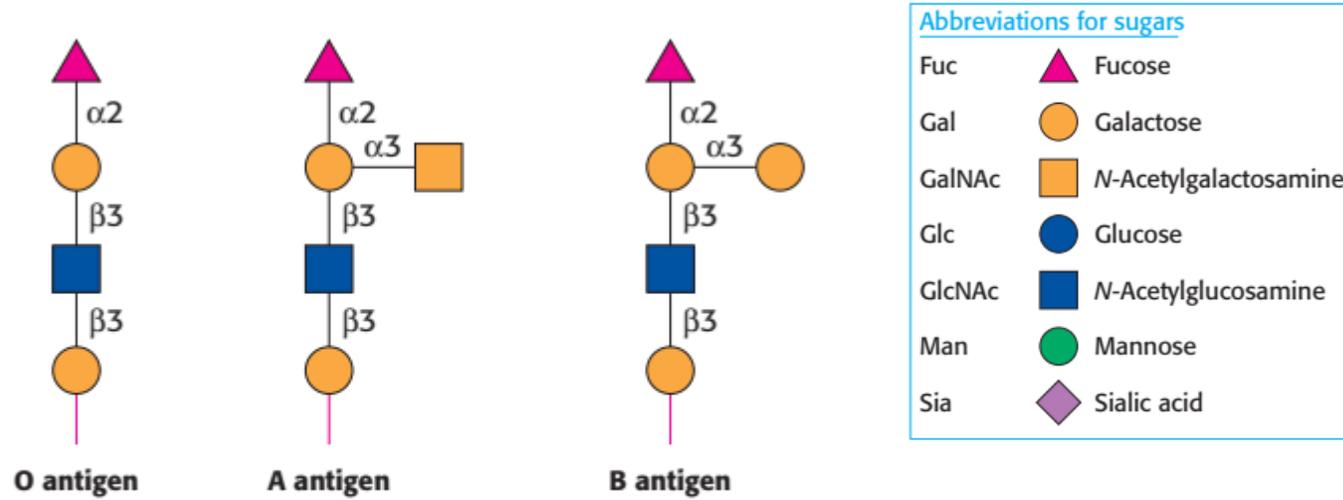


Figure 11.26 Structures of A, B, and O oligosaccharide antigens. The carbohydrate structures shown are depicted symbolically by employing a scheme (see the key in Figure 11.16) that is becoming widely used.

