The concept of Glycochemistry and Glycobiology

References

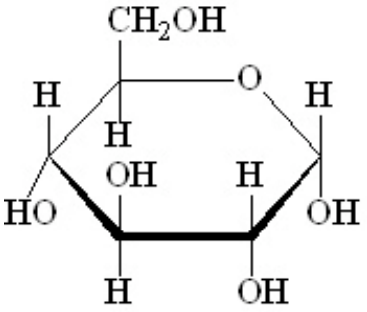
- "Carbohydrate Chemistry" Benjamin G. Davis Oxford University Press 2002
- "Introduction to Glycobiology" 2nd Ed. Maureen E. Taylor Oxford University Press 2003
- "Biochemistry" Garrett, 4th Ed. 2008
- A varieties of papers
- "Essentials of Glycobiology" 2nd Ed. Ajit Varki 2009
- "Functional and Molecular Glycobiology" BIOS scientific publishers 2002

Outline

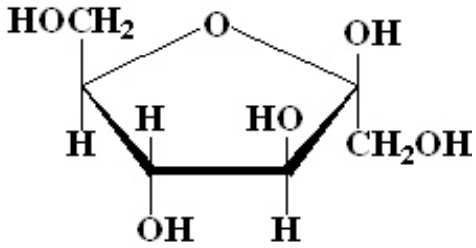
- The concept of glycochemistry and glycobiology
- Fischer Projection and the story behind
- Open chain and ring structure of monosaccharides
- Reactions of the hydroxyl groups
- Reactions of the anomeric centre
- Classical Polysaccharides/as biocompatible materials
- The development of Lock-key concept
- *N*-linked glycosylation

Outline

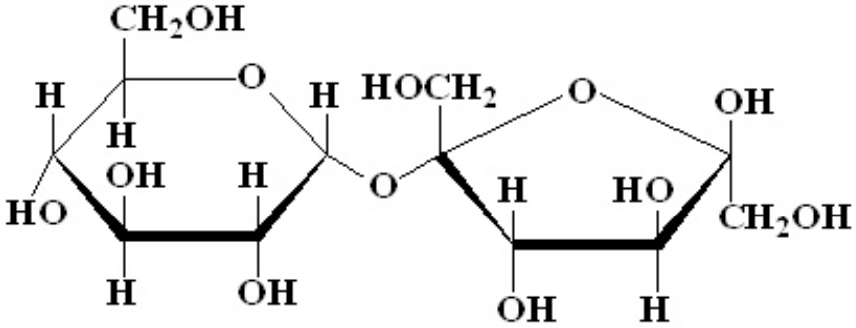
- *O*-linked glycosylation
- Glycolipid and membrane protein glycosylation
- Modern chemical and chemoenzymatic synthesis of oligosaccharides
- Effect of glycosylation on protein structure and function
- Carbohydrate recognition in cell adhesion and signaling
- Cyclodextrins/our research
- Update and Outlook



glucose



fructose



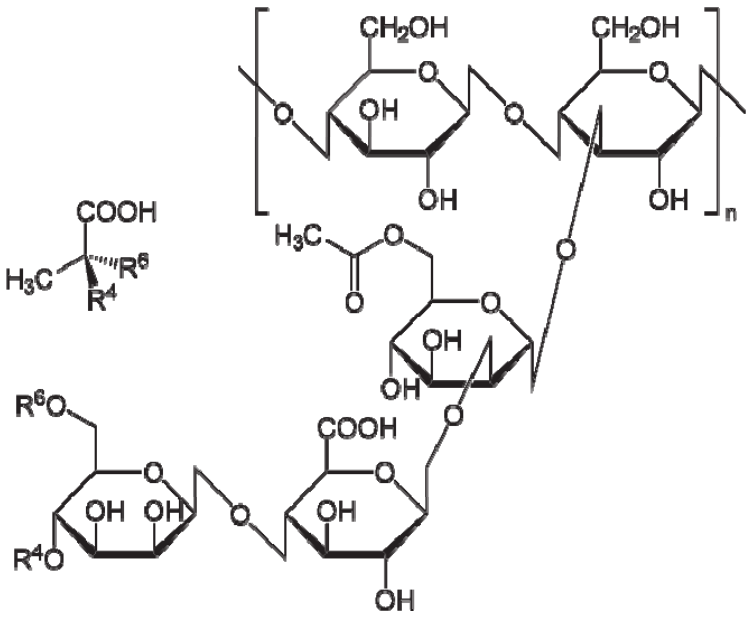
sucrose

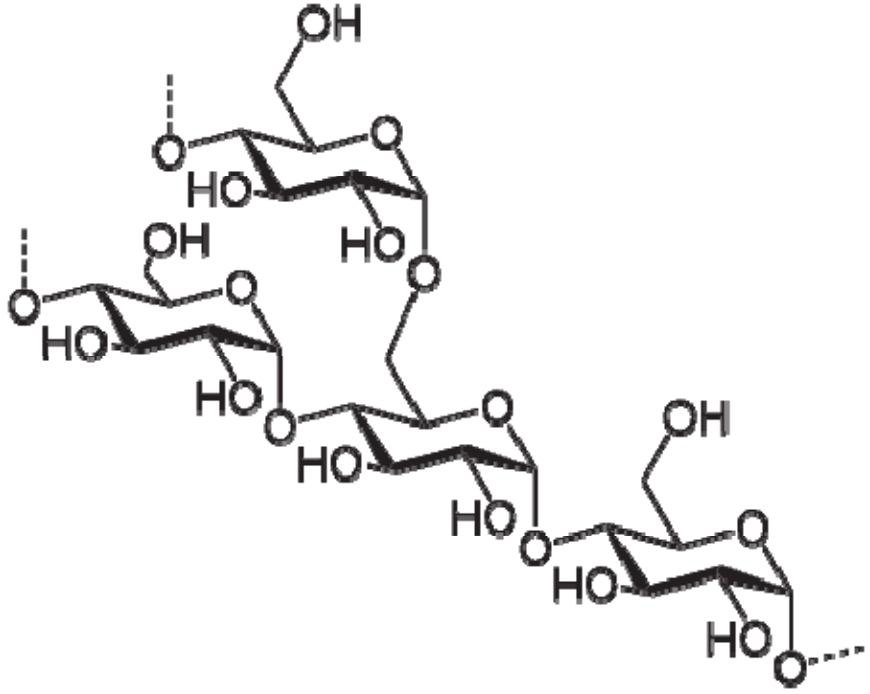
Lactose

Amylose

Amylopectin

Xanthan gum





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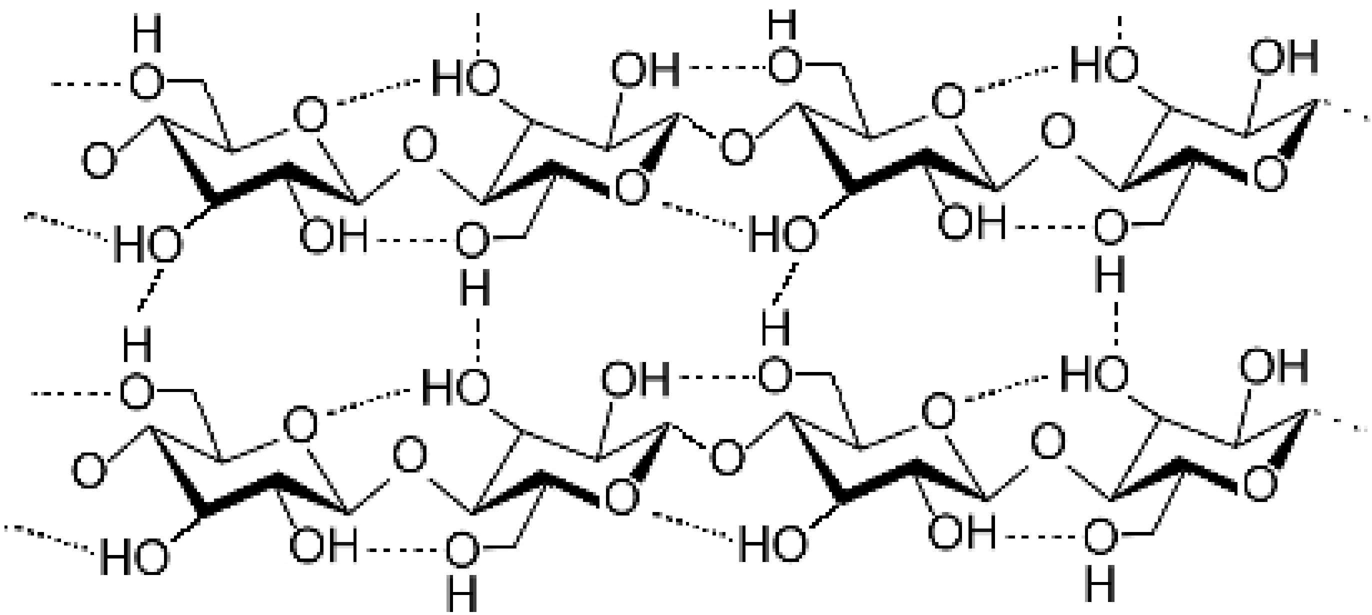
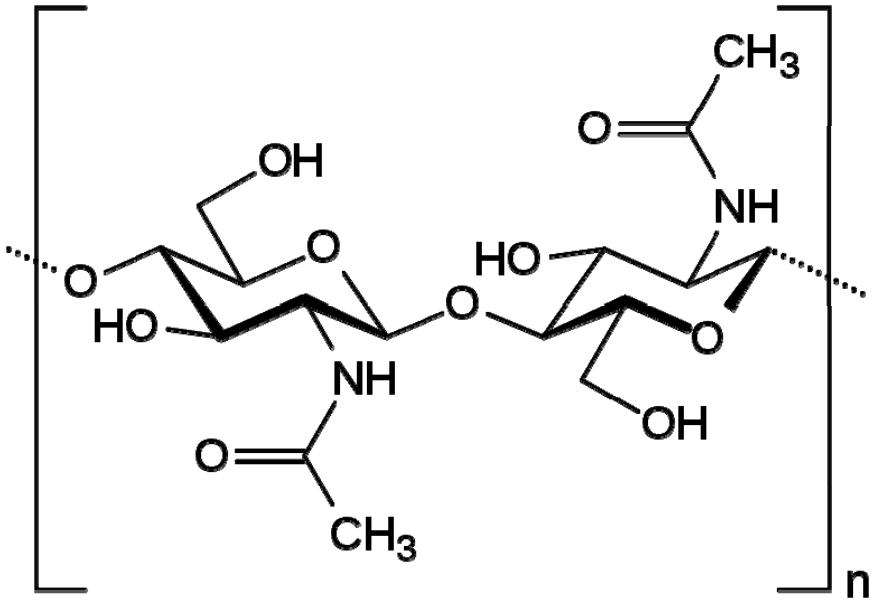
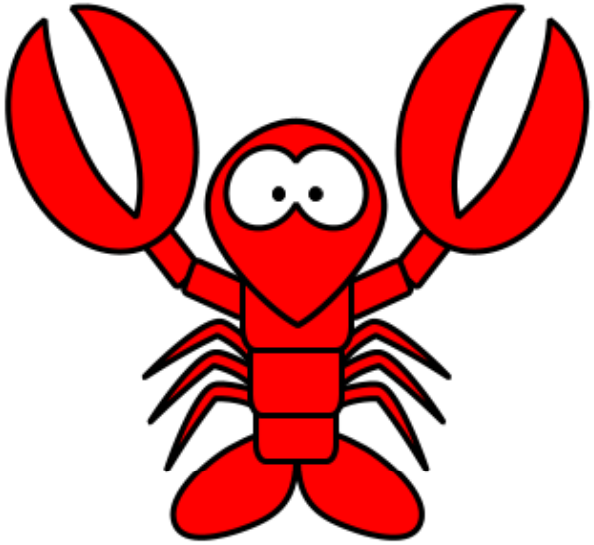
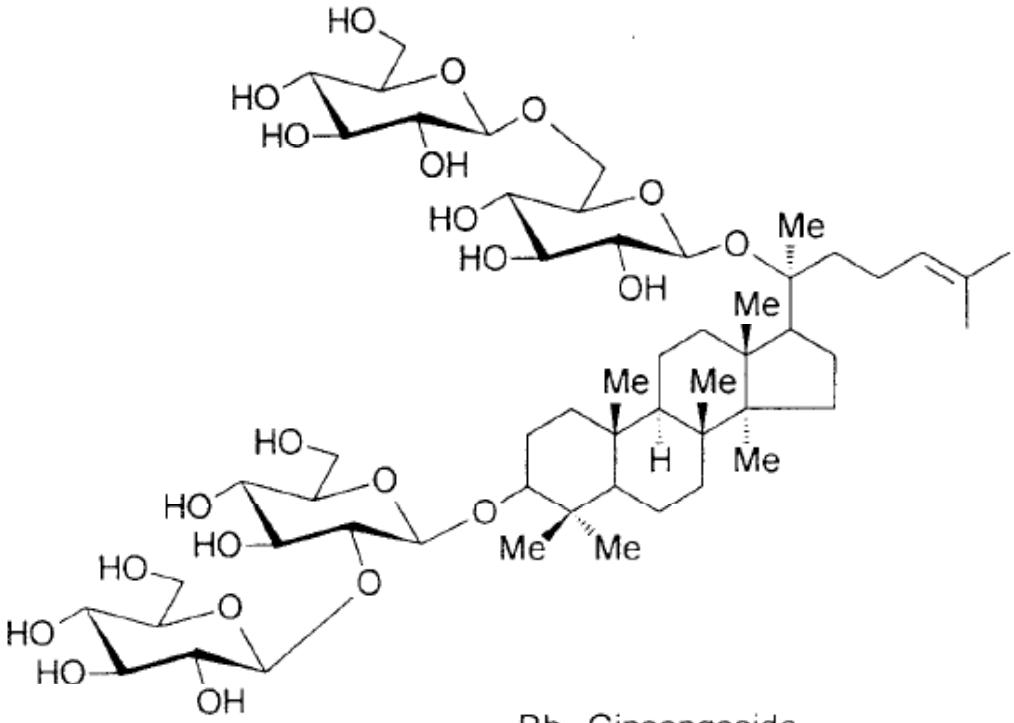


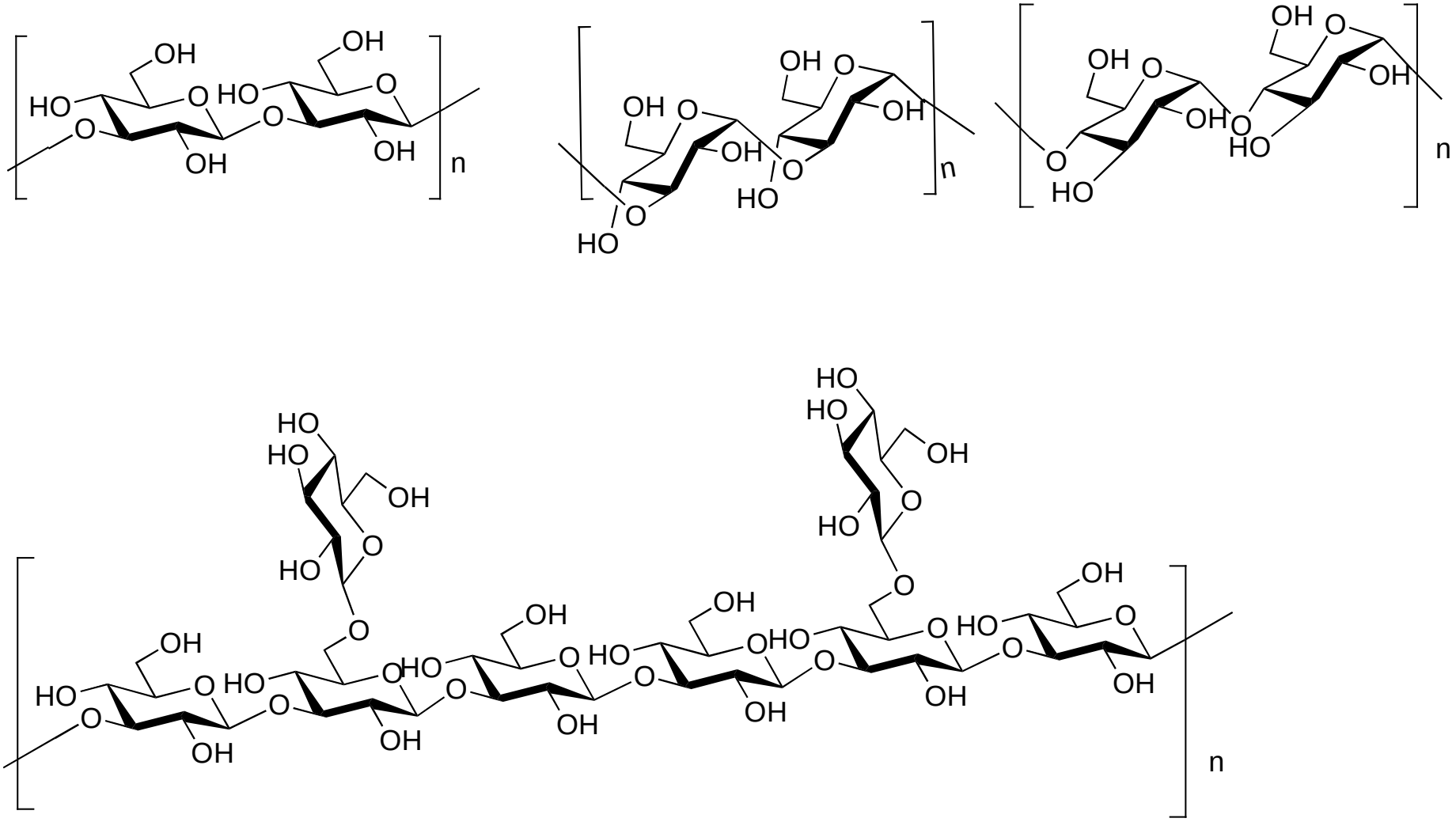


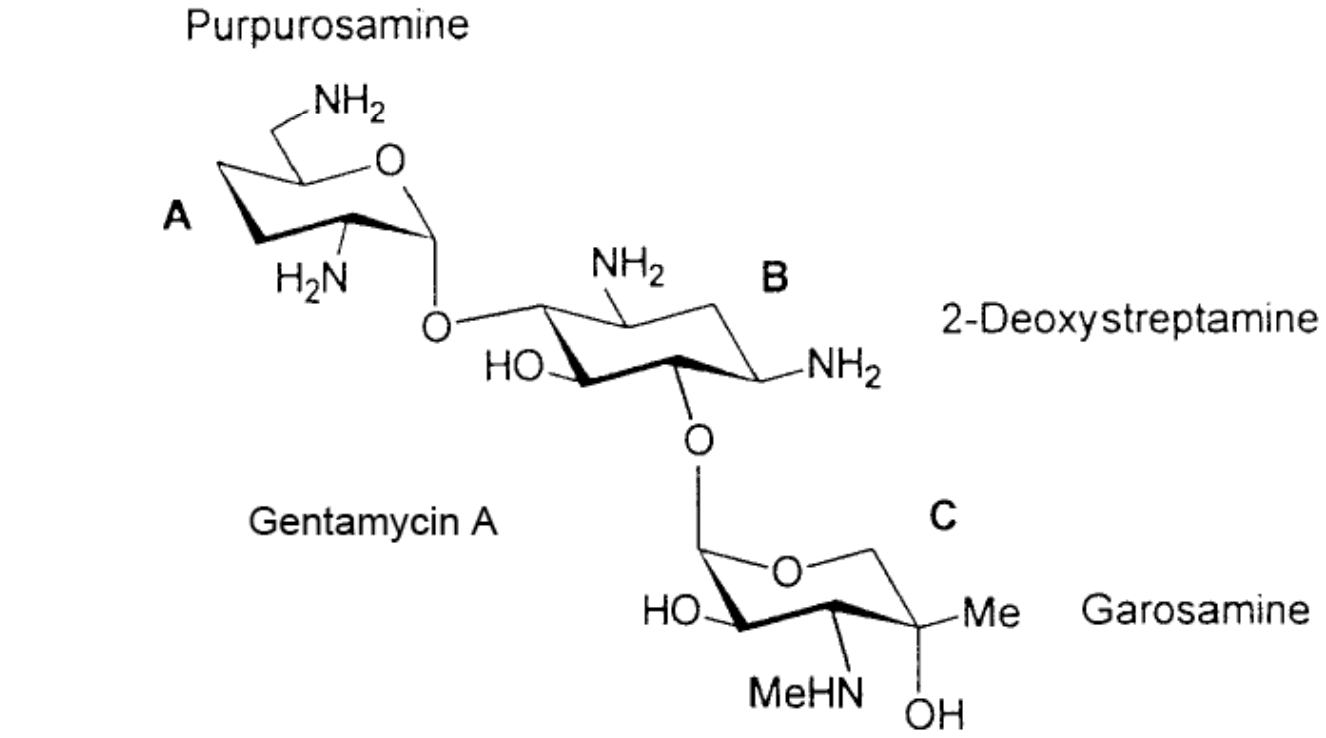


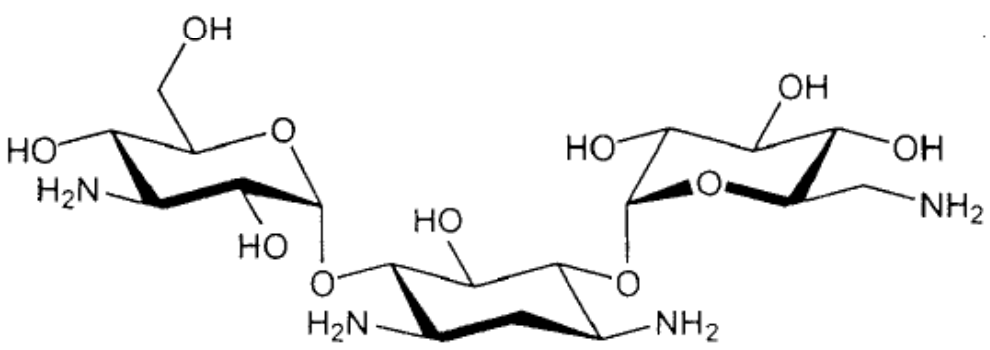
Chitin



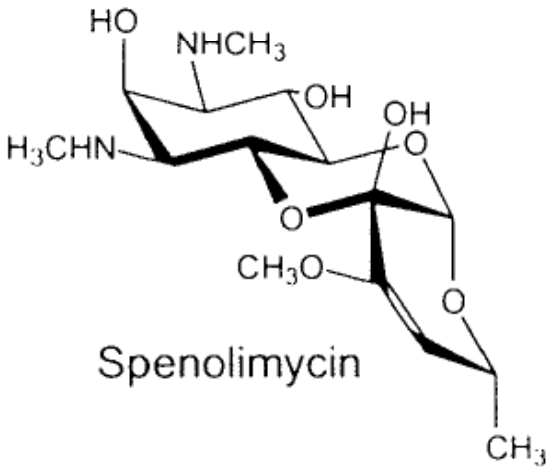
Rb_1 Ginsengoside


OH
HO
O
n





Kanamycin A

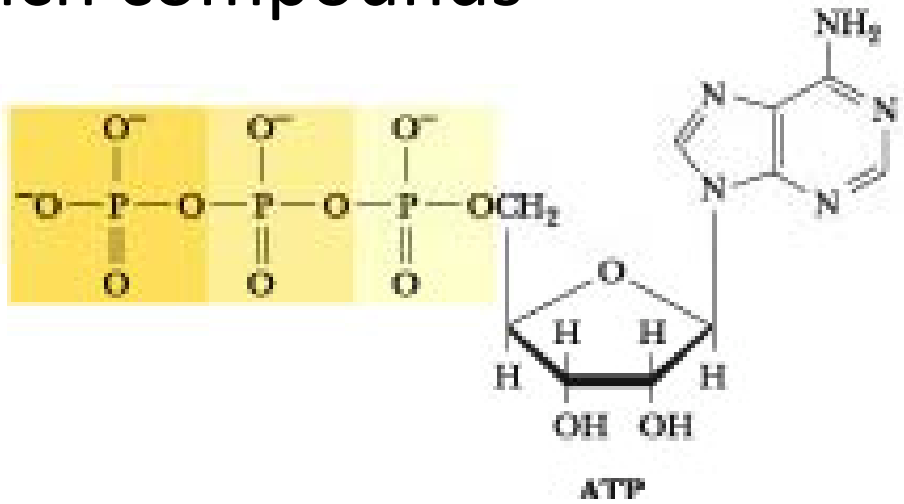


Spenolimycin

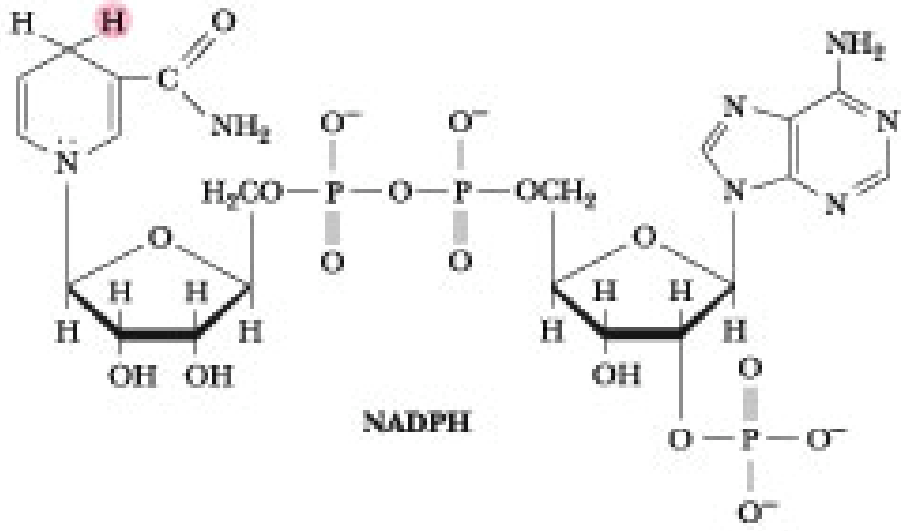
Sugars are everywhere in the world,

especially in our body.

ATP and NADPH, two biochemically important energy-rich compounds

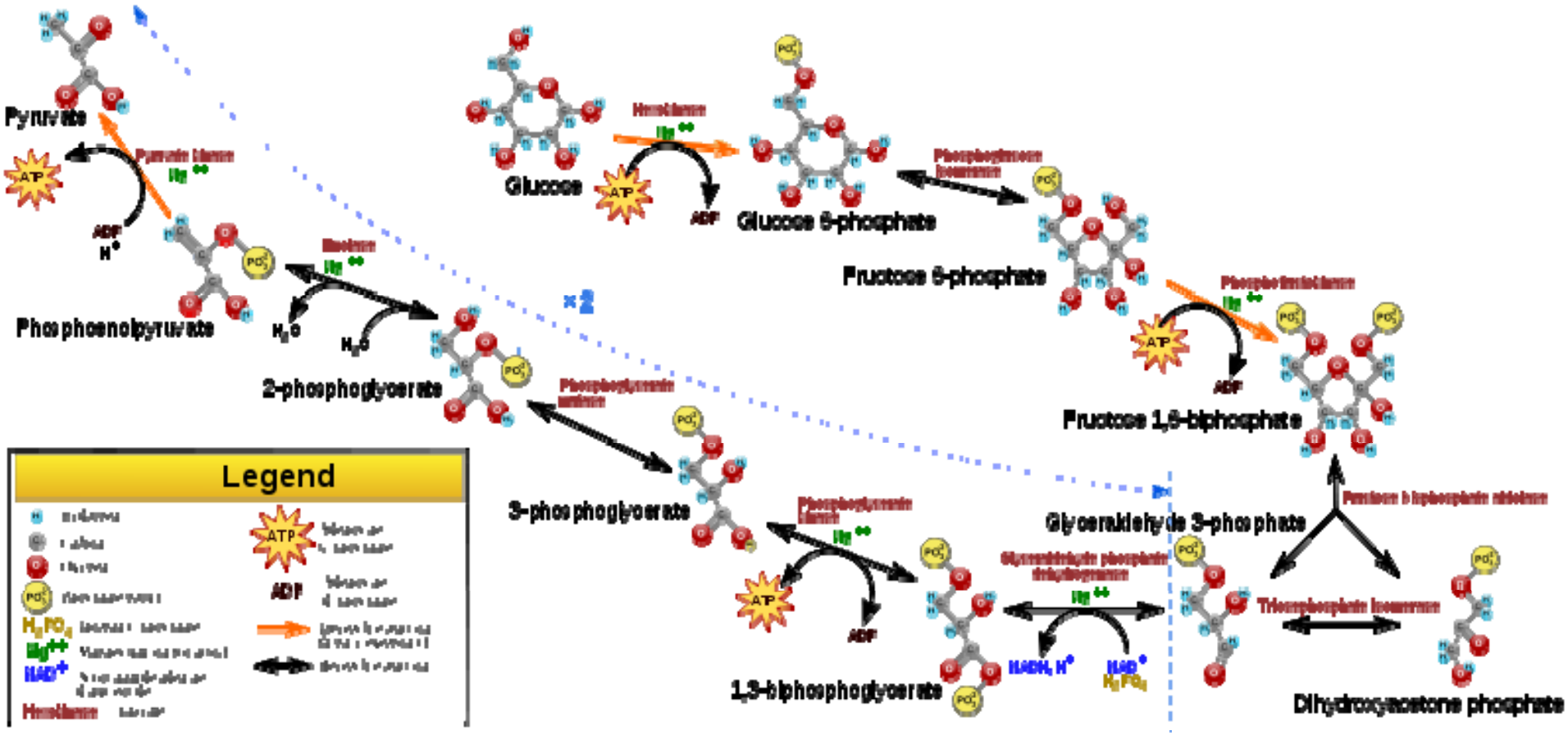


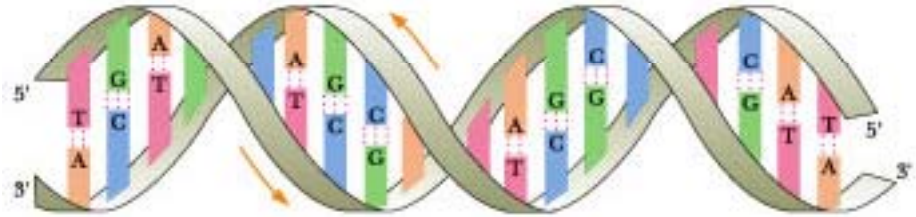
ATP

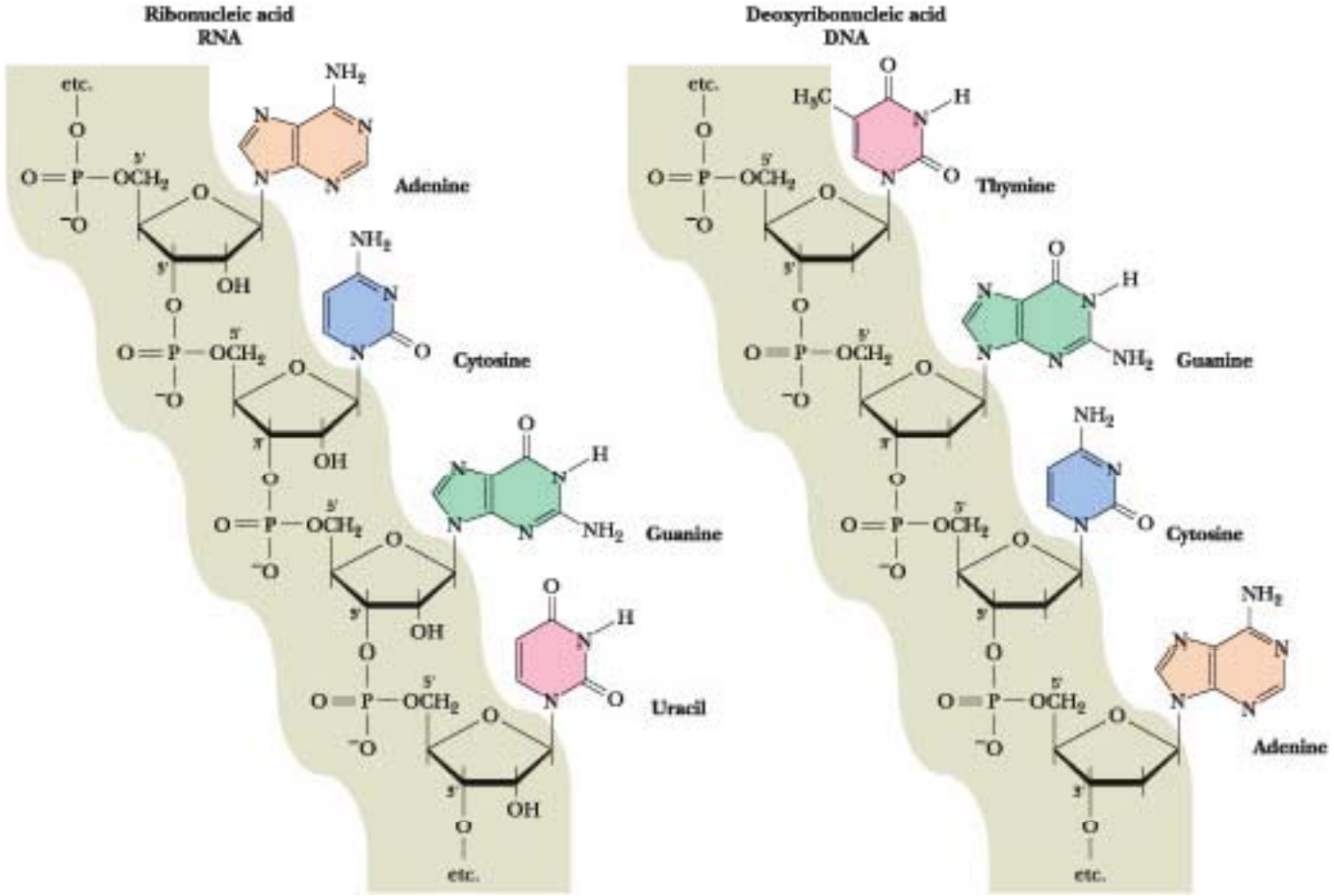


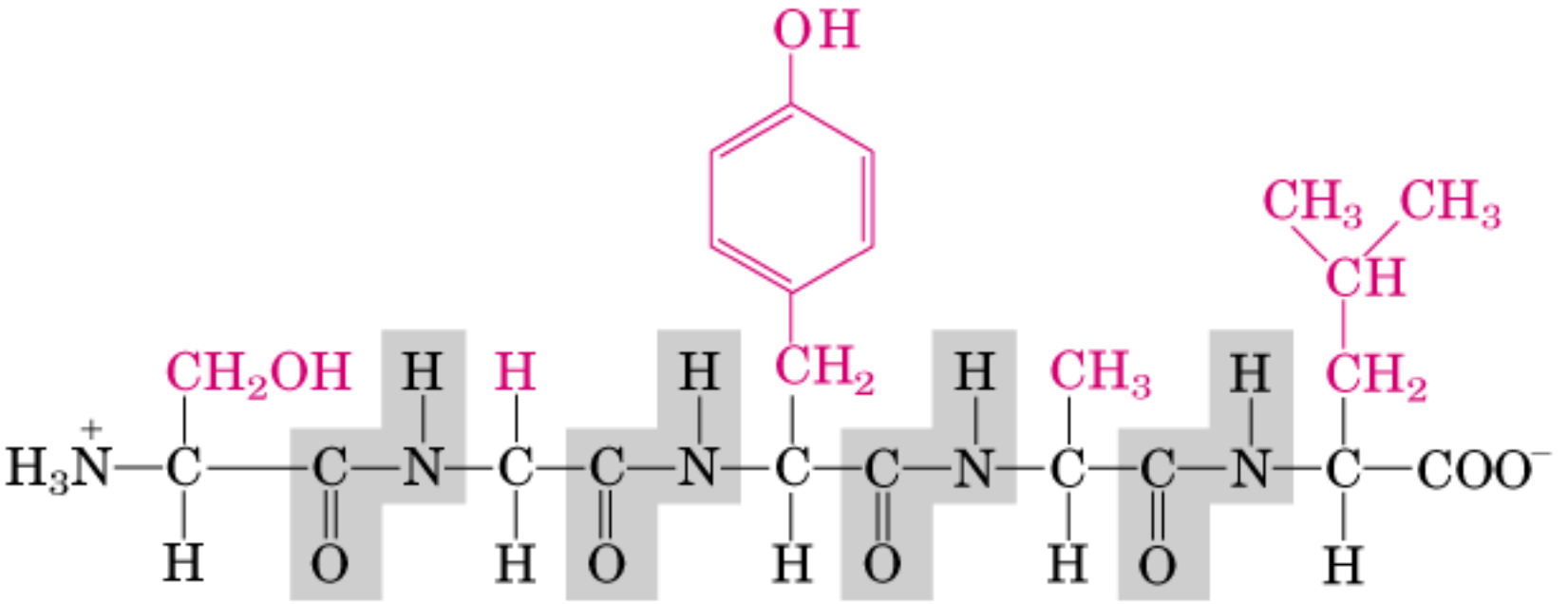
NADPH

Glycolysis

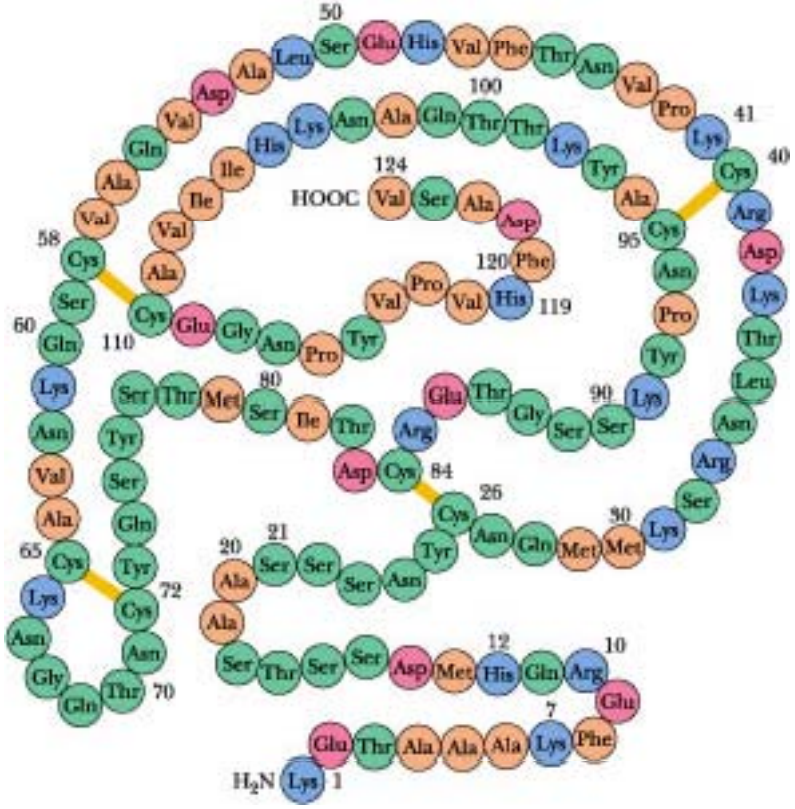

Pyruvate
ATP
ADF
H+
Phosphoenolpyruvate
H2O
H2O
2-phosphoglycerate
×2
3-phosphoglycerate
ATP
ADF
1,3-biphosphoglycerate
NADH, H+
Glucose
ATP
ADF
Glucose 6-phosphate
Fructose 6-phosphate
ATP
ADF
Fructose 1,6-biphosphate
Glyceraldehyde 3-phosphate
Triosephosphate isomerase
Dihydroxyacetone phosphate
Legend
ATP
ADF


5'
3'
5'
3'


Ribonucleic acid
RNA
Adenine
Cytosine
Guanine
Uracil
Deoxyribonucleic acid
DNA
Thymine
Guanine
Cytosine
Adenine



http://www.biochem.arizona.edu/classes/bioc462/462a/NOTES/Amino_Acids/amino_acids.htm



Bovine pancreatic ribonuclease A

Schematic representation of the Thy-1 glycoprotein

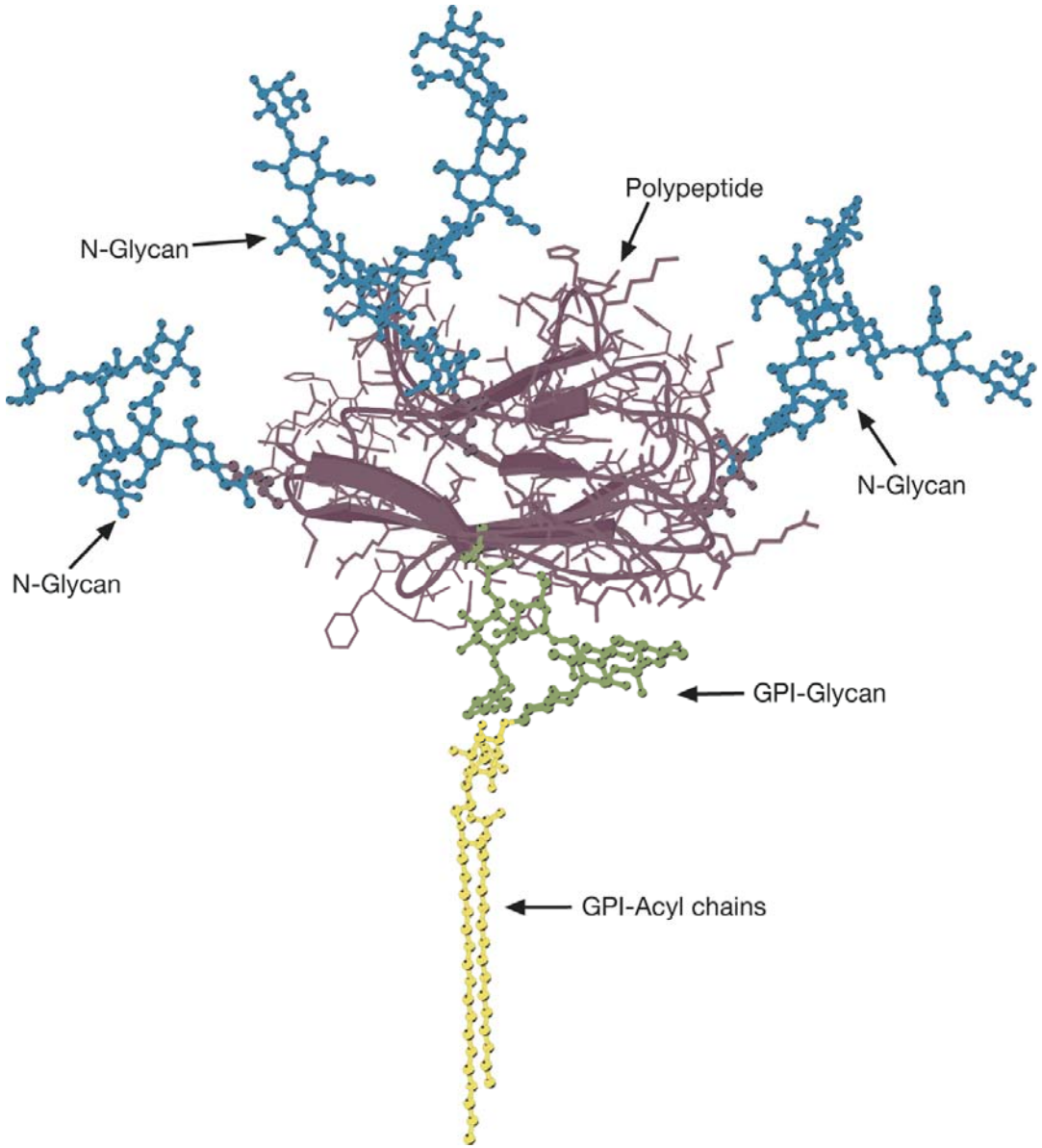
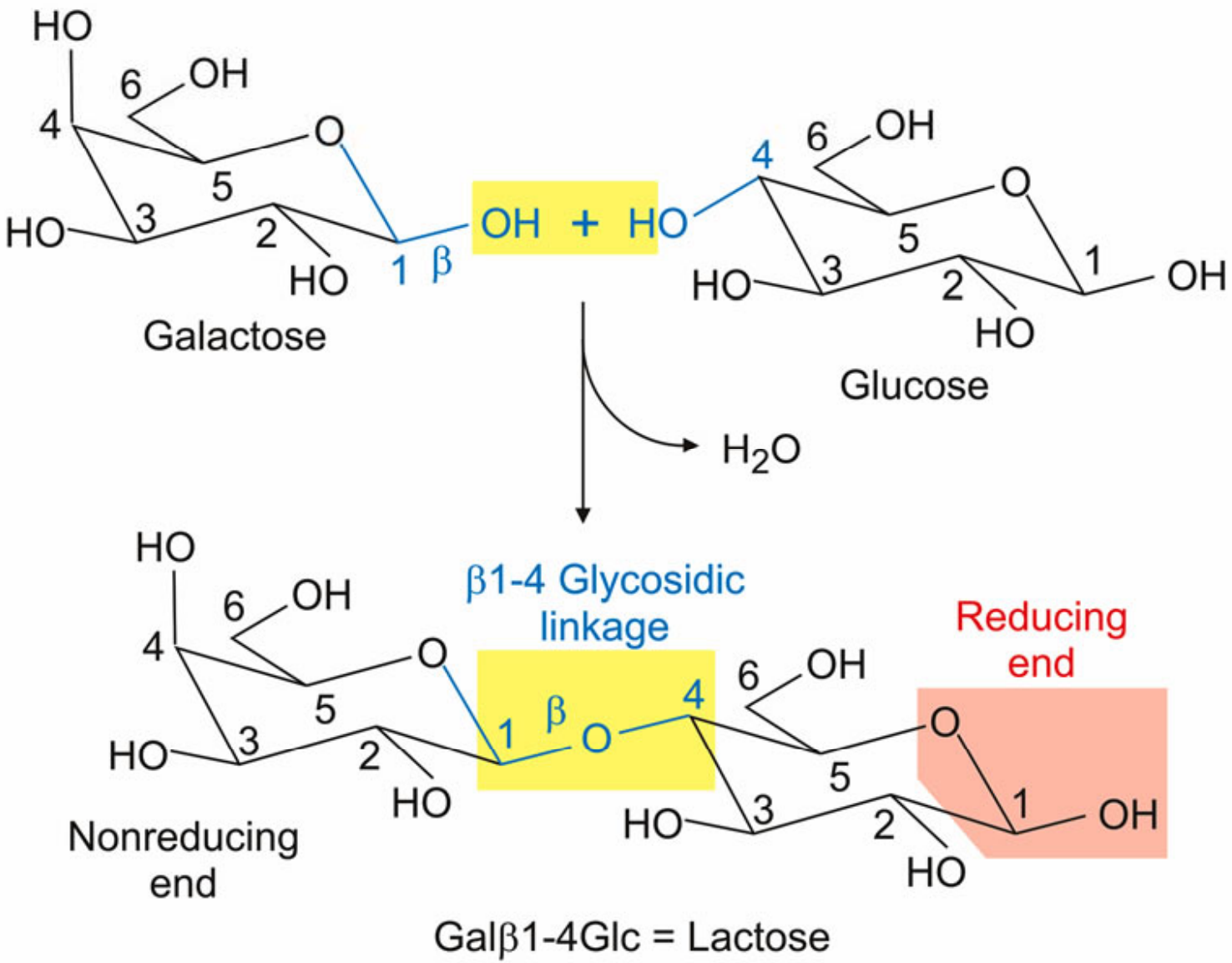
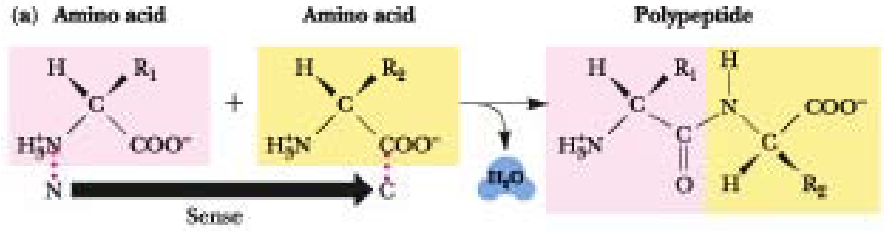
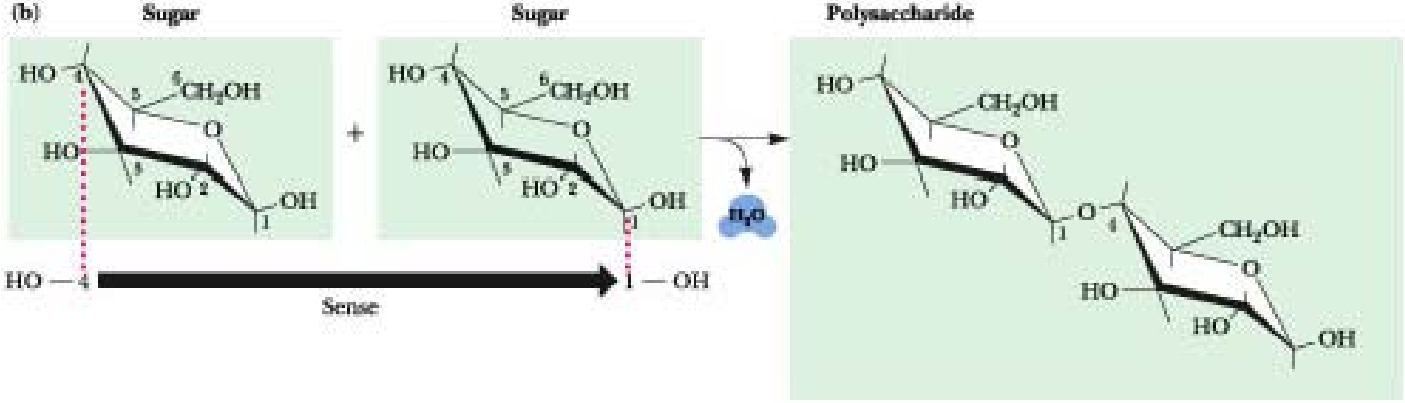
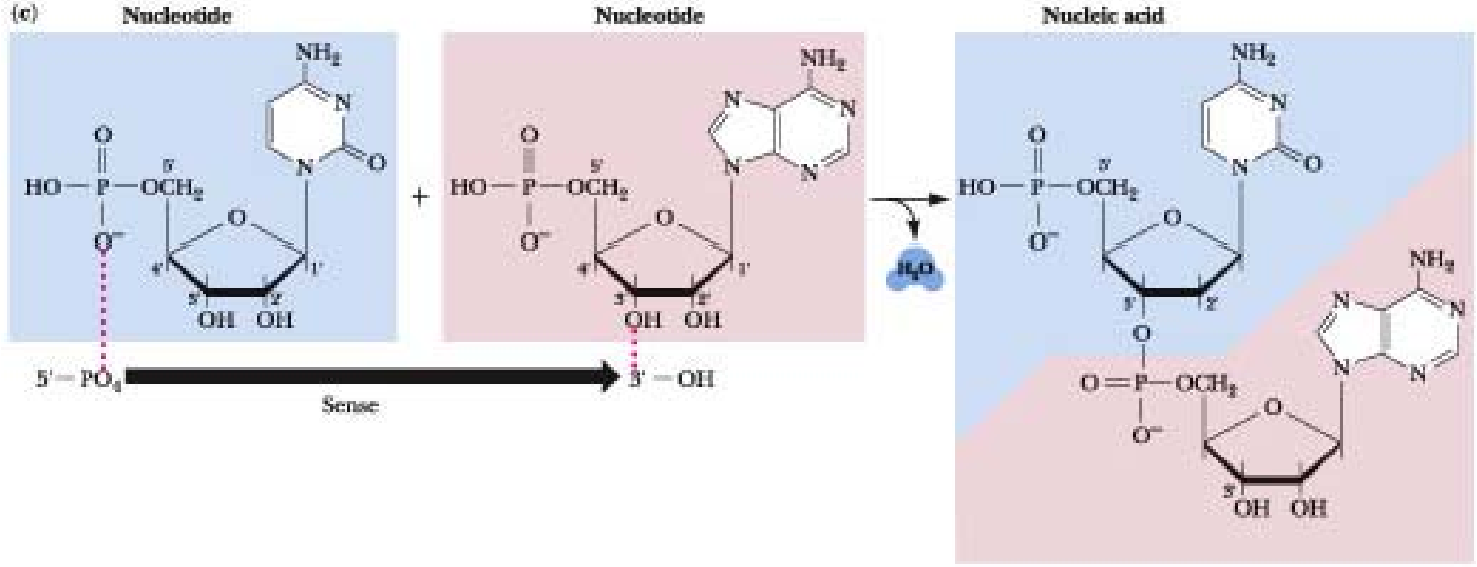


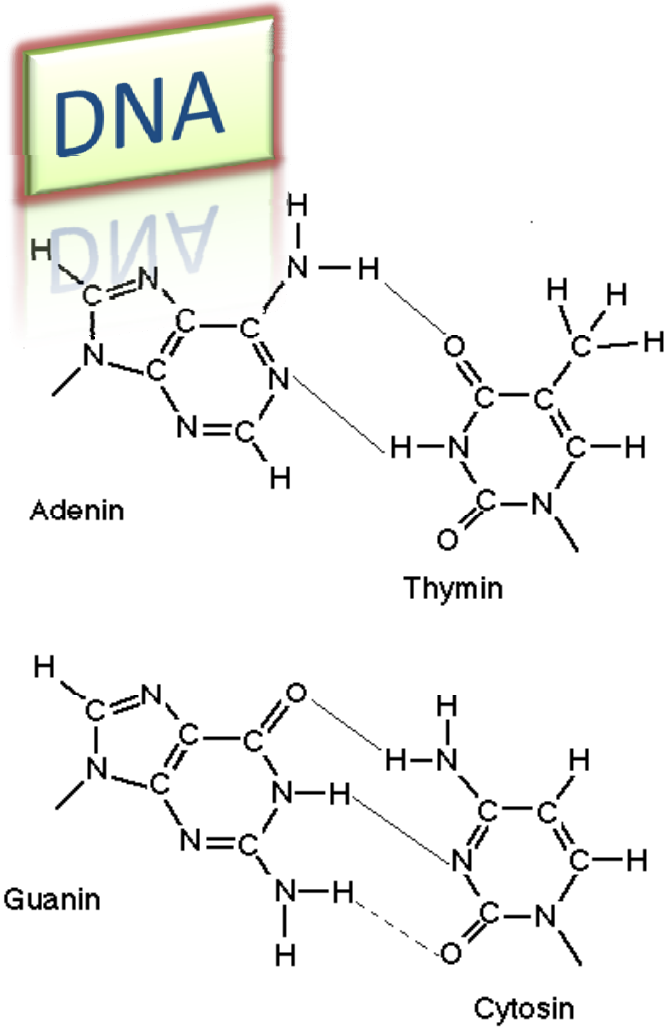
Figure 1.8 Formation of a glycosidic linkage

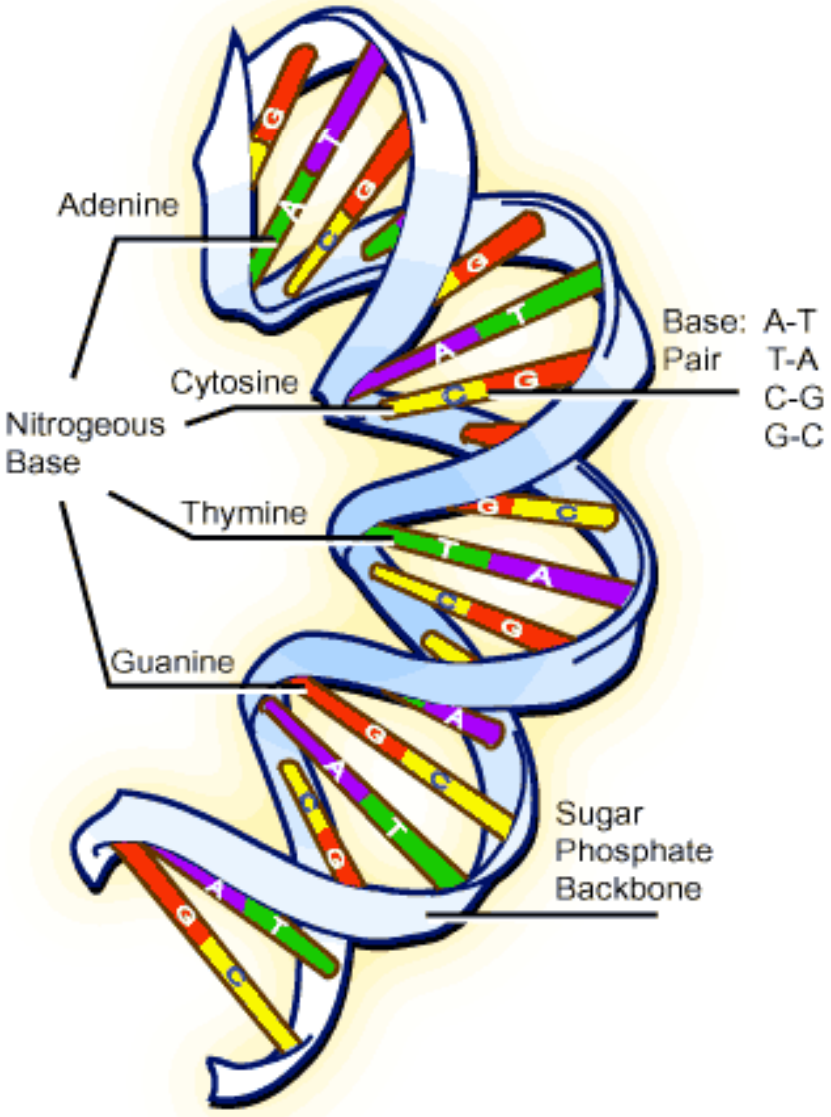



(a) Amino acid
Amino acid
Polypeptide
Sense


(b)
Sugar
Sugar
Polysaccharide
Sense


(c)
Nucleotide
Nucleotide
Nucleic acid
Sense

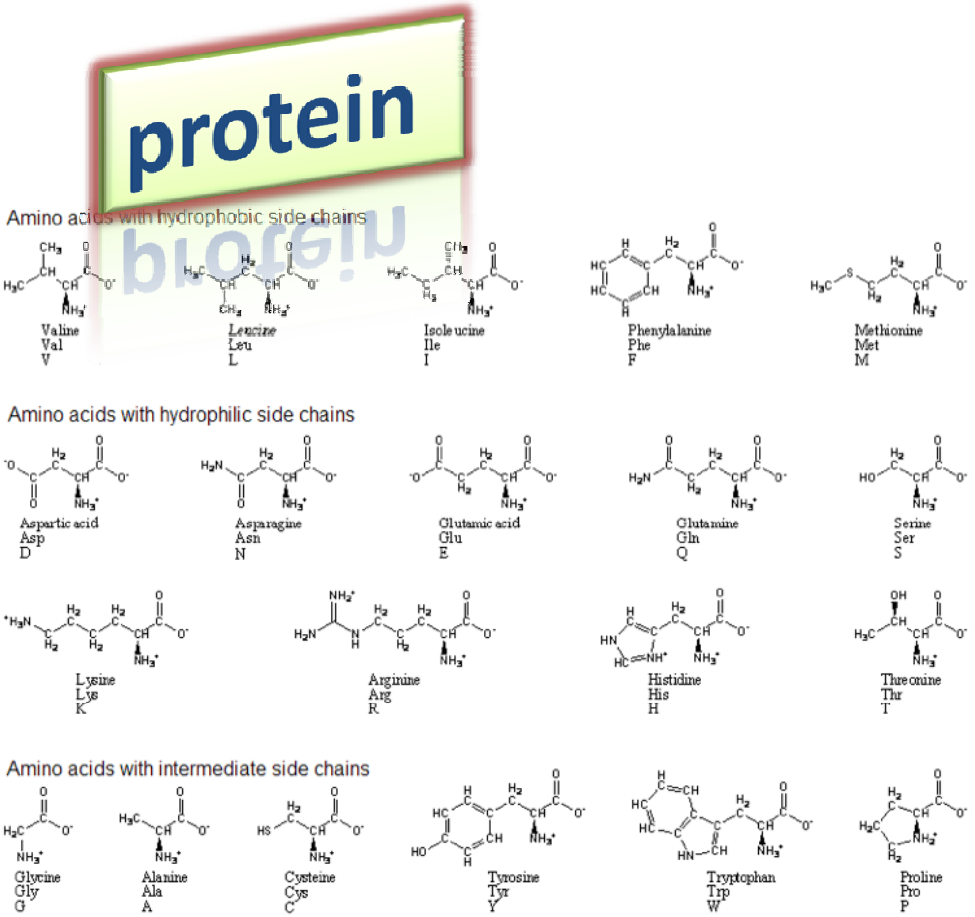


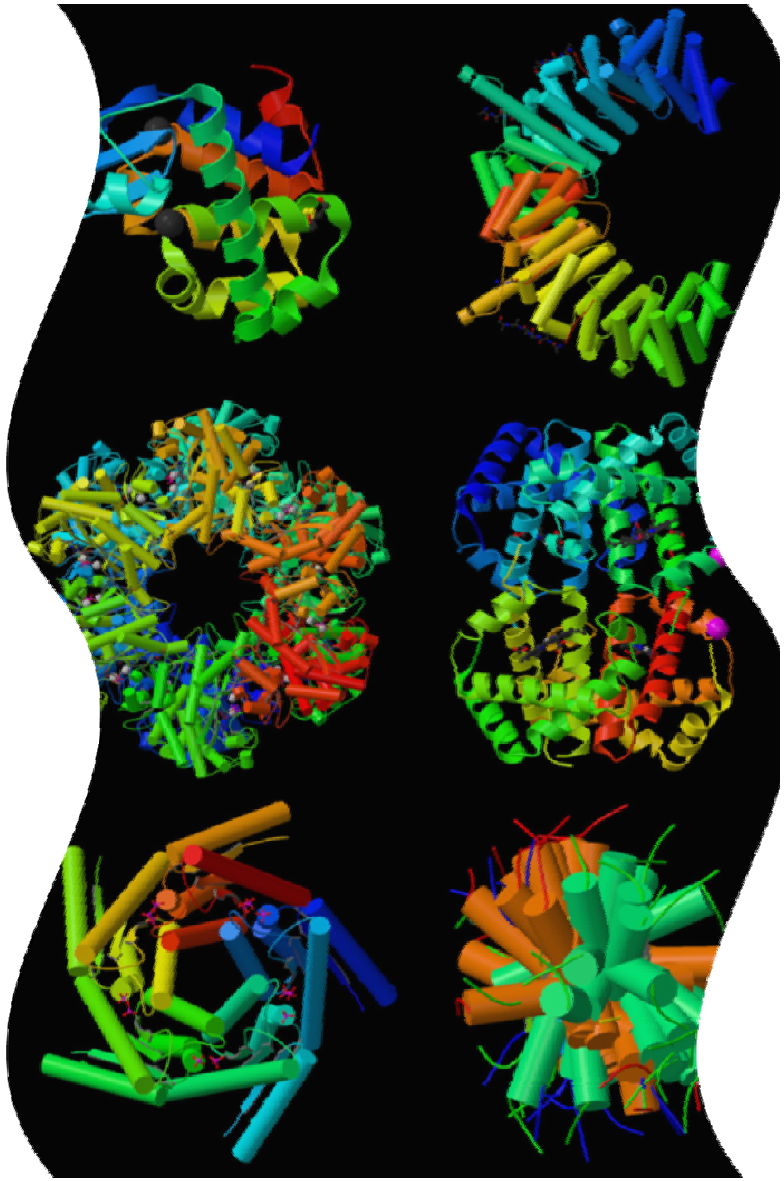


Basis set of 4

Biological 'words' of 4096

www.scq.ubc.ca/wp-content/dna.gif





Basis set of 20

Biological ‘words’ of 6.4×10^{7}

http://calstate.fullerton.edu/news/arts/2003_5_molecules.html

www.bioinformaticsatschool.eu/basicsa.html

Figure 1.5 Relationships between the common hexoses and N-acetylhexosamines

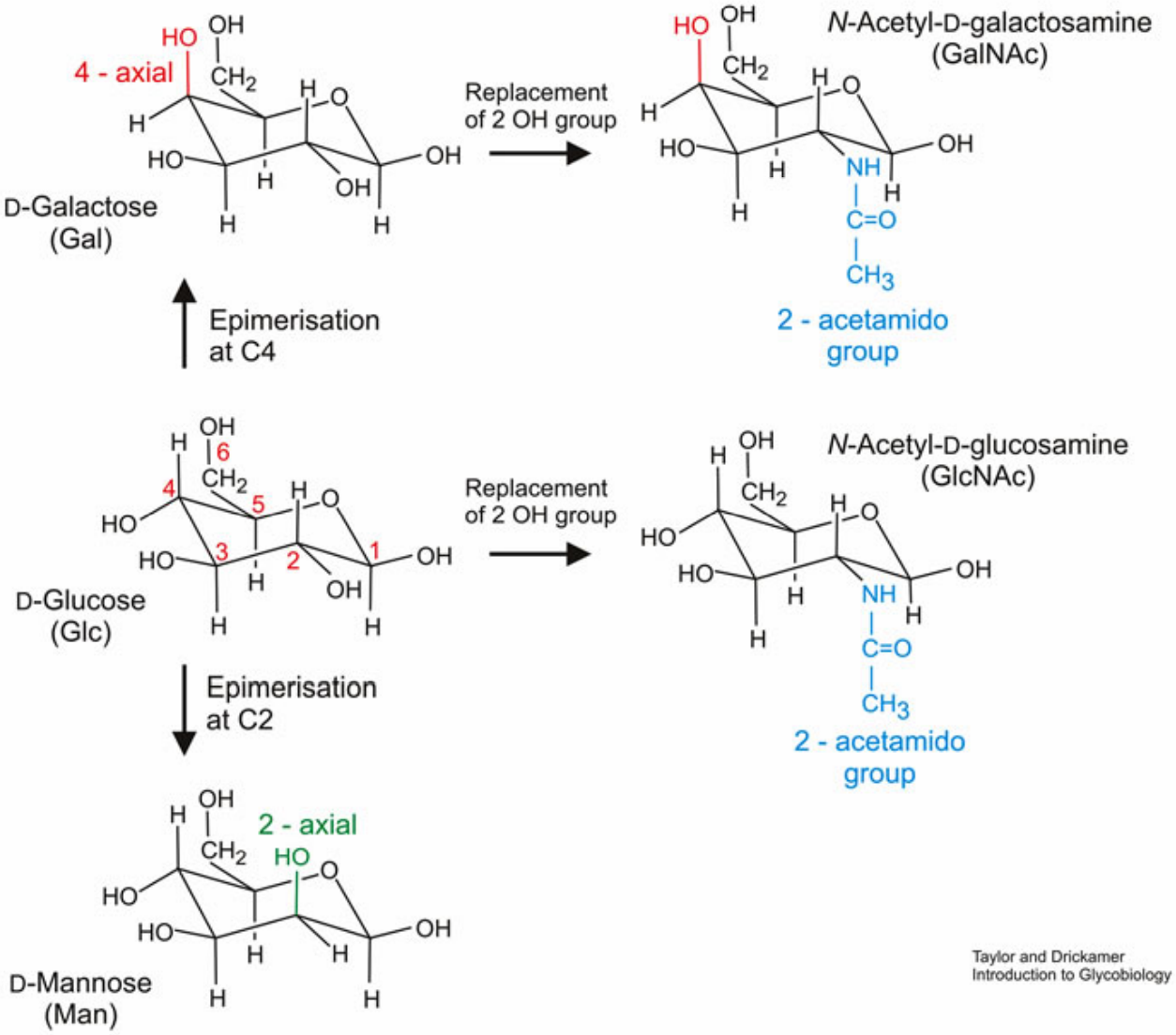
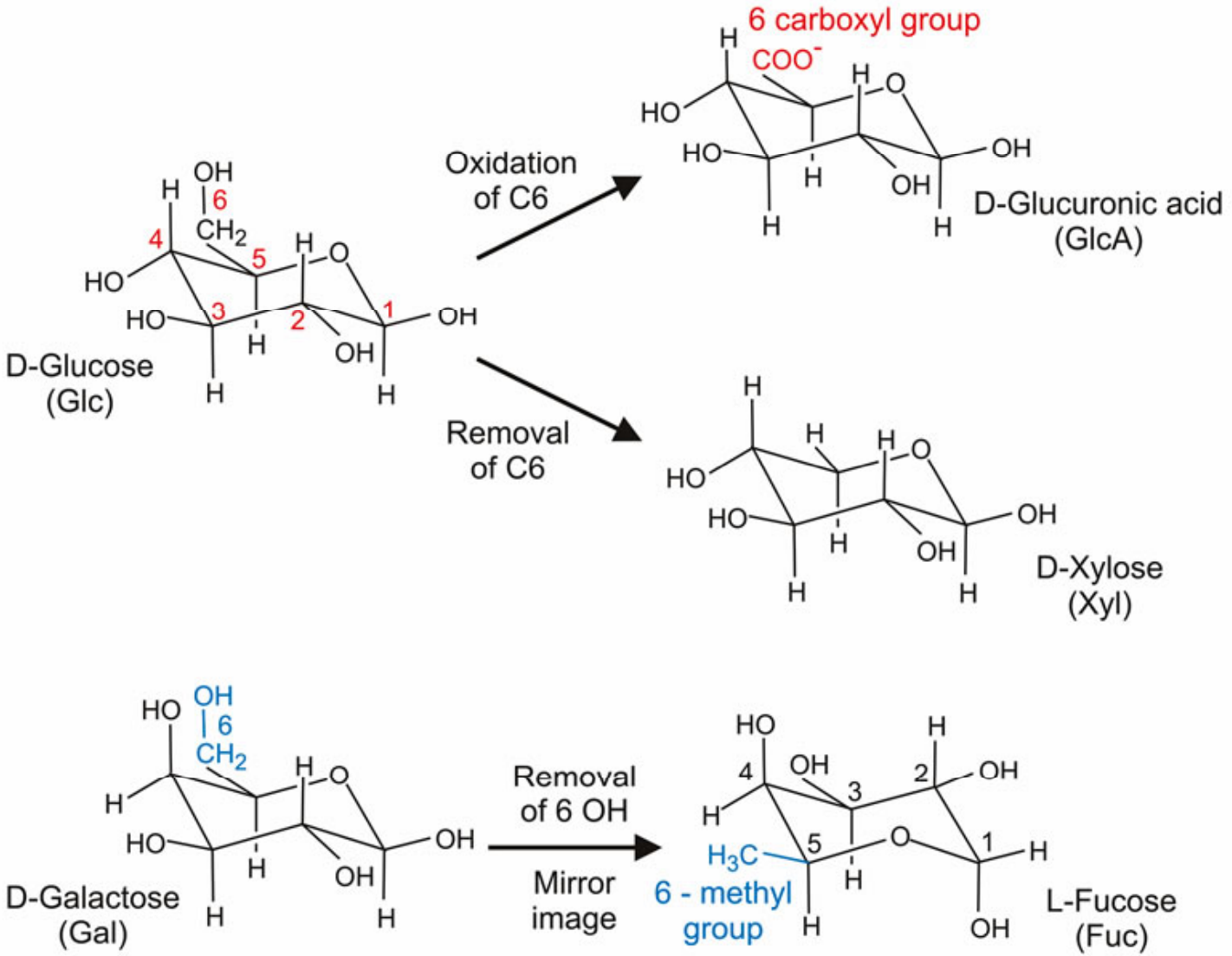


Figure 1.6 Structures of some common derivatives of the hexoses



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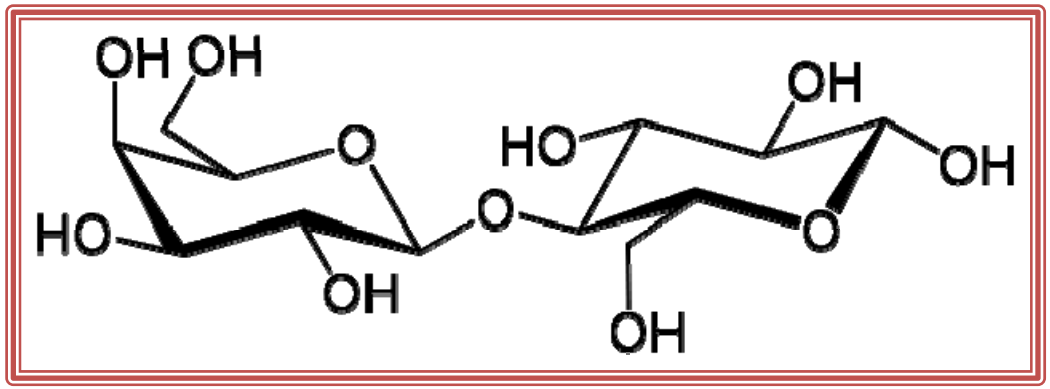
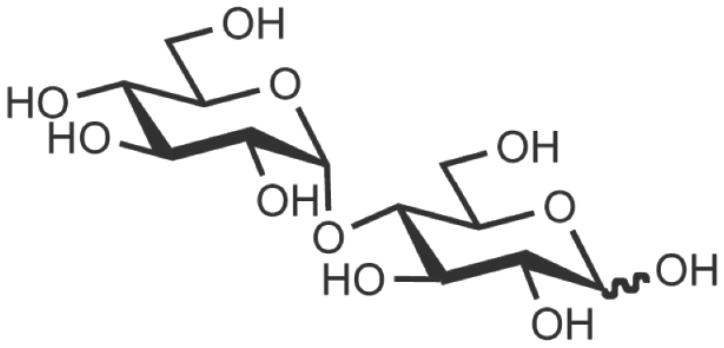
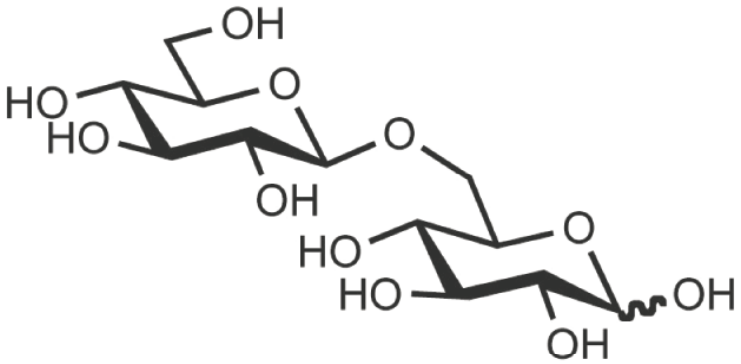
Two isomeric disaccharides



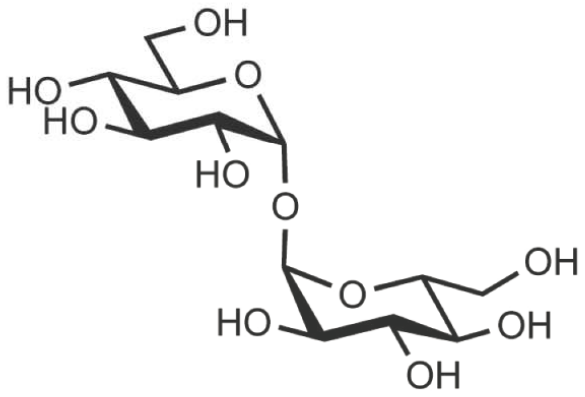


Glcα1-4Glc
(maltose)

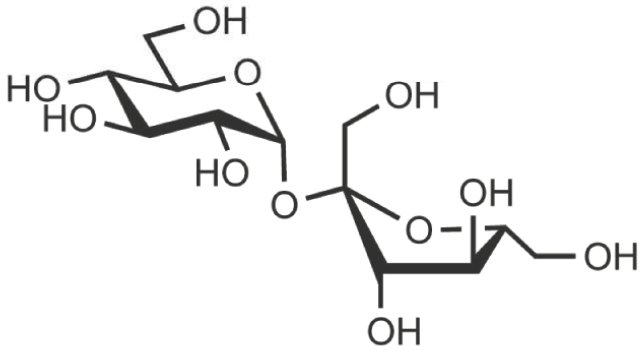


Glcβ1-6Glc
(gentiobiose)

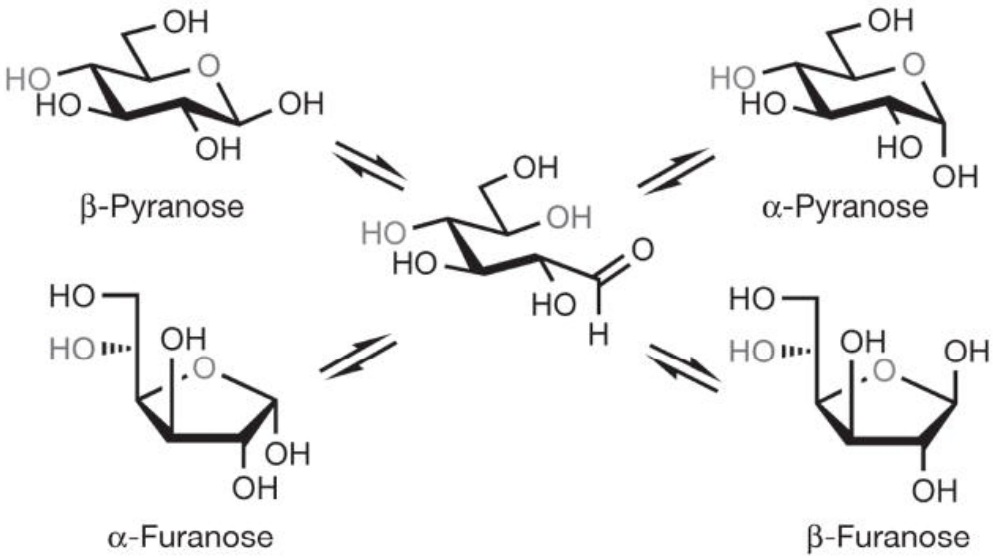
Nonreducing disaccharides



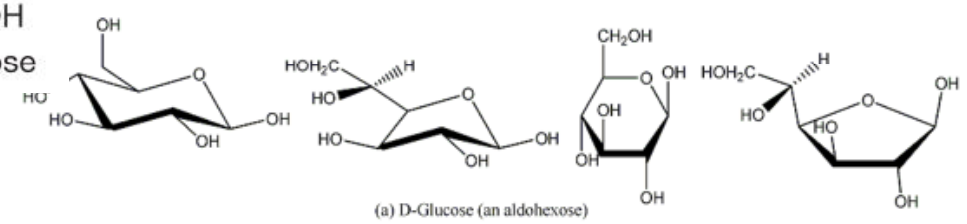
Glcα1Glcα1
(trehalose)



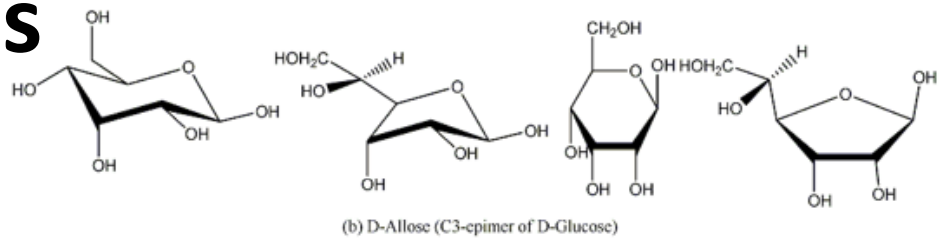
Glcα2Fruβ
(sucrose)



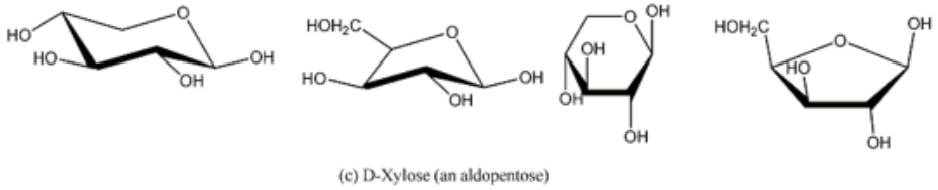
Sulfation
Phosphorylation
Methylation
Acylation
……

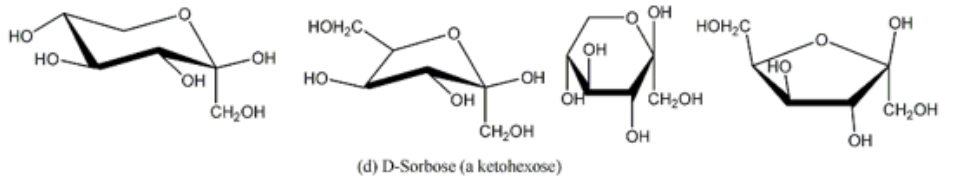


> 1.05×10^{12} variations



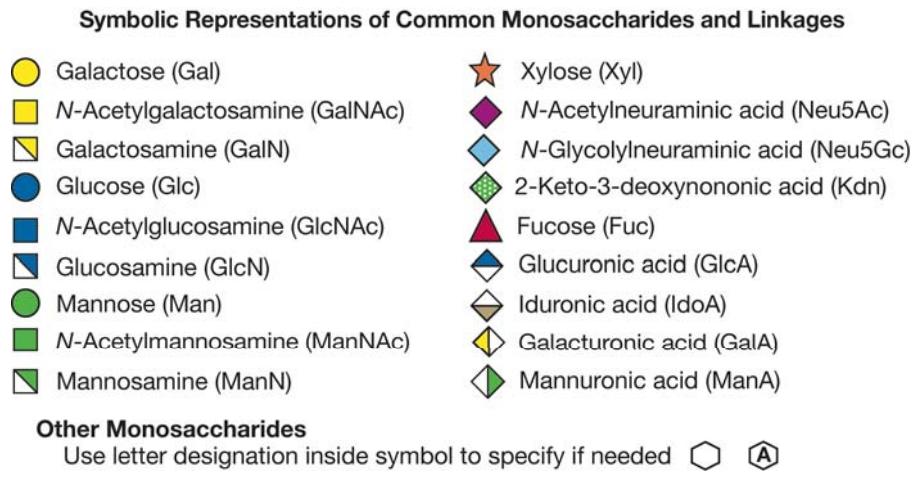
Even if we ere able to make a different hexasaccharide every day, the world would still end before we made all the possibilities
----B. G. Davis "Carbohydrate Chemsitry"



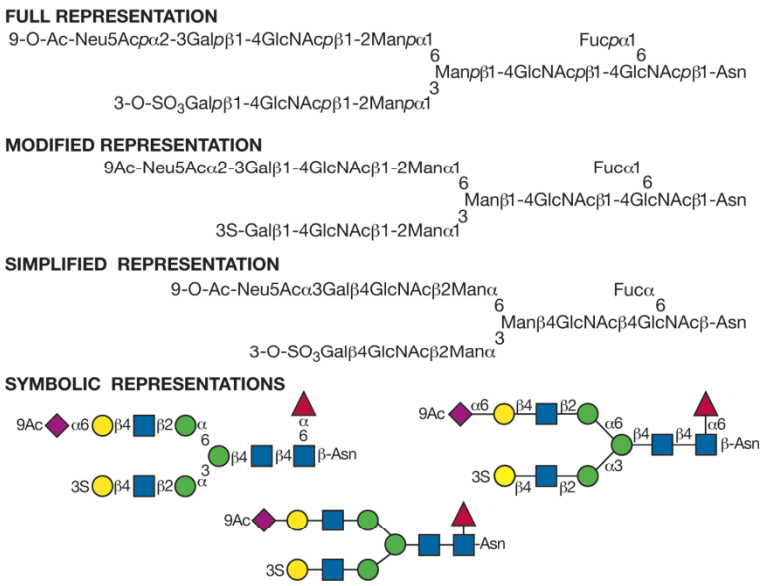


Monosaccharide symbol set

a



b



c

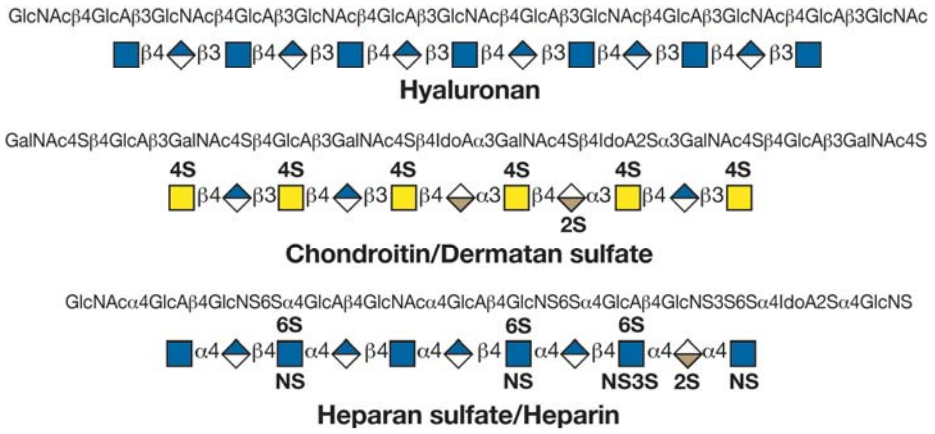
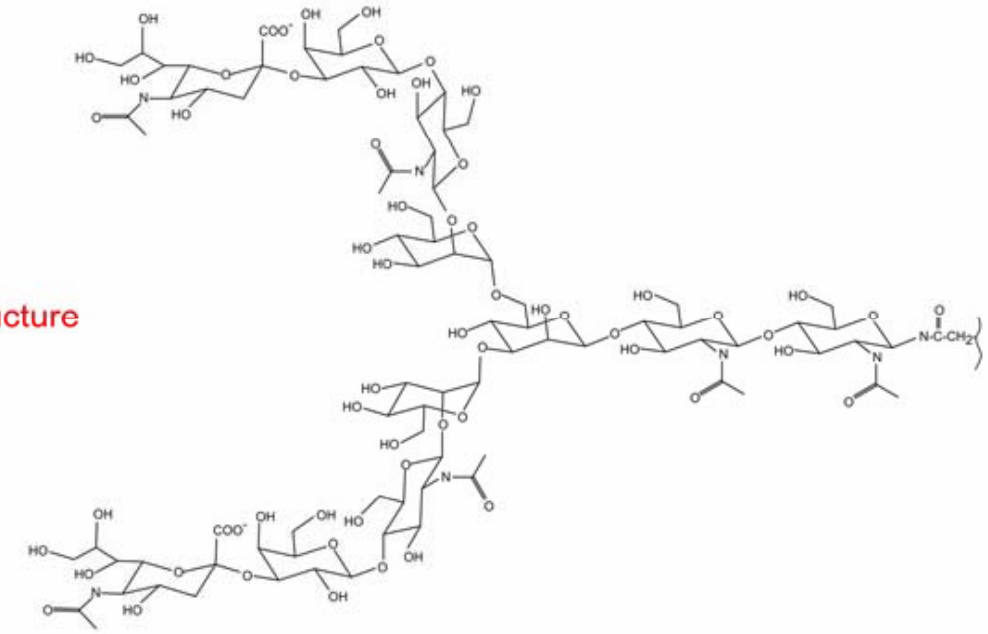


Figure 1.9 Representations of a typical N-linked glycan from a glycoprotein

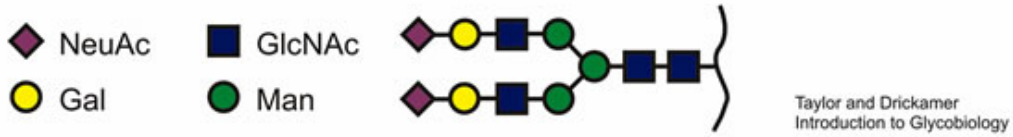
Complete chemical structure



Word structure

NeuAcα2-3Galβ1-4GlcNAcβ1-2Manα1 \
6 \
3 Manβ1-4GlcNAcβ1-4GlcNAcβ1-Asn \
NeuAcα2-3Galβ1-4GlcNAcβ1-2Manα1

Symbol representation



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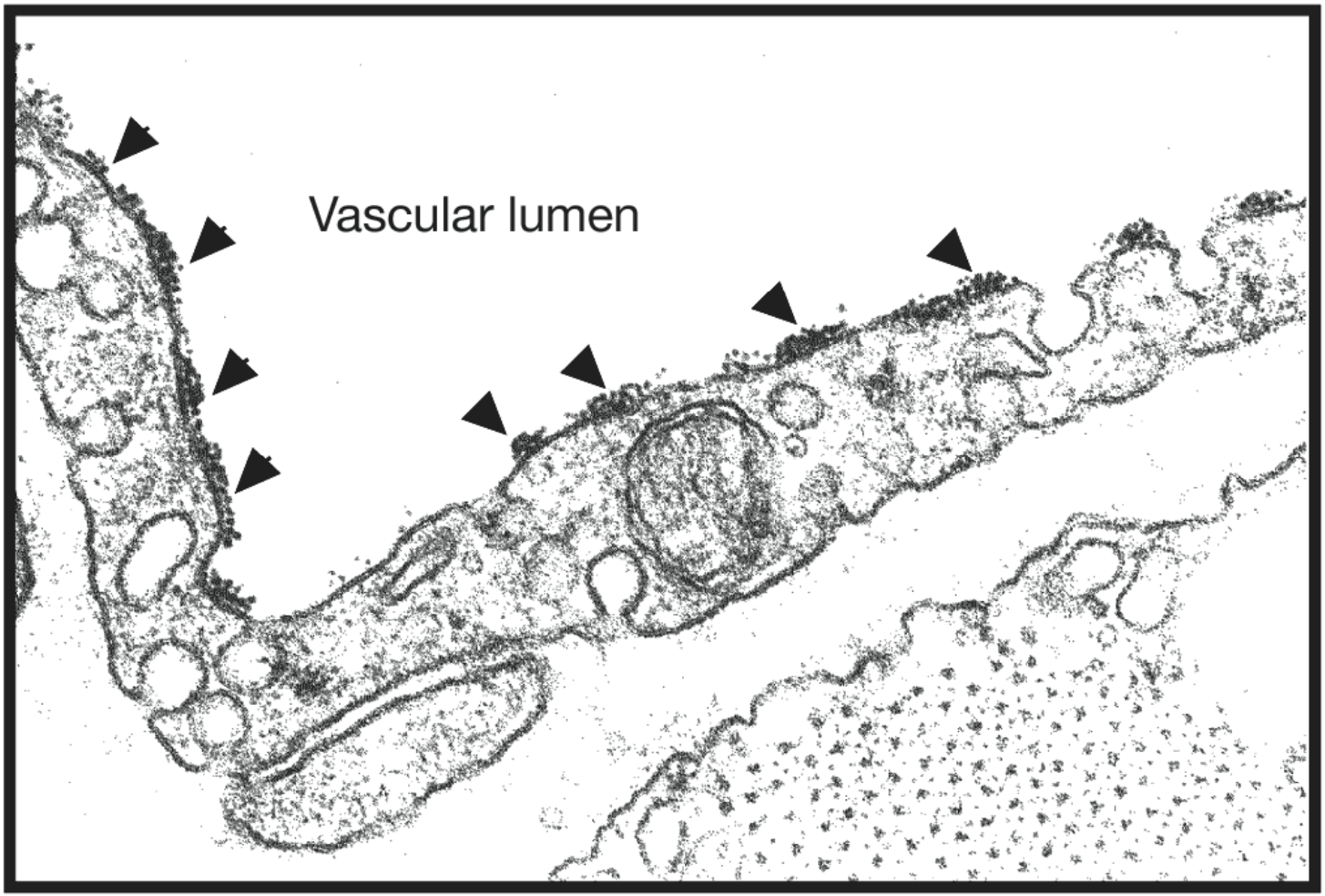
Electron micrograph of endothelial cells from a blood capillary



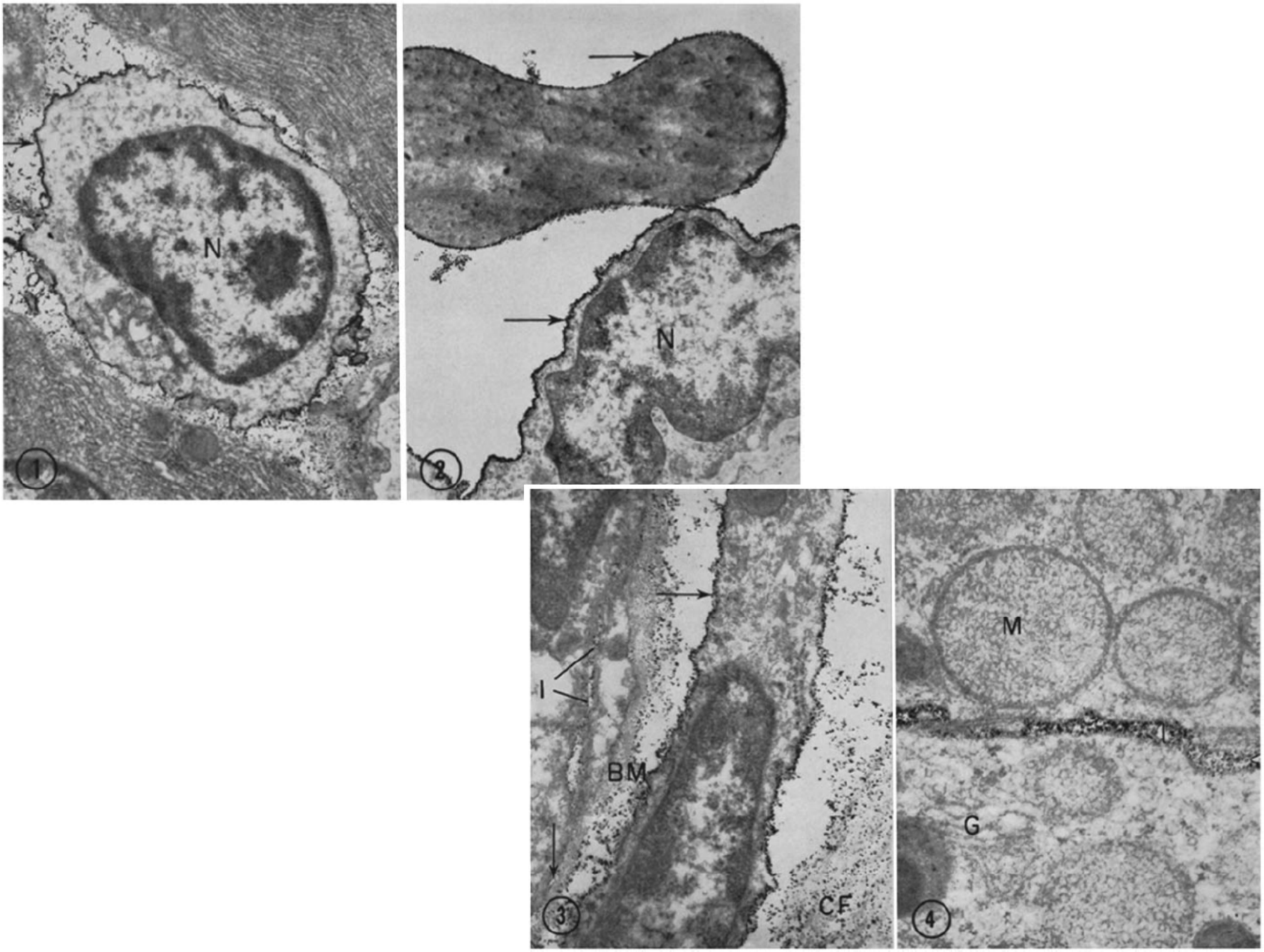
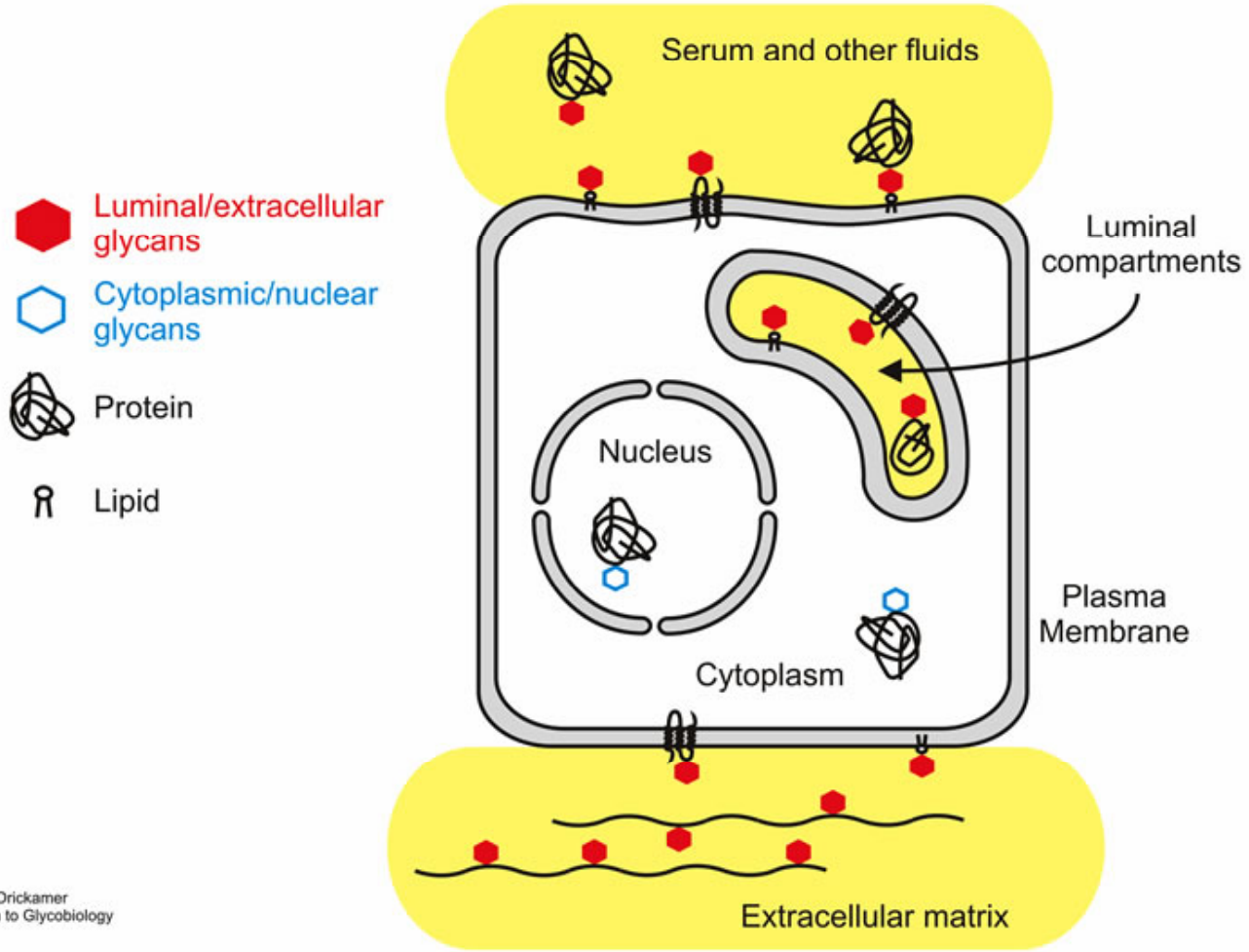

N
1
N
2
I
BM
CF
3
M
I
G
4

Figure 1.2 Localization of glycoconjugates in intracellular and extracellular compartments



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Prof. Raymond Dwek

Raymond Dwek, FRS, is Professor and Director of Oxford Glycobiology

Oxford GlycoSciences. He is of United Therapeutics and a wholly owned company of O was created to exploit its int He has received several hon Wellcome Trust Award for R related to Medicine (1994), t ation Leadership Award, USA Romanian Order of Merit (2 He is a member of the Europ Organization and Fellow of t Royal Society of Chemistry. torates from Katholieke Uni Ben Gurion University of the The Scripps Research Institu Babes-Bolyai University, Clu Professor Dwek has publishe 490 articles and 70 patents.

email: raymond.dwek@exet

glycobiology, (ˌglʌɪkəʊbaɪˈɒlədʒɪ), *n. Biochem.*
[f. GLYCO- + BIOLOGY *n.*: coined by Prof. Raymond Dwek (see quot. 1988[2]).] The branch of science concerned with the role of sugars in biological processes.

1988 *Oxford Times* 5 Feb. 1/2 A Glycobiology Institute is planned in the University Science area.
1988 *Oxf. Univ.* Gaz. 28 July 1010/2 Council has conferred the title Professor of Glycobiology on R. A. Dwek … with effect from 1 August 1988 for so long as he is Director of the Oxford Glycobiology Unit. **1990** (*journal title*) Glycobiology. **1991** *Times* 26 Sept. 14/5 Glycobiology … is expected to be one of the most exciting development of the 1990s.

R. Dwek *Biochemist*, 2006, 28, 4

Common classes of animal glycans

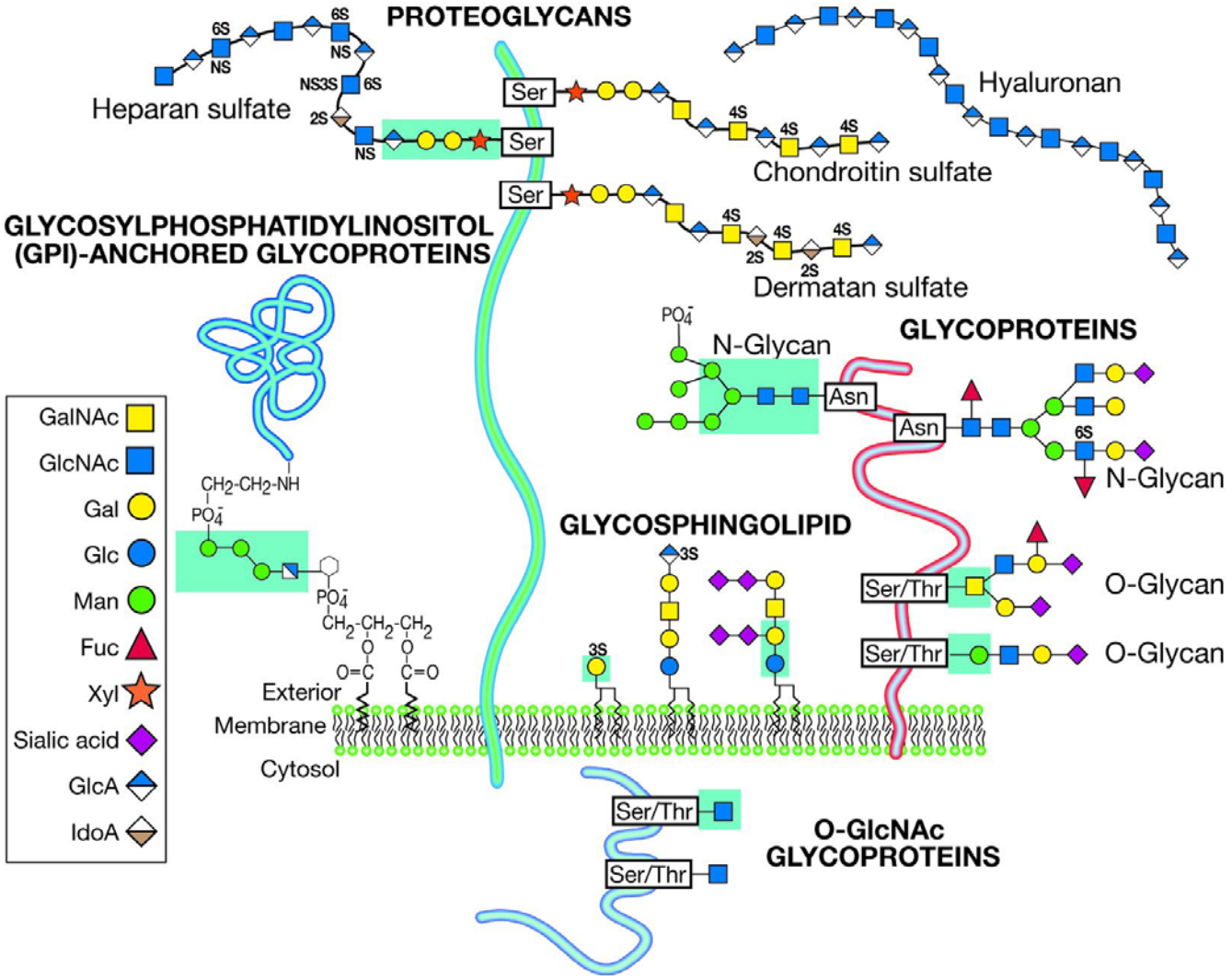
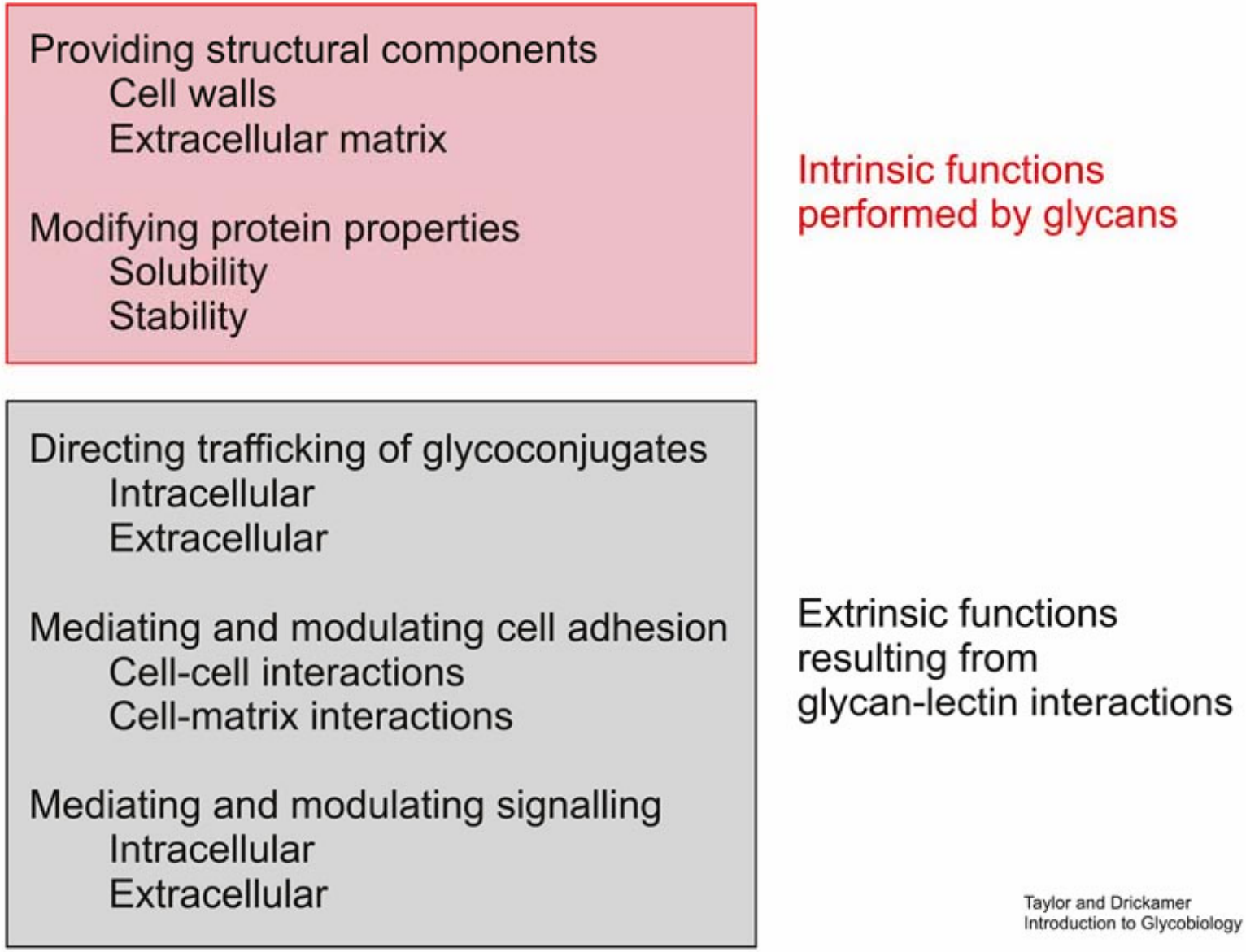


Figure 1.1 Summary of some of the functions of glycans



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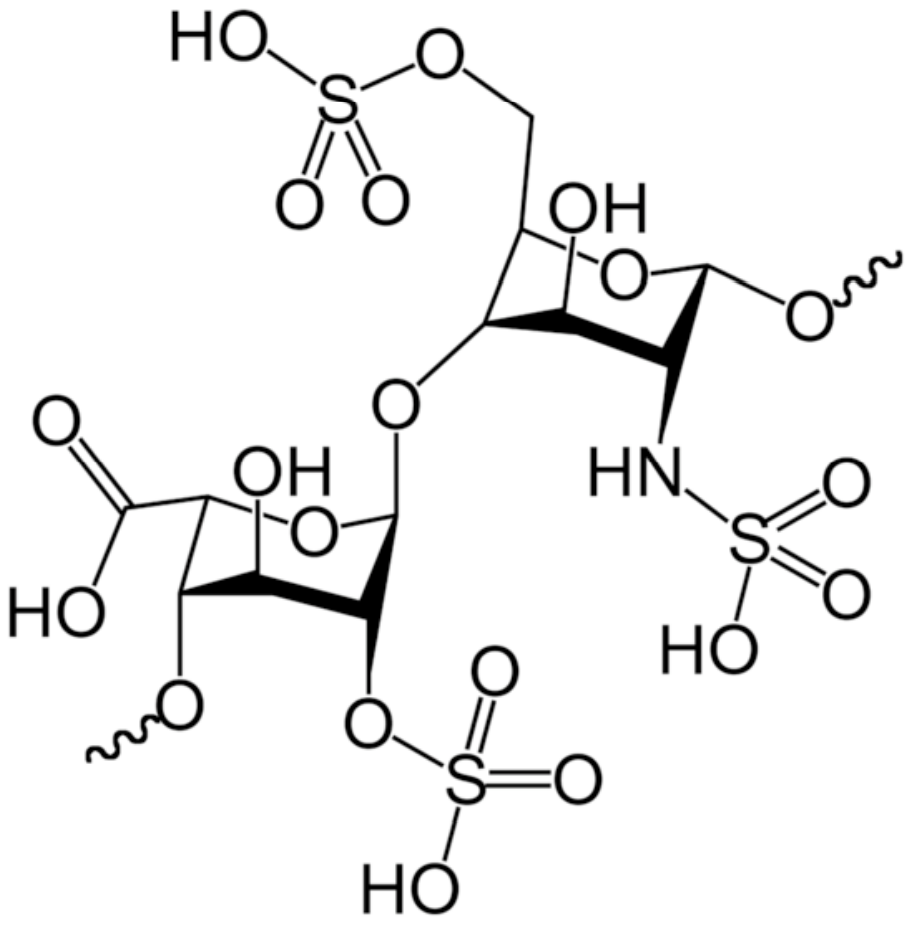
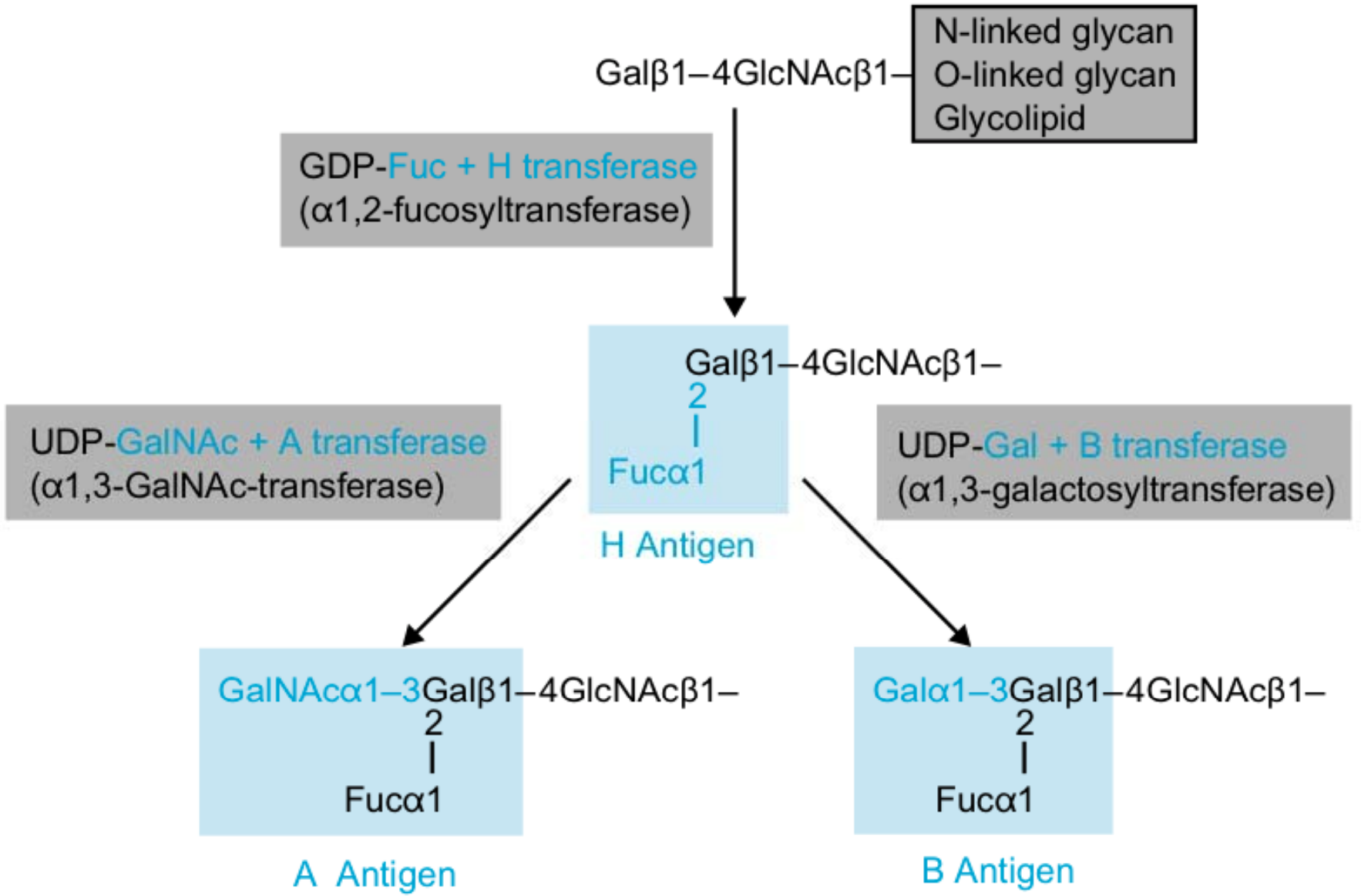


Associated Press


Galβ1–4GlcNAcβ1–
N-linked glycan
O-linked glycan
Glycolipid
GDP-Fuc + H transferase
(α1,2-fucosyltransferase)
Galβ1–4GlcNAcβ1–
2
Fucα1
H Antigen
UDP-GalNAc + A transferase
(α1,3-GalNAc-transferase)
UDP-Gal + B transferase
(α1,3-galactosyltransferase)
GalNAcα1–3Galβ1–4GlcNAcβ1–
2
Fucα1
A Antigen
Galα1–3Galβ1–4GlcNAcβ1–
2
Fucα1
B Antigen

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Howard R. A
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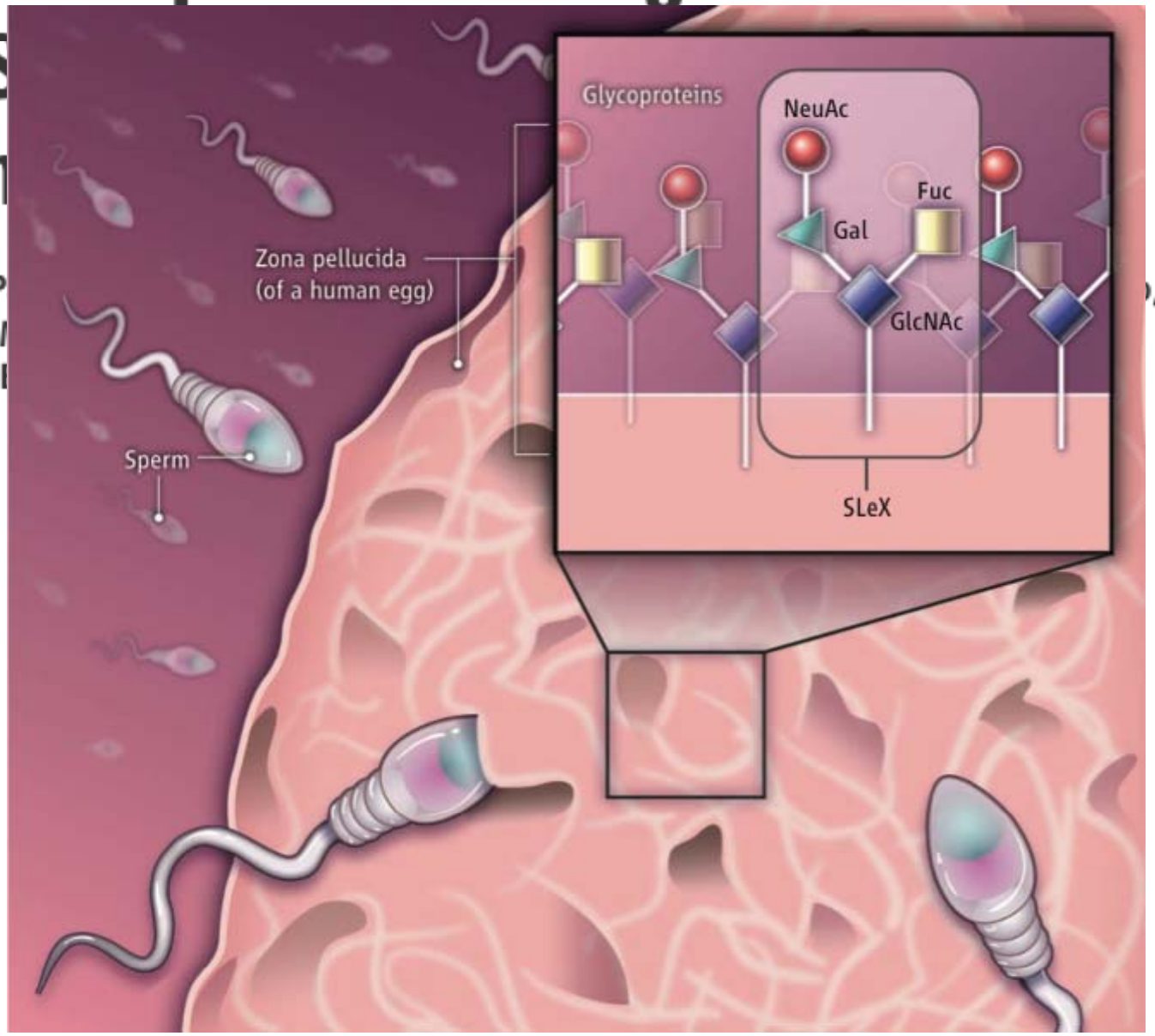

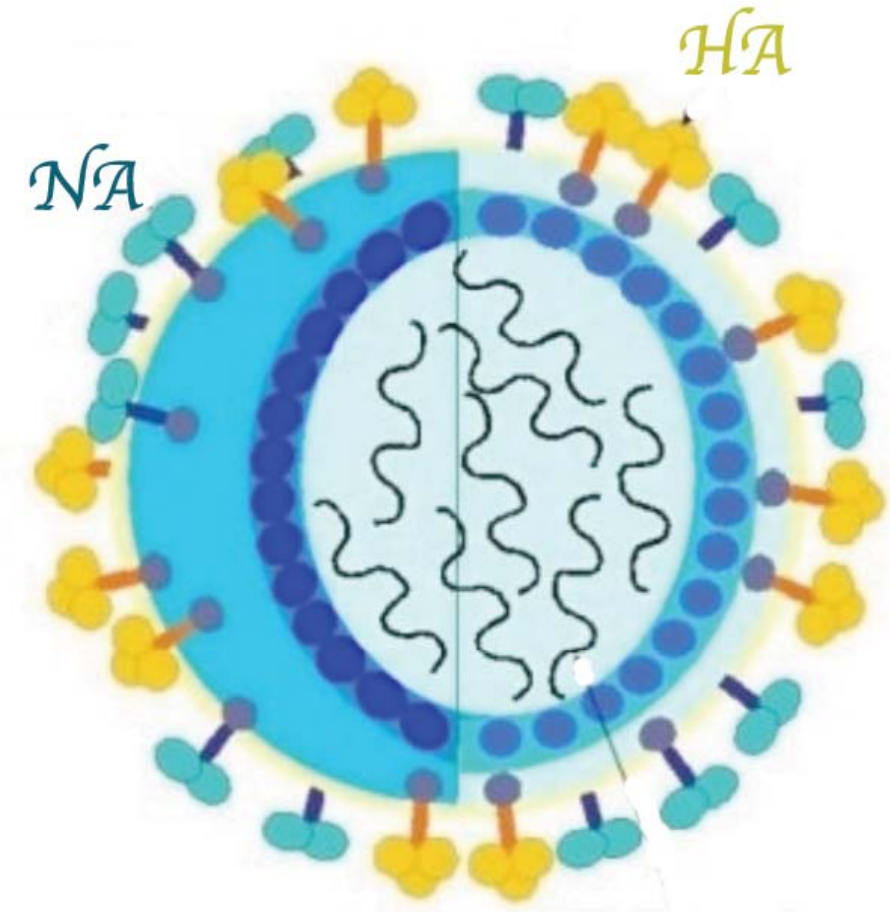

http://www.hipo-online.de/images/Image_HIPO_EN_250204.jpg

Occurrence

All cells in nature are covered with a dense and complex array of sugar chains (glycans).

The cell walls of bacteria and archea are composed of several classes of glycans and glycoconjugates.

Most secreted proteins of eukaryotes carry large amounts of covalently attached glycans.

The extracellular matrix of eukaryotes is also rich in such secreted glycans.

Cytosolic and nuclear glycans are common in eukaryotes.

Chemistry and structure

Glycosidic linkages can be in α- or β-linkage forms, which are biologically recognized as completely distinct.

Glycan chains can be linear or branched.

Glycans can be modified by a variety of different substituents, such as acetylation and sulfation.

Complete sequencing of glycans is feasible but usually requires combinatorial or iterative methods.

Modern methods allow in vitro chemoenzymatic synthesis of both simple and complex glycans.