Computational Biochemistry

Lecture 8
Introduction to Glycobiology

Introduction to glycobiology

- The scope and state of glycobiology (academic and translational)
- The nature of glycans, from their monosaccharide building blocks to the diversity of oligosaccharide structures
- Glycans in space
- Glycans in biological context

What is glycobiology

A term frequently attributed to Raymond Dwek (circa 1990) to encompass the body of research that contributes to understanding:

The structure, biosynthesis, and biology of saccharides

- The diversity of glycan structures
- The processes by which glycans are synthesized
- The determinants of glycan structure
- The mechanisms of glycan-protein interactions
- The impact of glycans on the structure and function of the molecules to which they are attached
- The contribution of glycans to normal cellular function and tissue development
- The participation of glycans in diverse pathologies

Impact of glycobiology

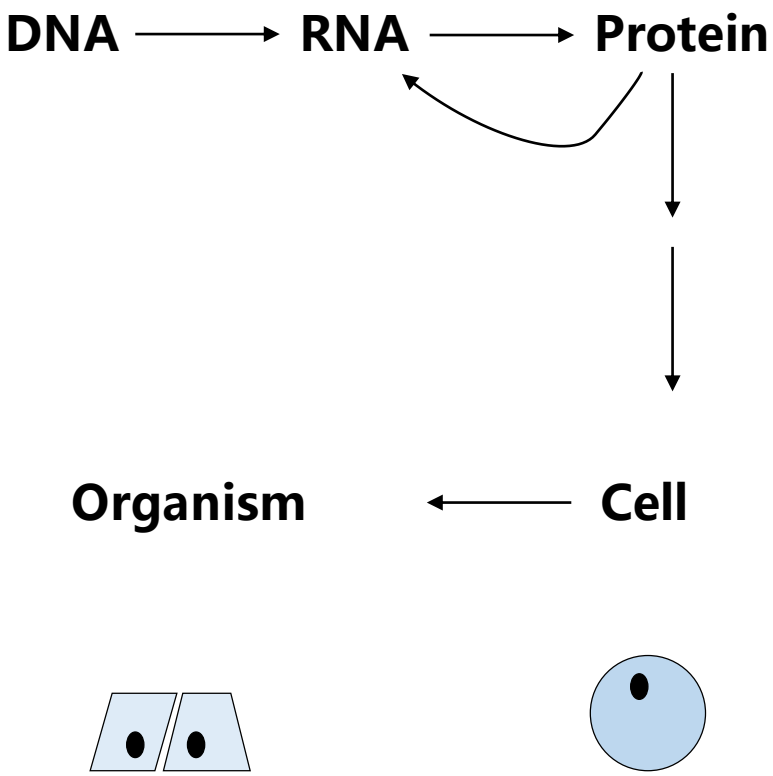
Aspects of glycobiology impact a broad range of disciplines:

organic synthetic chemistry
protein biochemistry
enzymology
analytic chemistry
structural biochemistry
cell biology membrane
developmental biology
genetics
genomics
proteomics
parasitology

neurobiology
reproductive medicine
endocrinology
cell signaling
stem cell biology
biophysics
microbiology
cancer biology
immunology
microbiology
biotechnology

And, in fact, glycobiology impacts life, itself, from conception (sperm-egg interactions) to death (apoptosis, multiple systemic pathologies)

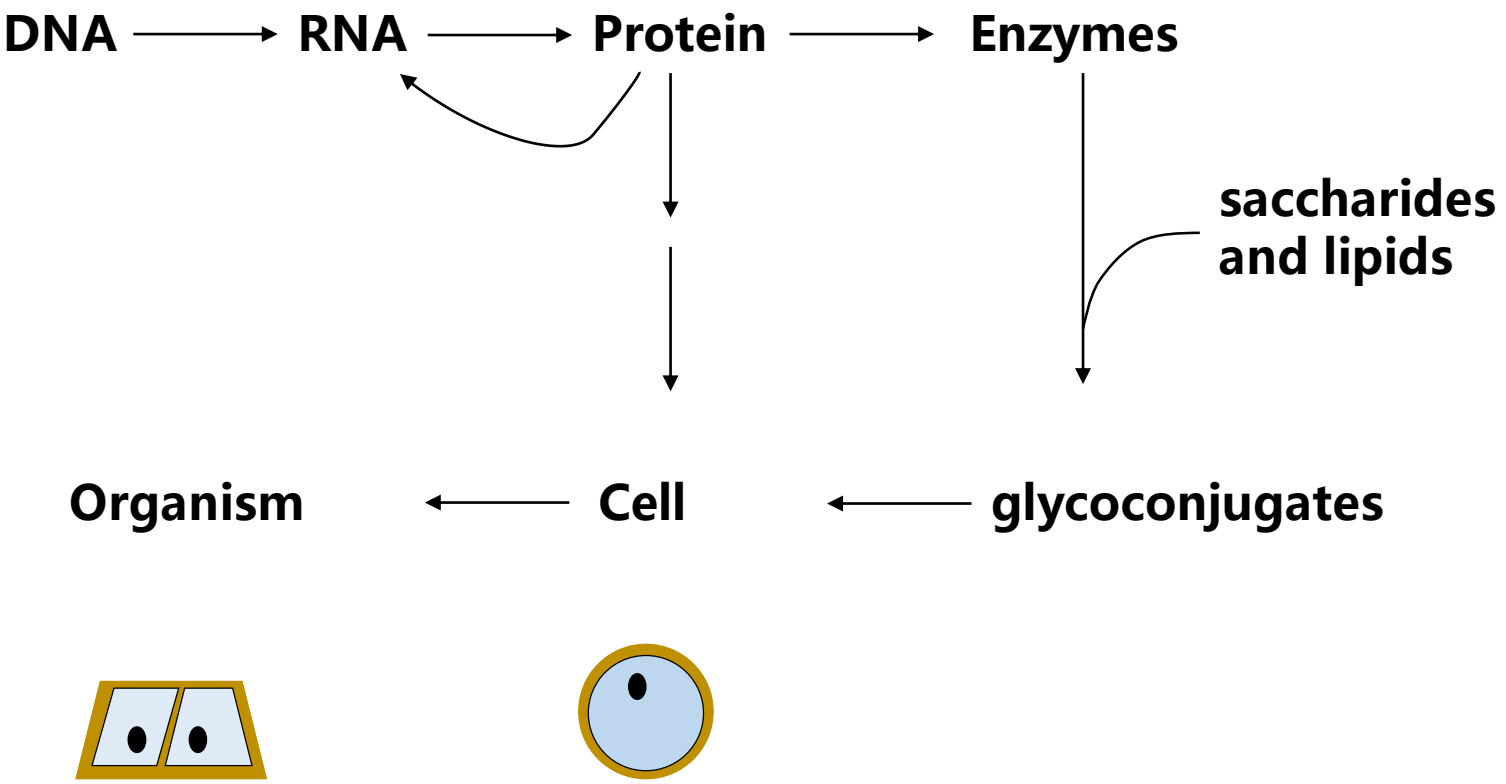
An expanded central dogma



Ignores a role for lipids and carbohydrates, especially at the cell surface

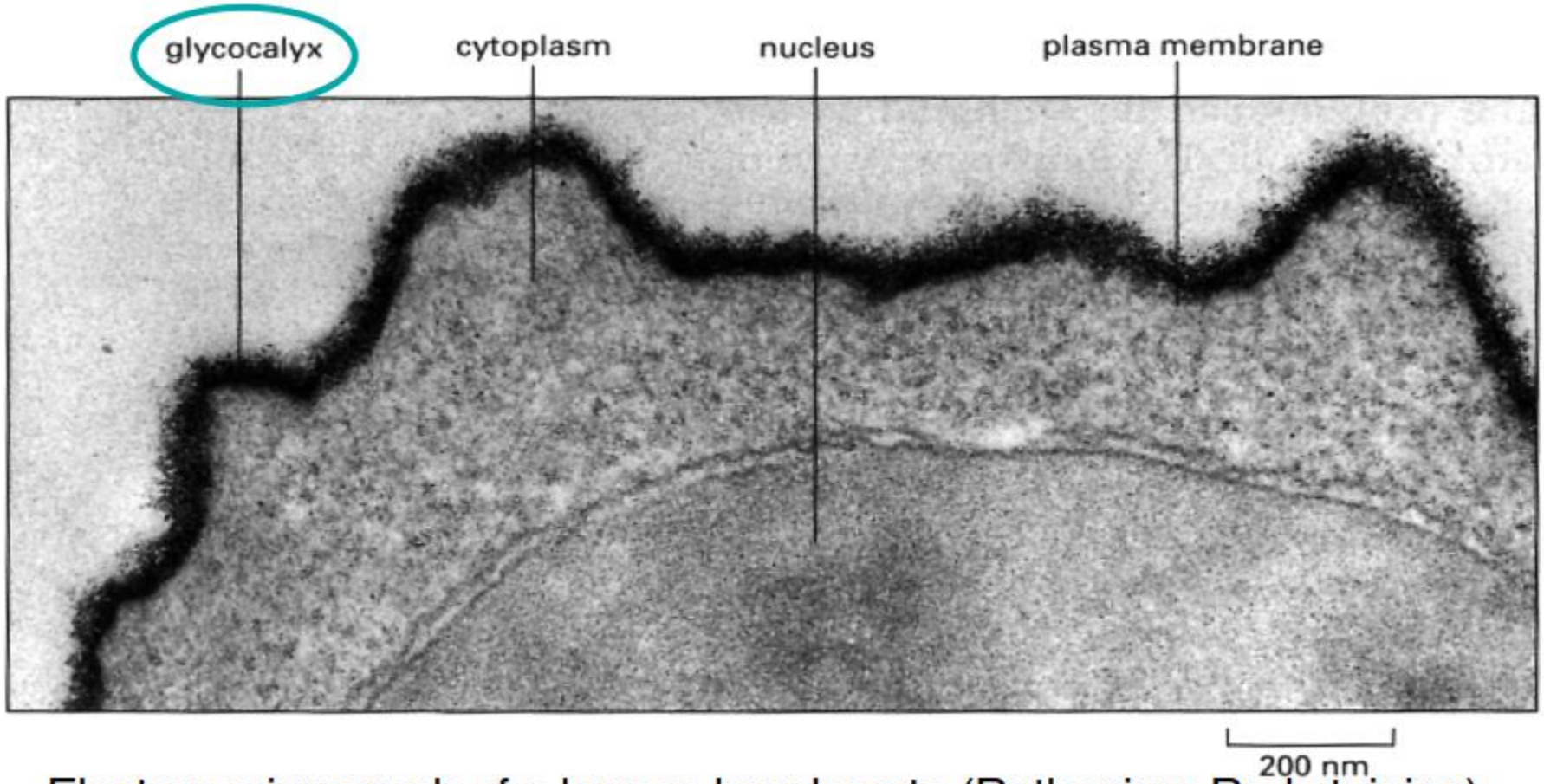
After Varki, A

An expanded central dogma



After Varki, A

Existence of sugars in cell



Electron micrograph of a human lymphocyte (Ruthenium Red staining)

Carbohydrates – Basic terms

Monosaccharide – a simple sugar

A carbohydrate that can not be broken down into smaller carbohydrates by treatment with acids

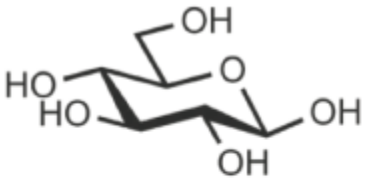
Oligosaccharide

Approximately 4-12 mono units

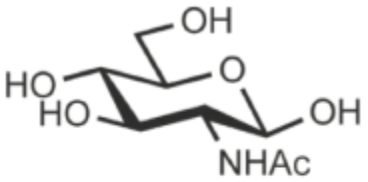
Polysaccharide

- Usually greater then 12 mono units
- Often a long linear repeating chain consiting of a single monosaccharide type or a repeating disaccharide with or without small side chains

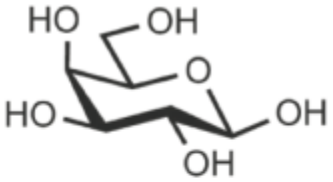
Common monosaccharides in vertebrates



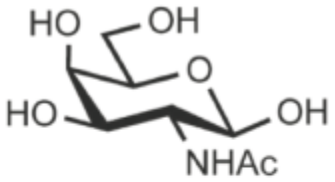
D-Glucose
(Glc)



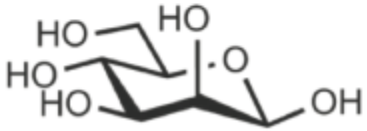
N-Acetyl-D-glucosamine
(GlcNAc)



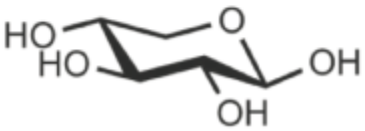
D-Galactose
(Gal)



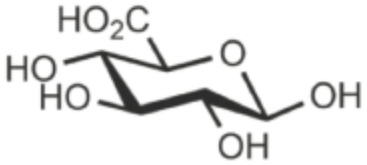
N-Acetyl-D-galactosamine
(GalNAc)



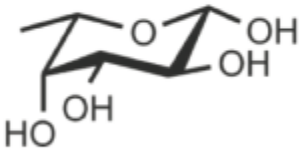
D-Mannose
(Man)



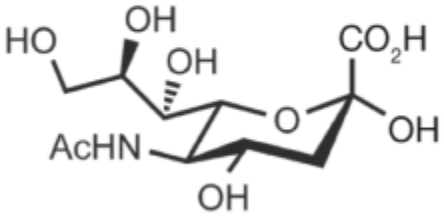
D-Xylose
(Xyl)



D-Glucuronic acid
(GlcA)



L-Fucose
(Fuc)

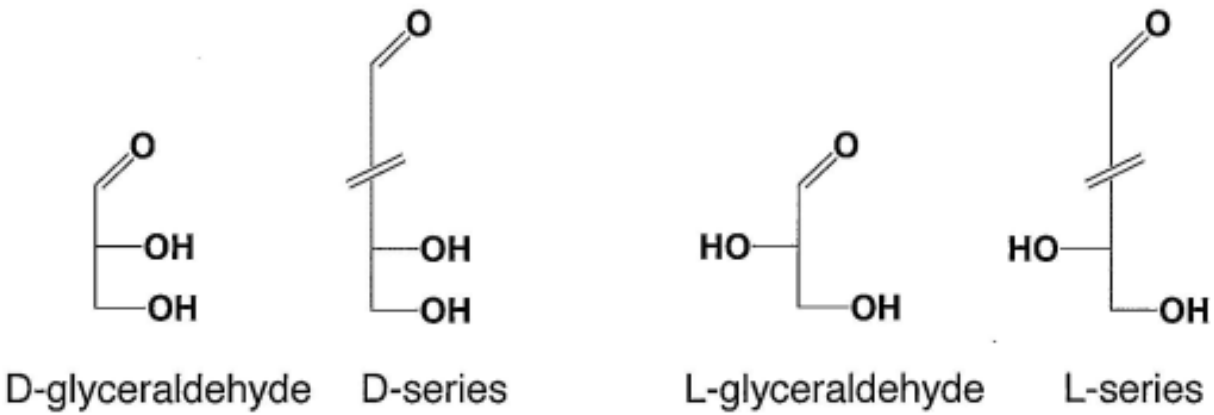


N-Acetylneuraminic acid
(NeuAc)

Complexity of glycan structures

Macromolecule	Building Block	Aproximate Mass	Possible Variations in a Trimer
Protein	Amino acids	125 → 10^4-10^5	6
Nucleic Acid	Nucleotides	330 → 10^3-10^9	6
Carbohydrate	Monosaccharides	200 → 10^2-10^6	1,056 to 27,648!

“Construct” carbohydrate molecules



"Construct" carbohydrate molecules

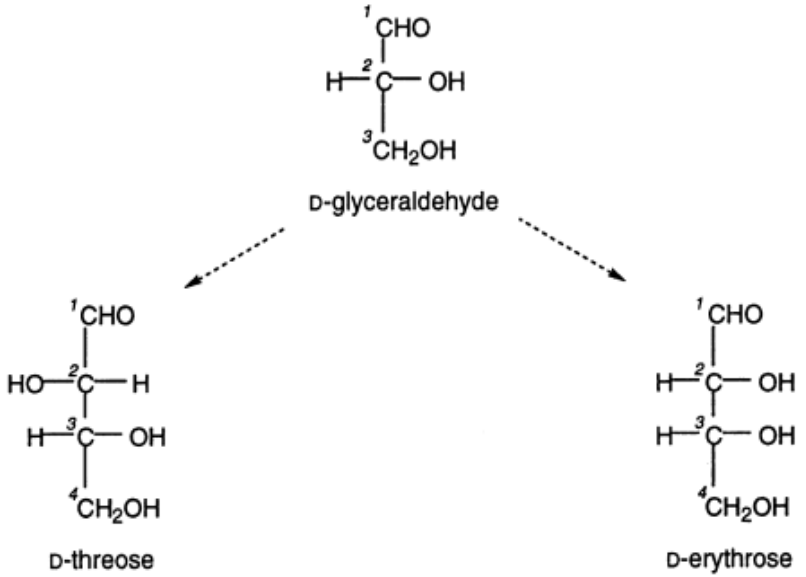
D-"Aldoses" with 4 Carbons

Two possible isomers at each new carbon center.

Mentally insert new carbon center between aldehyde terminus (C1) and what was previously C2.

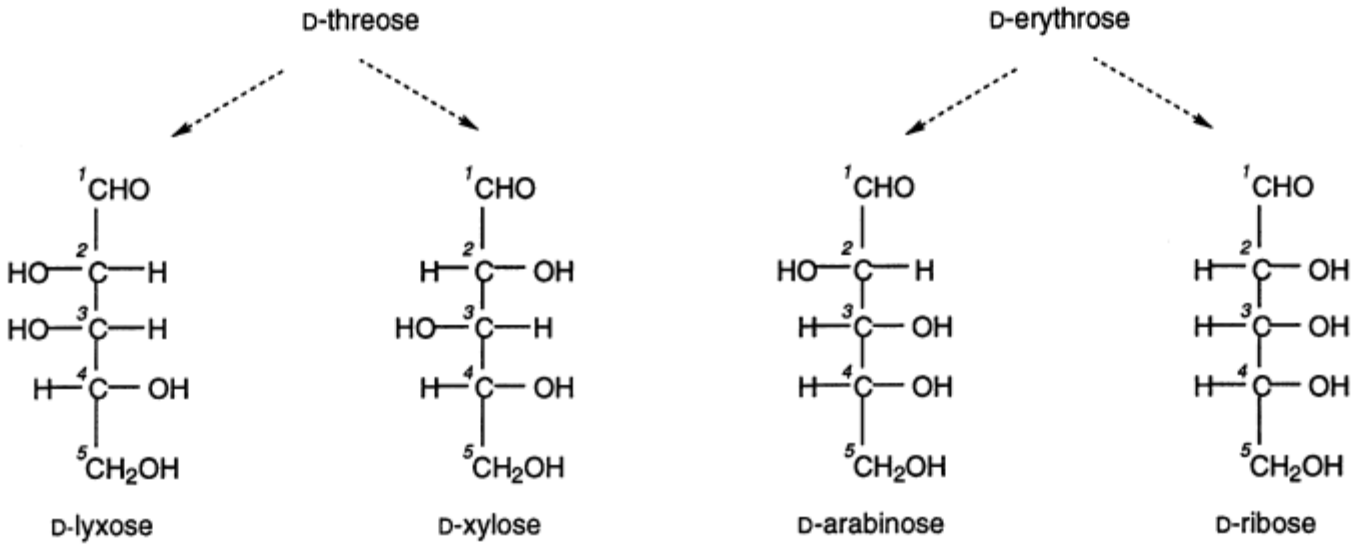
Note that *D* configuration is retained.

Two sugars that differ only in the configuration around a single chiral carbon are called **EPIMERS**



“Construct” carbohydrate molecules

D-”Aldoses” with 5 Carbons



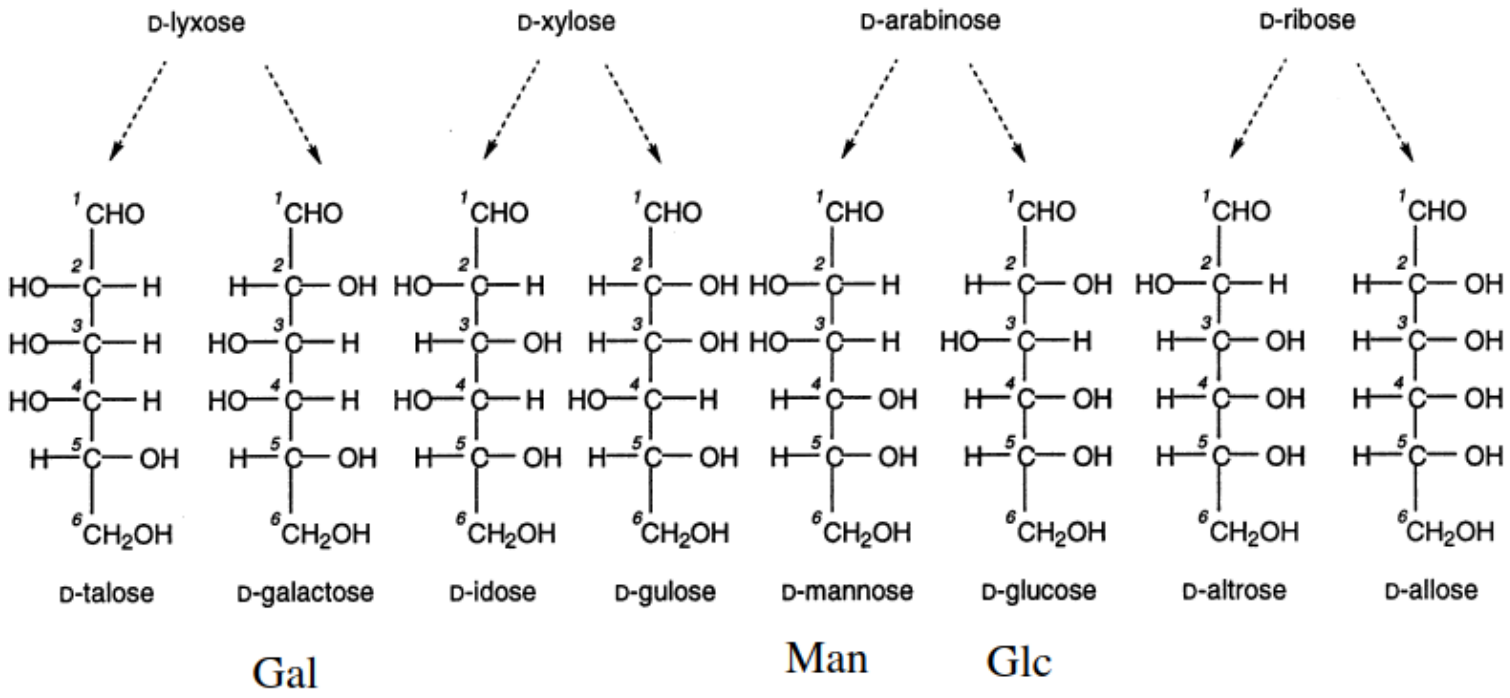
Xyl

Rib

"Construct" carbohydrate molecules

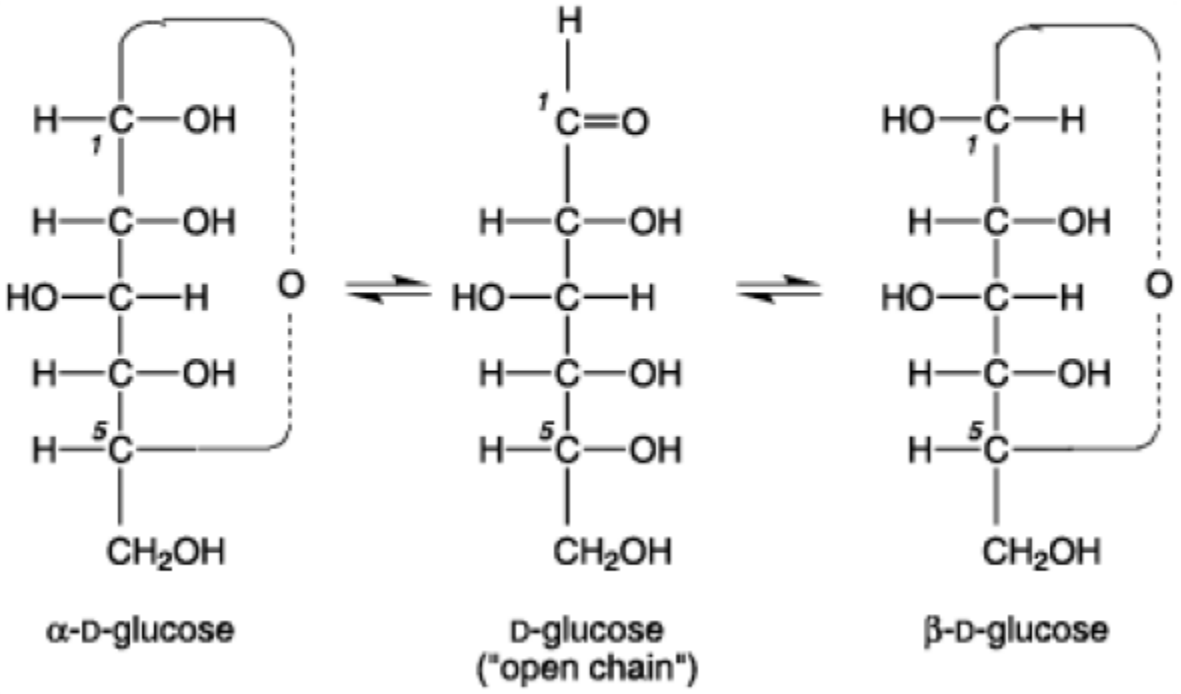
D-"Aldoses" with 6 Carbons

** special attention to Gal, Man, and Glc abbreviations



“Construct” carbohydrate molecules

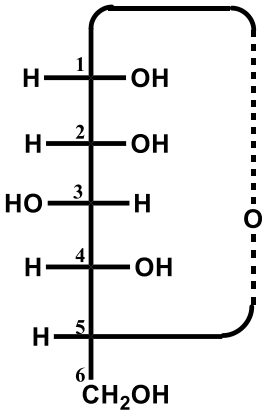
Cyclization Can Produce Multiple Isomers



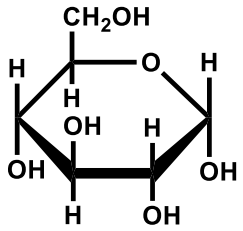
Fischer Projection is NOT good enough

Representation carbohydrate molecules

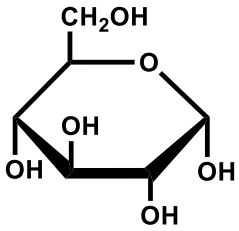
Fischer



Haworth



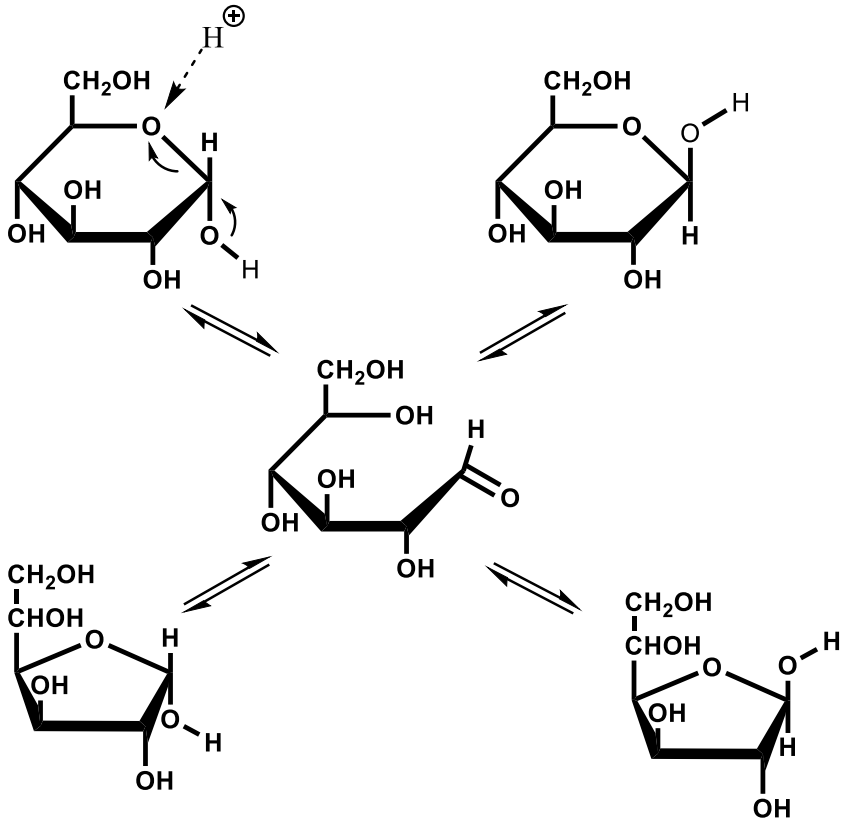
abbreviated Haworth



α-D-glucopyranose

α-D-Glc*p*

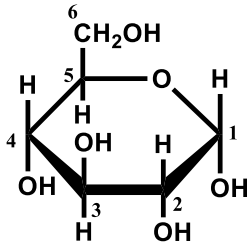
β-D-Glc*p*

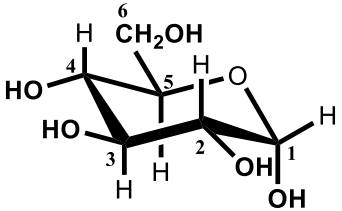


α-D-Glc*f*

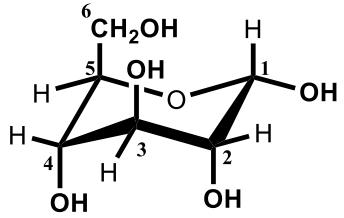
β-D-Glc*f*

Representation carbohydrate molecules





$^{4}C_{1}$ chair



$^{1}C_{4}$ chair