Class Business

Projects due next Thursday
The “central dogma” of life:

Transcription: DNA → RNA
Translation: RNA → protein
The “central dogma” of life

DNA ➔ RNA ➔ protein

- Transfer RNA (tRNA)
- Ribosomal RNA (rRNA)
- Messenger RNA (mRNA)
- Many other RNAs!!!
The “central dogma” of life

DNA $\rightarrow$ RNA $\rightarrow$ protein

- Microtubule
- Rhinovirus
- Ribosome
- GroEL/ES
Now What?
The other biomolecules…
structure, chemistry, and function

- Carbohydrates (today)

- Lipids (next week)
Biological Importance of Carbohydrates

1. Carbohydrates serve as energy stores, fuels, & metabolic intermediates

2. Ribose & deoxyribose sugars form part of the structural framework of RNA & DNA

3. Polysaccharides are structural elements in the cell walls of bacteria and plants. Cellulose is the most abundant organic compound in the biosphere

4. Carbohydrates are linked to many proteins and lipids, key role in mediating interactions among cells - made possible by their huge structural diversity
Hierarchy of Carbohydrates

- **Monosaccharide** – a simple carbohydrate such as glucose
- **Disaccharide** – hydrolysis results in two monosaccharide units
- **Oligosaccharide** – hydrolysis yields three to ten monosaccharides
- **Polysaccharide** – hydrolysis results in greater than 10 monosaccharides
Monosaccharides

- Simplest carbohydrates, aldehydes or ketones with two or more hydroxyl groups
- Empirical formula, \((C\cdot H_2O)_n\), literally a “carbon hydrate”

Smallest monosaccharides are trioses \((n = 3)\)

Fisher Projections
Carbonyl on top
Position of hydroxyl on the distal chiral carbon determines \(L\) or \(D\)

Enantiomers
Glyceraldehyde

\(L\)-Isomer
\(d\)-Isomer

Dihydroxy-acetone
D-Aldoses (3, 4, 5, & 6 carbons)

Aldehyde group, blue
Distal asymmetric center
Numbering

Epimer
D-Ketoses (3, 4, 5, & 6 carbons)

Keto group, blue
Numbering
Distal asymmetric center
Why do biochemists care about stereochemistry?
Symbolic Representations of Common Monosaccharides and Linkages

- △ = Glucose (Glc)  ○ = Mannose (Man)  ● = Galactose (Gal)
-  ■ = N-acetylglucosamine (GlcNAc)  □ = N-acetylglucosaminic acid (GlcNAc)
-  △ = Fucose (Fuc)  △ = Xylose (Xyl)
-  ◆ = Sialic acid, unspecified (Sia)  ◆ = Glucuronic acid (GlcA)
-  ◆ = Iduronic acid (IdoA)  ◆ = Uronic acid, unspecified (HexA)
-  Ac = O-acetyl  P = Phosphate  S = O-Sulfate  NS = N-Sulfate  NH₂ = free amino group

EXAMPLES OF SYMBOLIC REPRESENTATIONS

SIMPLIFIED TRADITIONAL REPRESENTATION

\[
\text{Fuc}_3 \\
\text{Sia}_3\text{Gal}_\beta\text{GlcNAc}_\beta\text{Man}_\alpha \\
9\text{Ac-Sia}_6\text{Gal}_\beta\text{GlcNAc}_\beta\text{Man}_\alpha
\]

FULL TRADITIONAL REPRESENTATION

\[
\text{Fuc}_\alpha_1 \\
\text{Siap}_2-3\text{Galp}_\beta_1-4\text{GlcNAcp}_\beta_1-2\text{Manp}_\alpha_1 \\
9\text{OAc-Siap}_2-6\text{Galp}_\beta_1-4\text{GlcNAcp}_\beta_1-2\text{Manp}_\alpha_1
\]
Cyclic forms of monosaccharides

Alcohol + Aldehyde ⇌ Hemiacetal

Alcohol + Ketone ⇌ Hemiketal

© 2005 Brooks/Cole - Thomson
An example of hemiacetal formation

Most favorable for five and six membered rings
Five membered – furanose
Six membered - pyranose

α-d-Glucopyranose
β-d-Glucopyranose
HAWORTH PROJECTION FORMULAE
FISCHER PROJECTION FORMULAS
An example of hemiketal formation

**d-Fructose**

**Furan**

**α-d-Fructofuranose**

**β-d-Fructofuranose**

**HAWORTH PROJECTION FORMULAS**

**FISCHER PROJECTION FORMULAS**
Mutarotation of D-glucose
Conformations of Pyranose Sugars

(a) Axis

Chair

Boat

a = axial bond

e = equatorial bond

(b)

© 2005 Brooks/Cole - Thomson
Conformations of furanose

Envelope form of β-D-ribose

C₃-endo

C₂-endo
Modified monosaccharides
Frequently expressed on cell surfaces

\[ \beta-L-\text{Fucose (Fuc)} \]

\[ \beta-d-\text{Acetylglactosamine (GalNAc)} \]

\[ \beta-d-\text{Acetylglucosamine (GlcNAc)} \]

\[ \text{Sialic acid (Sia) (N-Acetylneuramininate)} \]
Disaccharides

- Lactose (galactose-β-1,4-glucose)
- Maltose (glucose-α-1,4-glucose)
- Sucrose (glucose-α-1,2-fructose)
- Celllobiose (glucose-β-1,4-glucose)
- Isomaltose (glucose-α-1,6-glucose)

Hydrolyzed by sucrase
Oligosaccharides

- Melezitose (a constituent of honey)
- Amygdalin (occurs in seeds of *Rosaceae*
  glycoside of bitter almonds, in kernels of cherries, peaches, apricots)
- Laetrile (claimed to be an anticancer agent, but there is no rigorous scientific evidence for this)
- Stachyose (a constituent of many plants: white jasmine, yellow lupine, soybeans, lentils, etc.; causes flatulence since humans cannot digest it)
- Cycloheptaamylose (a breakdown product of starch; useful in chromatographic separations)
- Dextrantriose (a constituent of saké and honeydew)
Polysaccharides

*Functions: storage, structure, recognition*

- Nomenclature: homopolysaccharide vs. heteropolysaccharide
- Starch and glycogen are storage molecules
- Chitin and cellulose are structural molecules
- Cell surface polysaccharides are recognition molecules
Glycosidic bonds determine structure

Bent chains, good for storage

Cellulose
(β-1,4 linkages)

Straight chains, good for structure

Starch and Glycogen
(α-1,4 linkages)
Storage Polysaccharide

Two forms of starch – amylase and amylopectin

Linear linkages 1→4
Branches in amylopectin 1→6

\[ \alpha \text{-amylase} \]
Cleavage of amylose

Nonreducing end

Amylose

Reducing end

Starch phosphorylase

α-D-Glucose-1-phosphate

HPO$_4^{2-}$
Structural Polysaccharides
Composition similar to storage polysaccharides, but small structural differences greatly influence properties.

Cellulose
Major structural polymer of plants, one of the most abundant organic compounds in the biosphere.
Cellulose

Parallel arrangement
Chitin

• Three forms $\alpha$, $\beta$, and $\gamma$
Glycosaminoglycans, Anionic Polysaccharides

Made of repeating disaccharide units, containing a derivative of an amino sugar, glucosamine or galactosamine

At least 1 of the sugars has a negatively charged carboxyl or sulfate group

Usually attached to proteins to form proteoglycan (95% carb)
Polysaccharides in Bacteria
(a) Gram-positive bacteria

Polysaccharide coat

Peptidoglycan layers (cell wall)
(b) Gram-negative bacteria

Cell wall
- Outer lipid bilayer membrane
- Peptidoglycan
- Inner lipid bilayer membrane

Lipopolysaccharide
Structure of Peptidoglycans

(a) Gram-positive cell wall

N-Acetylmuramic acid (NAM)

N-Acetylgluosamine (NAG)

1-Ala
D-Glu
L-Lys
D-Ala

Pentaglycine crosslink

(b) Gram-negative cell wall

γ-Carboxyl linkage to L-Lys

L-Ala
CH(CH₂)₄N

Lys

CH₂

Lys

CH₂

D-Ala

Gram-negative

Gram-positive

© 2005 Brooks/Cole - Thomson
Polysaccharides in Eukaryotes
Glycoproteins
Many functions
Glycoprotein modifications
O-linked saccharides

(a) O-linked saccharides

\[ \beta\text{-Galactosyl-1,3-}\alpha\text{-N-acetylgalactosyl-serine} \]

\[ \alpha\text{-Xylosyl-threonine} \]

\[ \alpha\text{-Mannosyl-serine} \]
Glycoprotein modifications
N-linked saccharides

(b) Core oligosaccharides in N-linked glycoproteins

High mannose content

(c) N-linked glycoproteins

High mannose

Complex

Hybrid

© 2005 Brooks/Cole - Thomson
Protein Glycosylation in the ER
Glycosylation used as a protein fold checkpoint
A, B, & O oligosaccharide antigens (blood groups)

- **O antigen**: Foundation oligo (frameshift mutant gene), one from each parent

- **A antigen**
  - Fuc \(\alpha-1,2\) Gal \(\beta-1,3\) GlcNAc \(\beta-1,3\) Gal
  - Specific glycosyltransferases add group to O antigen

- **B antigen**
  - Fuc \(\alpha-1,2\) Gal \(\beta-1,3\) GlcNAc \(\beta-1,3\) Gal
Elastase, secreted glycoprotein in serum

Most proteins in blood serum are glycoproteins
One of several from ovalbumin
Various serum glycoproteins

Fig. 7-42, p.238
Fig. 7-42, p.238

Ribonuclease B

- Man
- Man
- Man
- Man
- GlcNAc
- GlcNAc
- ...
- Asn

Human IgG

- Sia
- Gal
- GlcNAc
- Man
- GlcNAc
- ...
- Asn
- Fuc
Mannose-6-P groups in certain lysosomal enzymes

Sulfated oligosaccharide from bovine luteinizing hormone

© 2005 Brooks/Cole - Thomson
Proteoglycans
Assembled in the Golgi
Predominantly glycosaminoglycans

Versican

Serglycin

Rat cartilage proteoglycan

Decoran

Syndican
### Glycosaminoglycans

<table>
<thead>
<tr>
<th>Chondroitin-4-sulfate</th>
<th>Heparin</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Chemical Structure" /></td>
<td><img src="image2" alt="Chemical Structure" /></td>
</tr>
<tr>
<td>d-Glucuronate</td>
<td>N-Acetyl-d-galactosamine-4-sulfate</td>
</tr>
<tr>
<td></td>
<td>d-Glucuronate-2-sulfate</td>
</tr>
<tr>
<td></td>
<td>N-Sulfo-d-galactosamine-6-sulfate</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chondroitin-6-sulfate</th>
<th>Hyaluronate</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image3" alt="Chemical Structure" /></td>
<td><img src="image4" alt="Chemical Structure" /></td>
</tr>
<tr>
<td>d-Glucuronate</td>
<td>N-Acetyl-d-galactosamine-6-sulfate</td>
</tr>
<tr>
<td></td>
<td>d-Glucuronate</td>
</tr>
<tr>
<td></td>
<td>N-Acetyl-d-glucosamine</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dermatan sulfate</th>
<th>Keratan sulfate</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image5" alt="Chemical Structure" /></td>
<td><img src="image6" alt="Chemical Structure" /></td>
</tr>
<tr>
<td>L-Gluronate</td>
<td>N-Acetyl-d-galactosamine-4-sulfate</td>
</tr>
<tr>
<td></td>
<td>d-Galactose</td>
</tr>
<tr>
<td></td>
<td>N-Acetyl-d-glucosamine-6-sulfate</td>
</tr>
</tbody>
</table>
Proteoglycans serve a variety of functions on the cytoplasmic and extracellular surfaces of the plasma membrane. Many of these functions appear to involve the binding of specific proteins to the glycosaminoglycan groups.
Hyaluronate – found in cartilage
O-linked oligosaccharides

- Ser
- O
- Xyl
- Gal
- Gal

N-linked oligosaccharides

- Asn
- O
- N
- GlcNAc
- GlcNAc
- Gal
- Man
- GlcNAc
- Gal
- NeuNAc

Sulfate group

- GluA
- GluNAc
- GluA
- GluNAc

Chondroitin sulfate

Keratan sulfate

© 2005 Brooks/Cole - Thomson