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Reference Books

- Physical Chemistry for the Life Sciences (Engel, Drobny and Reid)
- Physical Chemistry for the Life Sciences (Atkins and de Paula)
- General, Organic, and Biochemistry (Denniston, Topping and Caret)
- Biochemistry (Berg, Tymoczko and Stryer)

生物

化學

物理

空間尺度越來越小

物質

表面上是粒子，
實際上是波動。

波

力

表面上是粒子。

能量描述

目的：反推回去
瞭解生物現象

歲月會記得我們這個世紀，不是因為曾發生過的野蠻戰爭，而是對基礎科學知識的主要貢獻。在這個世紀中，遺傳學已經被簡化成單純的化學作用，而化學作用又簡化成原子和分子的量子物理作用。……

Alan Cromer,

Uncommon Sense: The Heretical Nature of Science, Oxford University Press 1993 equipment, and to Dr. G. E. R. Deacon and the captain and officers of R.R.S. *Discovery II* for their part in making the observations.

[1] Young, F. B., Gerrard, H., and Jevons, W., *Phil. Mag.*, 40, 149 (1949).
[2] Longuet-Higgins, M. S., *Mon. Not. Roy. Astro. Soc., Geophys. Supp.*, 5, 285 (1949).
[3] Von Arx, W. S., Woods Hole Papers in Phys. Oceanog. Meteor., 11 (3) (1950).
[4] Ekman, V. W., *Arkiv Mat. Astron. Fysik.* (Stockholm), 2 (11) (1905).

MOLECULAR STRUCTURE OF NUCLEIC ACIDS

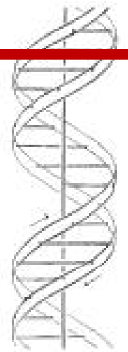
A Structure for Deoxyribose Nucleic Acid

WE wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.

A structure for nucleic acid has already been proposed by Pauling and Corey[1]. They kindly made their manuscript available to us in advance of publication. Their model consists of three inter-twined chains, with the phosphates near the fibre axis, and the bases on the outside. In our opinion, this structure is unsatisfactory for two reasons: (1) We believe that the material which gives the X-ray diagrams is the salt, not the free acid. Without the acidic hydrogen atoms it is not clear what forces would hold the structure together, especially as the negatively charged phosphates near the axis will repel each other. (2) Some of the van der Waals distances appear to be too small.

Another three-chain structure has also been suggested by Fraser (in the press). In his model the phosphates are on the outside and the bases on the inside, linked together by hydrogen bonds. This structure as described is rather ill-defined, and for this reason we shall not comment on it.

We wish to put forward a radically different structure for [illegible] acid. This structure has two helical chains each coiled round the same axis (see diagram). We have made the usual chemical assumptions, namely, that each chain consists of phosphate di-ester groups joining β-D-deoxy-ribofuranose residues with 3',5' linkages. The two chains (but not their bases) are related by a dyad perpendicular to the fibre axis. Both chains follow right-handed helices, but owing to the dyad the sequences of the atoms in the two chains run in opposite directions. Each chain loosely resembles Furberg's[2] model No. 1; that is, the bases are on the inside of the helix and the phosphates on the outside. The configuration of the sugar and the atoms near it is close to Furberg's 'standard configuration', the sugar being roughly perpendicular to the attached base. There



This figure is purely diagrammatic. The two ribbons symbolize the two phosphate—sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis

is a residue on each chain every 3·4 A. in the z-direction. We have assumed an angle of 36° between adjacent residues in the same chain, so that the structure repeats after 10 residues on each chain, that is, after 34 A. The distance of a phosphorus atom from the fibre axis is 10 A. As the phosphates are on the outside, cations have easy access to them.

The structure is an open one, and its water content is rather high. At lower water contents we would expect the bases to tilt so that the structure could [illegible]

The novel feature of the structure is the manner in which the two chains are held together by the purine and pyrimidine bases. The planes of the bases are perpendicular to the fibre axis. They are joined together in pairs, a single base from one chain being hydrogen-bonded to a single base from the other chain, so that the two lie side by side with identical z-co-ordinates. One of the pair must be a purine and the other a pyrimidine for bonding to occur. The hydrogen bonds are made as follows: purine position 1 to pyrimidine position 1; purine position 6 to pyrimidine position 6.

If it is assumed that the bases only occur in the structure in the most plausible tautomeric forms (that is, with the keto rather than the enol configurations) it is found that only specific pairs of bases can bond together. These pairs are: adenine (purine) with thymine (pyrimidine), and guanine (purine) with cytosine (pyrimidine).

In other words, if an adenine forms one member of a pair, on either chain, then on these assumptions the other member must be thymine; similarly for guanine and cytosine. The sequence of bases on a single chain does not appear to be restricted in any way. However, if only specific pairs of bases can be formed, it follows that if the sequence of bases on one chain is given, then the sequence on the other chain is automatically determined.

It has been found experimentally[3,4] that the ratio of the amounts of adenine to thymine, and the ratio of guanine to cytosine, are always very close to unity for deoxyribose nucleic acid.

It is probably impossible to build this structure [illegible] the extra oxygen atom would make too close a van der Waals contact.

The previously published X-ray data[5,6] on deoxyribose nucleic acid are insufficient for a rigorous test of our structure. So far as we can tell, it is roughly compatible with the experimental data, but it must be regarded as unproved until it has been checked against more exact results. Some of these are given in the following communications. We were not aware of the details of the results presented there when we devised our structure, which rests mainly though not entirely on published experimental data and stereo-chemical arguments.

It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material.

Full details of the structure, including the conditions assumed in building it, together with a set of co-ordinates for the atoms, will be published elsewhere.

We are much indebted to Dr. Jerry Donohue for constant advice and criticism, especially on inter-atomic distances. We have also been stimulated by a knowledge of the general nature of the unpublished experimental results and ideas of Dr. M. H. F. Wilkins, Dr. R. E. Franklin and their co-workers at King's College, London. One of us (J. D. W.) has been aided by a fellowship from the National Foundation for Infantile Paralysis.

J. D. WATSON
F. H. C. CRICK
Medical Research Council Unit for the Study of the Molecular Structure of Biological Systems,
Cavendish Laboratory, Cambridge.
April 2.

[1] Pauling, L., and Corey, R. B., *Nature*, 171, 346 (1953); *Proc. U.S. Nat. Acad. Sci.*, 39, 84 (1953).
[2] Furberg, S., *Acta Chem. Scand.*, 6, 634 (1952).
[3] Chargaff, E., for references see Zamenhof, S., Brawerman, G., and Chargaff, E., *Biochim. et Biophys. Acta*, 9, 402 (1952).
[4] Wyatt, G. R., *J. Gen. Physiol.*, 36, 201 (1952).
[5] Astbury, W. T., Symp. Soc. Exp. Biol. 1, Nucleic Acid, 66 (Camb. Univ. Press, 1947).
[6] Wilkins, M. H. F., and Randall, J. T., *Biochim. et Biophys. Acta*, 10, 192 (1953).

Molecular Structure of Deoxypentose Nucleic Acids

WHILE the biological properties of deoxypentose nucleic acid suggest a molecular structure containing great complexity, X-ray diffraction studies described here (cf. Astbury[1]) show the basic molecular configuration has great simplicity. The purpose of this communication is to describe, in a preliminary way, some of the experimental evidence for the polynucleotide chain configuration being helical, and existing in this form when in the natural state. A fuller account of the work will be published shortly.

The structure of deoxypentose nucleic acid is the same in all species (although the nitrogen base ratios alter considerably) in nucleoprotein, extracted or in cells, and in purified nucleate. The same linear group of polynucleotide chains may pack together parallel in different ways to give crystalline[1-3], semi-crystalline or paracrystalline material. In all cases the X-ray diffraction photograph consists of two regions, one determined largely by the regular spacing of nucleotides along the chain, and the other by the longer spacings of the chain configuration. The sequence of different nitrogen bases along the chain is not made visible.

Oriented paracrystalline deoxypentose nucleic acid ('structure *B*' in the following communication by Franklin and Gosling) gives a fibre diagram as shown in Fig. 1 (cf. ref. 4). Astbury suggested that the strong 3·4-A. reflexion corresponded to the inter-nucleotide repeat along the fibre axis. The ~ 34 A. layer lines, *however*, are not due to a repeat of a polynucleotide composition, but to the chain configuration repeat, which causes strong diffraction as the nucleotide chains have higher density than the interstitial water. The absence of reflexions on or near the meridian immediately suggests a helical structure with axis parallel to fibre length.

Diffraction by Helices

It may be shown[5] (also Stokes, unpublished) that the intensity distribution in the diffraction pattern of a series of points equally spaced along a helix is given by the squares of Bessel functions. A uniform continuous helix gives a series of layer lines of spacing corresponding to the helix pitch, the intensity distribution along the *n*th layer line being proportional to the square of J_n, the *n*th order Bessel function. A straight line may be drawn approximately through

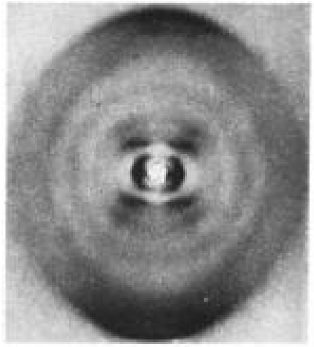


Fig. 1. Fibre diagram of deoxypentose nucleic acid from *B. coli*. Fibre axis vertical

the innermost maxima of each Bessel function and the origin. The angle this line makes with the equator is roughly equal to the angle between an element of the helix and the helix axis. If a unit repeats *n* times along the helix there will be a meridional reflexion (J_0^2) on the *n*th layer line. The helical configuration produces side-bands on this fundamental frequency, the effect[5] being to reproduce the intensity distribution about the origin around the new origin, on the *n*th layer line, corresponding to *C* in Fig. 2.

We will now briefly analyse in physical terms some of the effects of the shape and size of the repeat unit or nucleotide on the diffraction pattern. First, if the nucleotide consists of a unit having circular symmetry about an axis parallel to the helix axis, the whole diffraction pattern is modified by the form factor of the nucleotide. Second, if the nucleotide consists of a series of points on a radius at right-angles to the helix axis, the phases of radiation scattered by the helices of different diameter passing through each point are the same. Summation of the corresponding Bessel functions gives reinforcement for the inner-

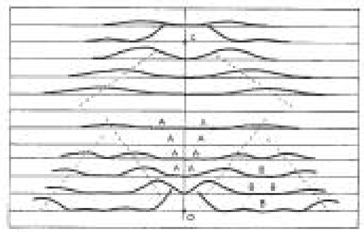


Fig. 2. Diffraction pattern of system of helices corresponding to structure of deoxypentose nucleic acid. The squares of Bessel functions are plotted about 0 on the equator and on the first, second, third and fifth layer lines for half of the nucleotide mass at 20 A. diameter and remainder distributed along a radius, the mass at a given radius being proportional to the radius. About C on the tenth layer line similar functions are plotted for an outer diameter of 12 A.

This structure has novel features which are of considerable biological interest.

become more compact.

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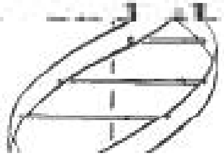
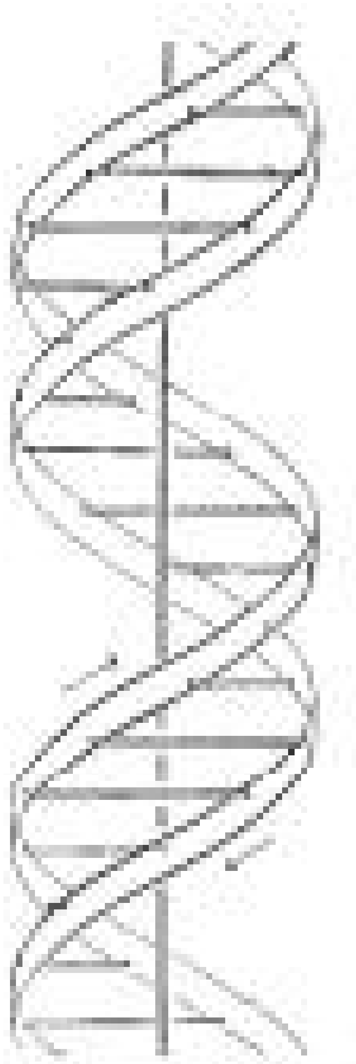
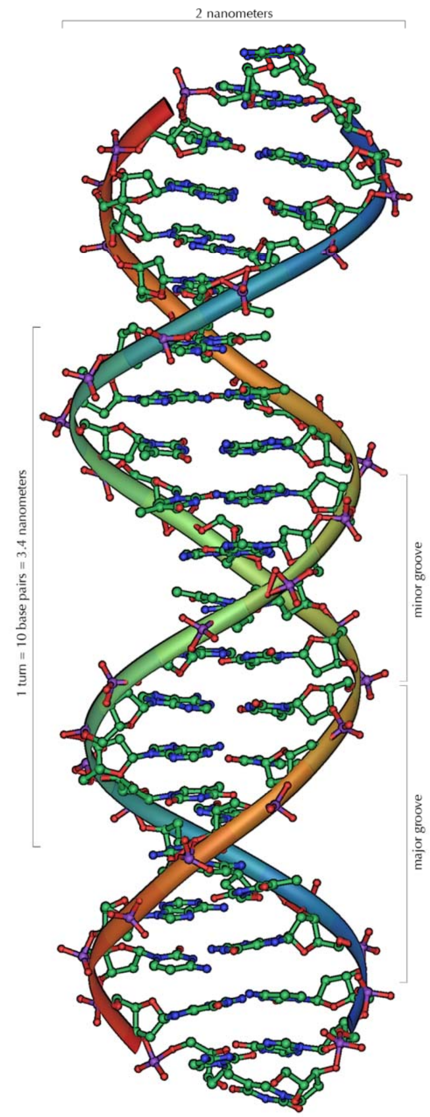


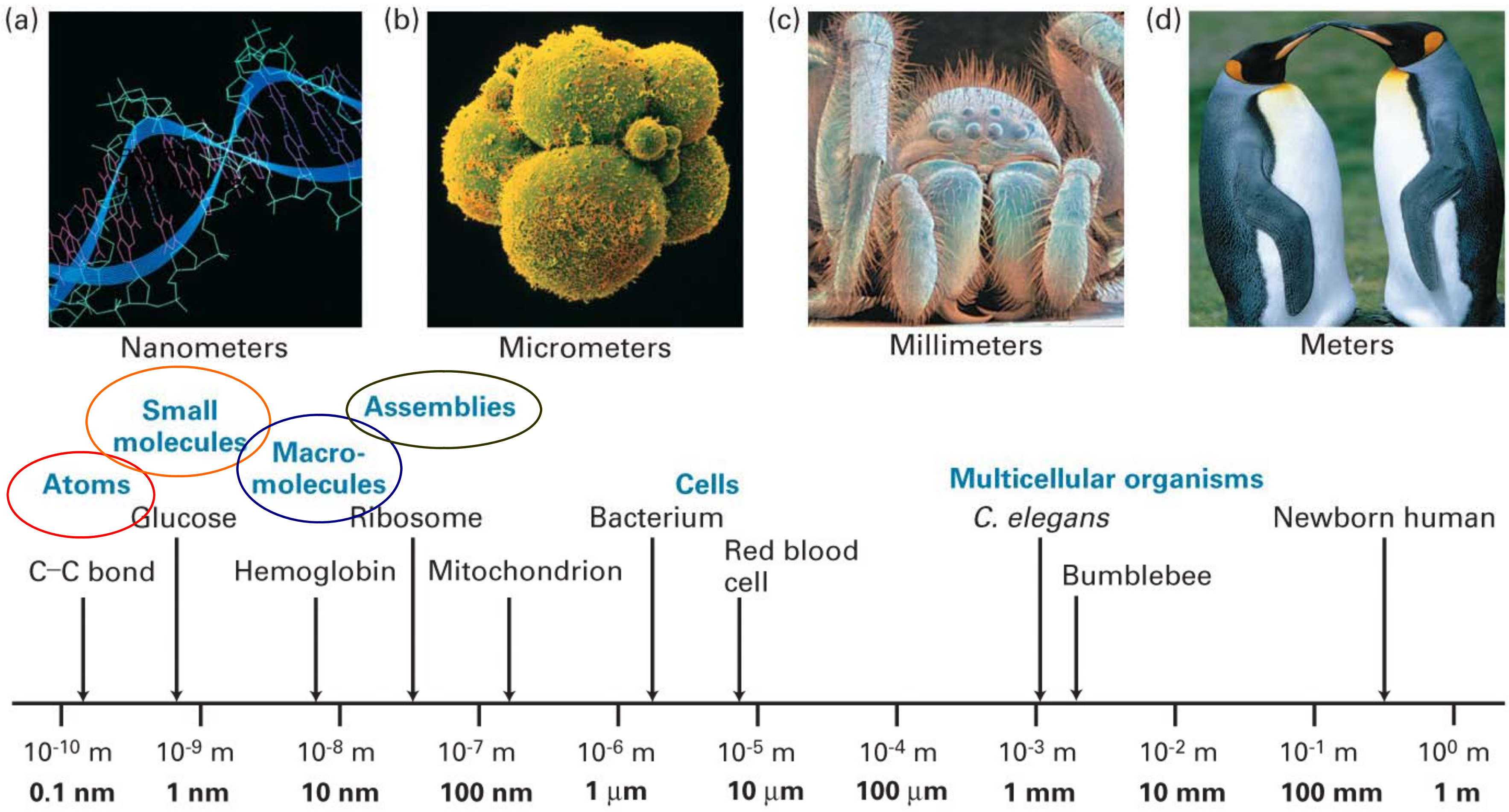
radically different structure for the salt of deoxyribose nucleic acid. This structure has two helical chains each coiled round

It is probably impossible to build this structure with a ribose sugar in place of the deoxyribose, as the extra oxygen atom would make too close a van der Waals contact.




2 nanometers
1 turn = 10 base pairs = 3.4 nanometers
minor groove
major groove

Guideline for biochemistry lectures



Questions

- Why does ice float on water?
- Why don't oil and water mix?
- Why does blood transport oxygen to our cells, whereas carbon monoxide inhibits this process?

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Alan Cromer,

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Lecture

The Structure of DNA

and more, RNA

「道生一，一生二，二生三，三生萬物。
萬物負陰而抱陽，沖氣以為和。」

～老子、道德經四十二章

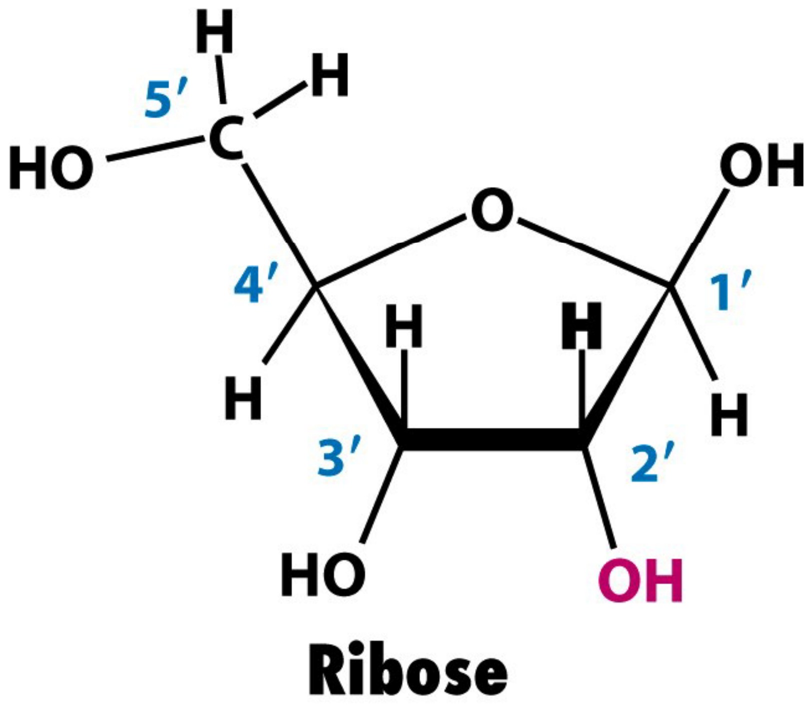
1. In the beginning was the Word, and the Word was with God, and the Word was God.

14. And the Word became flesh and tabernacled among us.

~ The Gospel According to JOHN, the New Testament

- Nucleotide: sugar + phosphate+ base
- Nucleoside: sugar + phosphate
- [Magic powered by] Hydroxyl group (−OH)

What's the sugar for DNA and RNA?



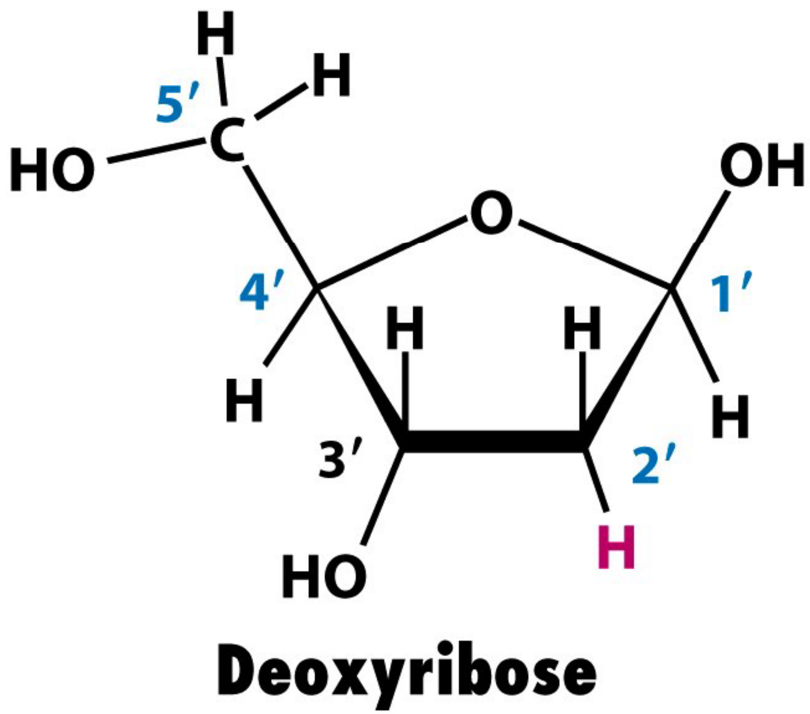


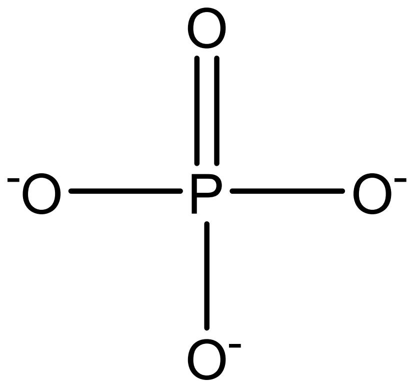
Figure 4-2
Biochemistry, Sixth Edition

What is Phosphate?

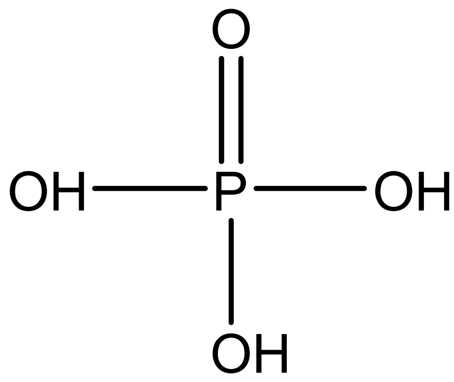
TABLE 3.3 Common Polyatomic Cations and Anions

Ion	Name
NH_4^+	Ammonium
NO_2^-	Nitrite
NO_3^-	Nitrate
SO_3^{2-}	Sulfite
SO_4^{2-}	Sulfate
HSO_4^-	Hydrogen sulfate
OH^-	Hydroxide
CN^-	Cyanide
PO_4^{3-}	Phosphate
HPO_4^{2-}	Hydrogen phosphate
$H_2PO_4^-$	Dihydrogen phosphate
CO_3^{2-}	Carbonate
HCO_3^-	Bicarbonate
ClO^-	Hypochlorite
ClO_2^-	Chlorite
ClO_3^-	Chlorate
ClO_4^-	Perchlorate
CH_3COO^- (or $C_2H_3O_2^-$)	Acetate
MnO_4^-	Permanganate
$Cr_2O_7^{2-}$	Dichromate
CrO_4^{2-}	Chromate
O_2^{2-}	Peroxide

Note: The most commonly encountered ions are highlighted in magenta.



phosphate



phosphoric acid

What's the base for A, T, G, C, U?

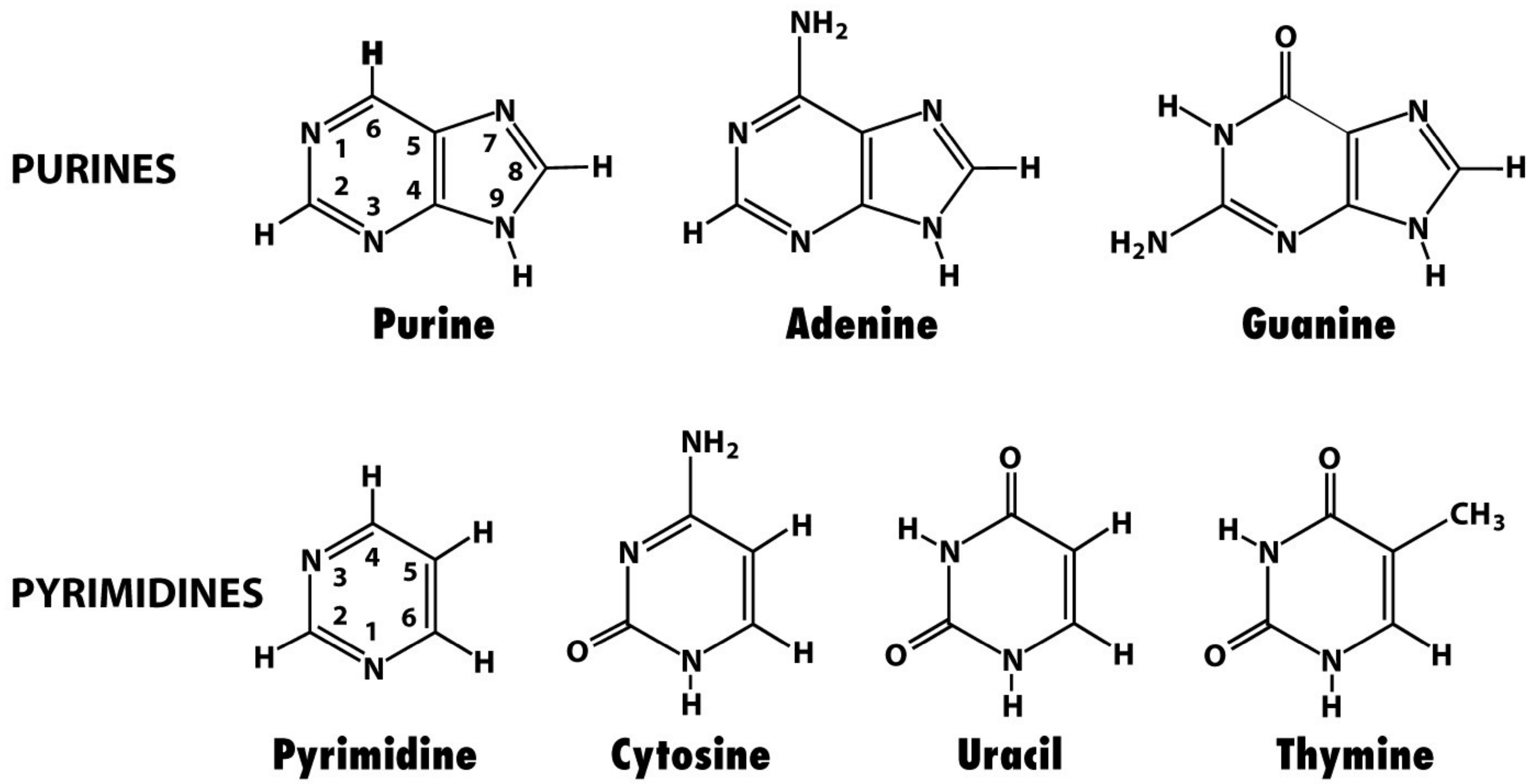


Figure 4-4
Biochemistry, Sixth Edition

How are they put together?

Phosphodiester bridge

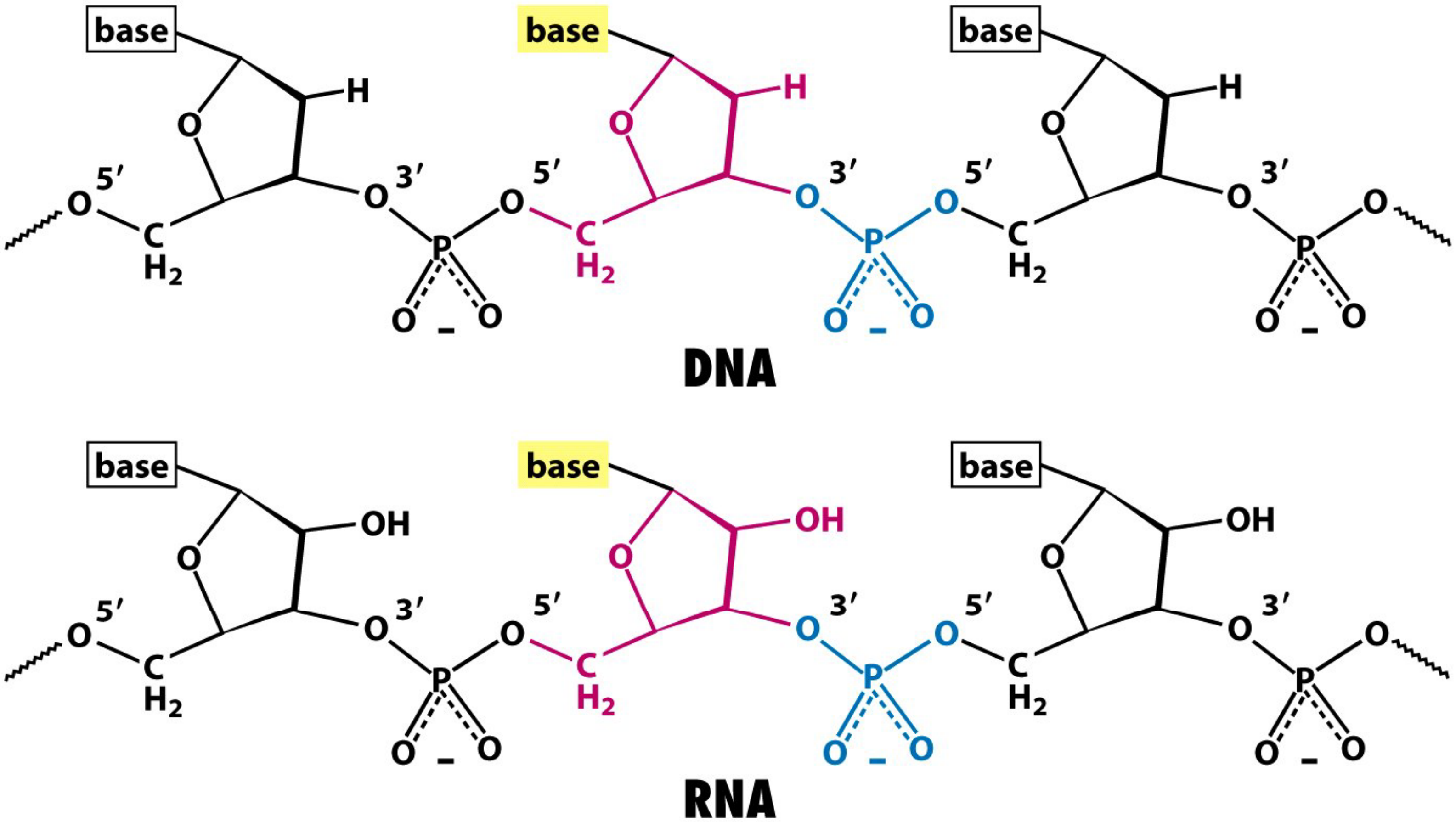


Figure 4-3
Biochemistry, Sixth Edition

β-Glycosidic linkage

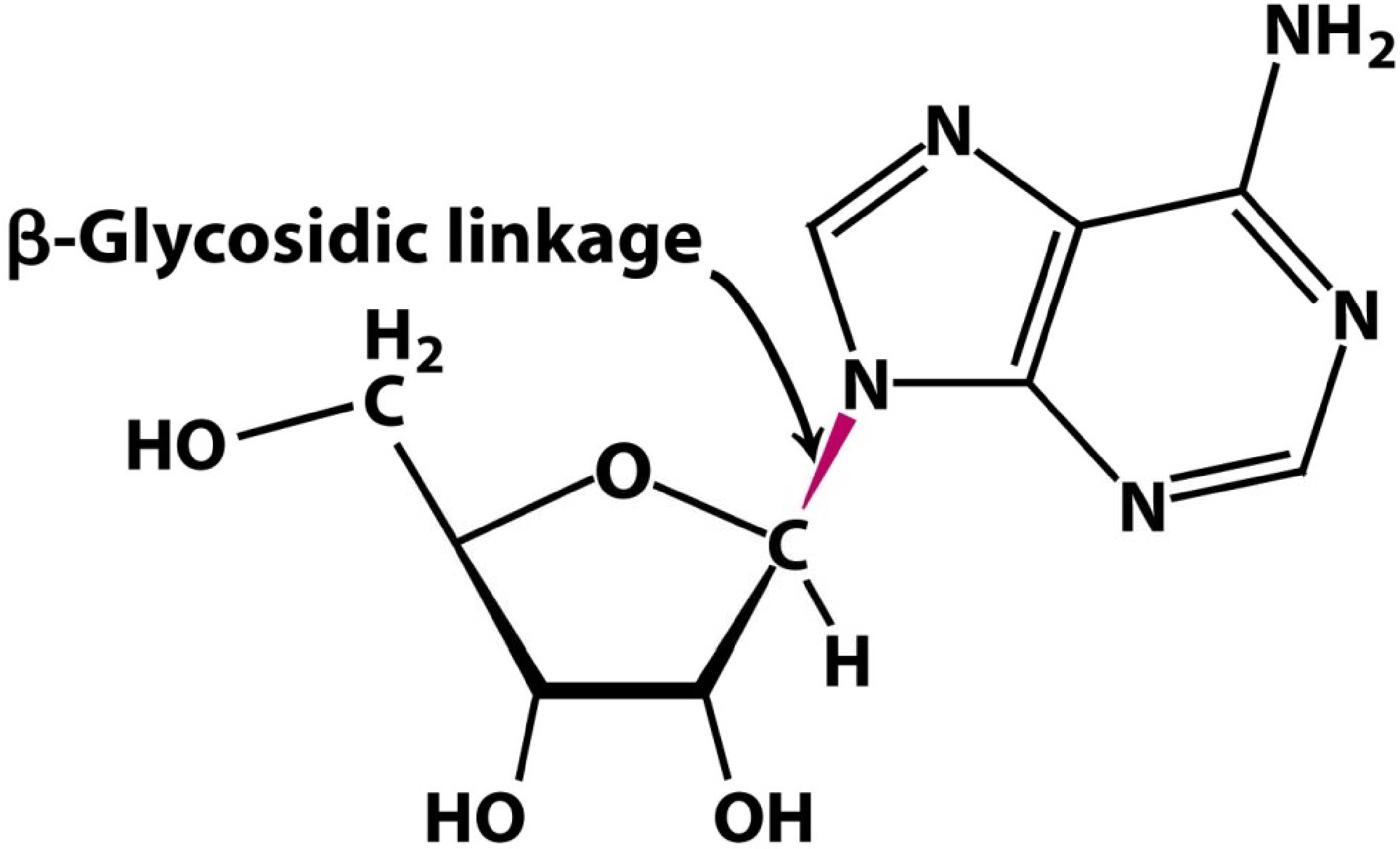


Figure 4-5
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DNA graph

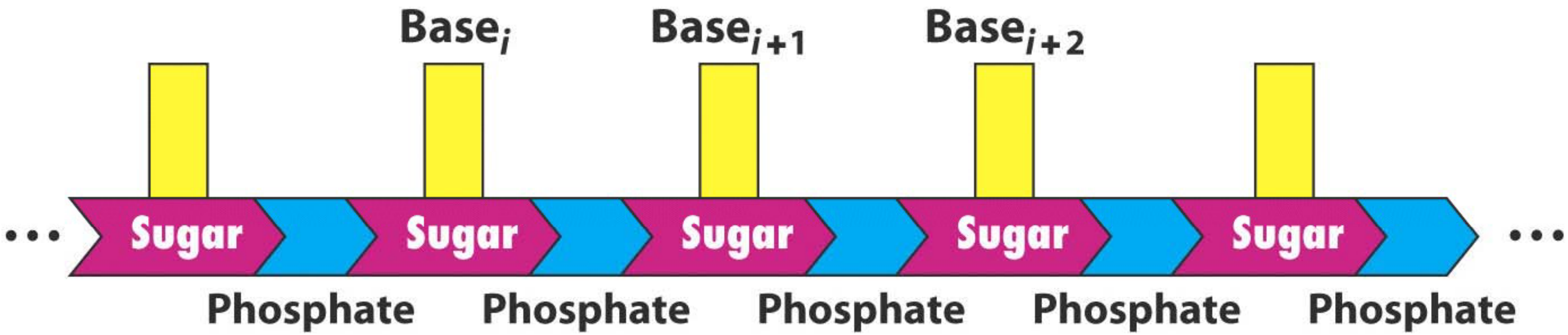

Figure 4-1
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DNA schema

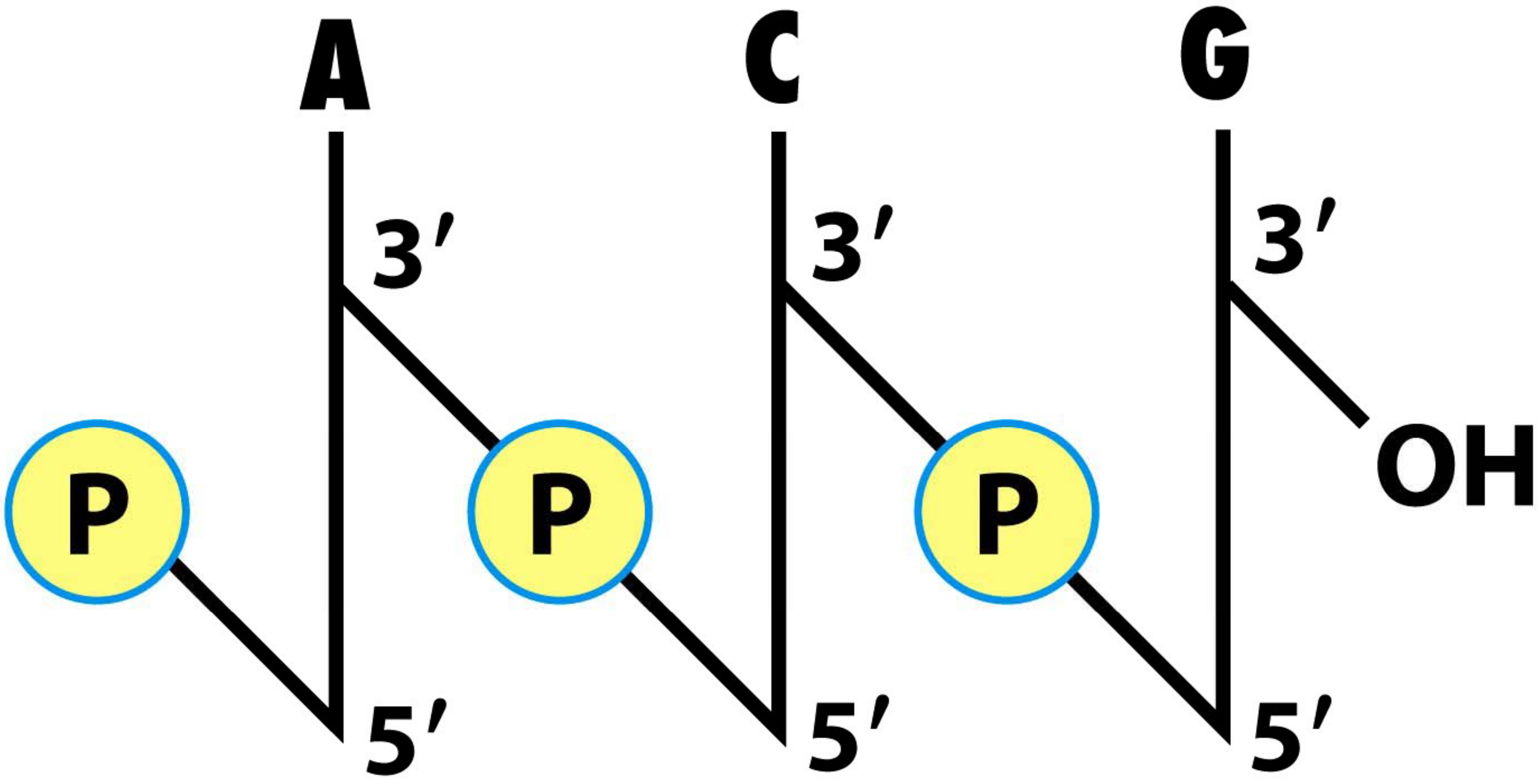

Figure 4-7
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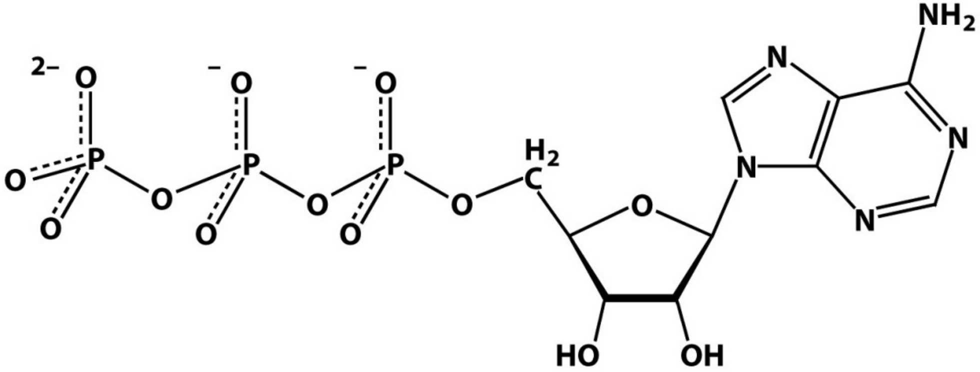
DNA abbreviation

pApCpGpApCpGpApCpGpApCpG

DNA letters

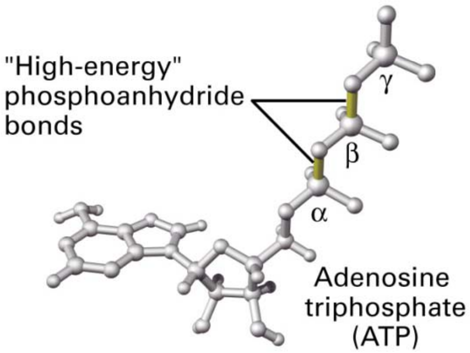
ACGACGACGACG

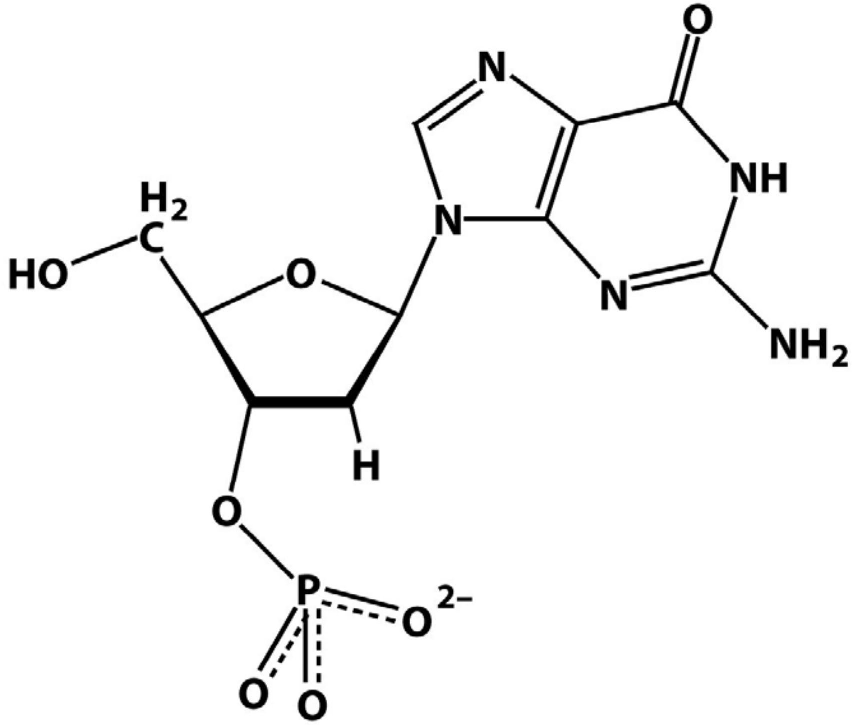
Other nucleotides



5′-ATP

Figure 4-6 part 1
Biochemistry, Sixth Edition





3′-dGMP

Figure 4-6 part 2
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Part of E. Coli genome

Figure 4-8
Biochemistry, Sixth Edition

The Indian muntjak and its chromosomes.

Figure 4-9a
Biochemistry, Sixth Edition

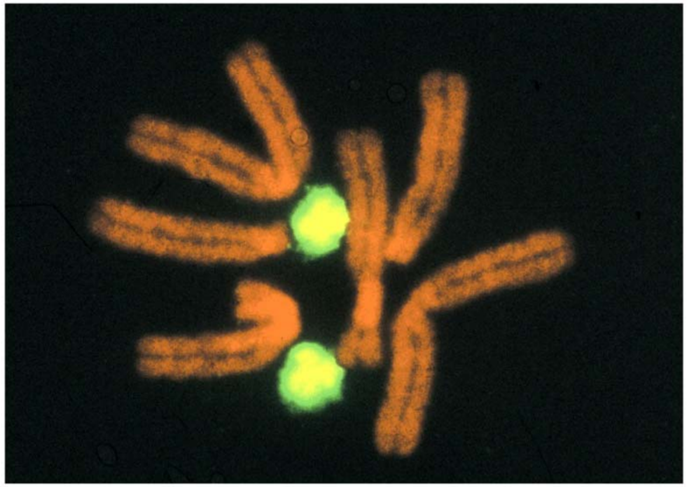

Figure 4-9b
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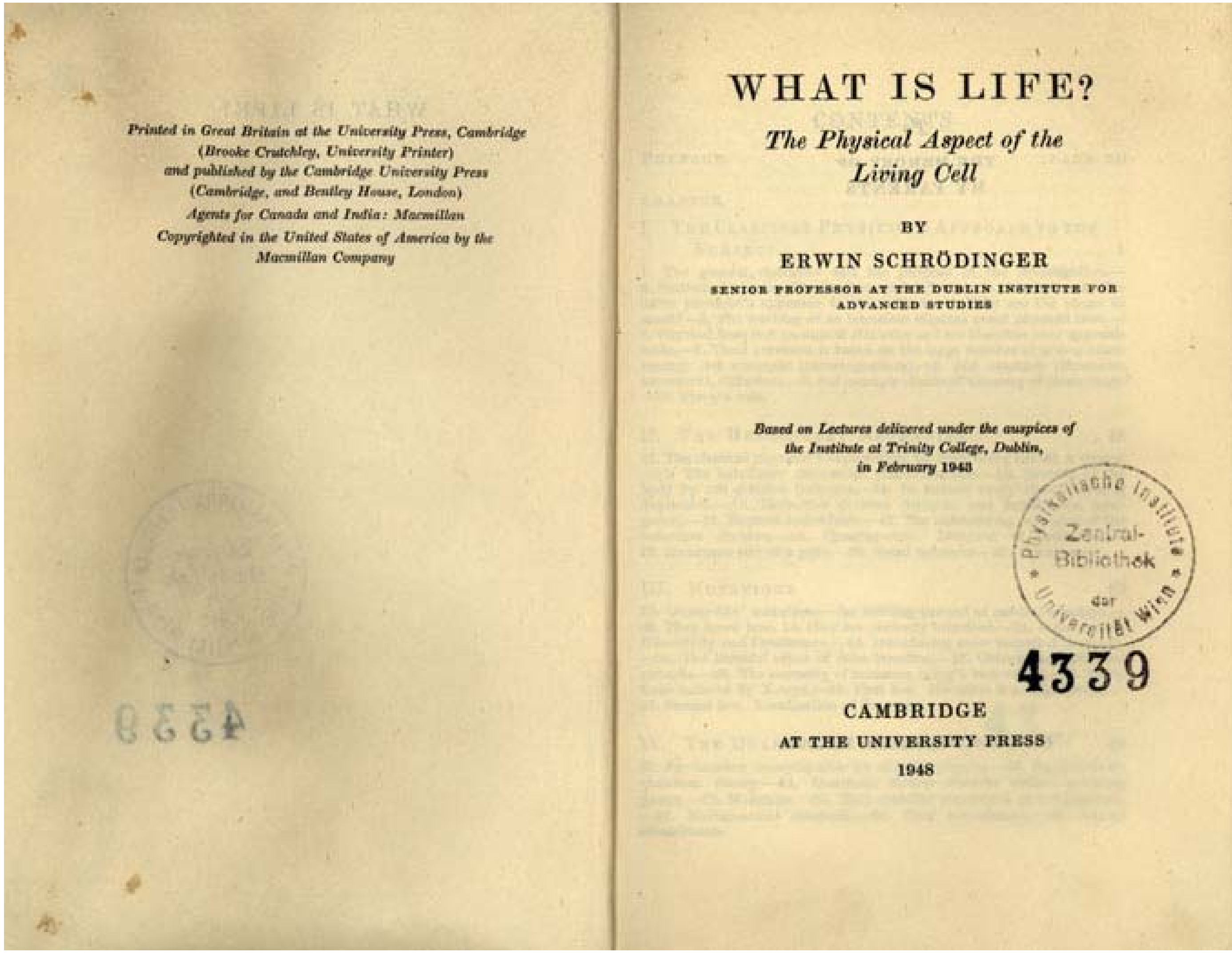
The advent of molecular biology



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WHAT IS LIFE?

The Physical Aspect of the Living Cell

BY

ERWIN SCHRÖDINGER

SENIOR PROFESSOR AT THE DUBLIN INSTITUTE FOR ADVANCED STUDIES

Based on Lectures delivered under the auspices of the Institute at Trinity College, Dublin, in February 1943

CAMBRIDGE
AT THE UNIVERSITY PRESS
1948

CORBIS-Bettmann

Figure 10.4 Erwin Schrödinger (1887–1961). Schrödinger proposed an expression of quantum mechanics that was different from but equivalent to Heisenberg's. His expression is useful because it expresses the behavior of electrons in terms of something we understand—waves. The Schrödinger equation is the central equation of quantum mechanics.

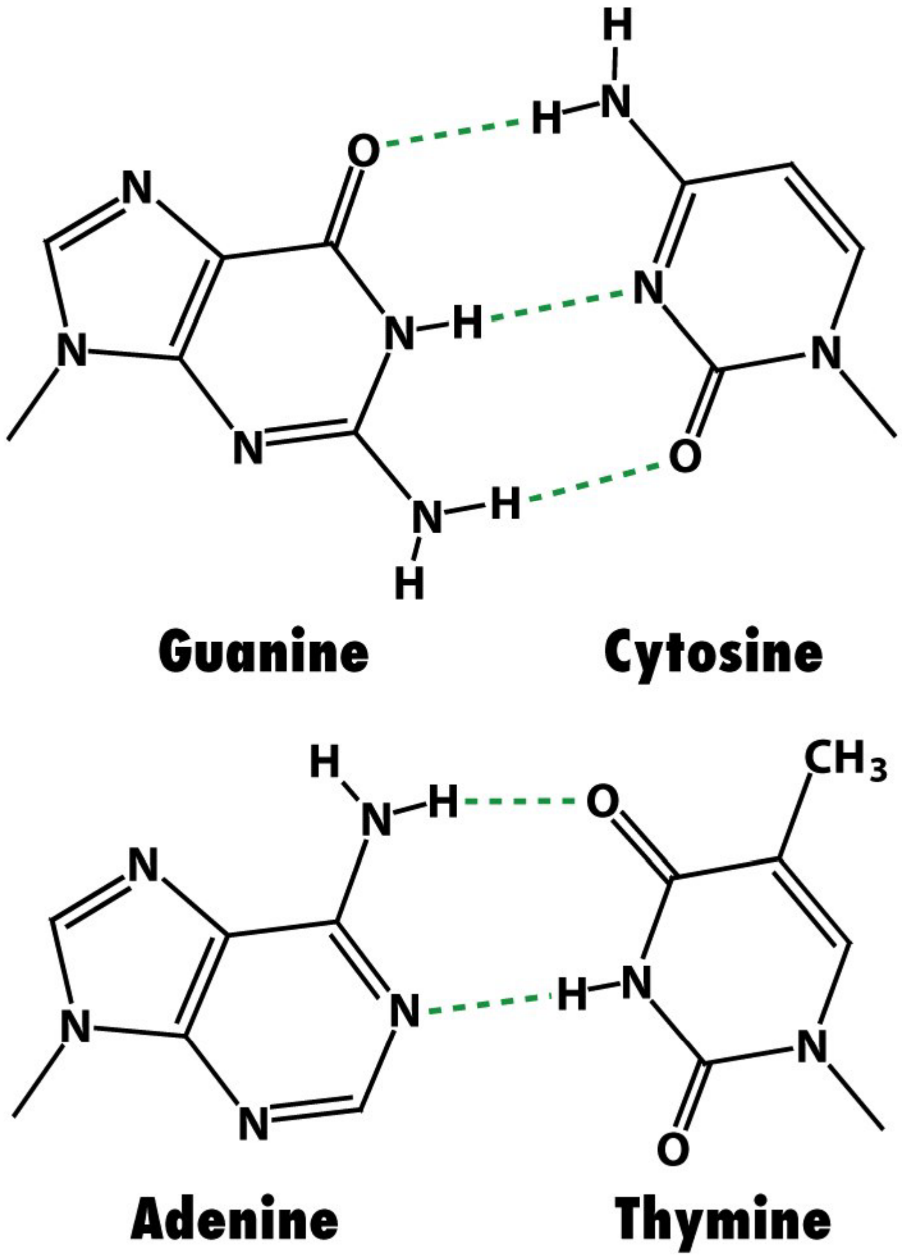

Figure 4-12
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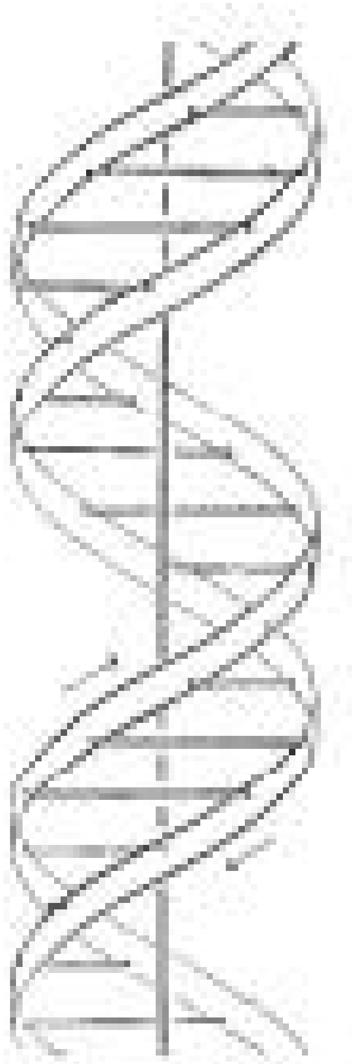

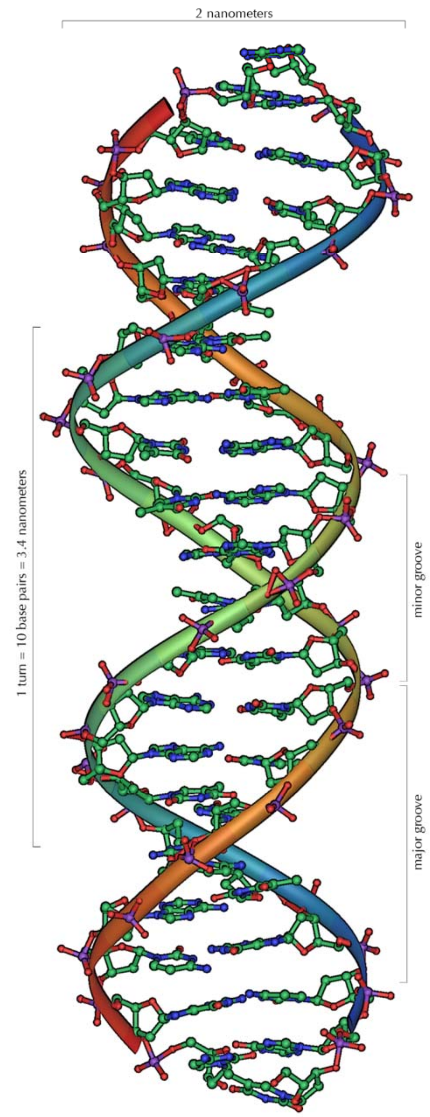
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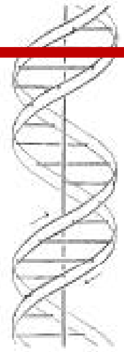

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The novel feature of the structure is the manner in which the two chains are held together by the purine and pyrimidine bases. The planes of the bases are perpendicular to the fibre axis. They are joined together in pairs, a single base from one chain being hydrogen-bonded to a single base from the other chain, so that the two lie side by side with identical z-co-ordinates. One of the pair must be a purine and the other a pyrimidine for bonding to occur. The hydrogen bonds are made as follows: purine position 1 to pyrimidine position 1; purine position 6 to pyrimidine position 6.

If it is assumed that the bases only occur in the structure in the most plausible tautomeric forms (that is, with the keto rather than the enol configurations) it is found that only specific pairs of bases can bond together. These pairs are: adenine (purine) with thymine (pyrimidine), and guanine (purine) with cytosine (pyrimidine).

In other words, if an adenine forms one member of a pair, on either chain, then on these assumptions the other member must be thymine; similarly for guanine and cytosine. The sequence of bases on a single chain does not appear to be restricted in any way. However, if only specific pairs of bases can be formed, it follows that if the sequence of bases on one chain is given, then the sequence on the other chain is automatically determined.

It has been found experimentally[3,4] that the ratio of the amounts of adenine to thymine, and the ratio of guanine to cytosine, are always very close to unity for deoxyribose nucleic acid.

It is probably impossible to build this structure with a ribose sugar in place of the deoxyribose, as the extra oxygen atom would make too close a van der Waals contact.

The previously published X-ray data[5,6] on deoxyribose nucleic acid are insufficient for a rigorous test of our structure. So far as we can tell, it is roughly compatible with the experimental data, but it must be regarded as unproved until it has been checked against more exact results. Some of these are given in the following communications. We were not aware of the details of the results presented there when we devised our structure, which rests mainly though not entirely on published experimental data and stereochemical arguments.

It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material.

Full details of the structure, including the conditions assumed in building it, together with a set of co-ordinates for the atoms, will be published elsewhere.

We are much indebted to Dr. Jerry Donohue for constant advice and criticism, especially on interatomic distances. We have also been stimulated by a knowledge of the general nature of the unpublished experimental results and ideas of Dr. M. H. F. Wilkins, Dr. R. E. Franklin and their co-workers at

King's College, London. One of us (J. D. W.) has been aided by a fellowship from the National Foundation for Infantile Paralysis.

J. D. WATSON
F. H. C. CRICK

Medical Research Council Unit for the Study of the Molecular Structure of Biological Systems,
Cavendish Laboratory, Cambridge.
April 2.

[1] Pauling, L., and Corey, R. B., *Nature*, 171, 346 (1953); *Proc. U.S. Nat. Acad. Sci.*, 39, 84 (1953).
[2] Furberg, S., *Acta Chem. Scand.*, 6, 634 (1952).
[3] Chargaff, E., for references see Zamenhof, S., Brawerman, G., and Chargaff, E., *Biochim. et Biophys. Acta*, 9, 402 (1952).
[4] Wyatt, G. R., *J. Gen. Physiol.*, 36, 201 (1952).
[5] Astbury, W. T., Symp. Soc. Exp. Biol. 1, Nucleic Acid, 66 (Camb. Univ. Press, 1947).
[6] Wilkins, M. H. F., and Randall, J. T., *Biochim. et Biophys. Acta*, 10, 192 (1953).

Molecular Structure of Deoxypentose Nucleic Acids

WHILE the biological properties of deoxypentose nucleic acid suggest a molecular structure containing great complexity, X-ray diffraction studies described here (cf. Astbury[1]) show the basic molecular configuration has great simplicity. The purpose of this communication is to describe, in a preliminary way, some of the experimental evidence for the polynucleotide chain configuration being helical, and existing in this form when in the natural state. A fuller account of the work will be published shortly.

The structure of deoxypentose nucleic acid is the same in all species (although the nitrogen base ratios alter considerably) in nucleoprotein, extracted or in cells, and in purified nucleate. The same linear group of polynucleotide chains may pack together parallel in different ways to give crystalline[1-3], semi-crystalline or paracrystalline material. In all cases the X-ray diffraction photograph consists of two regions, one determined largely by the regular spacing of nucleotides along the chain, and the other by the longer spacings of the chain configuration. The sequence of different nitrogen bases along the chain is not made visible.

Oriented paracrystalline deoxypentose nucleic acid ('structure B' in the following communication by Franklin and Gosling) gives a fibre diagram as shown in Fig. 1 (cf. ref. 4). Astbury suggested that the strong 3·4-A. reflexion corresponded to the internucleotide repeat along the fibre axis. The ~ 34 A. layer lines, however, are not due to a repeat of a polynucleotide composition, but to the chain configuration repeat, which causes strong diffraction as the nucleotide chains have higher density than the interstitial water. The absence of reflexions on or near the meridian immediately suggests a helical structure with axis parallel to fibre length.

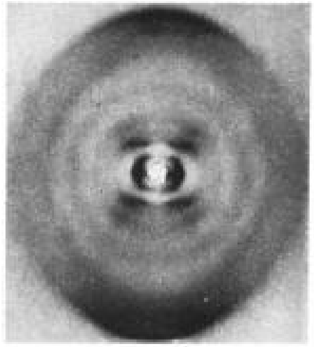

Fig. 1. Fibre diagram of deoxypentose nucleic acid from *B. coli*. Fibre axis vertical

Diffraction by Helices

It may be shown[5] (also Stokes, unpublished) that the intensity distribution in the diffraction pattern of a series of points equally spaced along a helix is given by the squares of Bessel functions. A uniform continuous helix gives a series of layer lines of spacing corresponding to the helix pitch, the intensity distribution along the *n*th layer line being proportional to the square of J_n, the *n*th order Bessel function. A straight line may be drawn approximately through the innermost maxima of each Bessel function and the origin. The angle this line makes with the equator is roughly equal to the angle between an element of the helix and the helix axis. If a unit repeats *n* times along the helix there will be a meridional reflexion (J_0^2) on the *n*th layer line. The helical configuration produces side-bands on this fundamental frequency, the effect[5] being to reproduce the intensity distribution about the origin around the new origin, on the *n*th layer line, corresponding to *C* in Fig. 2.

We will now briefly analyse in physical terms some of the effects of the shape and size of the repeat unit or nucleotide on the diffraction pattern. First, if the nucleotide consists of a unit having circular symmetry about an axis parallel to the helix axis, the whole diffraction pattern is modified by the form factor of the nucleotide. Second, if the nucleotide consists of a series of points on a radius at right-angles to the helix axis, the phases of radiation scattered by the helices of different diameter passing through each point are the same. Summation of the corresponding Bessel functions gives reinforcement for the inner-

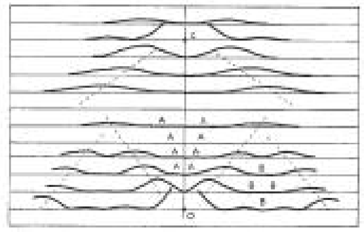

Fig. 2. Diffraction pattern of system of helices corresponding to structure of deoxypentose nucleic acid. The squares of Bessel functions are plotted about 0 on the equator and on the first, second, third and fifth layer lines for half of the nucleotide mass at 20 A. diameter and remainder distributed along a radius, the mass at a given radius being proportional to the radius. About *C* on the tenth layer line similar functions are plotted for an outer diameter of 12 A.

X-ray diffraction from B-form DNA

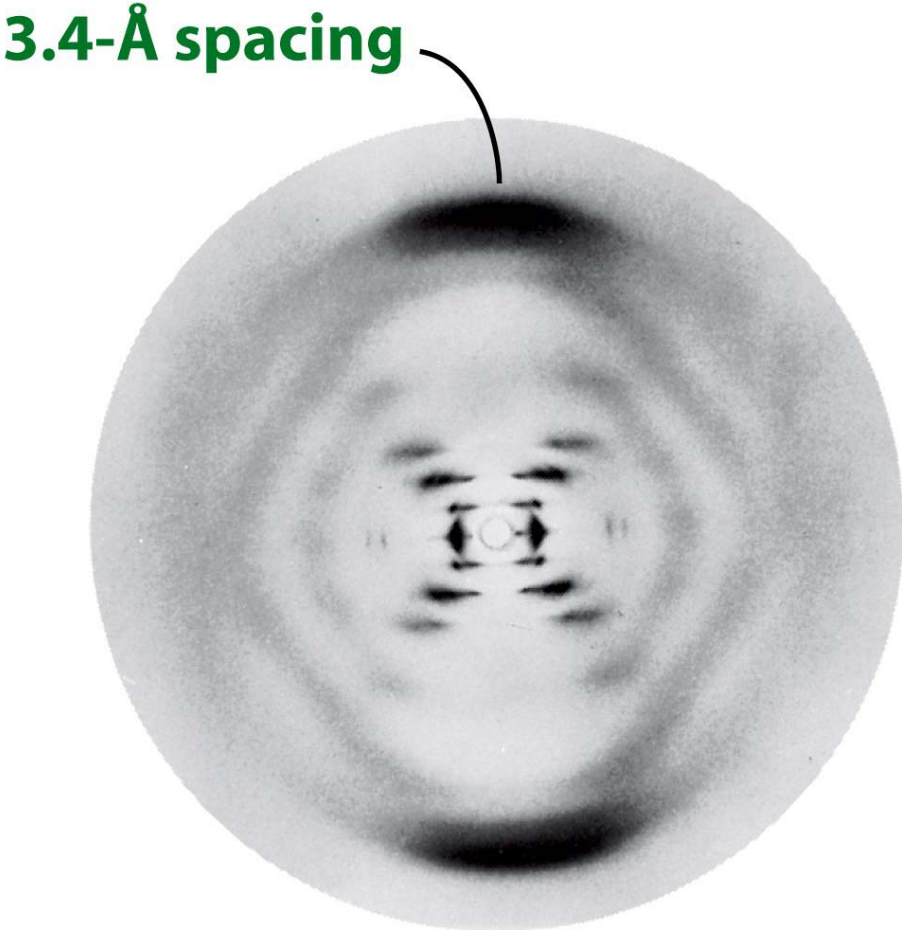

Figure 4-10
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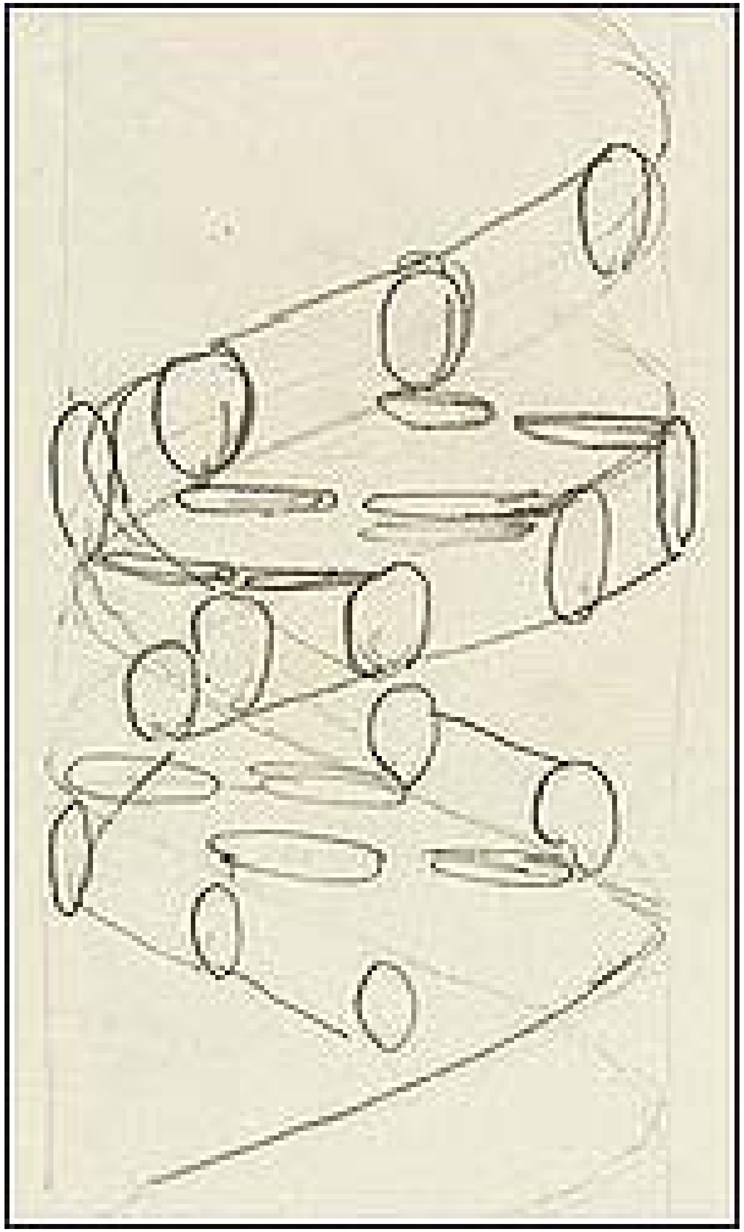
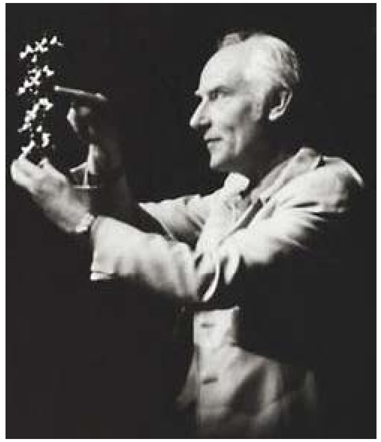
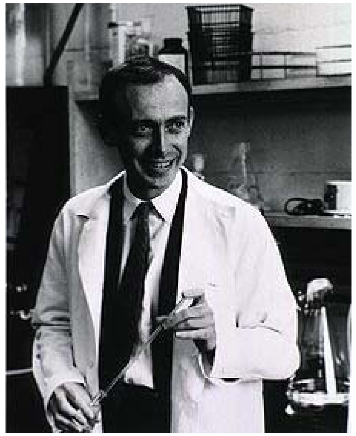




Francis Crick



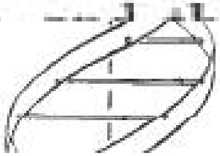
James Watson

This structure has novel features which are of considerable biological interest.

become more compact.

W of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.

A structure for nucleic acid has already been proposed by Pauling and Corey[1]. They kindly made their manuscript available to us in advance of publication. Their model consists of three intertwined chains, with the phosphates near the fibre



radically different structure for the salt of deoxyribose nucleic acid. This structure has two helical chains each coiled round

It is probably impossible to build this structure with a ribose sugar in place of the deoxyribose, as the extra oxygen atom would make too close a van der Waals contact.

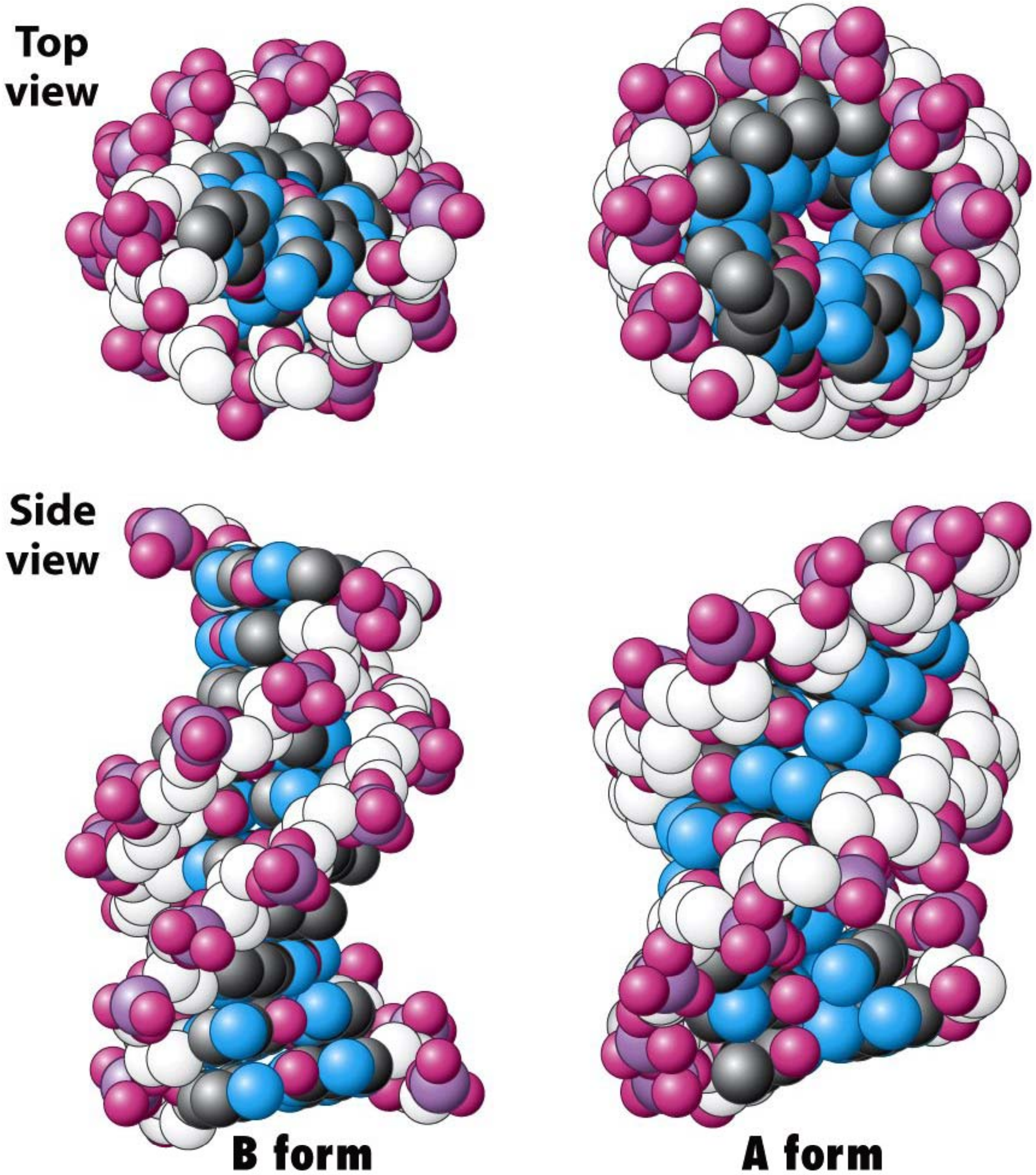
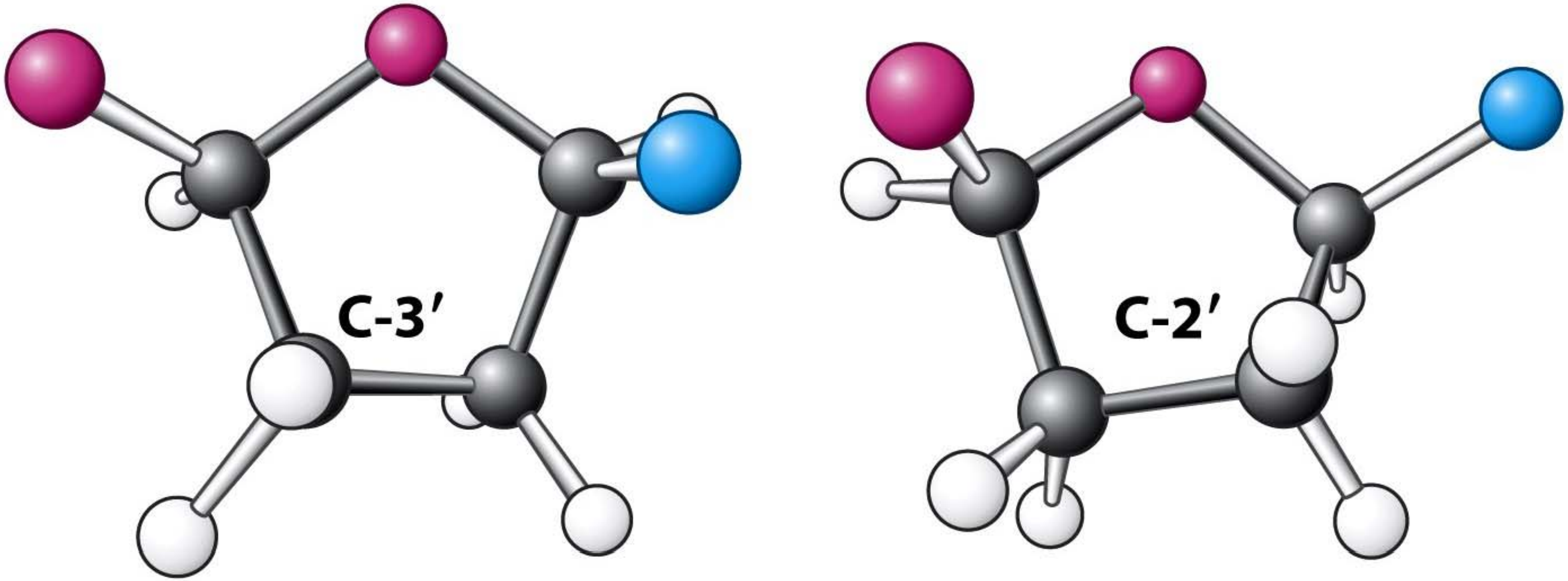


Figure 28-3
Biochemistry, Sixth Edition

esentation



C-3′ endo (A form)

C-2′ endo (B form)

Figure 28-4
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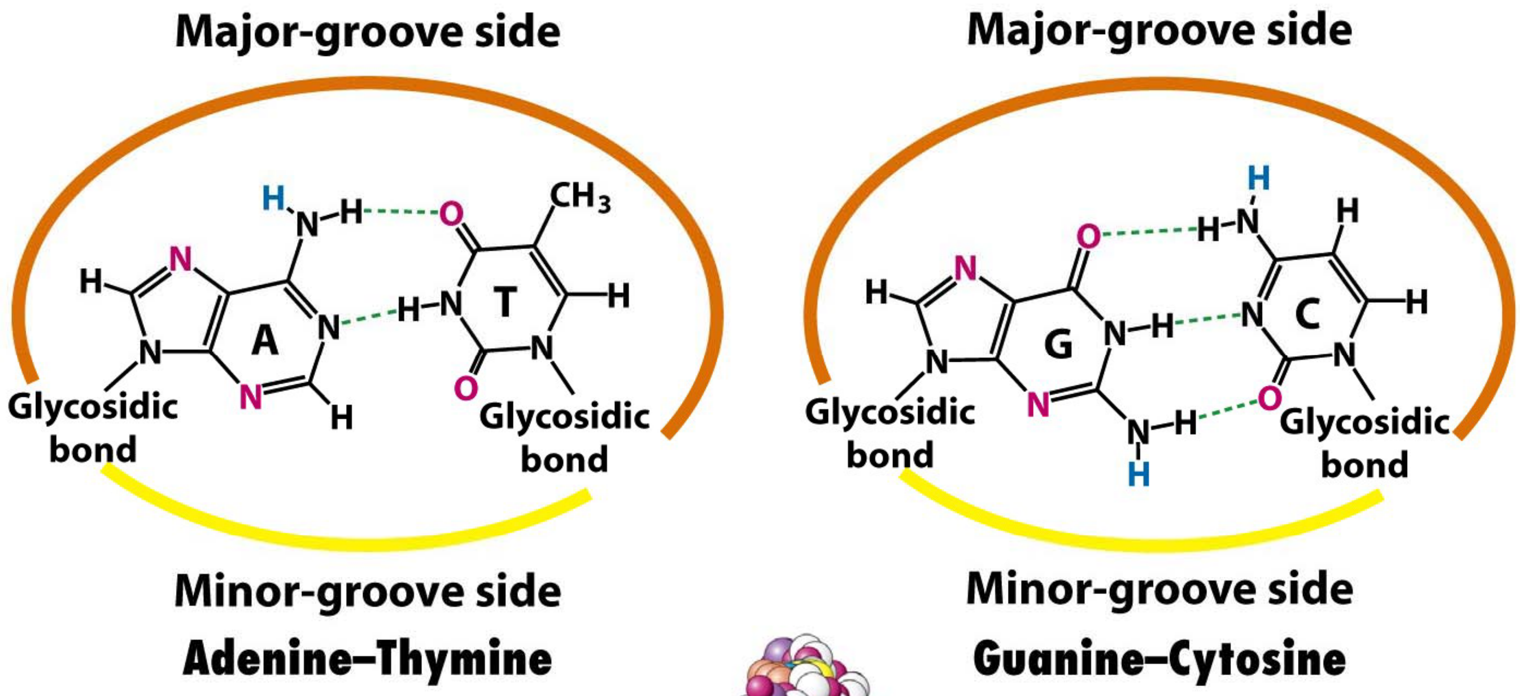

Figure 28-5
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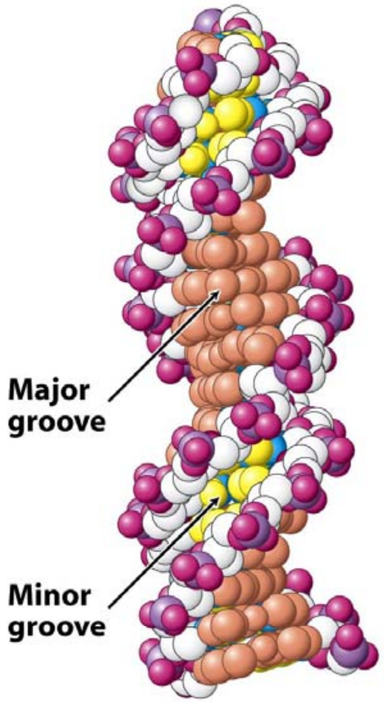

Figure 28-6
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Table 28.1 Comparison of A-, B-, and Z-DNA

	Helix type		
	A	**B**	**Z**
Shape	Broadest	Intermediate	Narrowest
Rise per base pair	2.3 Å	3.4 Å	3.8 Å
Helix diameter	25.5 Å	23.7 Å	18.4 Å
Screw sense	Right-handed	Right-handed	Left-handed
Glycosidic bond*	*anti*	*anti*	Alternating *anti* and *syn*
Base pairs per turn of helix	11	10.4	12
Pitch per turn of helix	25.3 Å	35.4 Å	45.6 Å
Tilt of base pairs from normal to helix axis	19°	1°	9°
Major groove	Narrow and very deep	Wide and quite deep	Flat
Minor groove	Very broad and shallow	Narrow and quite deep	Very narrow and deep

**Syn* and *anti* refer to the orientation of the *N*-glycosidic bond between the base and deoxyribose. In the *anti* orientation, the base extends away from the deoxyribose. In the *syn* orientation, the base is above the deoxyribose. Pyrimidine can be only in *anti* orientations, while purines can be *anti* or *syn*.

Table 28-1
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Single-Stranded DNA and RNA

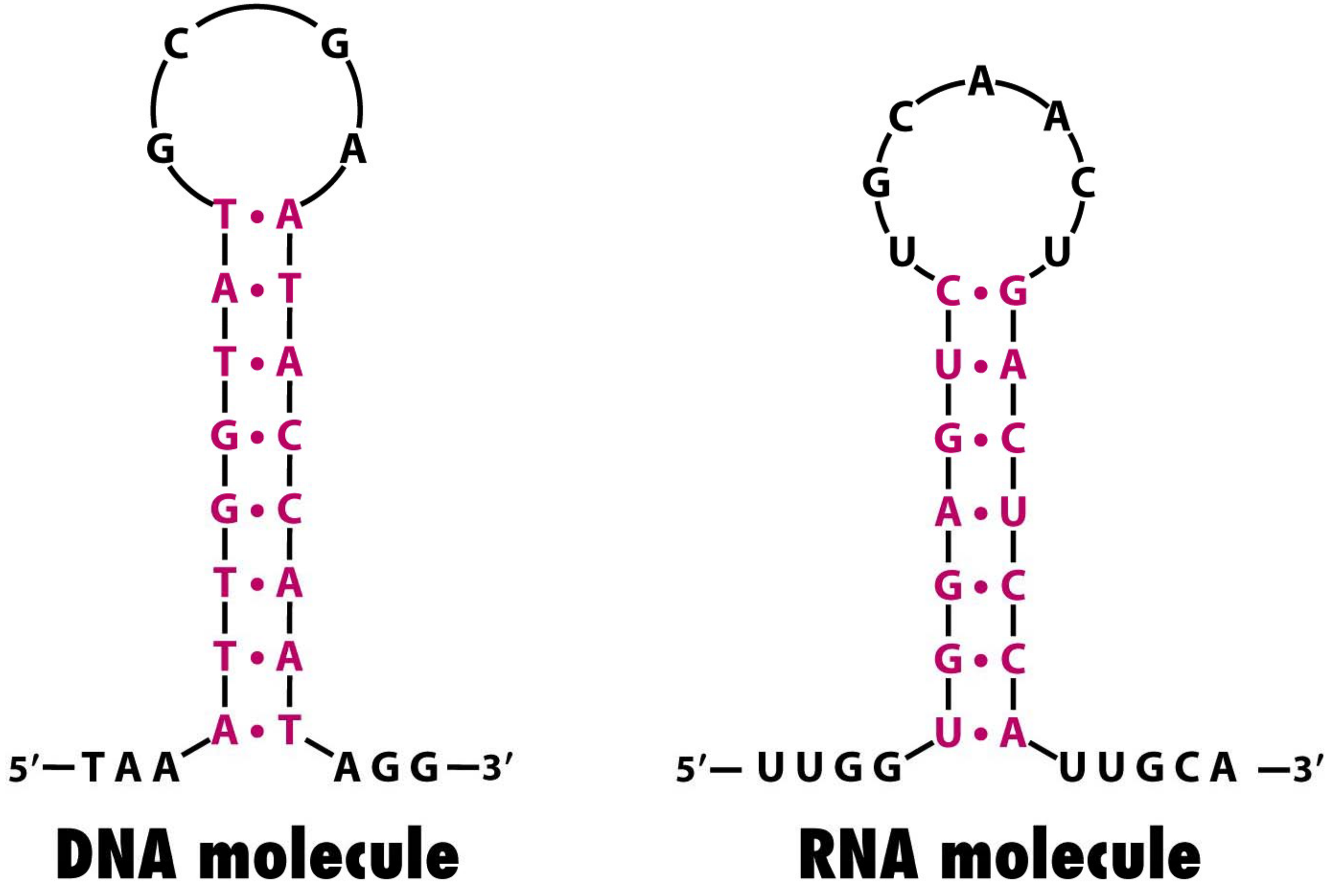

Figure 4-19
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The structure of RNA

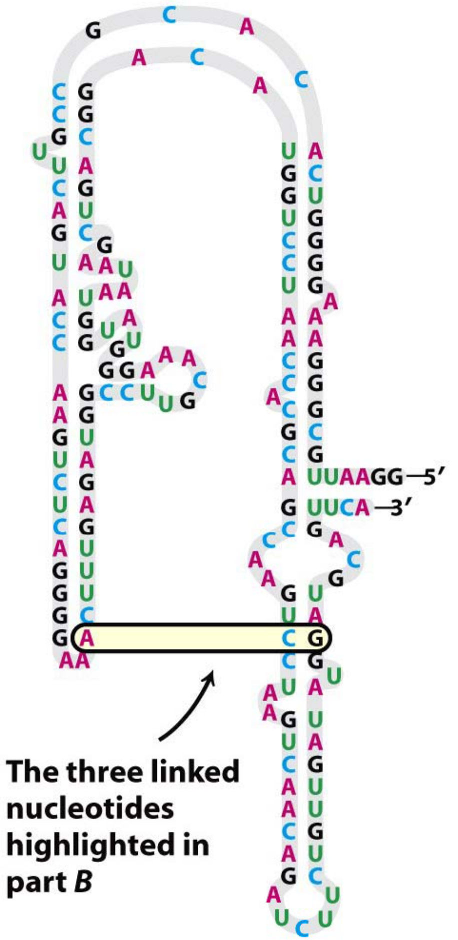

Figure 4-20a
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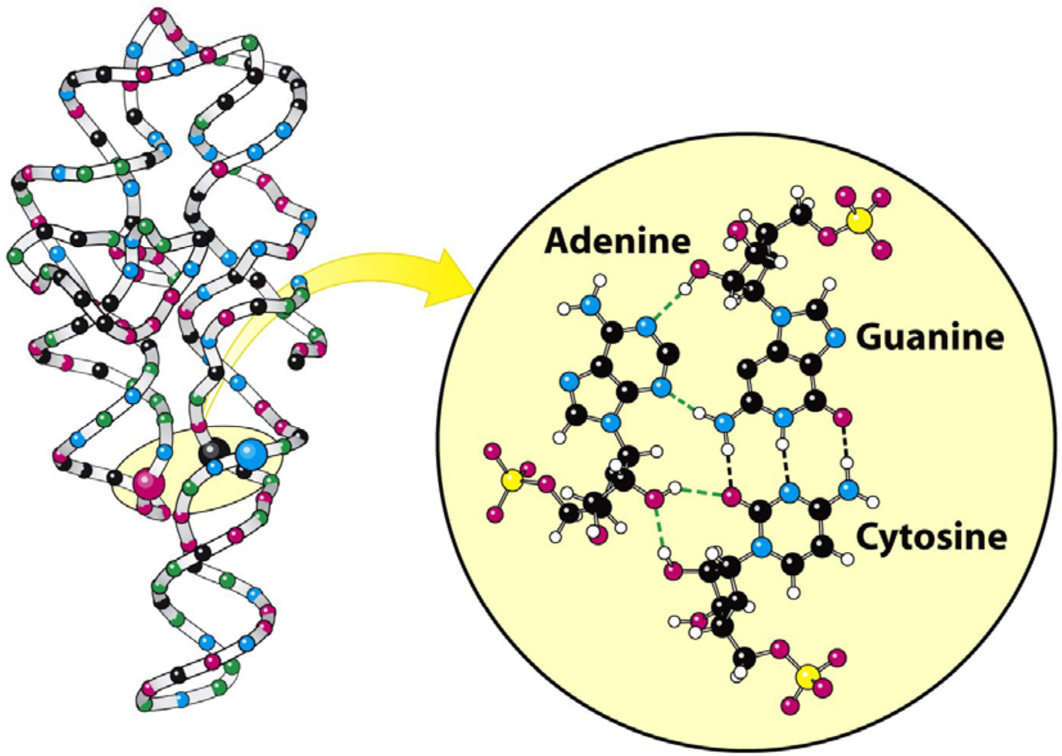

Figure 4-20b
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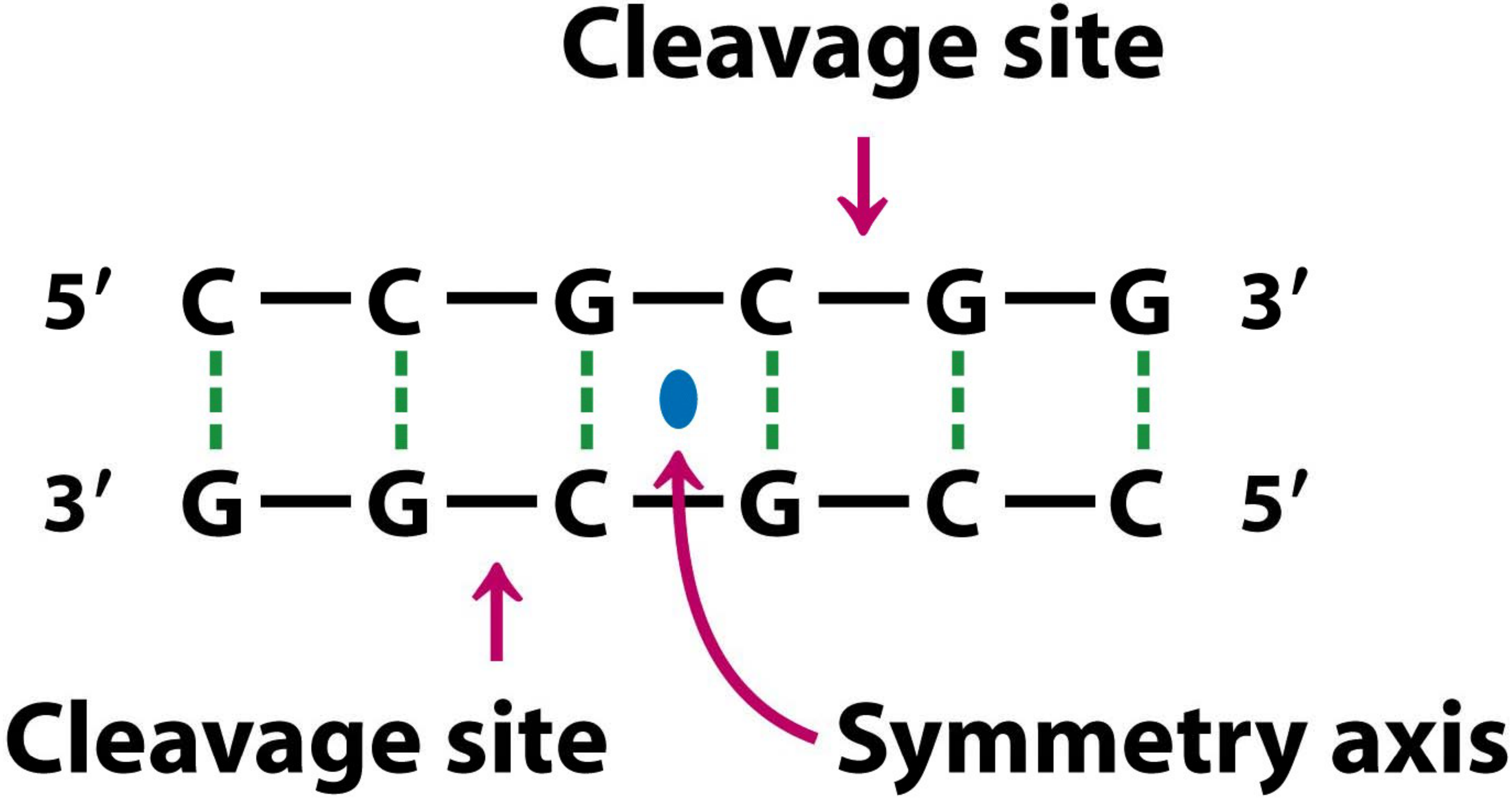
Several Kinds of RNA

- Ribosomal RNA (rRNA)
- Transfer RNA (tRNA)
- Messenger RNA (mRNA)
- Small nuclear RNA (snRNA)
- Micro RNA (miRNA)
- Small interfering RNA (siRNA)
- Others (signal-recognition, component of telomerase and etc.)

Regulations of DNA

- Restriction-enzyme. (Cut)
- Ligase. (Paste)
- Polymerase. (Copy)
- Topoisomerase. (Twist)

Restriction Enzyme



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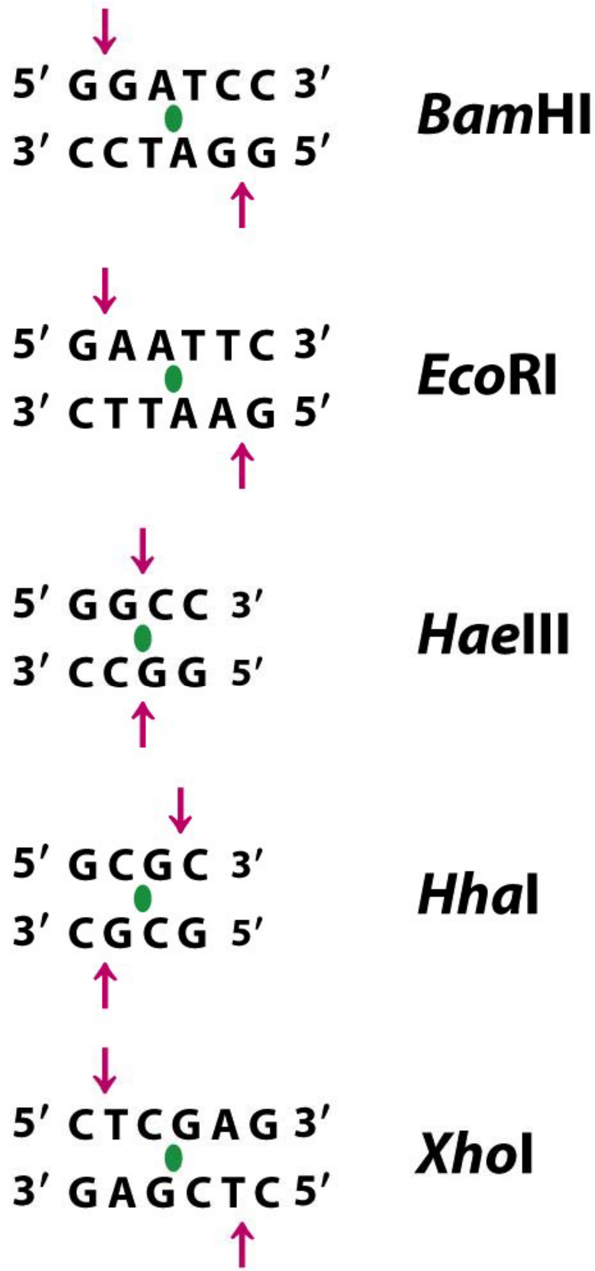

Figure 5-1
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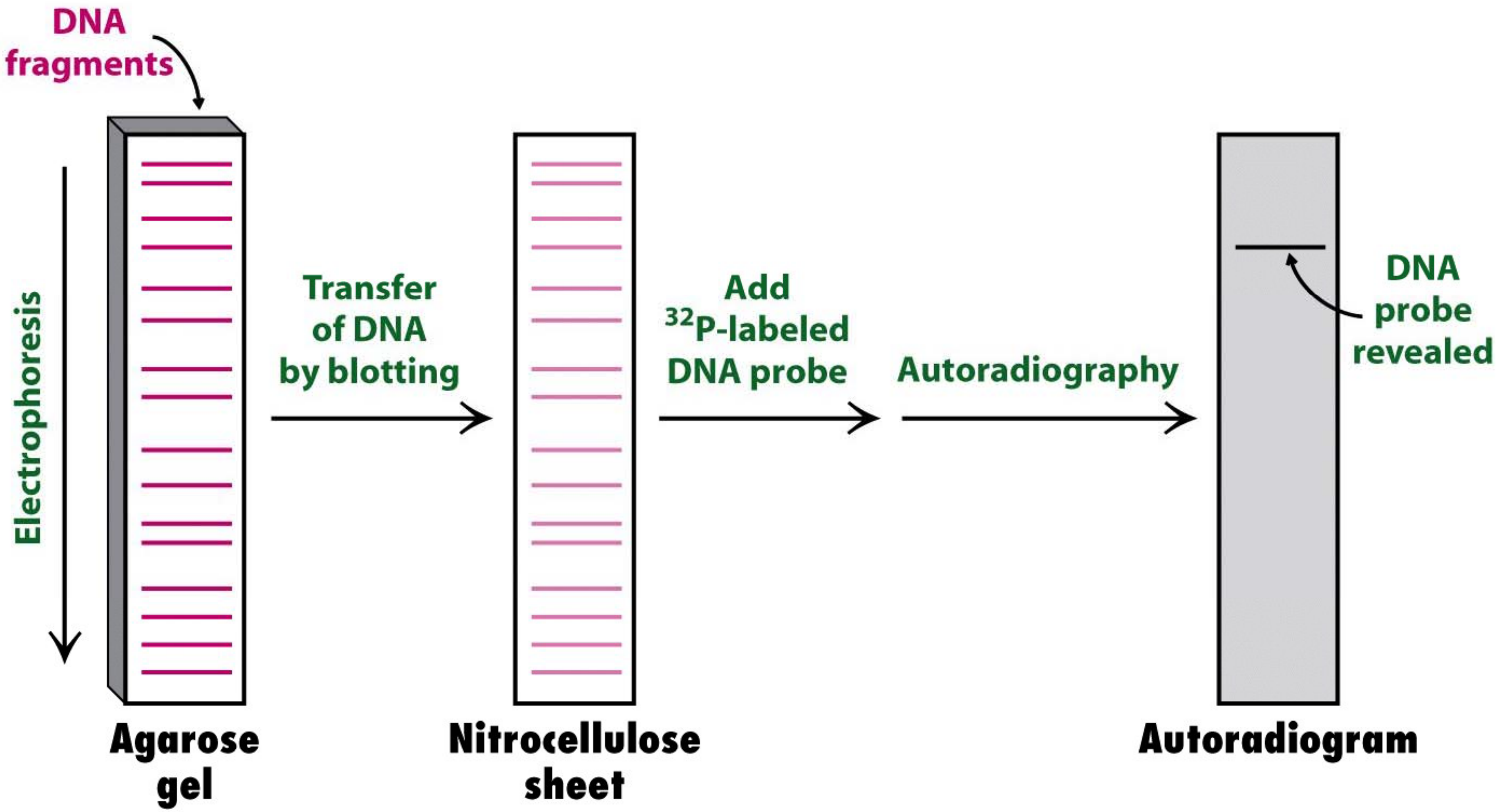

Figure 5-3
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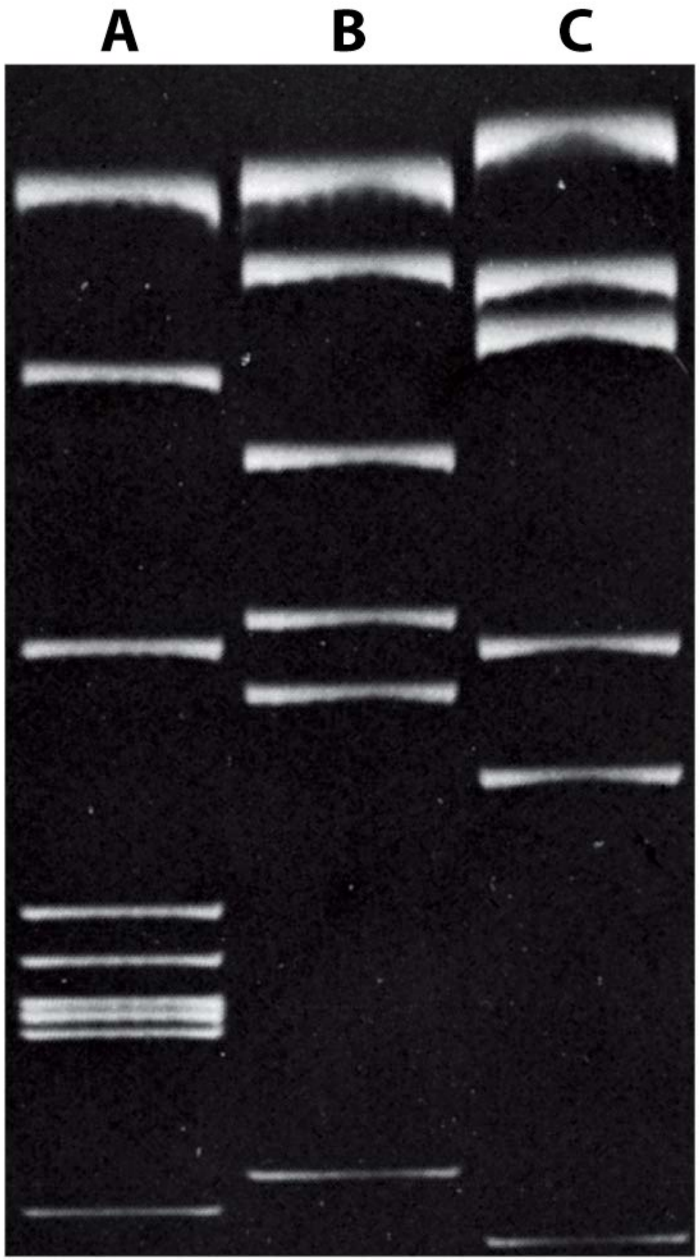

Figure 5-2
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DNA Ligase

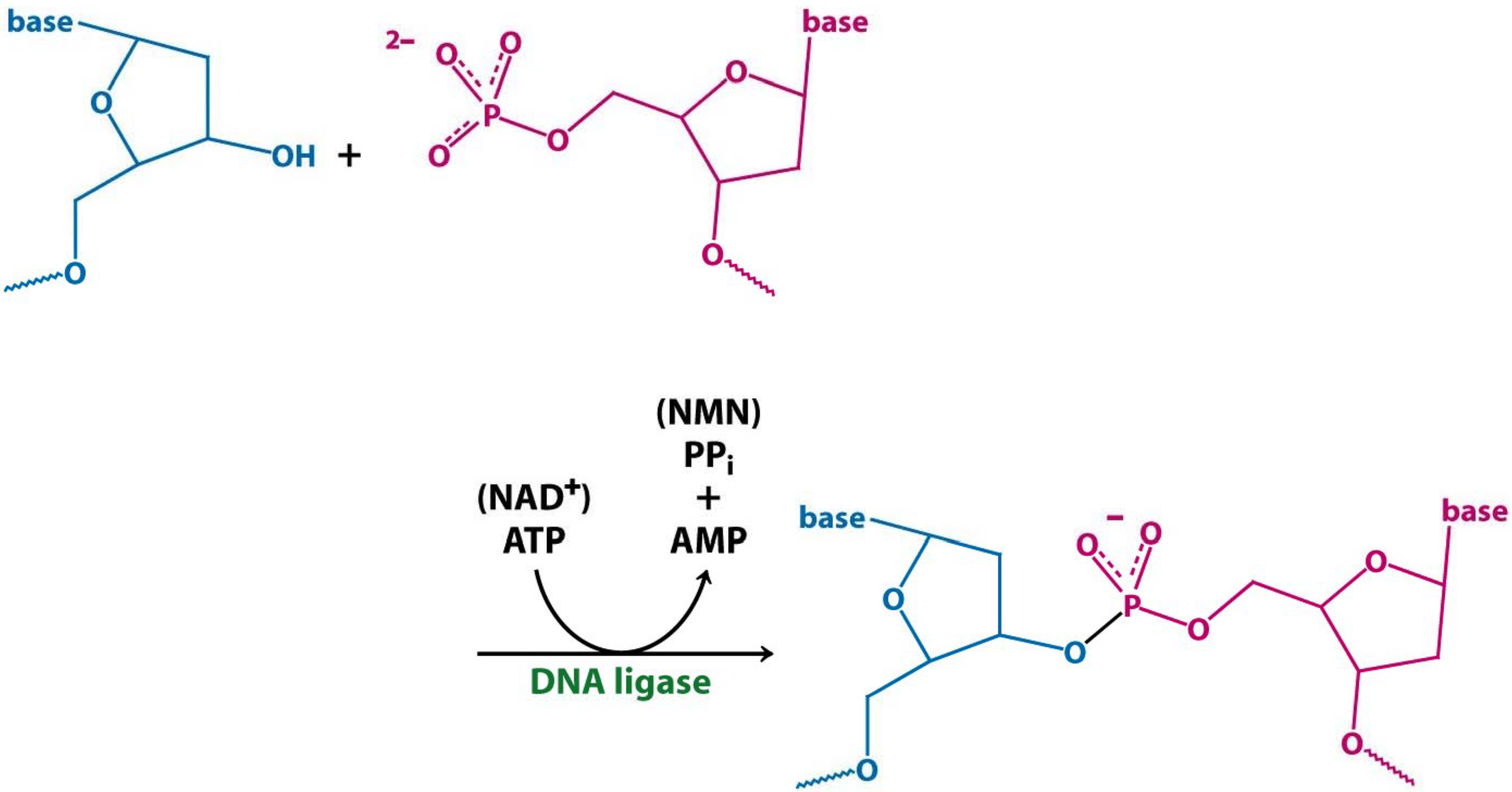

Figure 28-22
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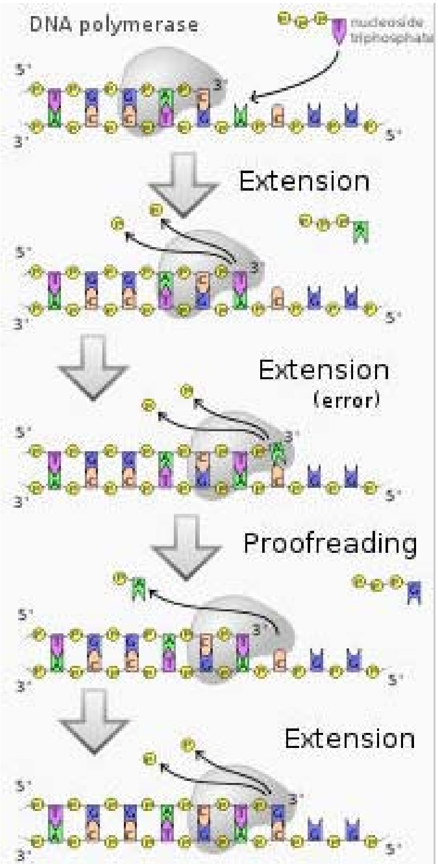
DNA Polymerase



From Wikipedia

Abbreviations

- dNTP: dATP, dGTP, dCTP and dTTP
- dN: deoxynucleoside
- TP: triphosphate
- PPi: pyrophospate ion

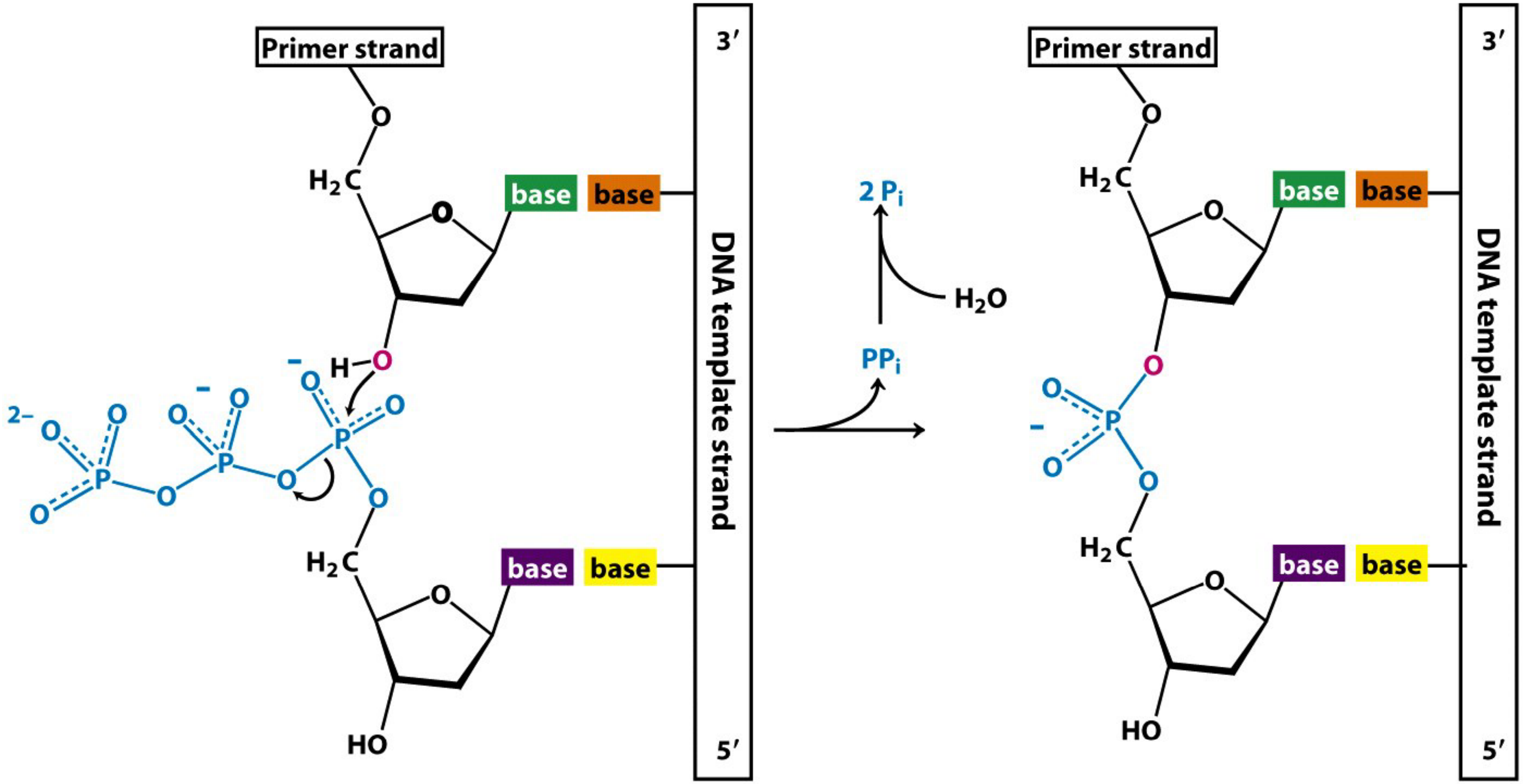


Figure 4-22
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- Primer with free 3’ -OH

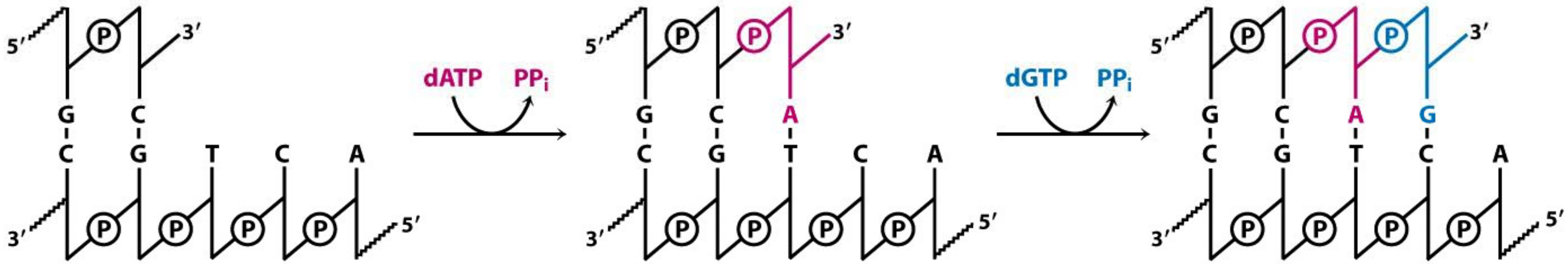

Figure 4-21
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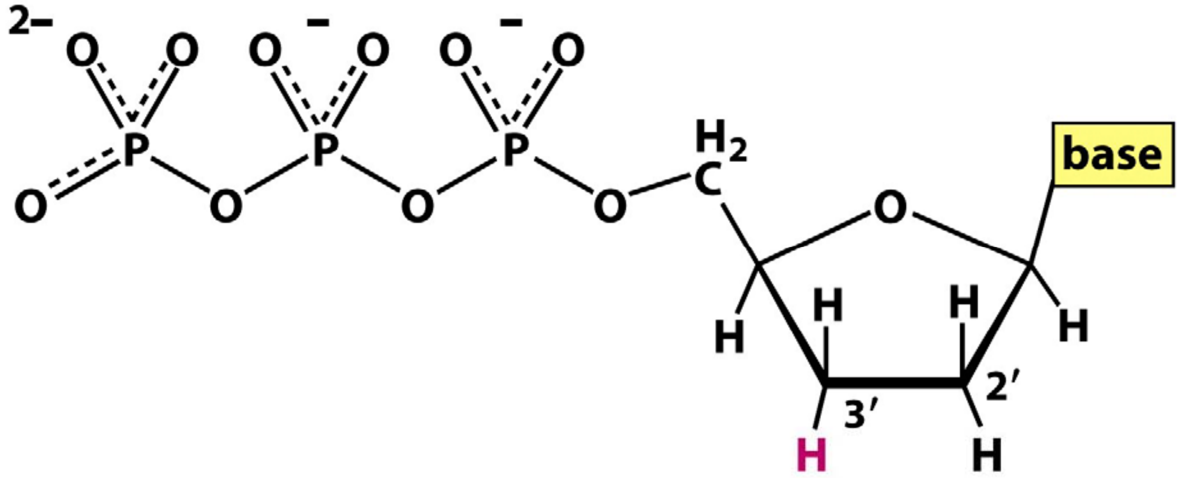
Applications of DNA

- The polymerase chain reaction (PCR).
- DNA sequencing.
- Southern Blotting.

DNA sequencing (1975)



2′, 3′-Dideoxy analog

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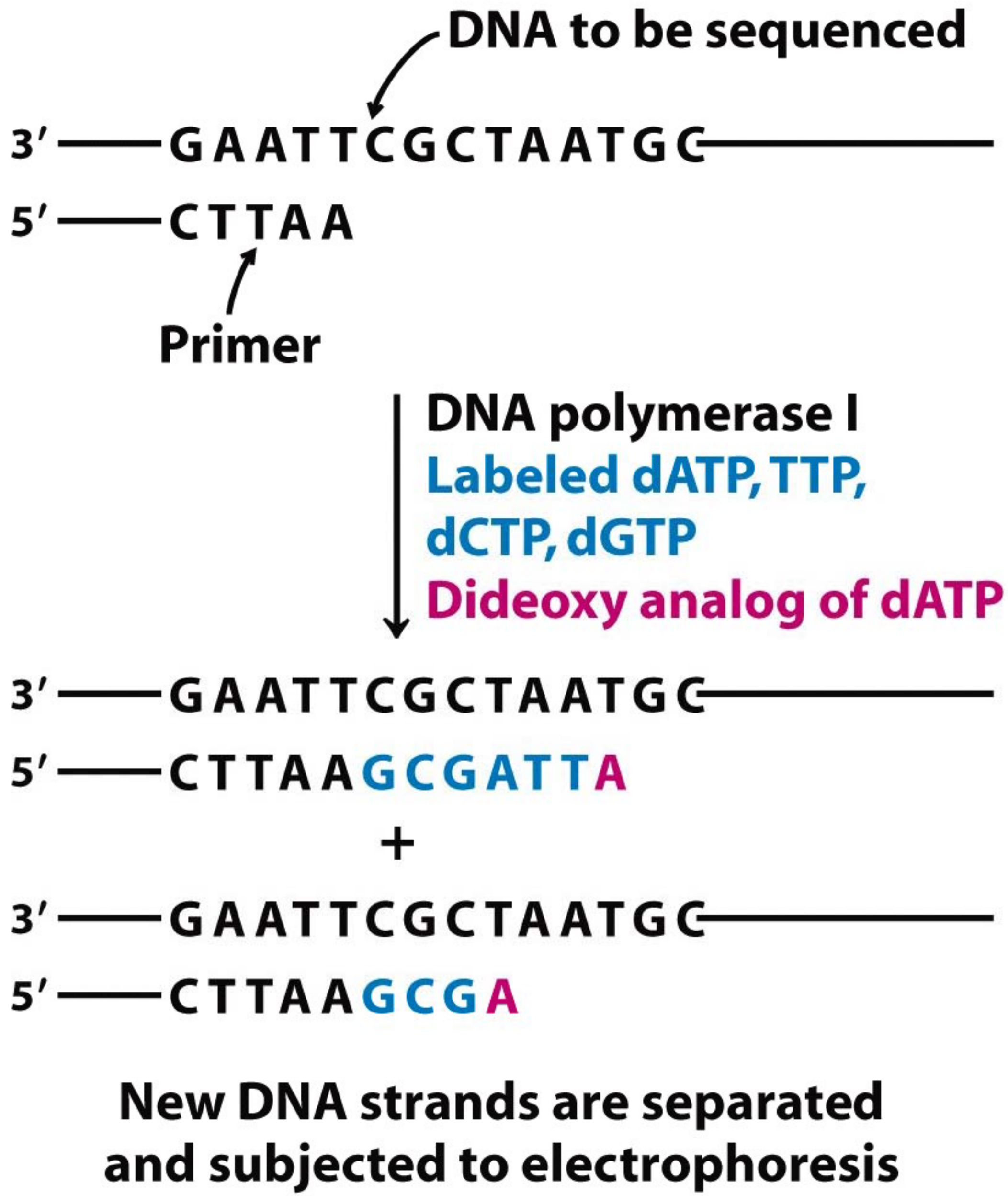

Figure 5-4
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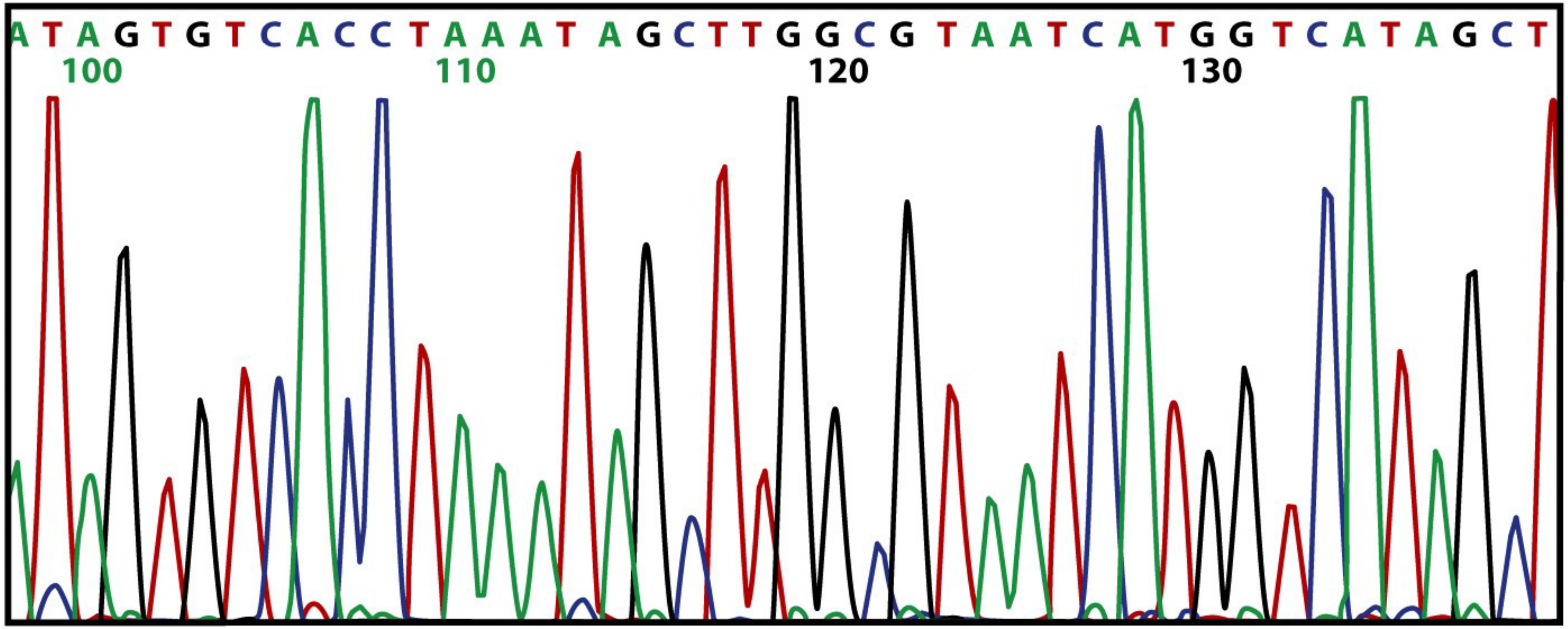

Figure 5-5
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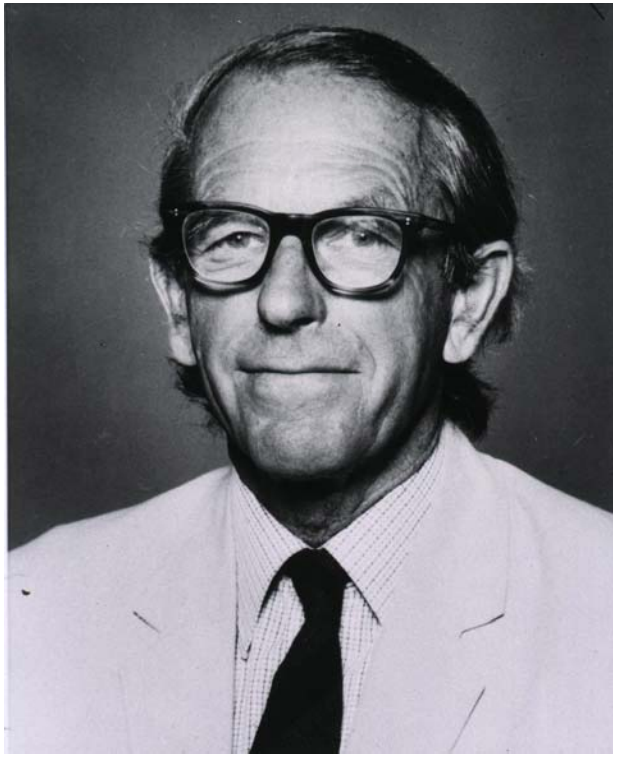
Frederick Sanger



- The Nobel Prize for Chemistry in 1980.

Several Kinds of RNA

- Ribosomal RNA (rRNA)
- Transfer RNA (tRNA)
- Messenger RNA (mRNA)
- Small nuclear RNA (snRNA)
- Micro RNA (miRNA)
- Small interfering RNA (siRNA)
- Others (signal-recognition, component of telomerase and etc.)

Ribosomal RNA (rRNA)

Table 4.1 Base compositions experimentally determined for a variety of organisms

Species	A:T	G:C	A:G
Human being	1.00	1.00	1.56
Salmon	1.02	1.02	1.43
Wheat	1.00	0.97	1.22
Yeast	1.03	1.02	1.67
Escherichia coli	1.09	0.99	1.05
Serratia marcescens	0.95	0.86	0.70

Table 4-1
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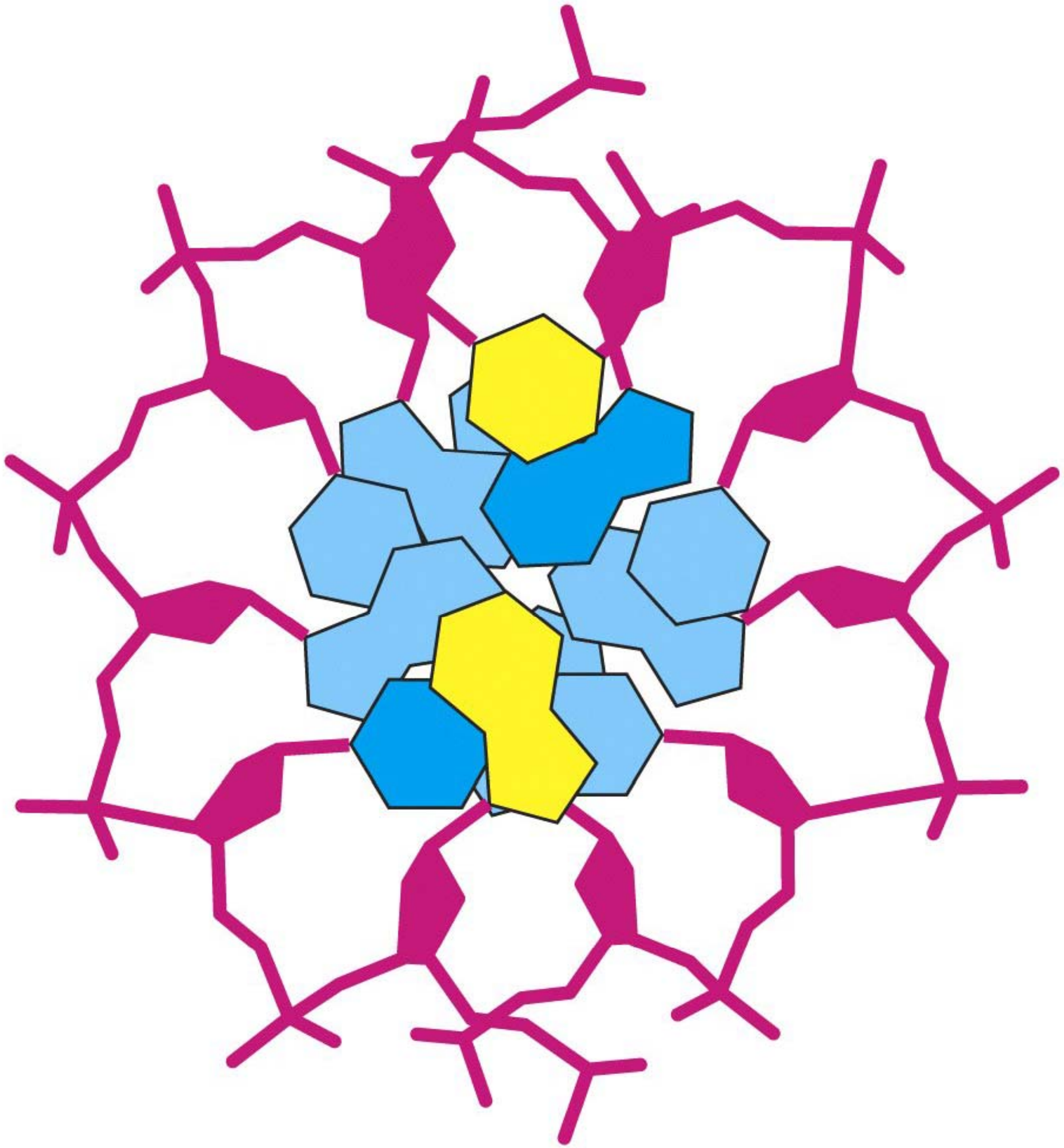

Figure 4-13
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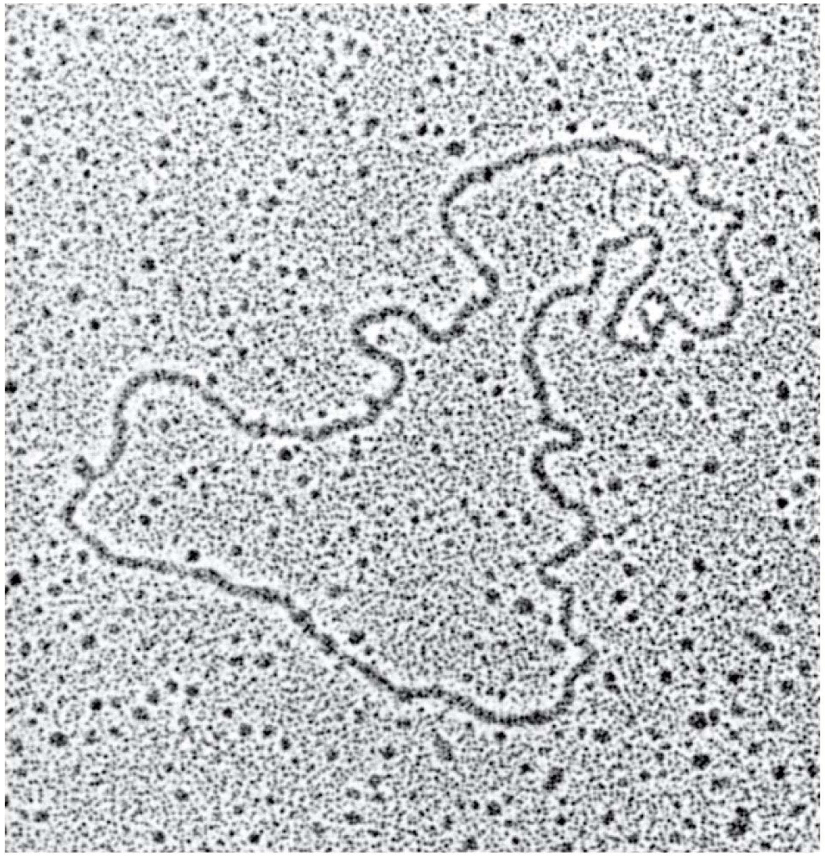

Figure 4-18a
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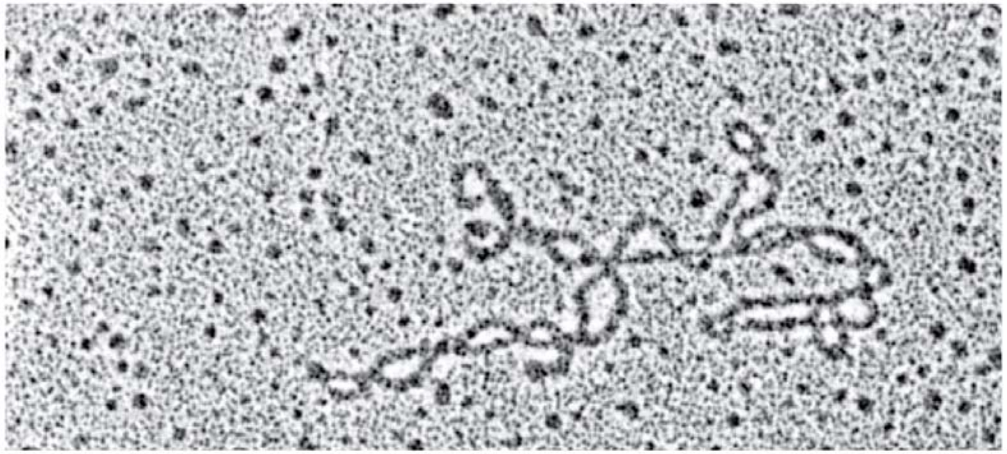

Figure 4-18b
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Learning Goals

- Explain the difference between complex and simple carbohydrates using Lewis symbol.
- Apply the systems of classifying and naming monosaccharides according to the functional group and number of carbons in chain.
- Determine whether a molecule has a chiral center.
- Explain stereoisomerism.
- Identify monosaccharides as either D- or L-.
- Draw and name the common monosaccharides using structural formulas.

Learning Goals

- Given the linear structure of a monosaccharide, draw the Haworth projection of its α- and β-cyclic forms and vice versa.
- By inspection of the structure, predict whether a sugar in a reducing or a nonreducing sugar.
- Discuss the use of the Benedict's reagent to measure the level of glucose in urine.
- Draw and name the common disaccharides and discuss their significance in biological systems.
- Describe the difference between galactosemia and lactose intolerance.
- Discuss the structural, chemical, and biochemical properties of starch, glycogen, and the cellulose.

Learning Goals

- Describe the physical and chemical properties and biological function of each of the families of lipids.
- Write the structures of saturated and unsaturated fatty acids.
- Compare and contrast the structure and properties of saturated and unsaturated fatty acids.
- Write equations representing the reactions that fatty acids undergo.
- Describe the functions of prostaglandins.
- Discuss the mechanism by which aspirin reduces pain.
- Draw the structure of the phospholipid and discuss its amphipathic nature.

Learning Goals

- Discuss the general classes of sphingolipids and their functions.
- Draw the structure of the steroid nucleus and discuss the functions of steroid hormones.
- Describe the function of lipoprotein in triglyceride and cholesterol transport in body.
- Draw the structure of the cell membrane and discuss its functions.
- Discuss passive and facilitated diffusion of materials through a cell membrane.
- Explain the process of osmosis.
- Describe the mechanism of action of a Na+-K+ ATPase.

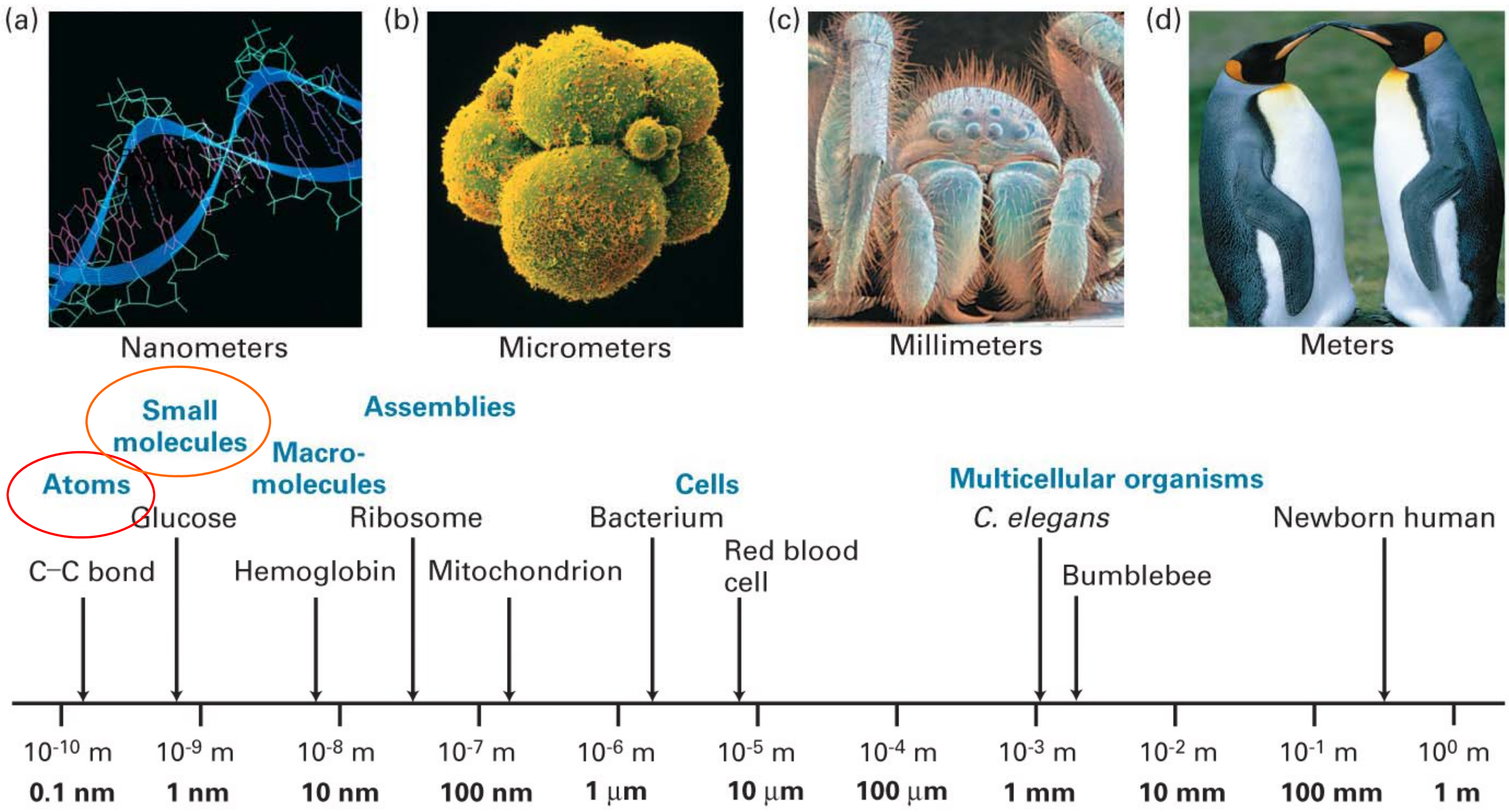
Learning Goals

- List the functions of proteins.
- Draw the general structure of an amino acids and classify amino acids based on their R groups.
- Describe the primary structure of proteins and structure of the peptide bond.
- Describe the structure of small peptides and name them.
- Describe the type of secondary structure of a protein.
- Discuss the forces that maintain secondary structure.
- Describe the structure and functions of fibrous protein.
- Describe the tertiary and quaternary structure of a portein.

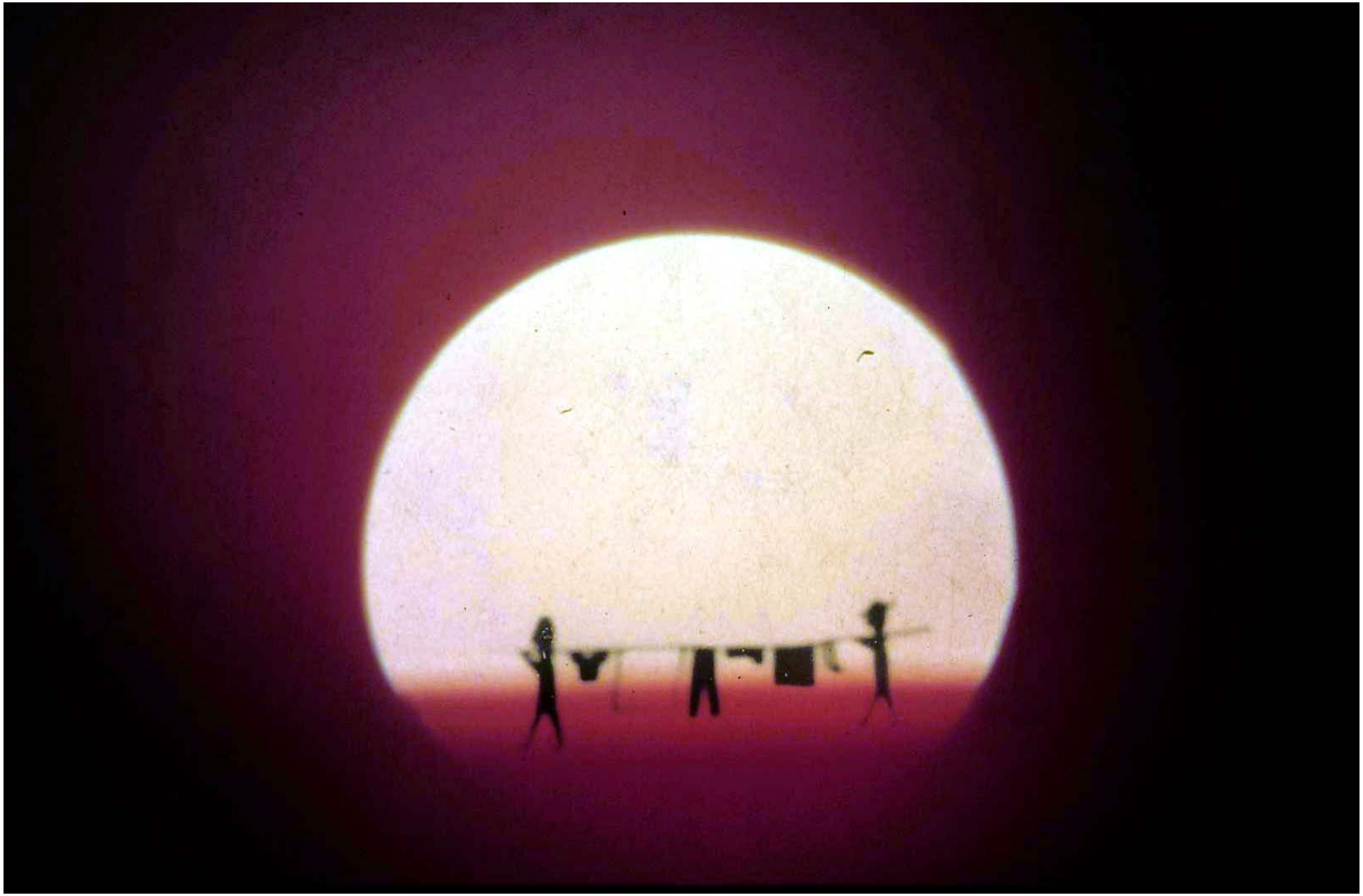
Learning Goals

- List the R group interactions that maintain protein conformation.
- List example of protein that require prosthetic groups and explain the way in which they function.
- Discuss the importance of the three-dimensional structure of protein to its function.
- Describe the roles of hemoglobin and myoglobin.
- Describe how extremes of pH and temperature cause denaturation of proteins.
- Explain the difference between essential and nonessential amino acids.

Guideline for biochemistry lectures

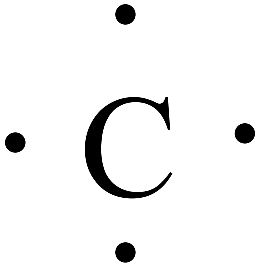


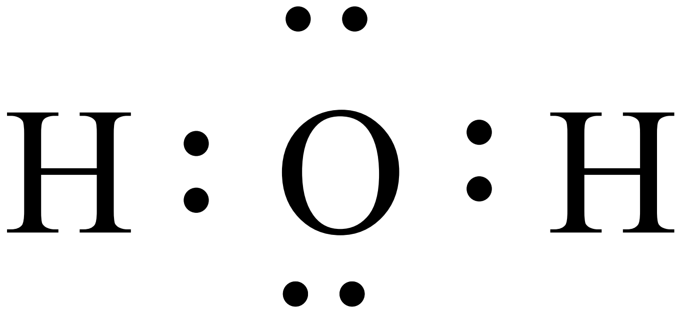
4.1 Carbohydrates



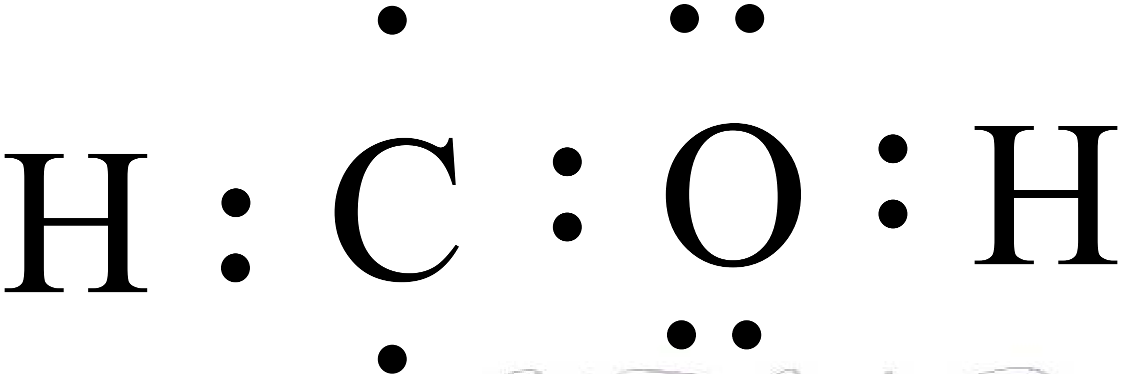
Y.T.Lin's Presentation

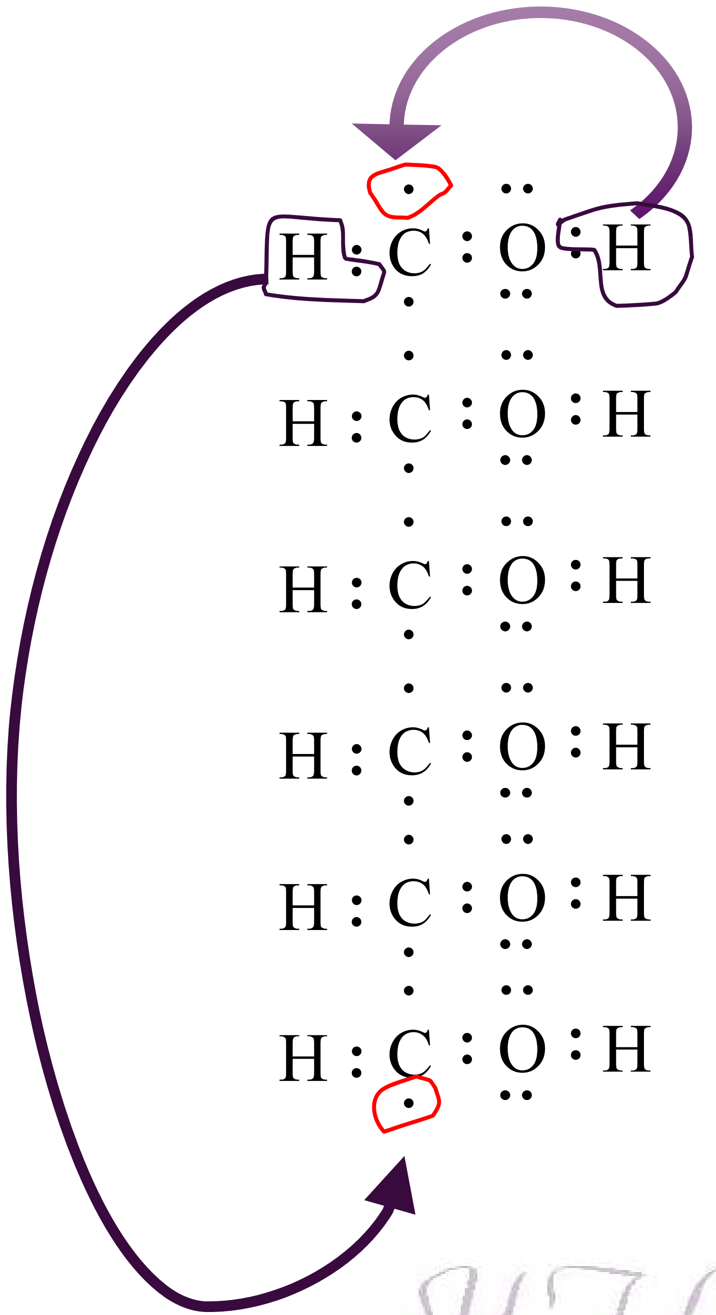
How to store the sunlight energy?





photosynthesis

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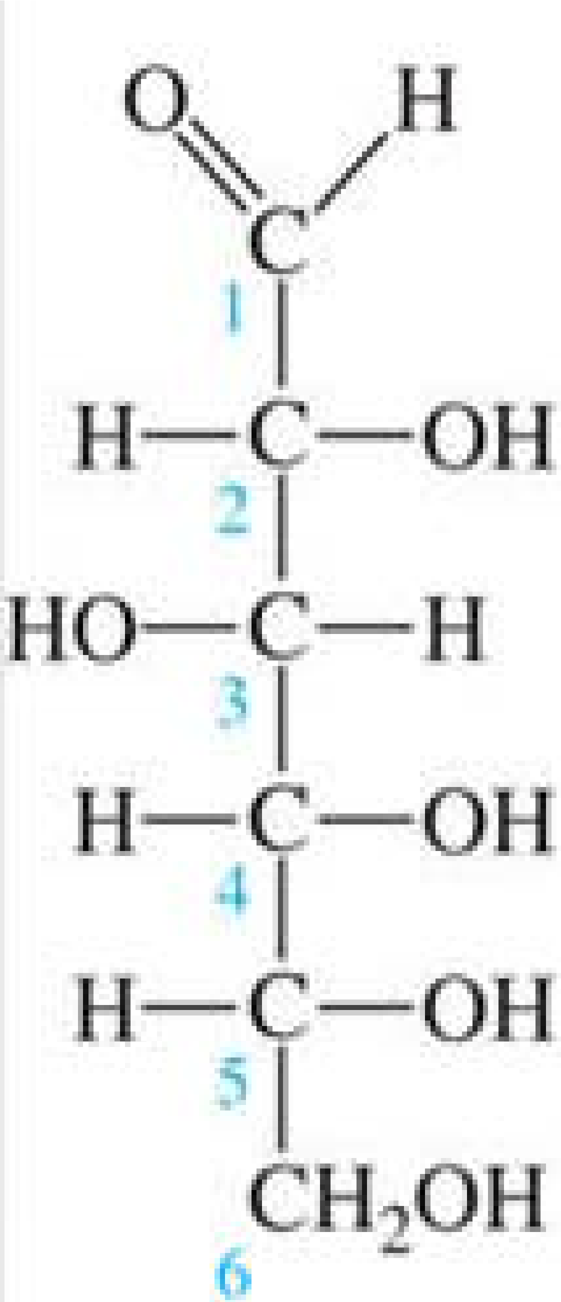

aldose

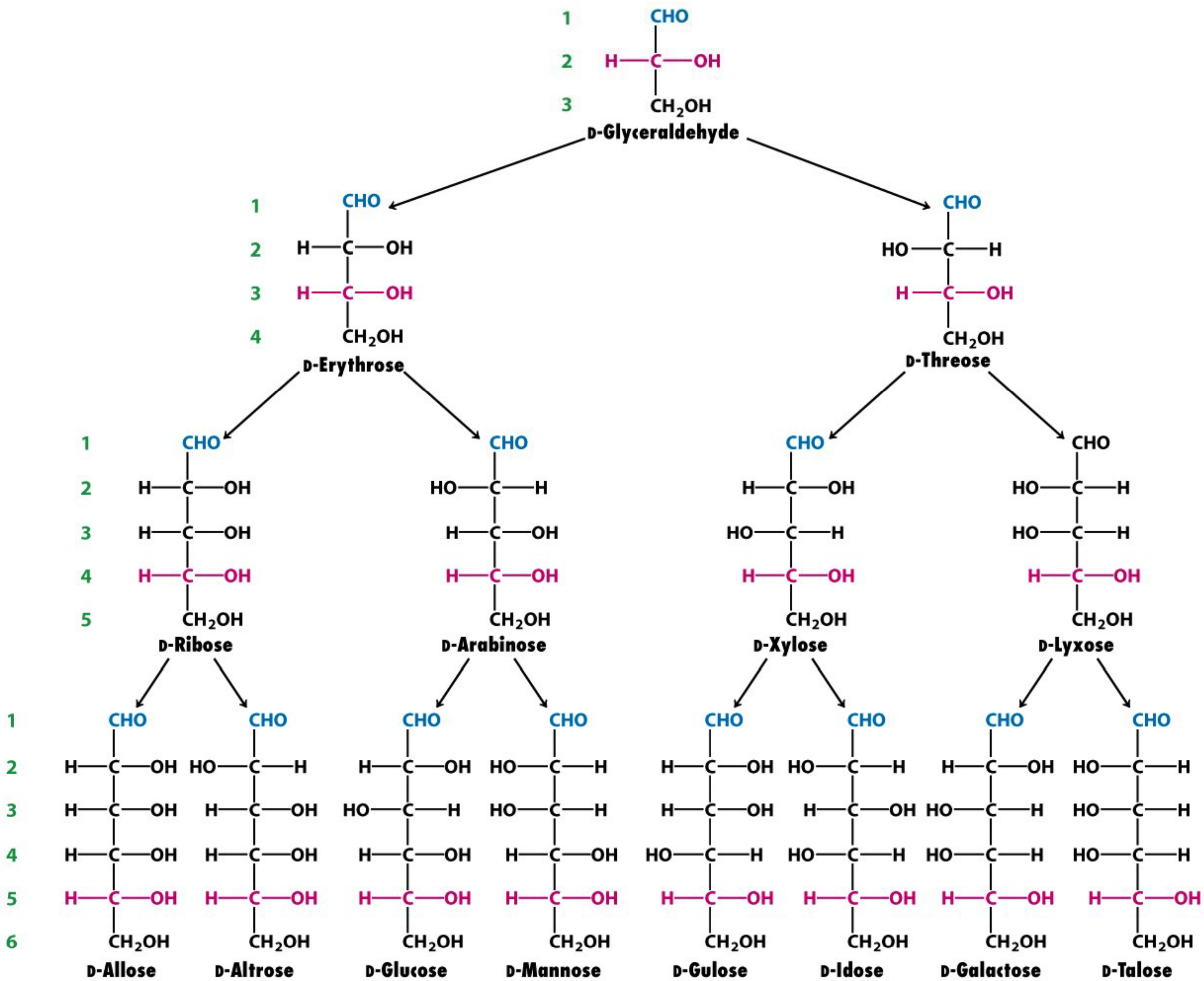

Figure 11-2
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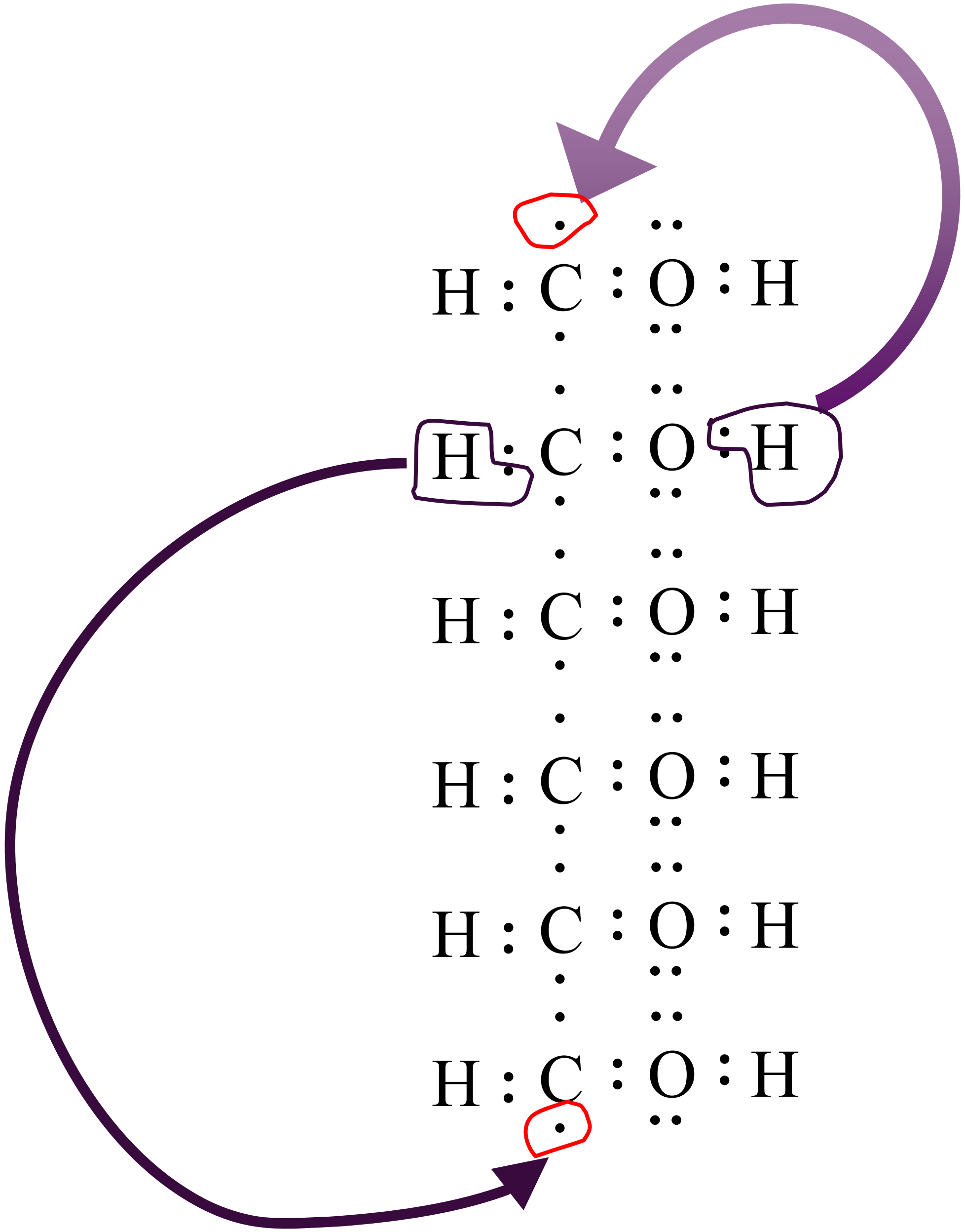

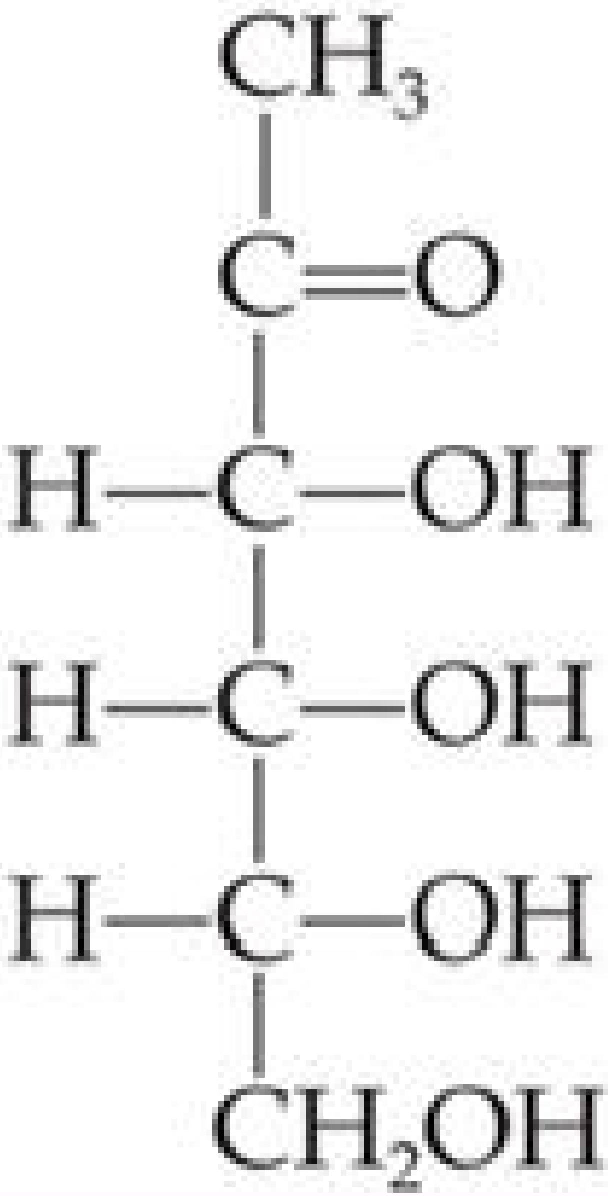

ketose

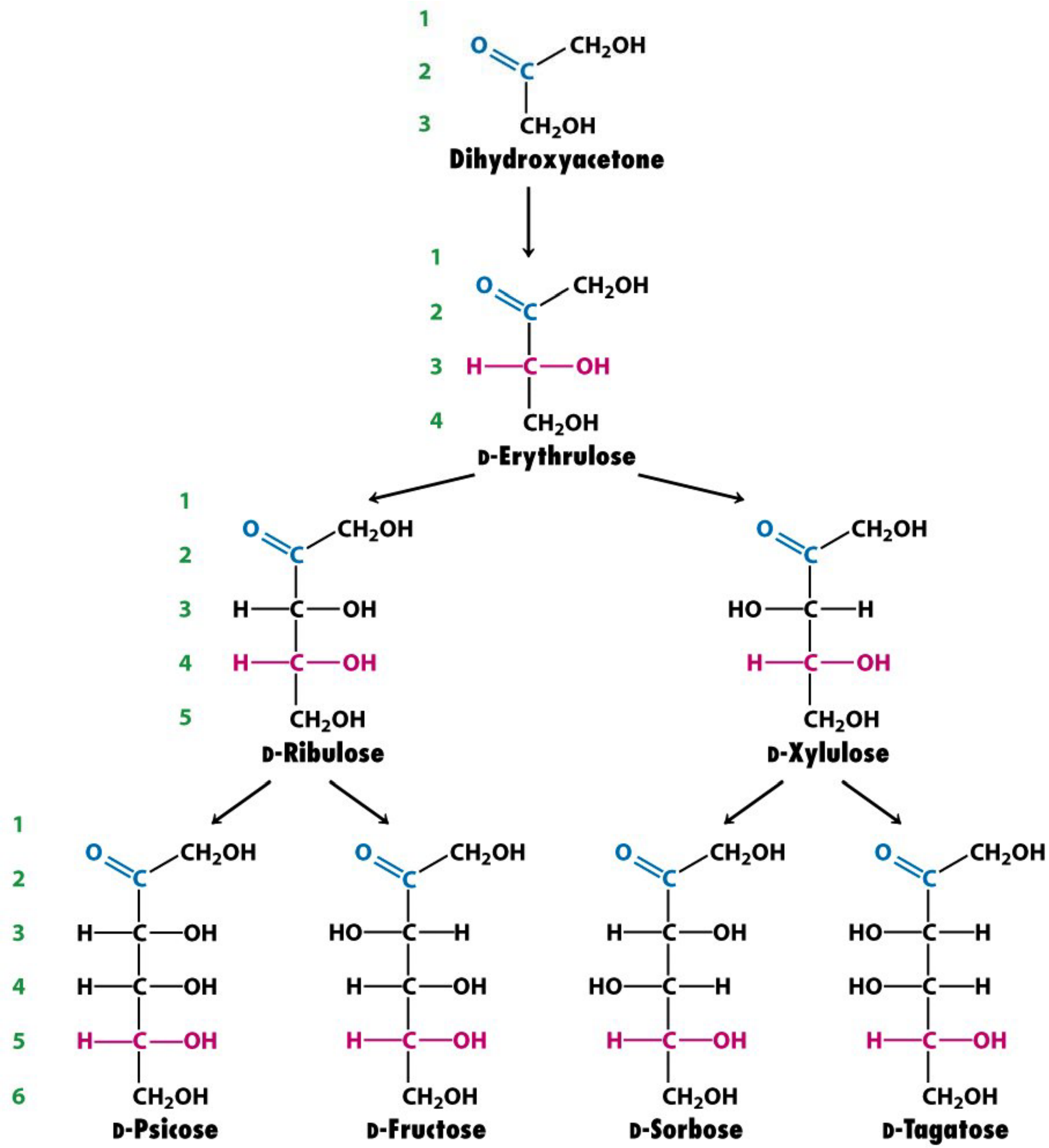

Figure 11-3
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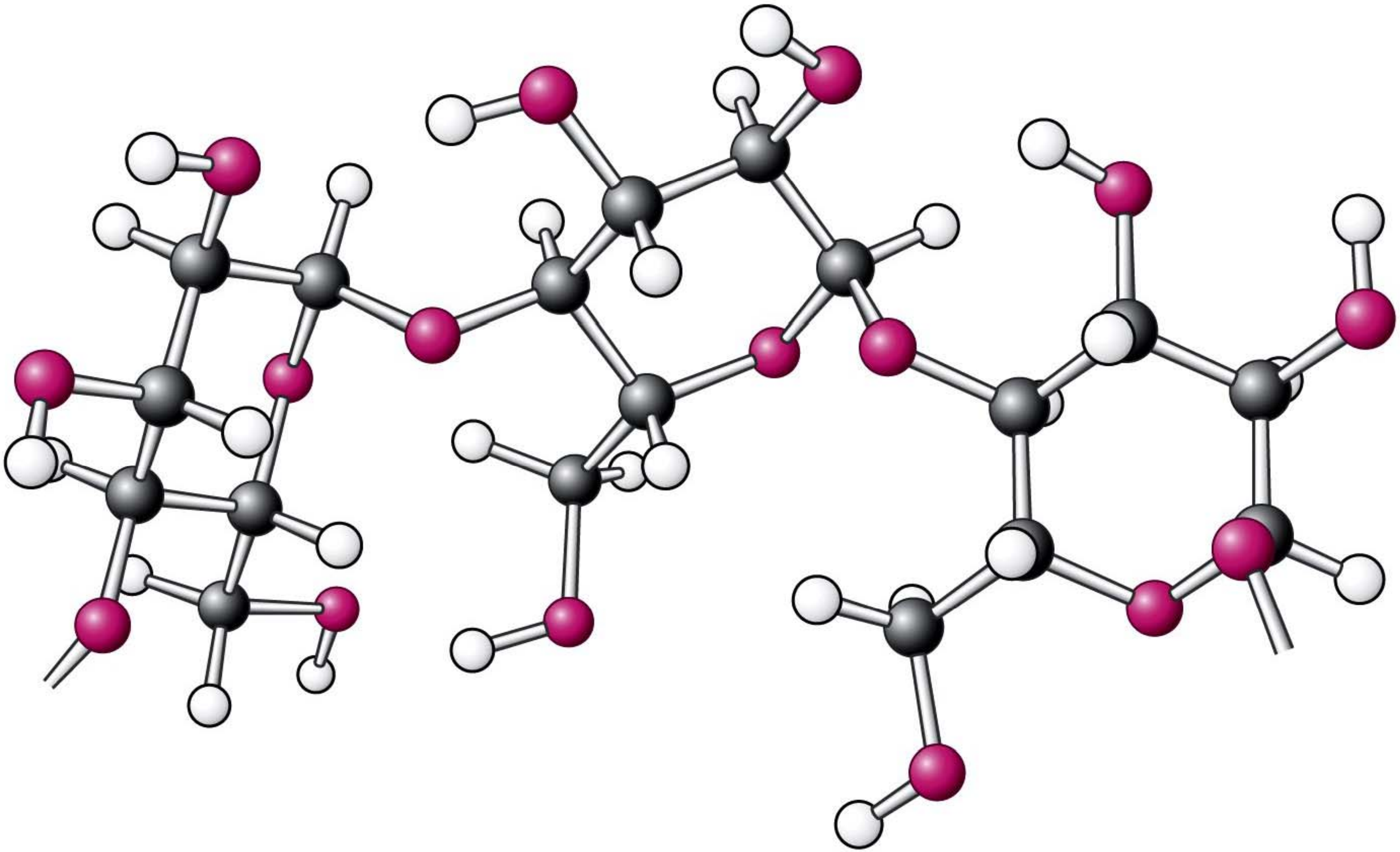


Chapter 11 Opener part 2
Biochemistry, Sixth Edition

- Carbohydrates are synthesized by photosynthesis in plants
  - Grains, cereals, bread, sugar cane
- Glucose is major energy source
  - A gram of digested carbohydrate gives about 4 kcal of energy
  - Complex carbohydrates are best for diet
  - FDA recommends about 58% daily calories from carbohydrates

Basic Carbohydrate Types

- Monosaccharides
  - *e.g.*, glucose, fructose
  - One sugar (saccharide) molecule
- Disaccharides
  - *e.g.*, sucrose, lactose
  - Two monosaccharides linked together
  - Linkage is called a glycosidic bond
- Oligosaccharides
  - Three to ten monosaccharides linked by glycosidic bonds
- Polysaccharides
  - *e.g.*, starch, glycogen, cellulose
  - Chains of linked monosaccharide units

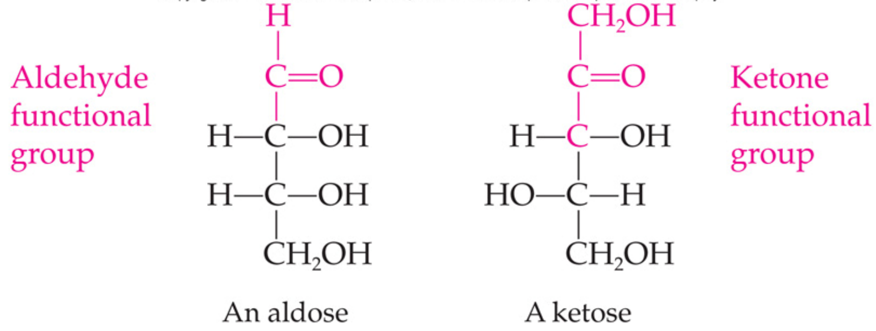
Monosaccharides

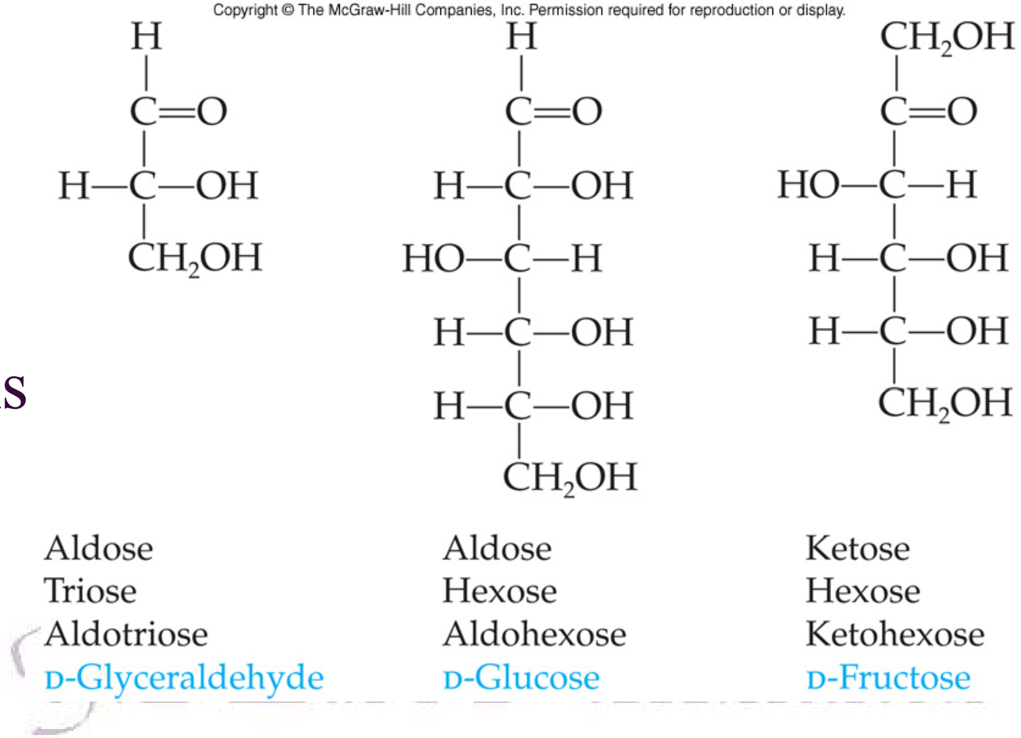
- Monosaccharides are composed of:
  - Carbon
  - Hydrogen
  - Oxygen
  - Basic Formula = $(CH_2O)_n$ n = any integer 3 – 7
- Many monosaccharides also contain chemical modifications
  - Amino groups
  - Phosphate groups

Naming Monosaccharides

Named on the basis of

- Functional groups
  - Ketone carbonyl = ketose
  - Aldehyde carbonyl = aldose
- Number of carbon atoms in the main skeleton
  - 3 carbons = triose
  - 4 carbons = tetrose
  - 5 carbons = pentose
  - 6 carbons = hexose
- Combine both systems gives even more information





A Human *Perspective*

Tooth Decay and Simple Sugars

How many times have you heard the lecture from parents or your dentist about brushing your teeth after a sugary snack? Annoying as this lecture might be, it is based on sound scientific data that demonstrate that the cause of tooth decay is plaque and acid formed by the bacterium *Streptococcus mutans* using sucrose as its substrate.

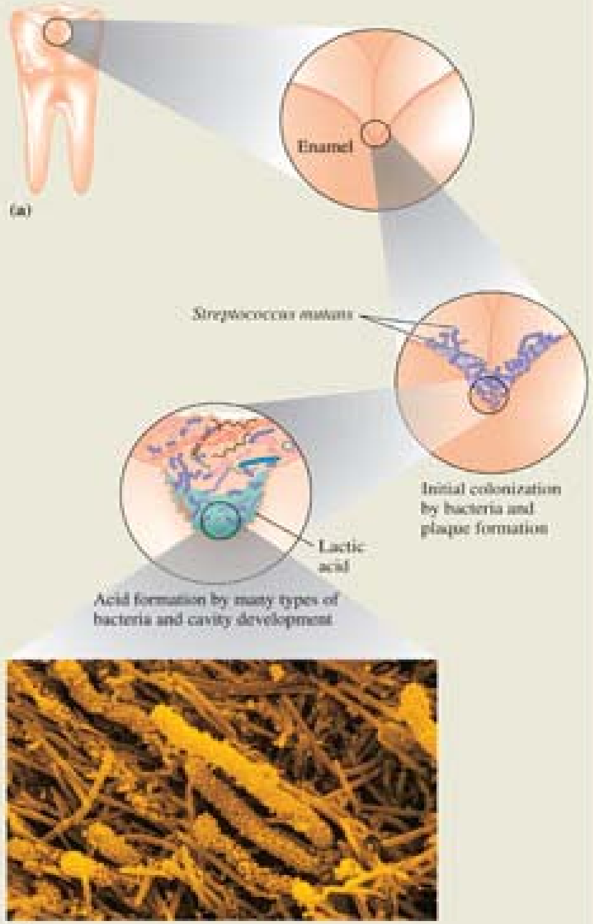
Saliva is teeming with bacteria in concentrations up to one hundred million (10^8) per milliliter of saliva! Within minutes after you brush your teeth, sticky glycoproteins in the saliva adhere to tooth surfaces. Then millions of oral bacteria immediately bind to this surface.

Although many oral bacteria stick to the tooth surface, as the diagram below shows, only *S. mutans* causes cavities. The reason for this is that this organism alone can make the enzyme *glucosyl transferase.* This enzyme acts only on the disaccharide sucrose, breaking it down into glucose and fructose. The glucose is immediately added to a growing polysaccharide called *dextran,* the glue that allows the bacteria to adhere to the tooth surface, contributing to the formation of plaque.

Now the bacteria embedded in the dextran take in the fructose and use it in the lactic acid fermentation. The lactic acid that is produced lowers the pH on the tooth surface and begins to dissolve calcium from the tooth enamel. Even though we produce about one liter of saliva each day, the acid cannot be washed away from the tooth surface because the dextran plaque is not permeable to saliva.

So what can we do to prevent tooth decay? Of course, brushing after each meal and flossing regularly reduce plaque buildup. Eating a diet rich in calcium also helps build strong tooth enamel. Foods rich in complex carbohydrates, such as fruits and vegetables, help prevent cavities in two ways. Glucosyl transferase can't use complex carbohydrates in its cavity-causing chemistry, and eating fruits and vegetables helps to mechanically remove plaque.

Perhaps the most effective way to prevent tooth decay is to avoid sucrose-containing snacks between meals. Studies have shown that eating sucrose-rich foods doesn't cause much tooth decay if followed immediately by brushing. However, even small amounts of sugar eaten between meals actively promote cavity formation.



(a) The complex process of tooth decay. (b) Electron micrograph of dental plaque.

For Further Understanding

It has been suggested that tooth decay could be prevented by a vaccine that would rid the mouth of *Streptococcus mutans.* Explain this from the point of view of the chemical reactions that are described above.

What steps could you take following a sugary snack to help prevent tooth decay, even when it is not possible to brush your teeth?

Stereoisomers and Stereochemistry

- Prefixes D- and L- in a monosaccharide name identify one of two isomeric forms
  - These isomers differ in the spatial arrangement of atoms and are stereoisomers
- Stereochemistry is the study of different spatial arrangements of atoms
- The stereoisomers D- and L- glyceraldehyde are nonsuperimposable mirror image molecules and are called enantiomers (a subset of stereoisomers)

Presentation

Chemistry *Connection*

Chemistry Through the Looking Glass

In his children's story *Through the Looking Glass,* Lewis Carroll's heroine Alice wonders whether "looking-glass milk" would be good to drink. As we will see in this chapter, many biological molecules, such as the sugars, exist as two stereoisomers, *enantiomers,* that are mirror images of one another. Because two mirror-image forms occur, it is rather remarkable that in our bodies, and in most of the biological world, only one of the two is found. For instance, the common sugars are members of the D-family, whereas all the common amino acids that make up our proteins are members of the L-family. It is not too surprising, then, that the enzymes in our bodies that break down the sugars and proteins we eat are *stereospecific,* that is, they recognize only one mirror-image isomer. Knowing this, we can make an educated guess that "looking-glass milk" could not be digested by our enzymes and therefore would not be a good source of food for us. It is even possible that it might be toxic to us!

Pharmaceutical chemists are becoming more and more concerned with the stereochemical purity of the drugs that we take. Consider a few examples. In 1960 the drug thalidomide was commonly prescribed in Europe as a sedative. However, during that year, hundreds of women who took thalidomide during pregnancy gave birth to babies with severe birth defects. Thalidomide, it turned out, was a mixture of two enantiomers. One is a sedative; the other is a teratogen, a chemical that causes birth defects.

One of the common side effects of taking antihistamines for colds or allergies is drowsiness. Again, this is the result of the fact that antihistamines are mixtures of enantiomers. One causes drowsiness; the other is a good decongestant.

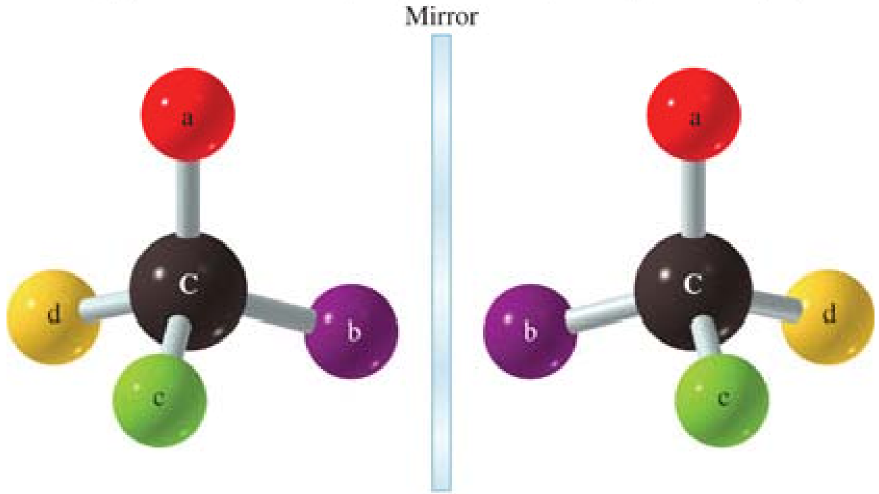
One enantiomer of the compound carvone is associated with the smell of spearmint; the other produces the aroma of caraway seeds or dill. One mirror-image form of limonene smells like lemons; the other has the aroma of oranges.

The pain reliever ibuprofen is currently sold as a mixture of enantiomers, but one is a much more effective analgesic than the other.

Taste, smell, and the biological effects of drugs in the body all depend on the stereochemical form of compounds and their interactions with cellular enzymes or receptors. As a result, chemists are actively working to devise methods of separating the isomers in pure form. Alternatively, methods of conducting stereospecific syntheses that produce only one stereoisomer are being sought. By preparing pure stereoisomers, the biological activity of a compound can be much more carefully controlled. This will lead to safer medications.

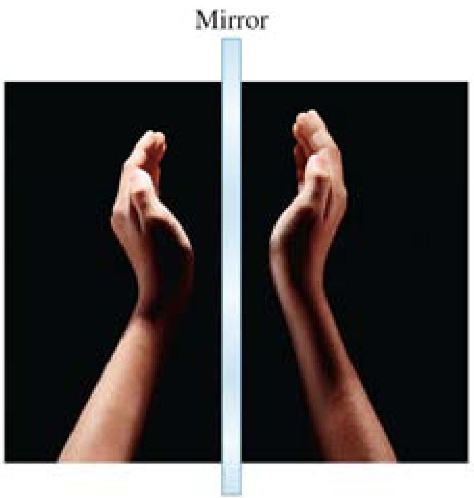
In this chapter we will begin our study of stereochemistry, the spatial arrangement of atoms in molecules, with the carbohydrates. Later, we will examine the stereochemistry of the amino acids that make up our proteins and consider the stereochemical specificity of the metabolic reactions that are essential to life. A more complete treatment of stereochemistry is found online at www.mhhe.com/denniston5e, in Stereochemistry and Stereoisomers Revisited.

Enantiomers



(a)

Nonsuperimposable mirror images:
enantiomers



(b)

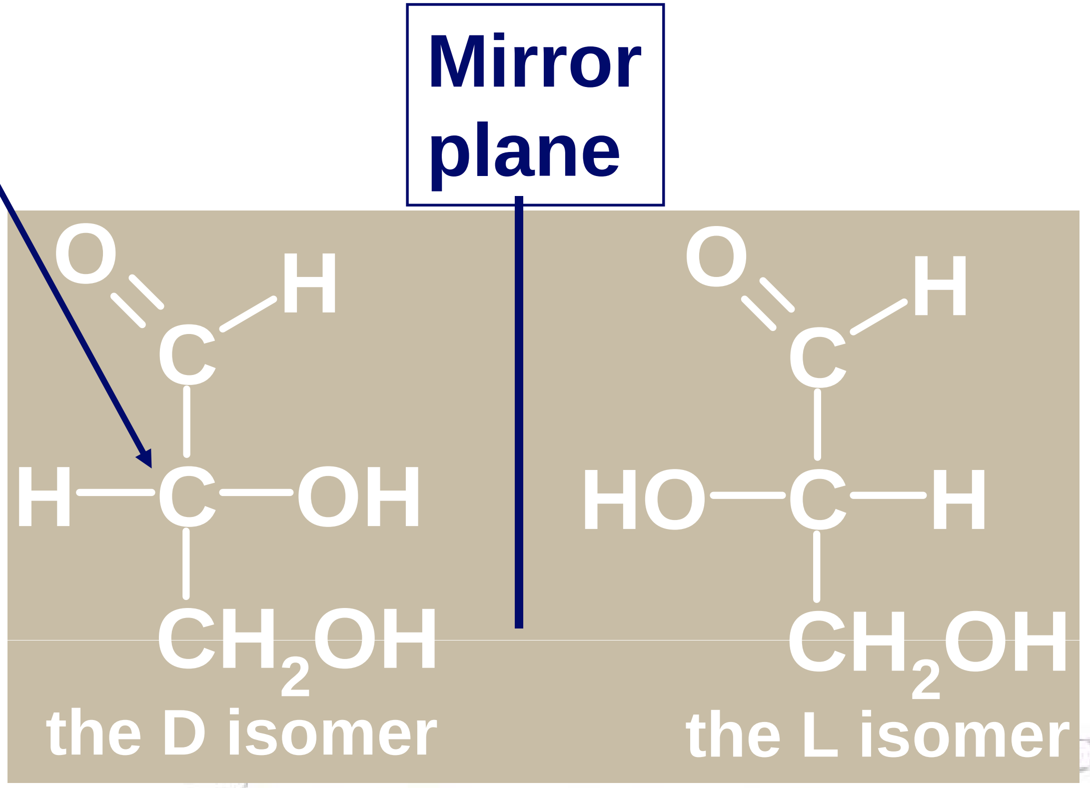
Chirality

- A carbon atom that has four different groups bonded to it is called a chiral carbon atom
- Any molecule containing a chiral carbon can exist as a pair of enantiomers
- Chirality in glyceraldehyde (the simplest carbohydrate) is conveyed by a chiral carbon
- Larger biological molecules often have more than one chiral carbon

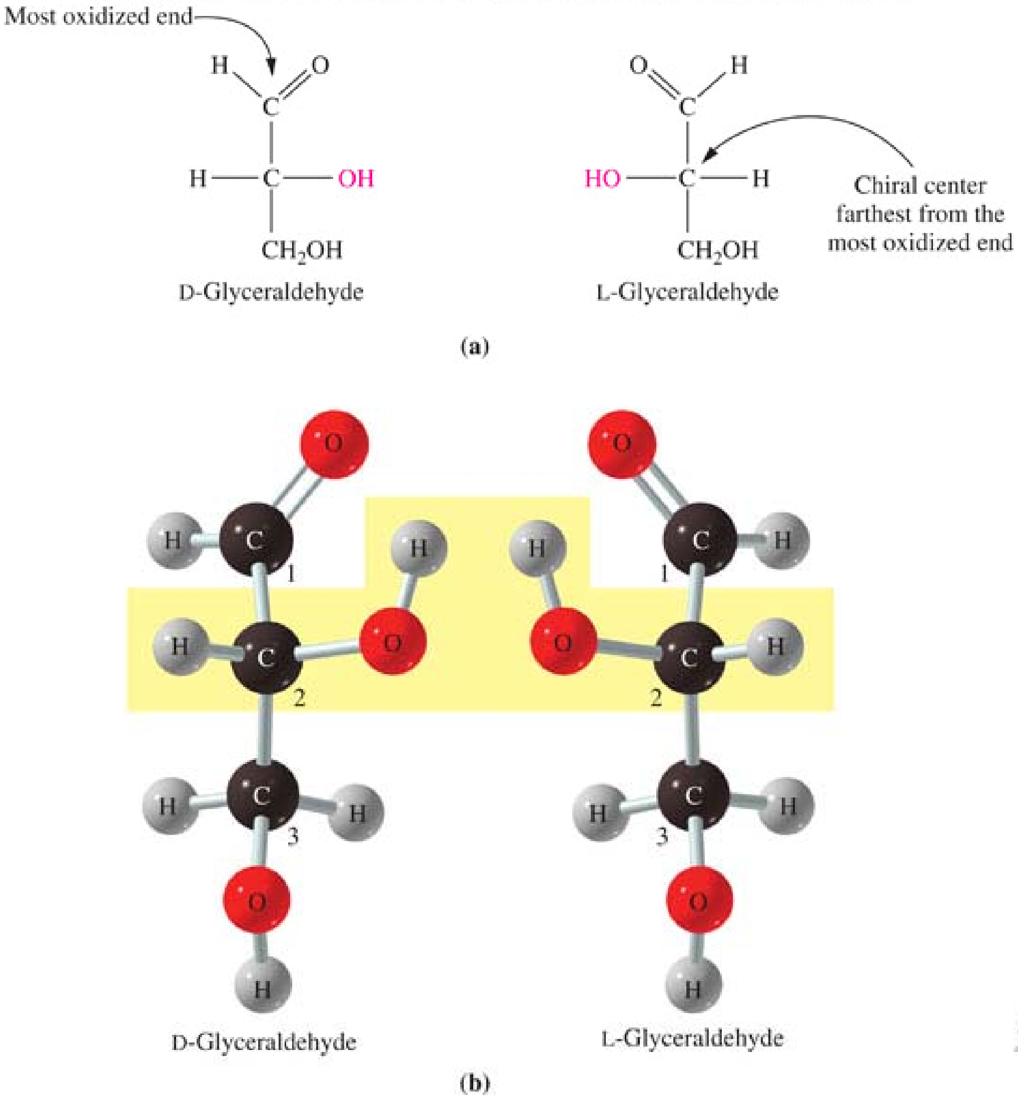
Chirality of Glyceraldehyde

- Glyceraldehyde has a chiral carbon and thus, has two enantiomers
  - The D isomer has the -OH on the stereocenter to the right
  - The L isomer has the -OH on the stereocenter to the left

Chiral Carbon: connected to four different atoms or groups



Structural Formulas of D- and L-Glyceraldehyde



4.1 Carbohydrates

sentation

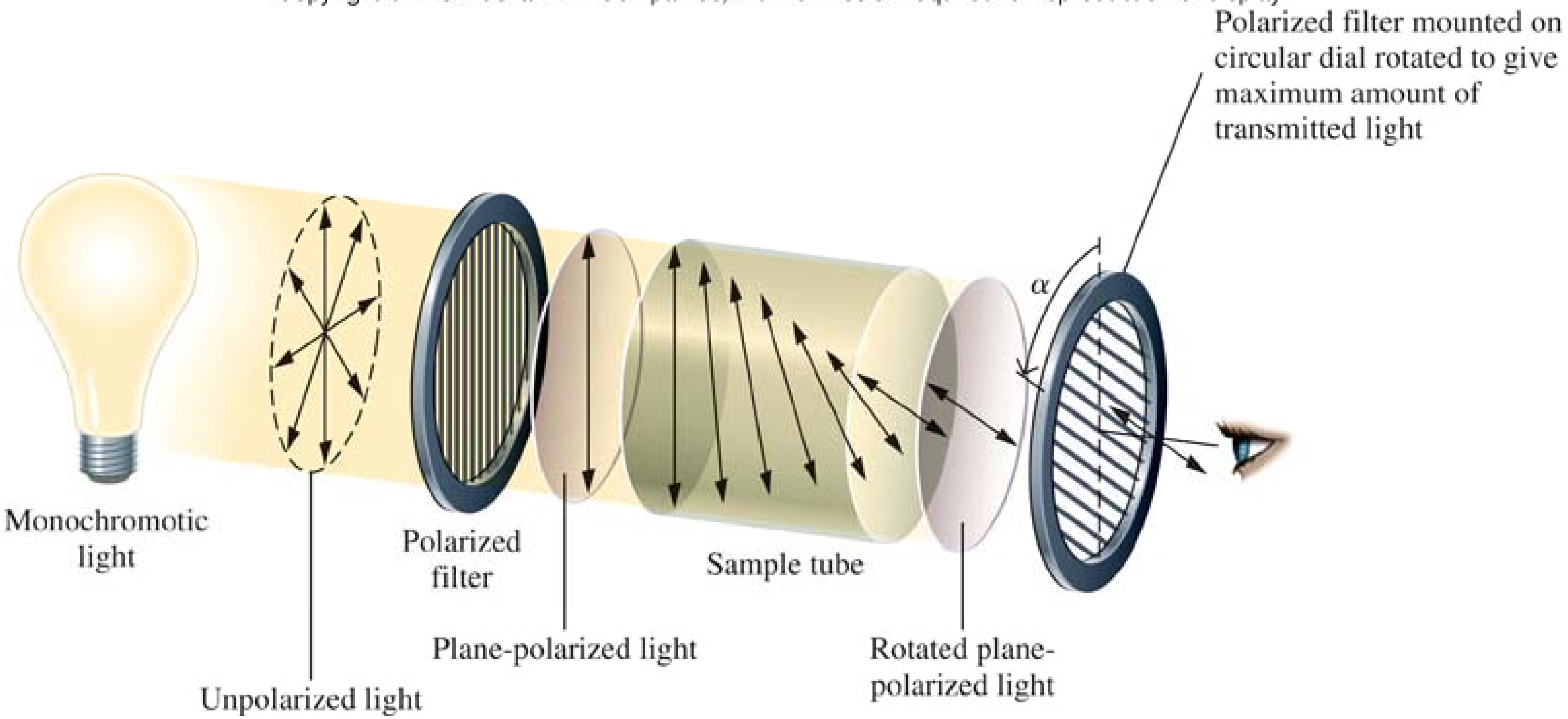
Optical Activity

- Enantiomers are also called optical isomers
- Enantiomers interact with plain polarized light to rotate the plane of the light in opposite directions
  - This interaction with polarized light is called optical activity
  - Optical activity distinguishes the isomers
  - It is measured in a device called a polarimeter

Polarized Light

- Normal light vibrates in an infinite number of directions perpendicular to the direction of travel
  - When the light passes through a polarizing filter (Polaroid sunglasses) only light vibrating in one plane reaches the other side of the filter
  - A polarimeter allows the determination of the specific rotation of a compound
    - Measures its ability to rotate plane-polarized light

Schematic Drawing of a Polarimeter

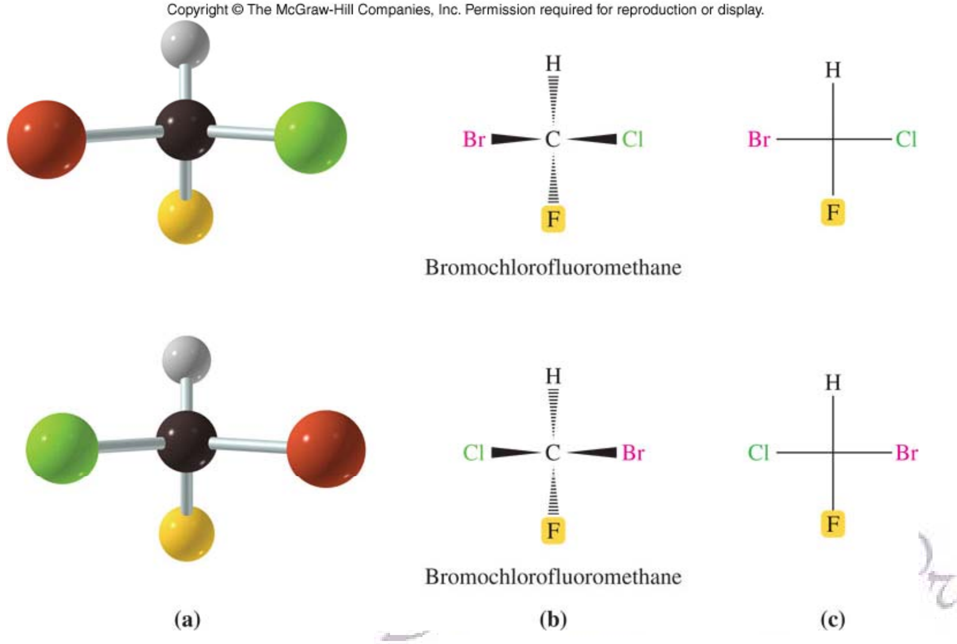


The Relationship Between Molecular Structure and Optical Activity

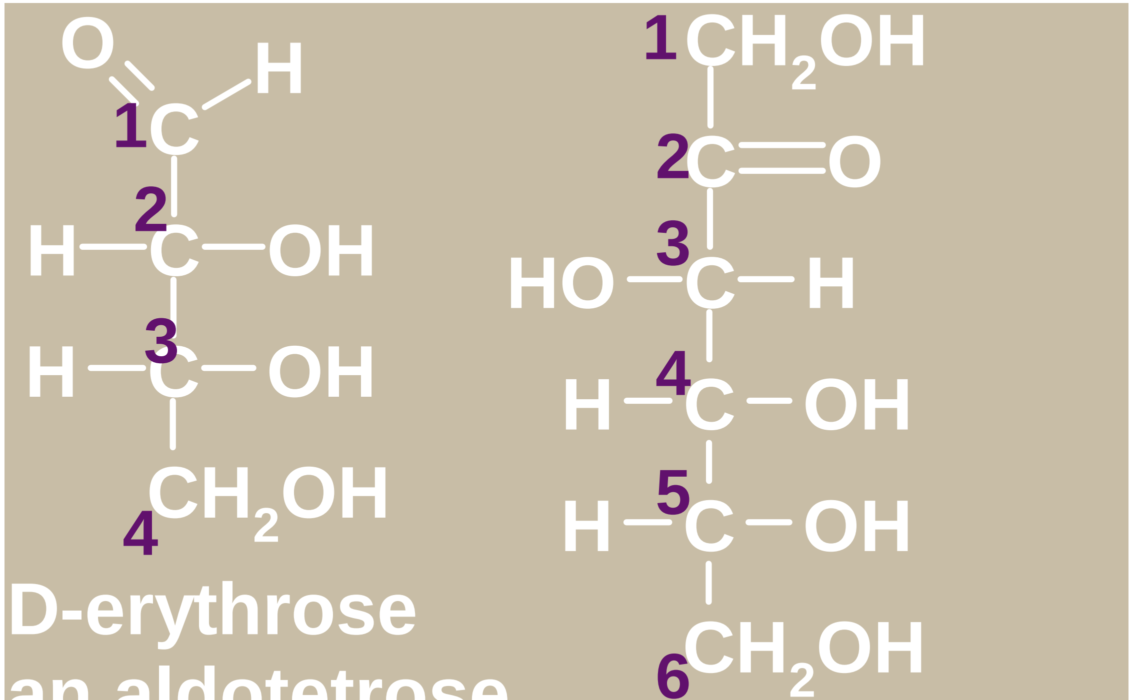
- When an enantiomer in a solution is placed in the polarimeter, the plane of rotation of the polarized light is rotated
  - One enantiomer always rotates light in a clockwise (+) direction
    - This is the dextrorotatory isomer
  - The other isomer rotates the light in a counterclockwise (-) direction
    - It is the levorotatory isomer
- Under identical conditions, the enantiomers always rotate light to exactly the same degree, but in opposite directions

Fischer Projection Formulas

- A Fischer projection uses lines crossing through a chiral carbon to represent bonds
  - Projecting out of the page (horizontal lines)
  - Projecting into the page (vertical lines)
- Compare the wedge to the Fischer diagrams



Fischer Projections of Monosaccharides



D-erythrose
an aldotetrose

D-fructose
a ketohexose

Drawing Fischer Projections for a Sugar

EXAMPLE 16.1

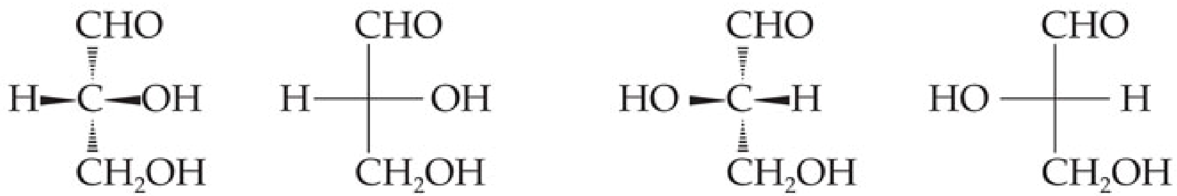
Draw the Fischer Projections for the stereoisomers of glyceraldehyde.

Solution

Review the structures of the two stereoisomers of glyceraldehydes (Figure 16.4b). The ball-and-stick models can be represented using three-dimensional wedge drawings. Remember that for sugars the most oxidized carbon (the aldehyde or ketone group) is always drawn at the top of the structure.

D-Glyceraldehyde L-Glyceraldehyde

Remember that in the wedge diagram, the solid wedges represent bonds directed toward the reader. The dashed wedges represent bonds directed away from the reader and into the page. In these molecules, the center carbon is the only chiral carbon in the structure. To convert these wedge representations to a Fischer Projection, simply use a horizontal line in place of each solid wedge and use a vertical line to represent each dashed wedge. The chiral carbon is represented by the point at which the vertical and horizontal lines cross, as shown below.

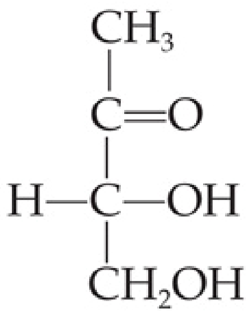


D-Glyceraldehyde L-Glyceraldehyde

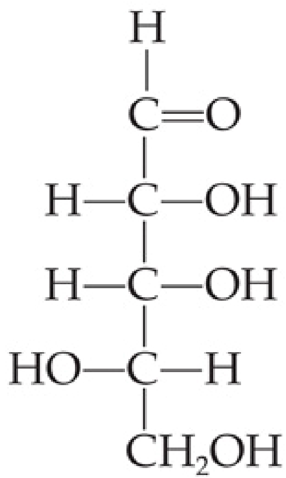
Aldose or Ketose?

Indicate whether each of the following molecules is an aldose or a ketose.

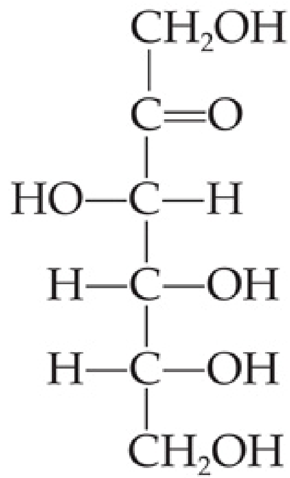
a.



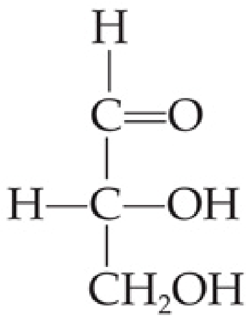
b.



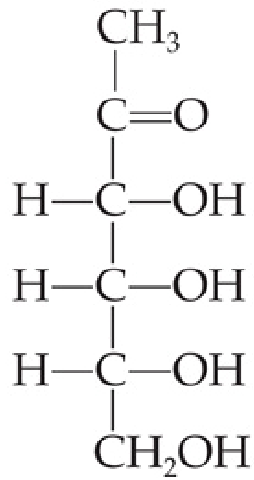
c.



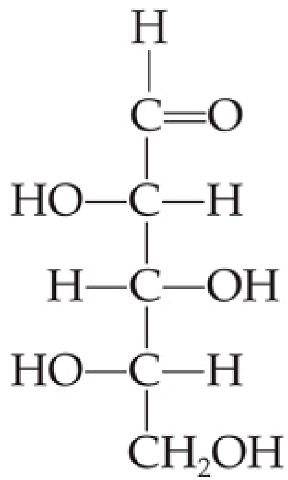
d.



e.

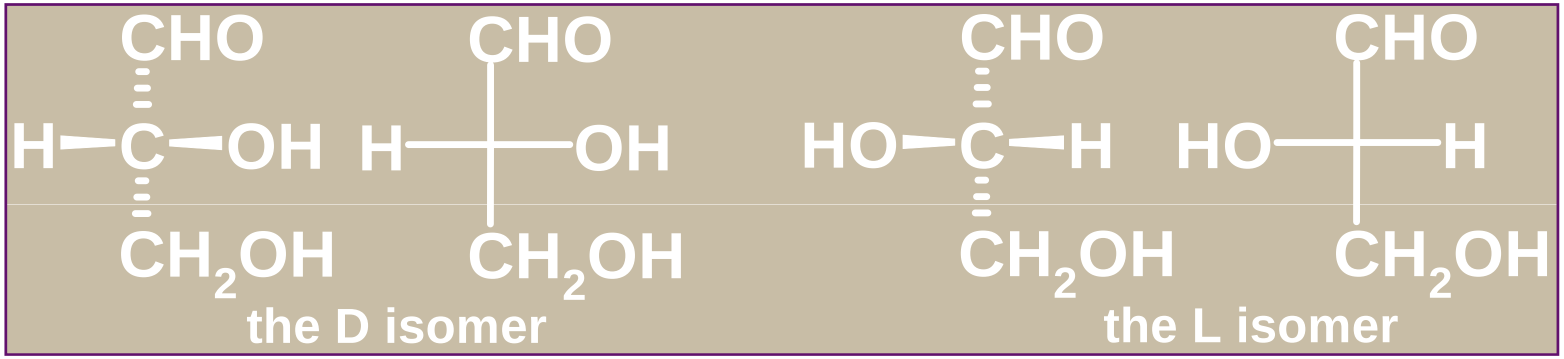


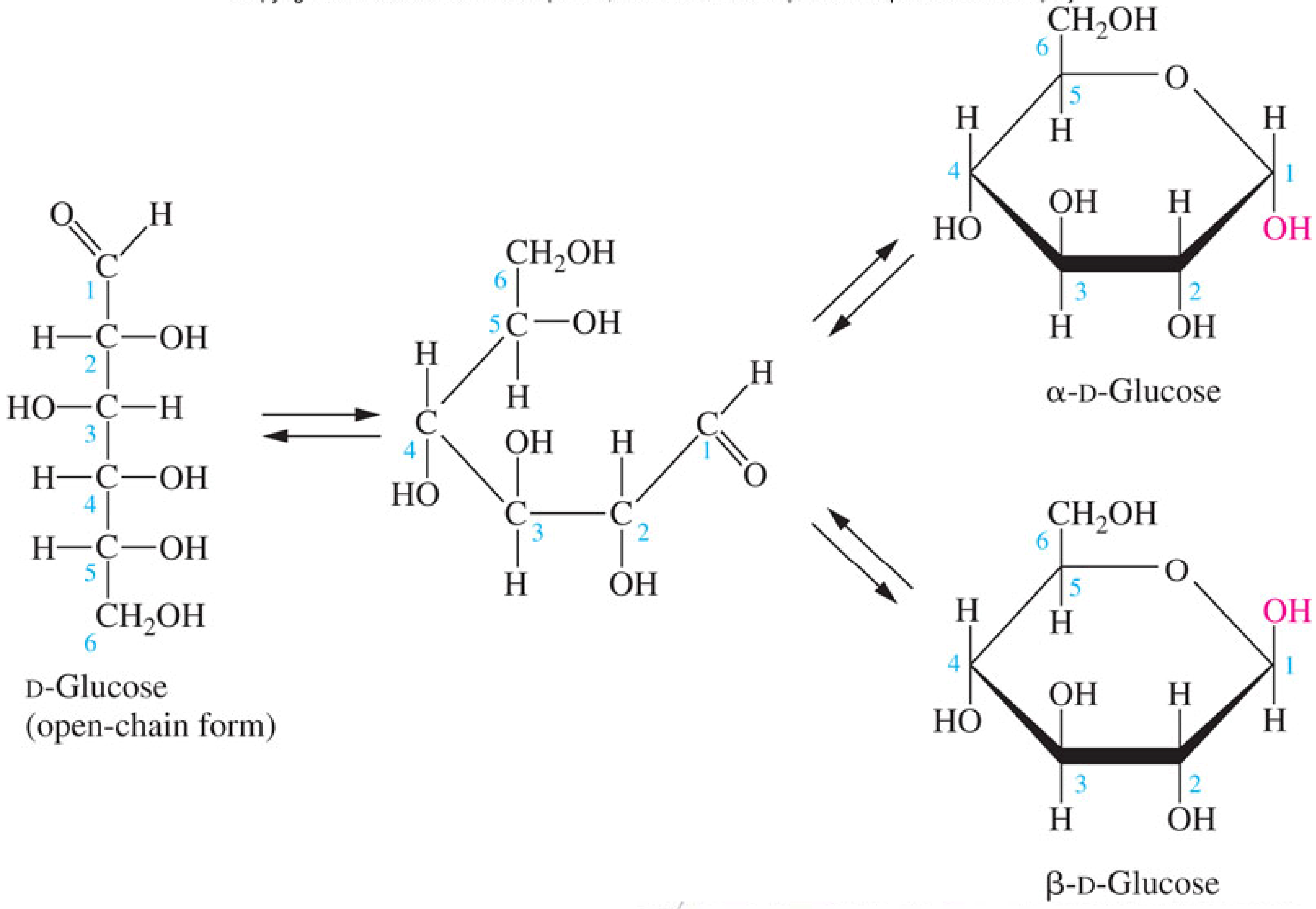
f.



The D- and L-System

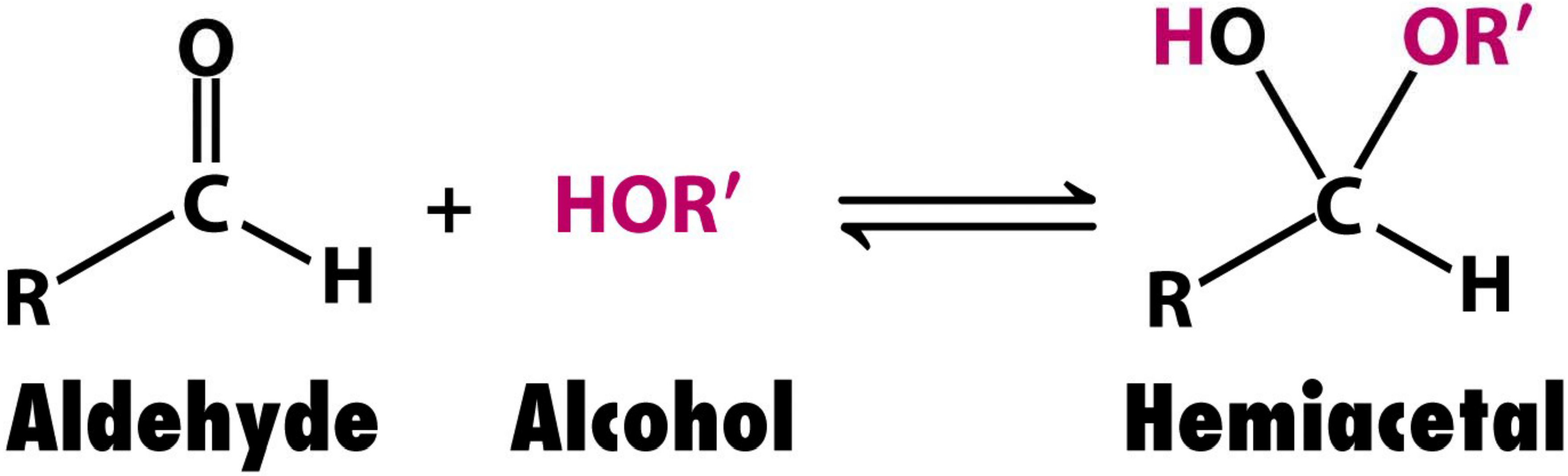
- Monosaccharides are drawn in Fischer projections
  - With the most oxidized carbon closest to the top
  - The carbons are numbered from the top
  - If the chiral carbon with the highest number has the OH to the right, the sugar is D
  - If the OH is to the left, the sugar is L
- Most common sugars are in the D form




D-Glucose
(open-chain form)
α-D-Glucose
β-D-Glucose

Biological Monosaccharides

- Glucose is the most important sugar in the human body
  - Found in many foods
  - Several common names include: dextrose and blood sugar
  - Its concentration in the blood is regulated by insulin and glucagon
- Under physiological conditions, glucose exists in a cyclic hemiacetal form where the C-5 hydroxyl reacts with the C-1 aldehyde group
  - Two isomers are formed which differ in the location of the -OH on the acetal carbon, C-1
- An aldohexose with molecular formula $C_6H_{12}O_6$



Unnumbered figure pg 306a
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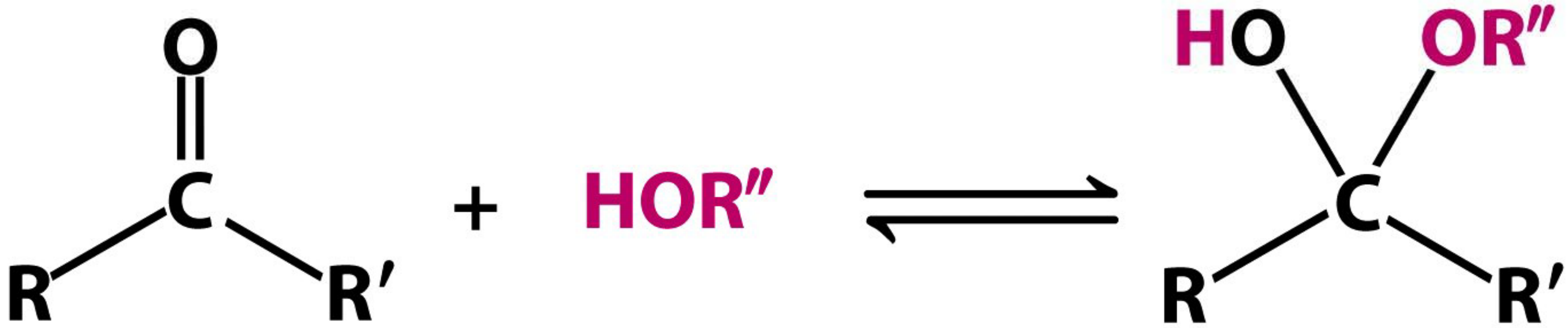

Ketone **Alcohol** **Hemiketal**

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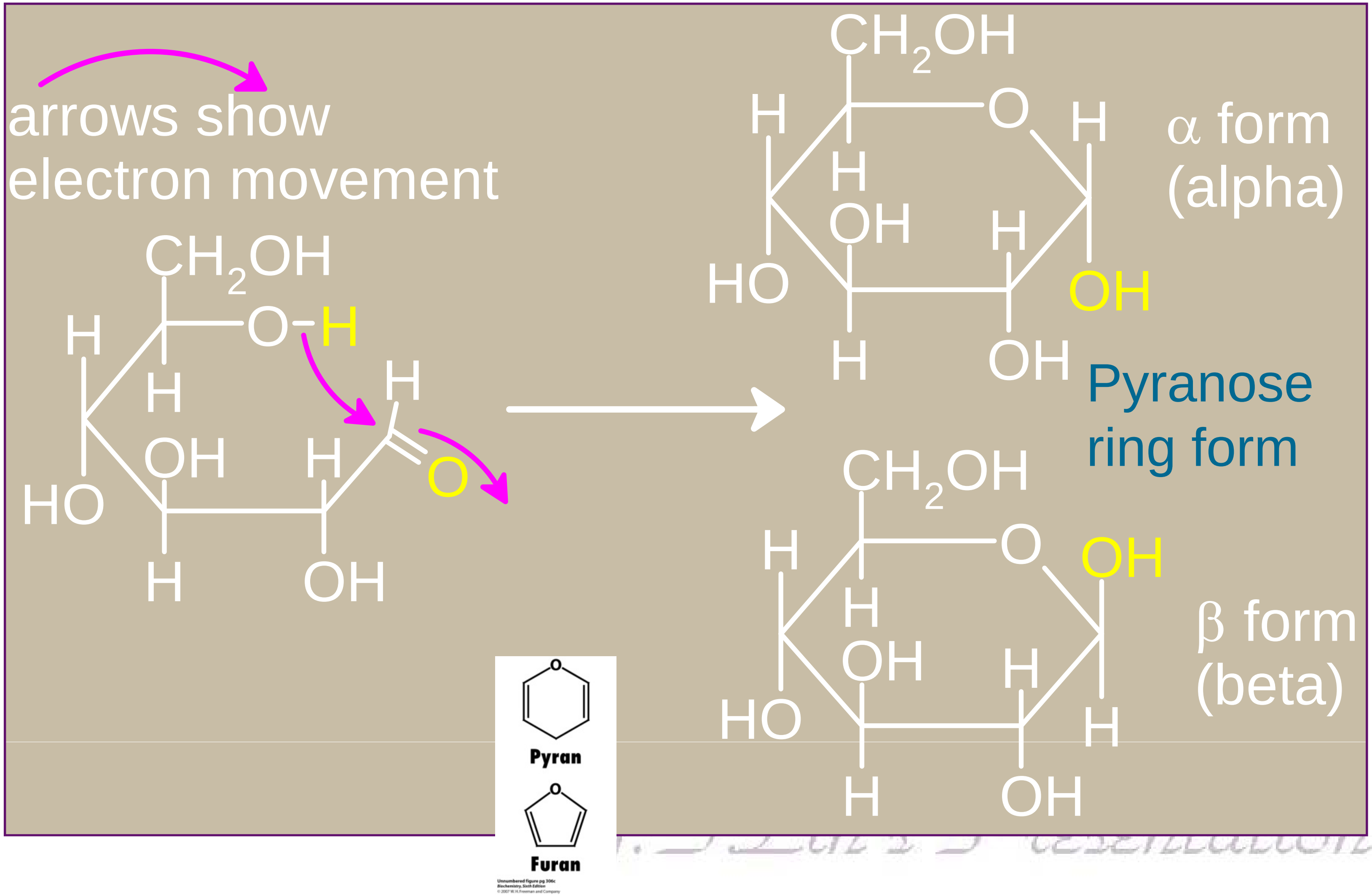
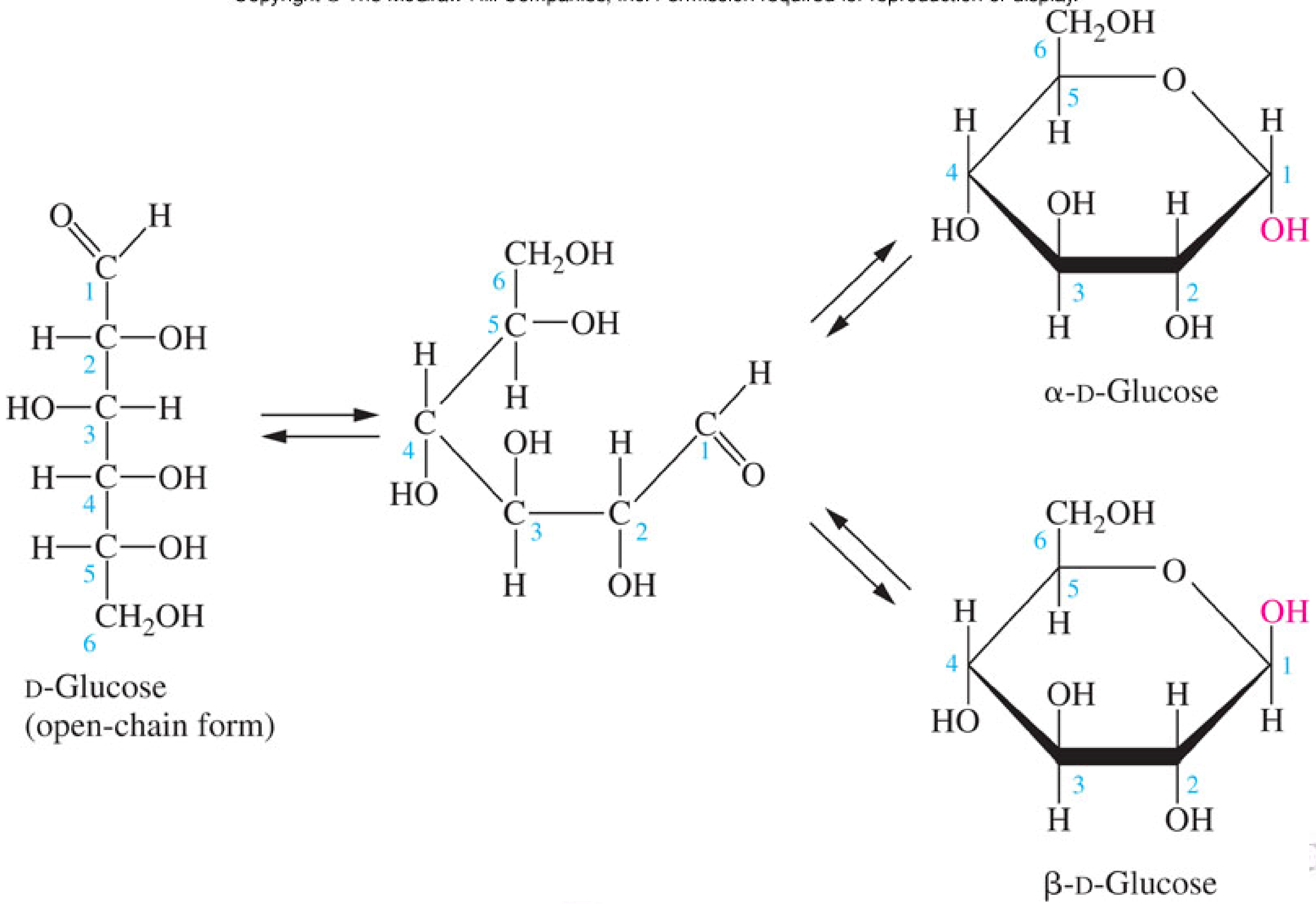
Cyclic Form of Glucose

- The cyclic form of glucose is shown as a Haworth projection



Cyclization of Glucose



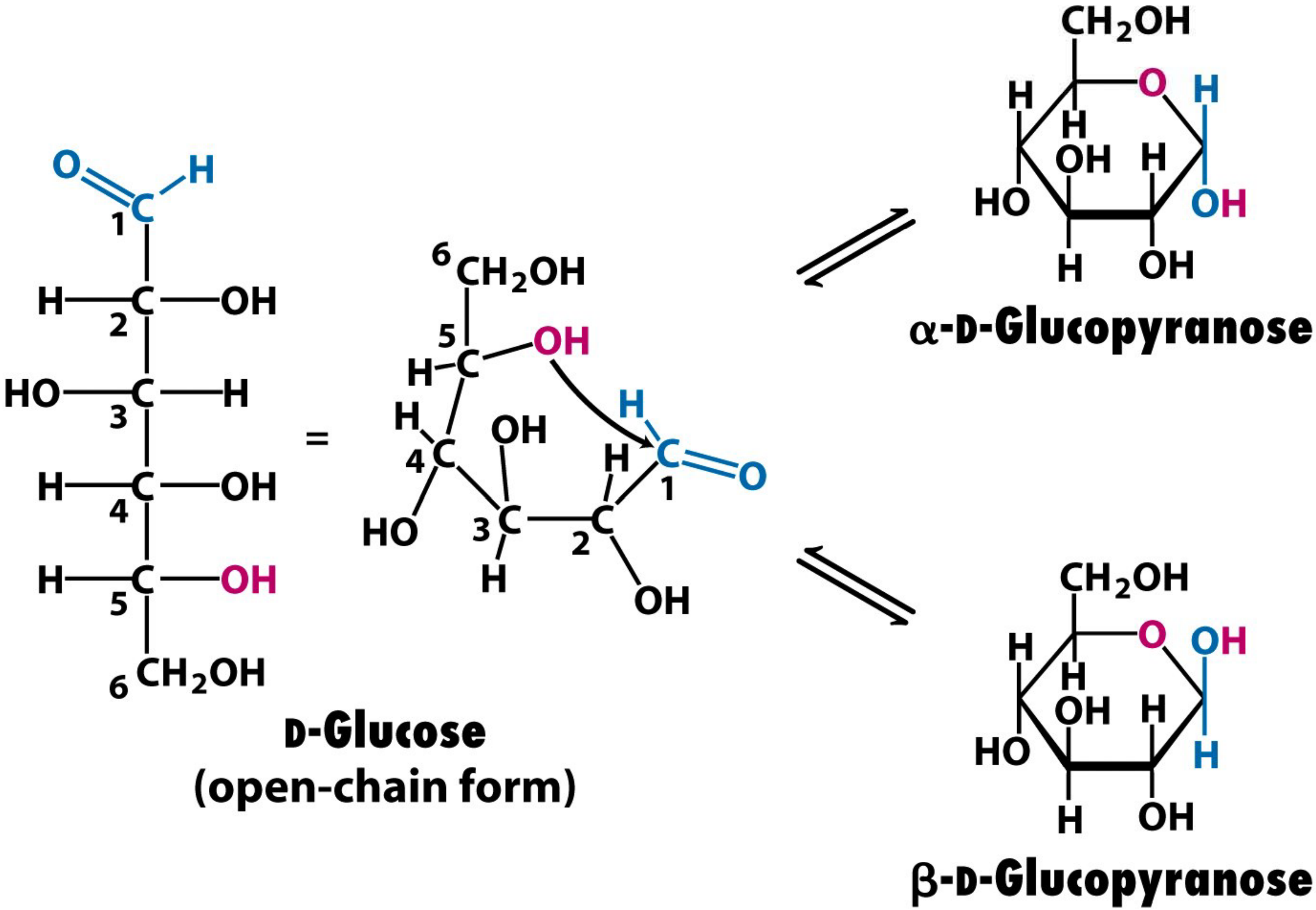


Figure 11-4
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Drawing the Structure of a Monosaccharide — EXAMPLE 16.2

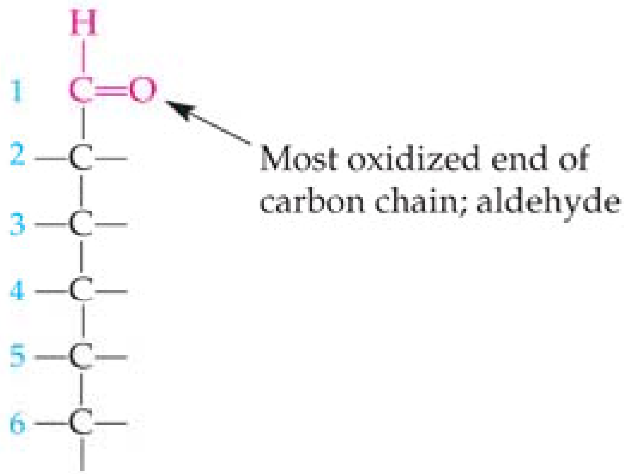
Draw the structure for D-glucose.

Solution

Glucose is an aldohexose.

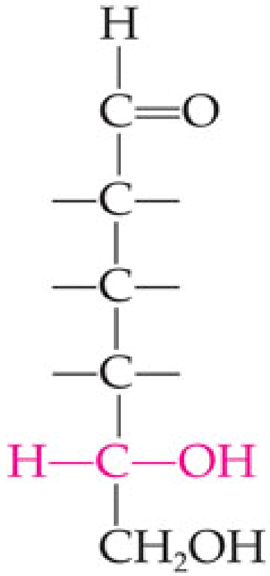
Step 1. Draw six carbons in a straight vertical line; each carbon is separated from the ones above and below it by a bond:

Step 2. The most highly oxidized carbon is, by convention, drawn as the uppermost carbon (carbon-1). In this case, carbon-1 is an aldehyde carbon:

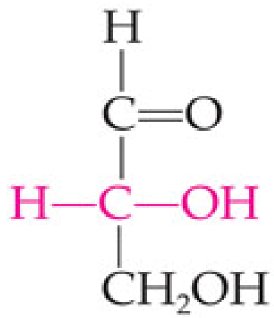


Continued—

Step 3. The atoms are added to the next to the last carbon atom, at the bottom of the chain, to give either the D- or L-configuration as desired. Remember, when the —OH group is to the right, you have D-glucose. When in doubt, compare your structure to D-glyceraldehyde!



D-Isomer



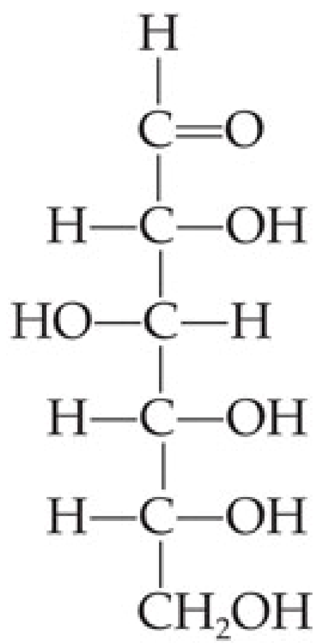
D-Glyceraldehyde

Compare chiral carbons farthest from the carbonyl group

Step 4. All the remaining atoms are then added to give the desired carbohydrate. For example, one would draw the following structure for D-glucose.

Continued—

EXAMPLE 16.2 —*Continued*



D-Glucose

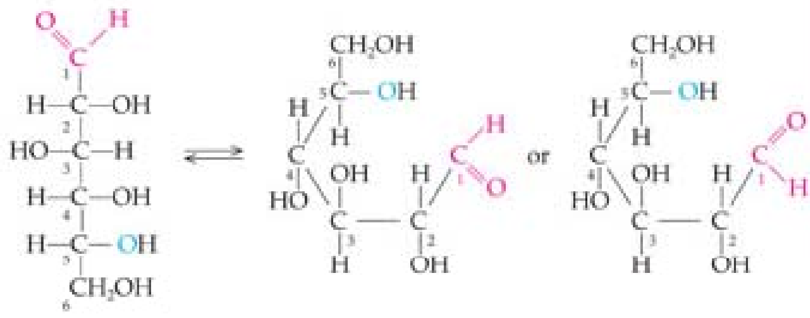
The positions for the hydrogen atoms and the hydroxyl groups on the remaining carbons must be learned for each sugar.

EXAMPLE 16.3 **Drawing the Haworth Projection of a Monosaccharide from the Structural Formula**

Draw the Haworth projections of α- and β-D-glucose.

Solution

1. Before attempting to draw a Haworth projection, look at the first steps of ring formation shown here:

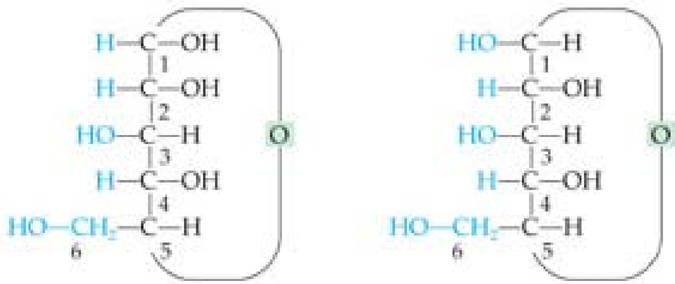


Glucose (open chain)

Glucose (intermediates in ring formation)

Try to imagine that you are seeing the molecules shown above in three dimensions. Some of the substituent groups on the molecule will be above the ring, and some will be beneath it. The question then becomes: How do you determine which groups to place above the ring and which to place beneath the ring?

2. Look at the two-dimensional structural formula. Note the groups (drawn in blue) to the left of the carbon chain. These are placed above the ring in the Haworth projection.

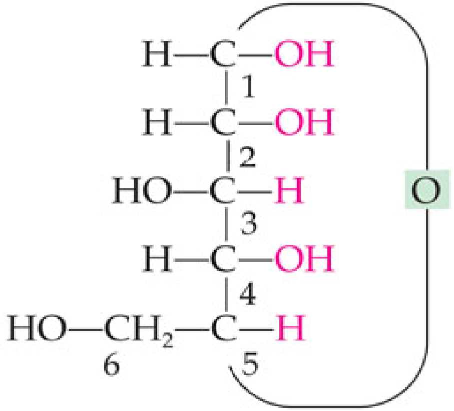


α-D-Glucose β-D-Glucose

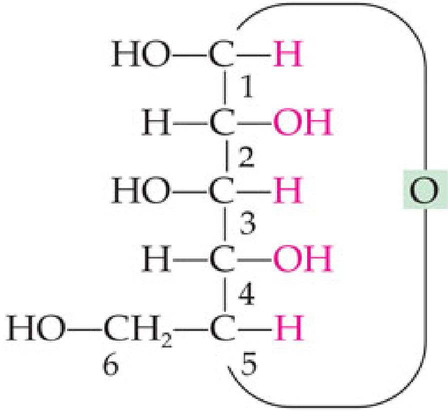
3. Now note the groups (drawn in red) to the right of the carbon chain. These will be located beneath the carbon ring in the Haworth projection.

Continued—

EXAMPLE 16.3 —*Continued*

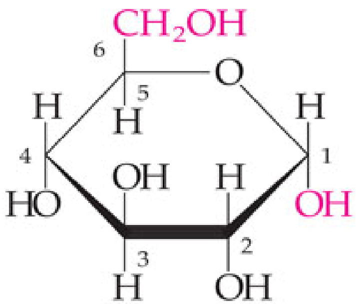


α-D-Glucose

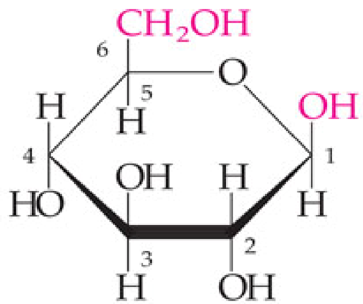


β-D-Glucose

4. Thus in the Haworth projection of the cyclic form of any D-sugar the —CH_2OH group is always "up." When the —OH group at C-1 is also "up," *cis* to the —CH_2OH group, the sugar is β-D-glucose. When the —OH group at C-1 is "down," *trans* to the —CH_2OH group, the sugar is α-D-glucose.



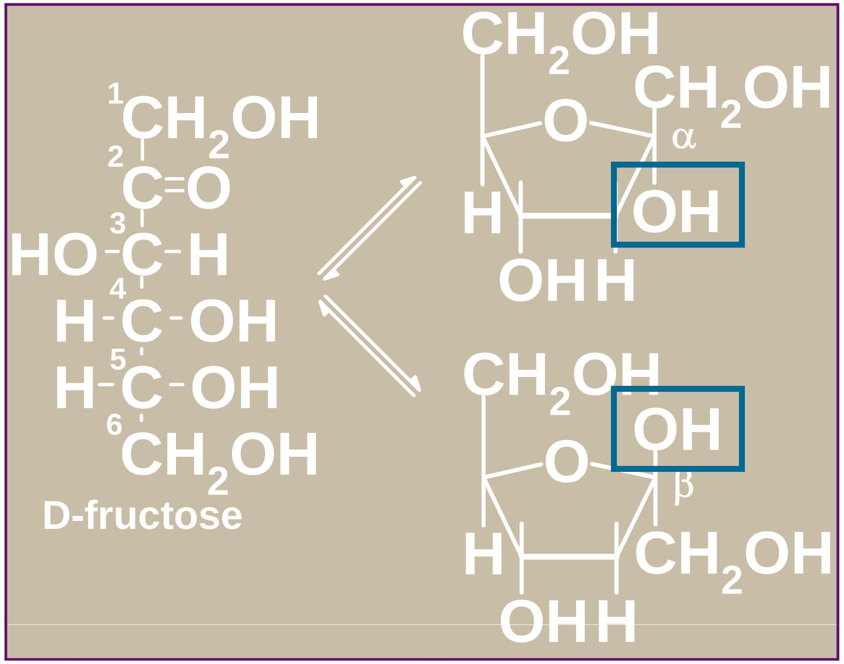
Haworth projection
α-D-Glucose



Haworth projection
β-D-Glucose

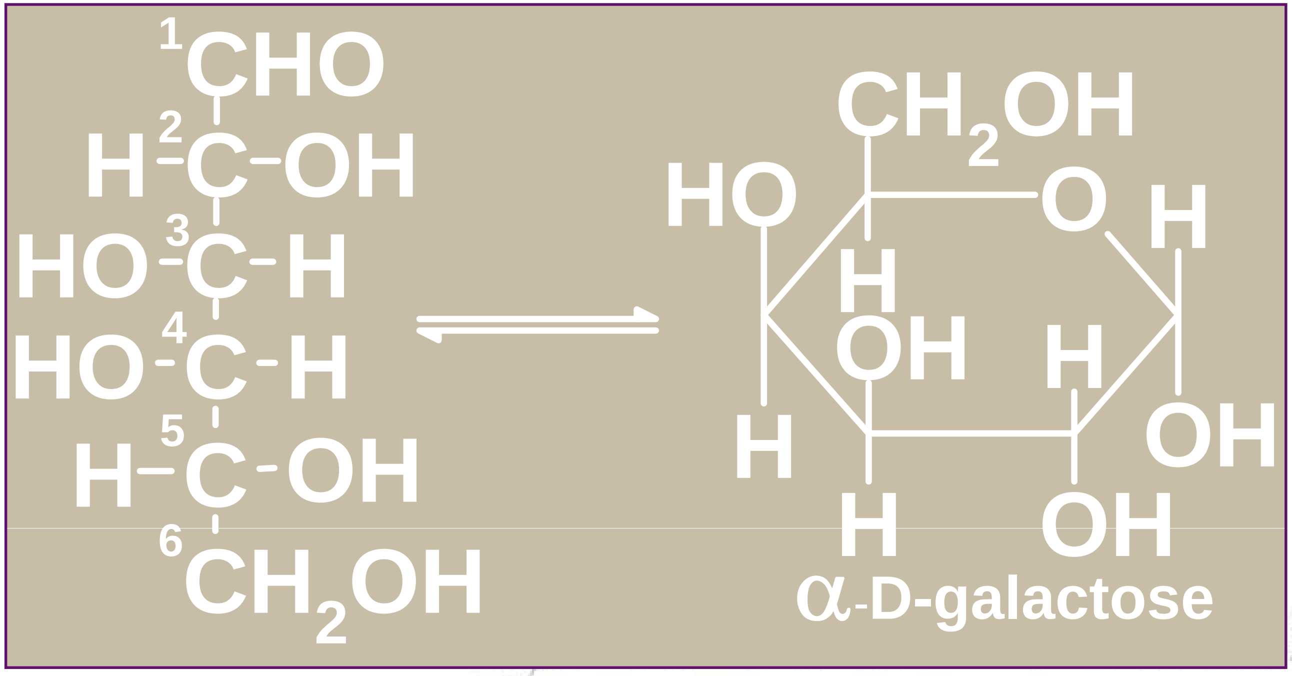
Fructose (果糖)

- Fructose is also called:
  - Levulose
  - Fruit sugar
- Found in large amounts in:
  - Honey
  - Corn syrup
  - Fruits
- The sweetest of all sugars
- Ketohexose



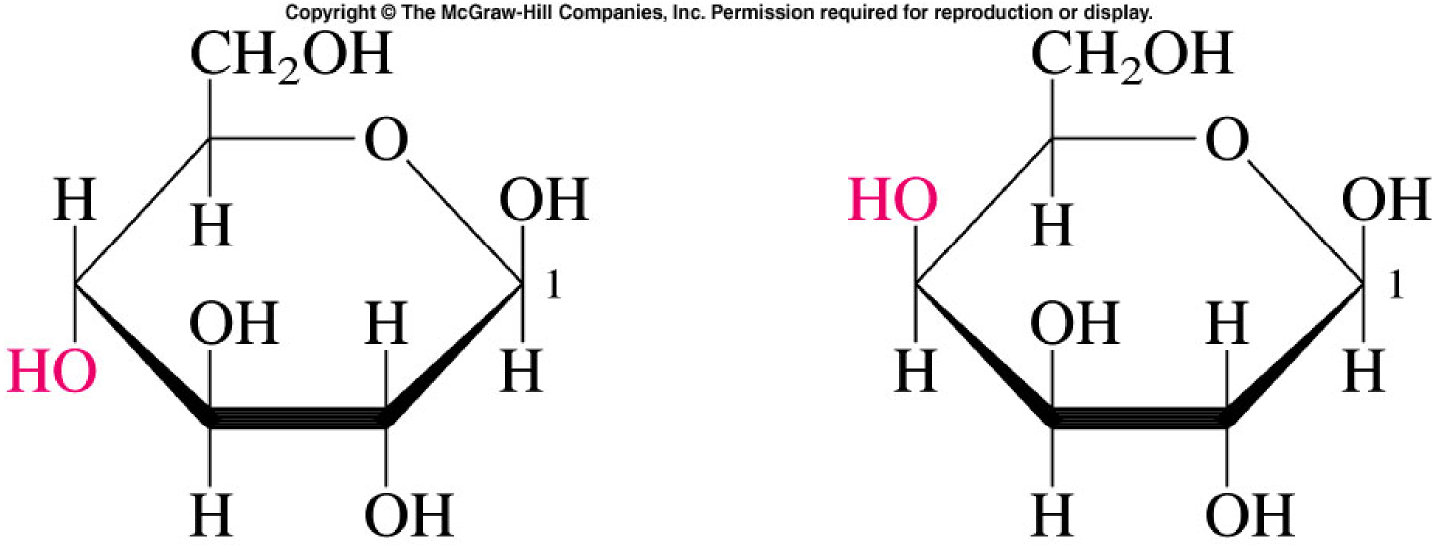
Galactose (半乳糖)

- Galactose is the principal sugar found in mammalian milk
- Aldohexose very similar to glucose
- β-D-galactosamine is a component of the blood group antigens



Galactose Orientation

Glucose and galactose differ only in the orientation of one hydroxyl group



β-D-Glucose *β*-D-Galactose

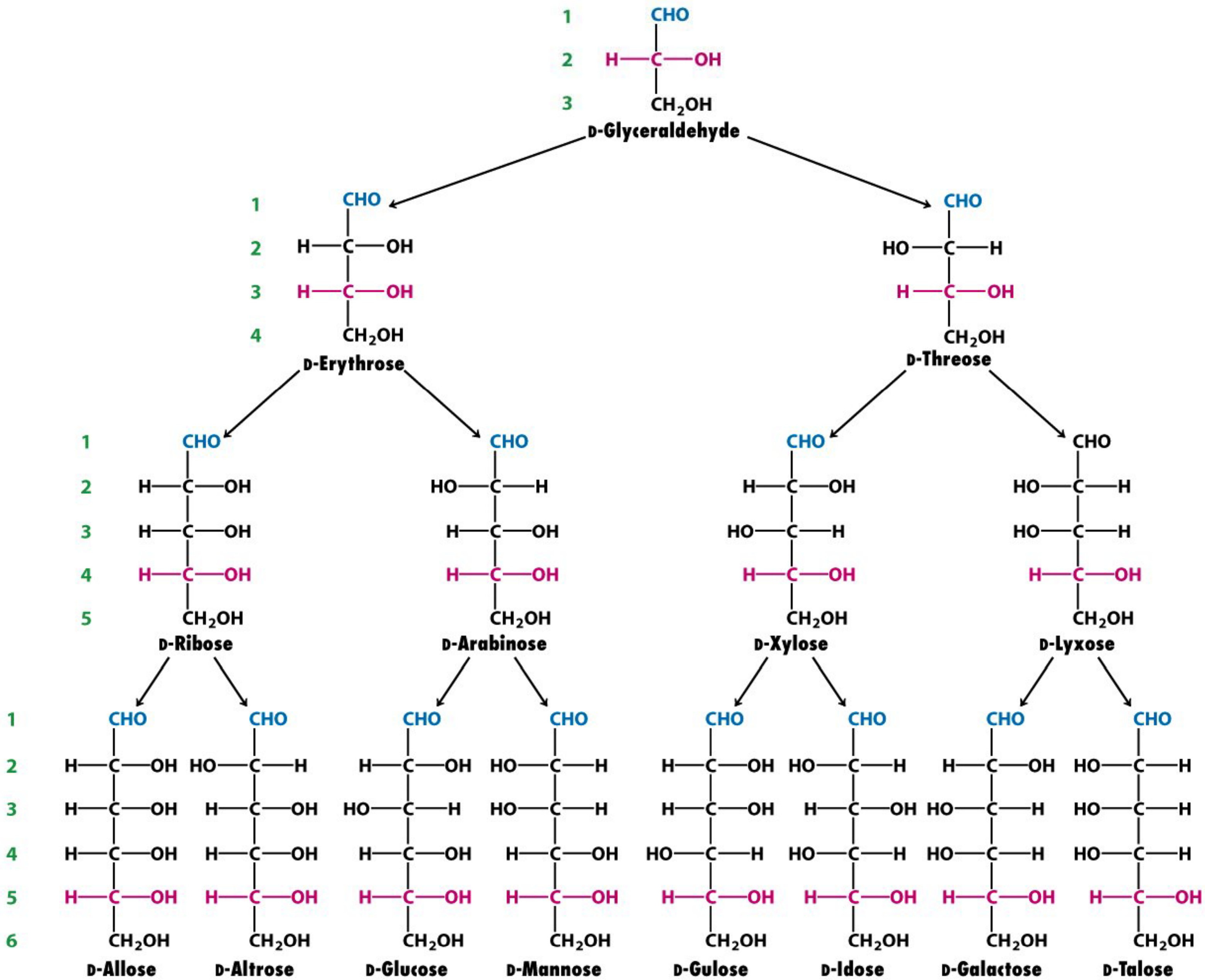


Figure 11-2
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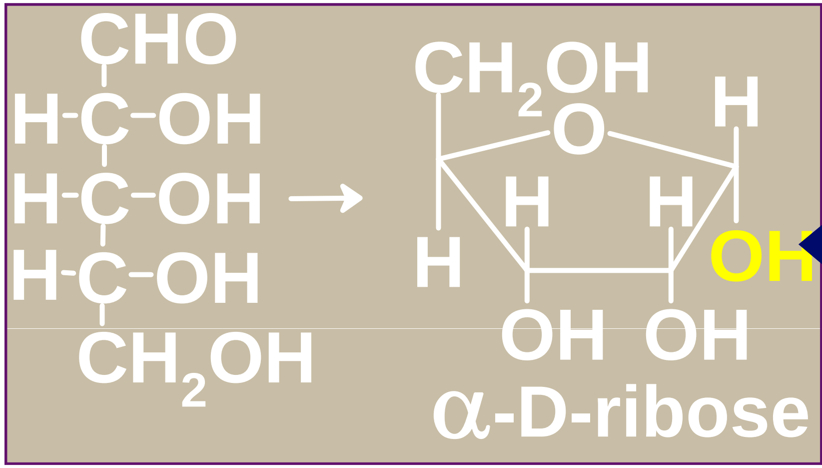
Ribose (核糖) and Deoxyribose (去氧核糖), Five-Carbon Sugars

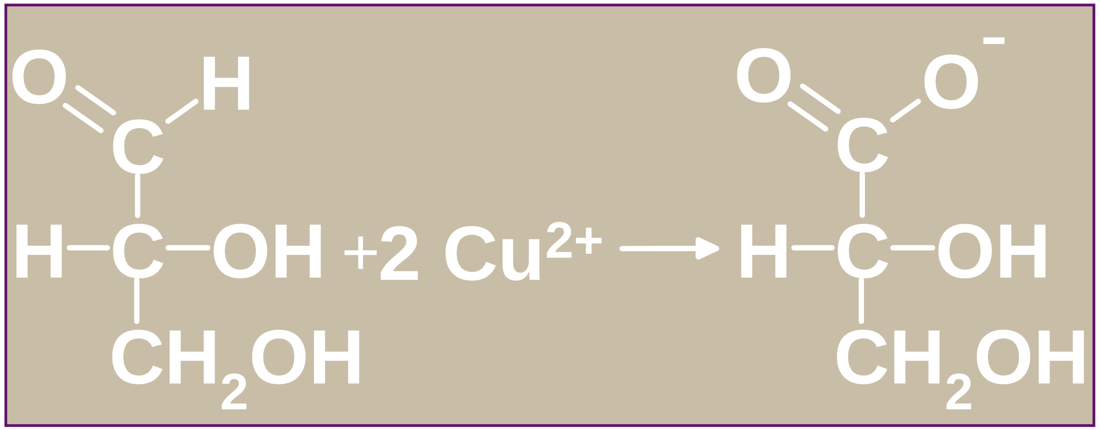
- Components of many biologically important molecules
- Exists mainly in the cyclic form
- Aldopentose



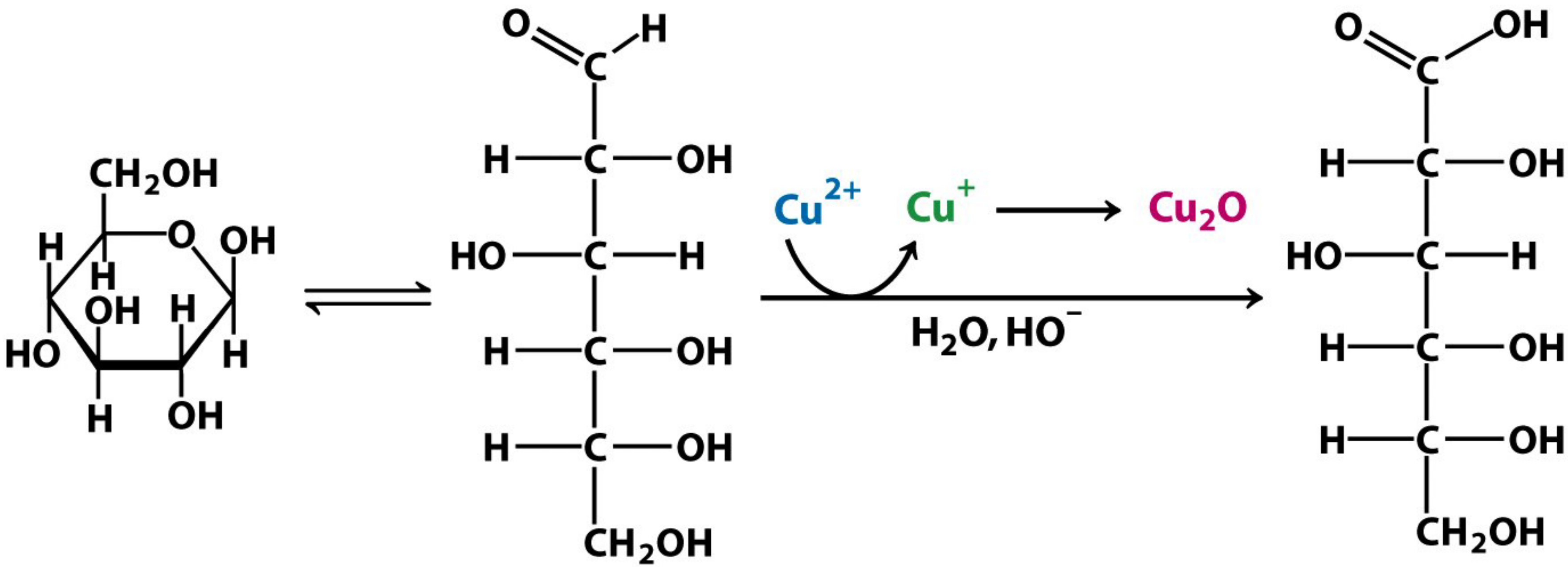
Deoxyribose has an -H here replacing the -OH

Reducing Sugars

- The aldehyde groups of aldoses are oxidized by Benedict's reagent, an alkaline copper(II) solution
- The blue color of the reagent fades as reaction occurs reducing Cu^{2+} to Cu^{+} with a red-orange precipitate forming as Cu_2O results
- Test can measure glucose in urine



+ Cu_2O (red-orange)



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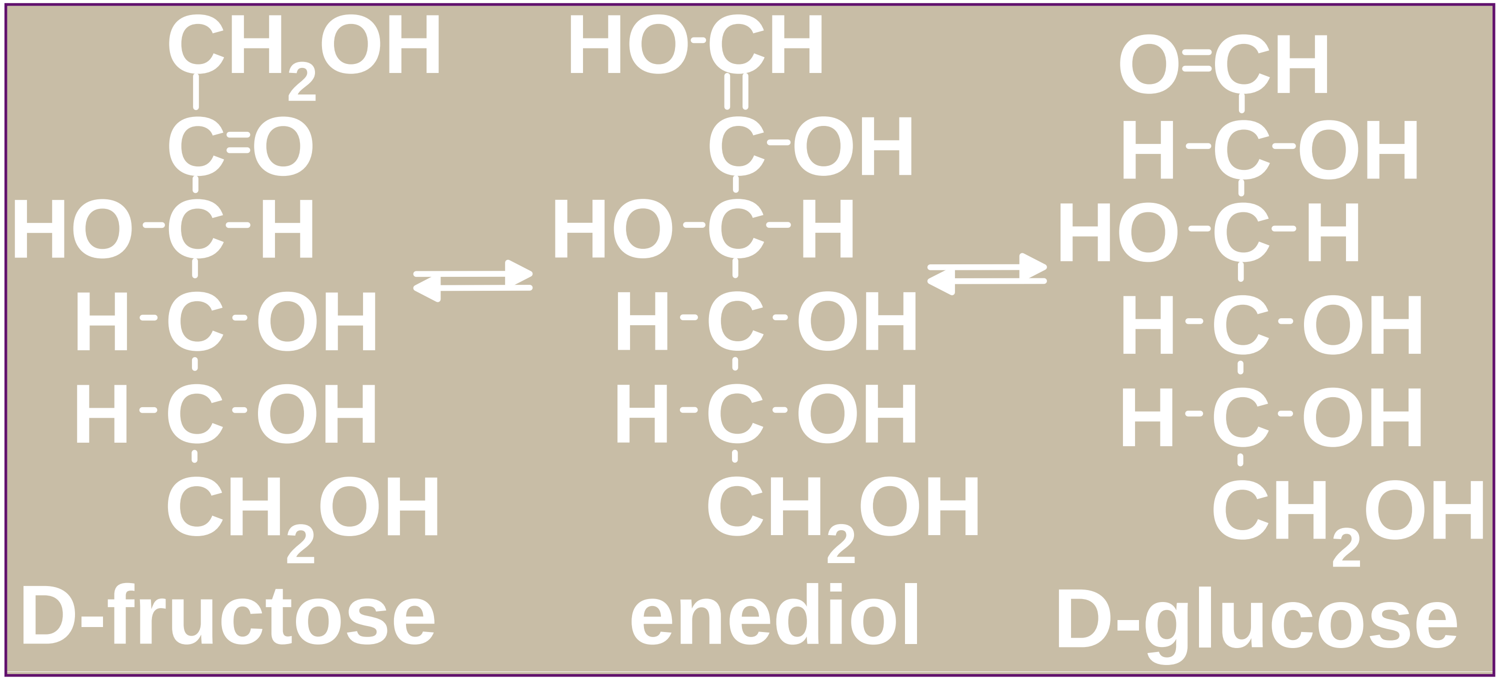
Reducing Sugars

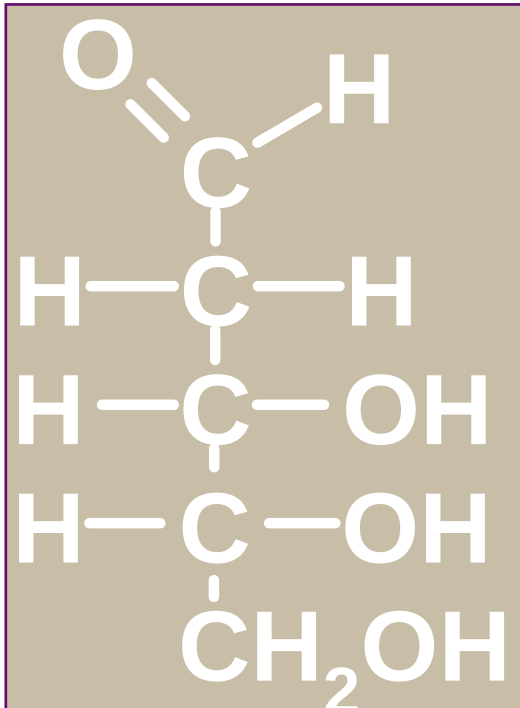
- All monosaccharides and the disaccharides except sucrose are reducing sugars
- Ketoses can isomerize to aldoses and react also



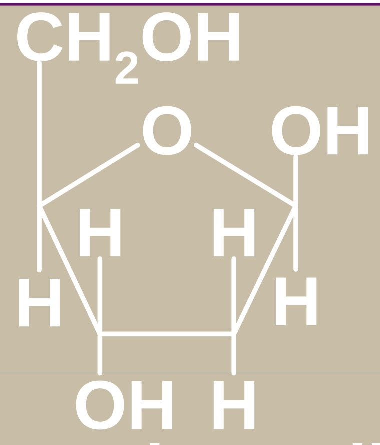
Biological Monosaccharides

A Reduced Sugar

- The most important reduced sugar is deoxyribose



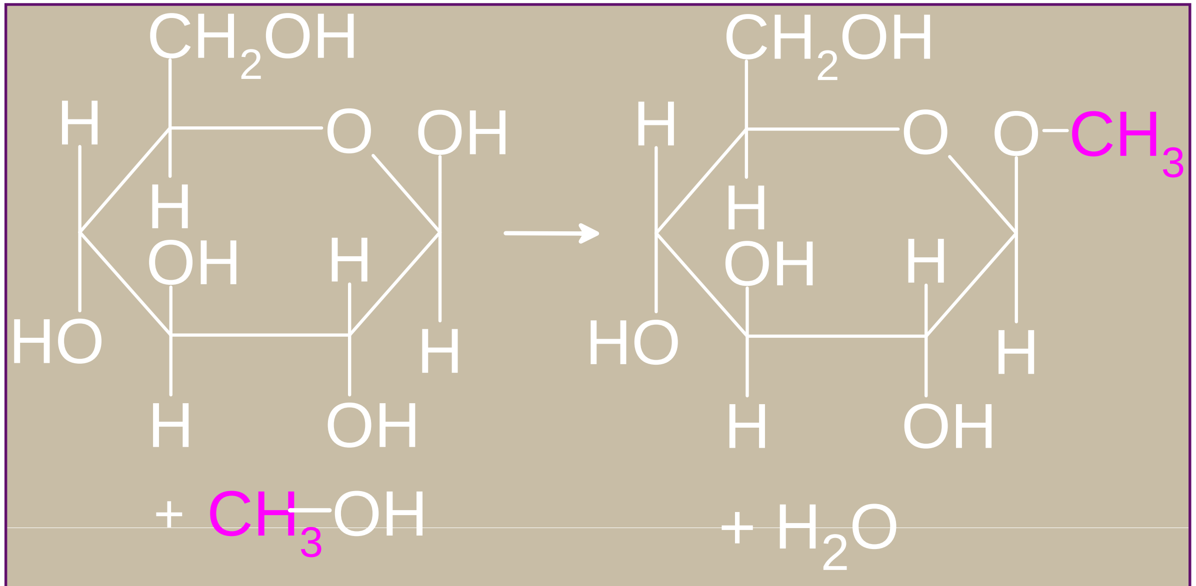
D-deoxyribose



β-D-2-deoxyribose

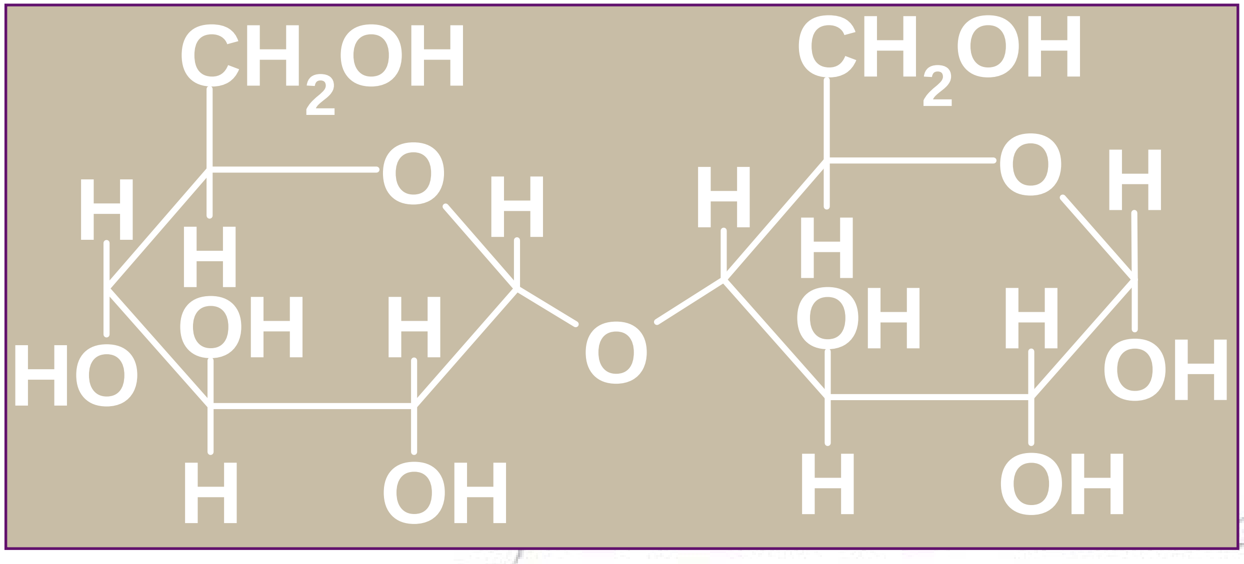
Biologically Important Disaccharides

- The anomeric -OH can react with another -OH on an alcohol or sugar
- Process is forming a glycosidic bond
- Water is lost to form an acetal

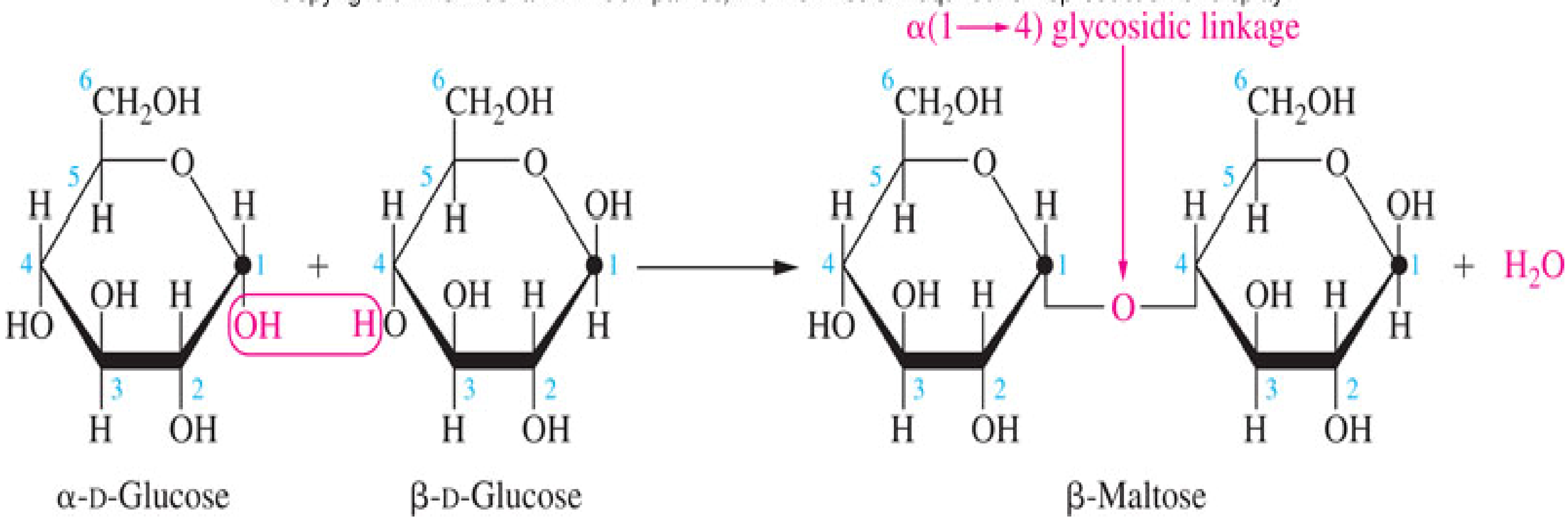


Maltose (麥芽糖)

- Maltose is formed by linking two α-D-glucose molecules to give a 1,4 glycosidic linkage
- Maltose is malt sugar
- Formed as an intermediate in starch hydrolysis
- Reducing sugar due to the hemiacetal hydroxyl



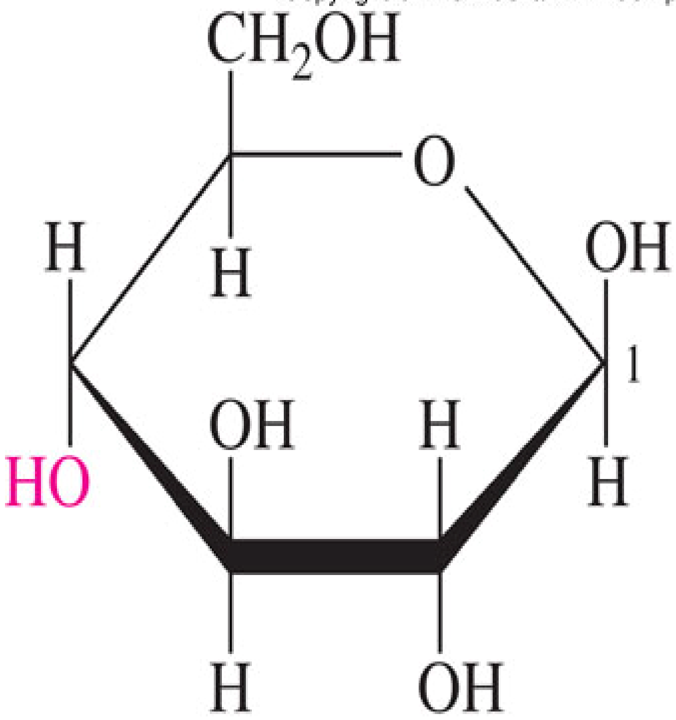
Formation of Maltose



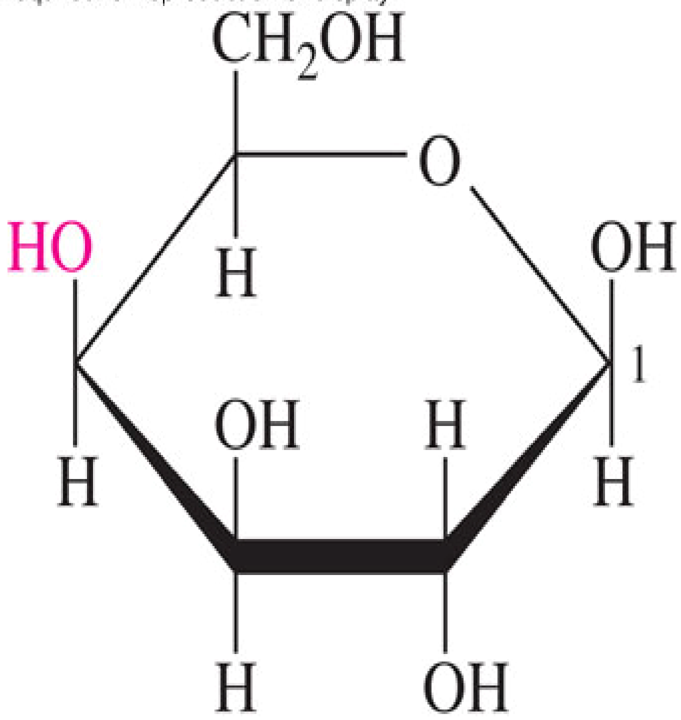
Lactose (乳糖)

- Lactose is formed by joining β–D-galactose to α-D-glucose to give a β–1,4-glycoside
- Lactose is milk sugar
  - For use as an energy source, must be hydrolyzed to glucose and galactose
  - Lactose intolerance results from lack of lactase to hydrolyze the glycosidic link of lactose

4.1 Carbohydrates

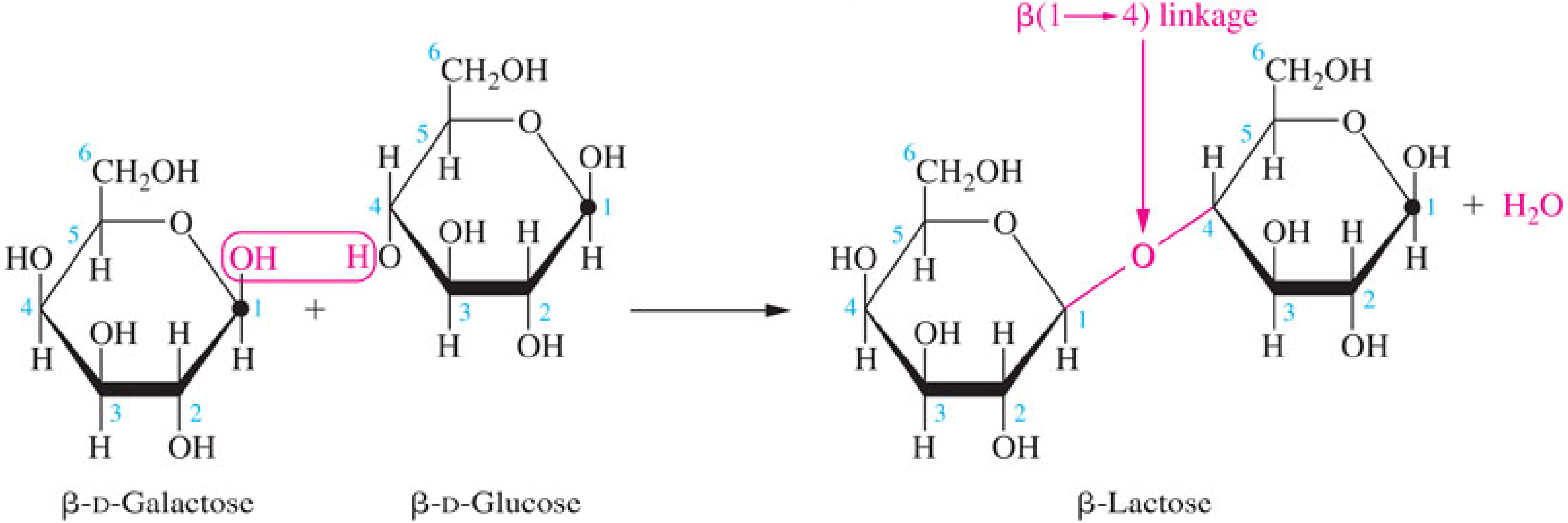


β-D-Glucose



β-D-Galactose

Lactose Glycosidic Bond



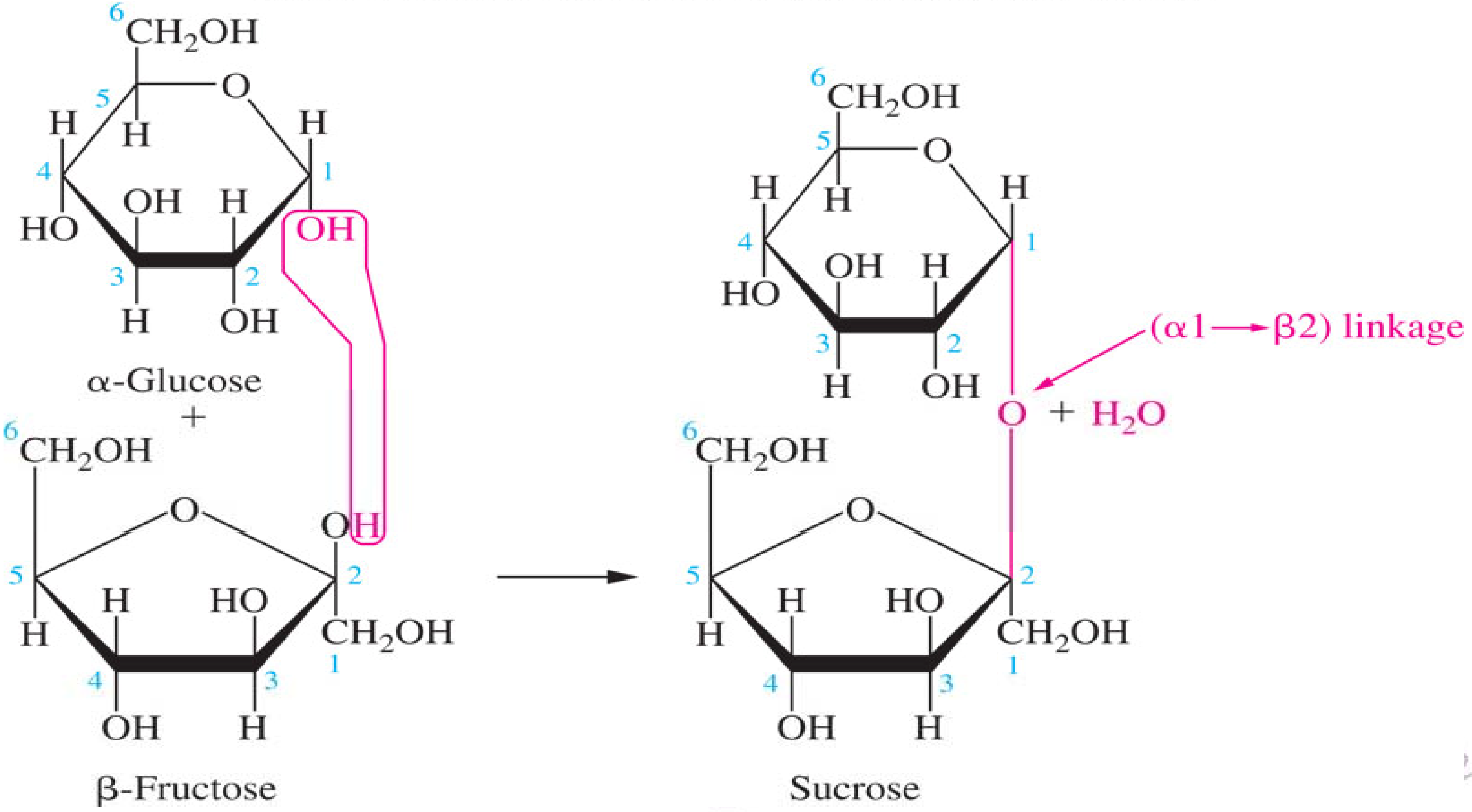
Galactosemia

- In order for lactose to be used as an energy source, galactose must be converted to a phosphorylated glucose molecule
- When enzymes necessary for this conversion are absent, the genetic disease galactosemia results
- People who lack the enzyme lactase (~20%) are unable to digest lactose and have the condition lactose intolerance

Sucrose

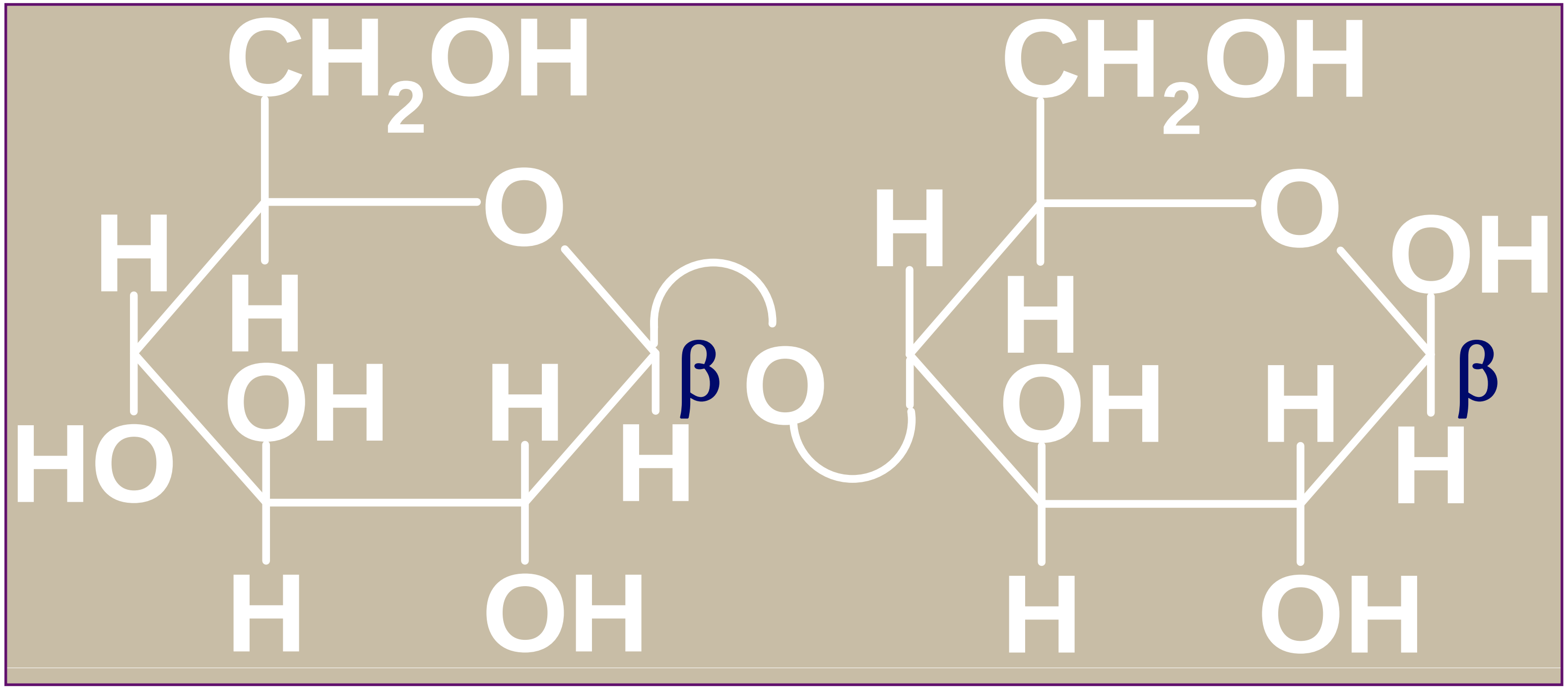
- Sucrose is formed by linking α–D-glucose with β–D-fructose to give a 1,2 glycosidic linkage
  - Nonreducing – negative reaction in Benedict test
  - The glycosidic O is part of an acetal and a ketal
- Important plant carbohydrate
  - Water soluble
  - Easily transported in plant circulatory system
- Cannot by synthesized by animals
- Sucrose called:
  - Table sugar
  - Cane sugar
  - Beet sugar
  - Linked to dental caries

Glycosidic Bond Formed in Sucrose



Cellobiose (纖維二糖)

- Cellobiose is formed by linking two β–D-glucose molecules to give a 1,4-glycosidic link
- It is a product of hydrolyzed cellulose

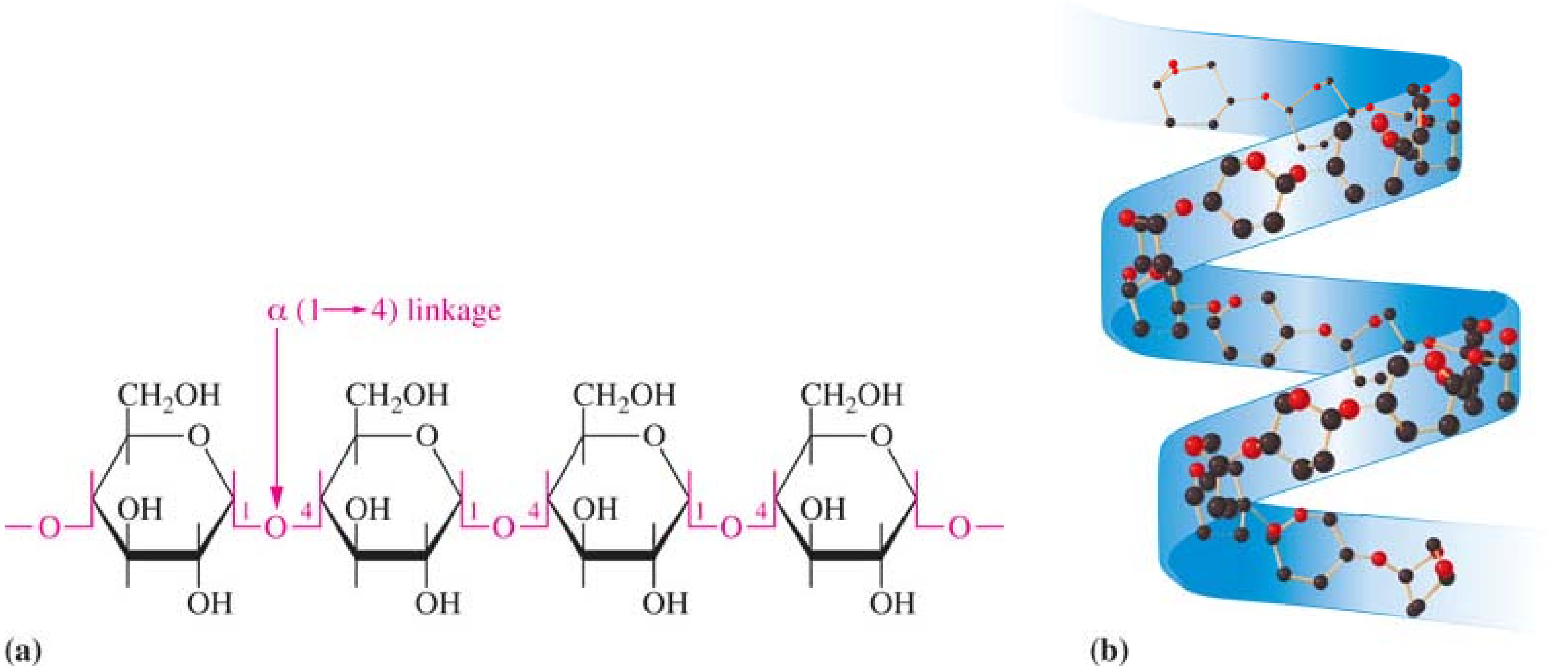


Polysaccharides

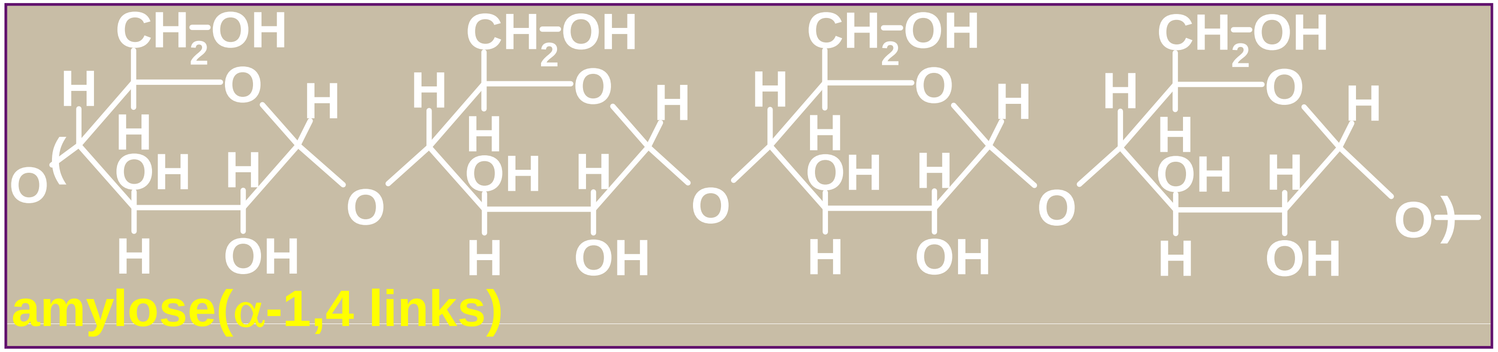
Starch

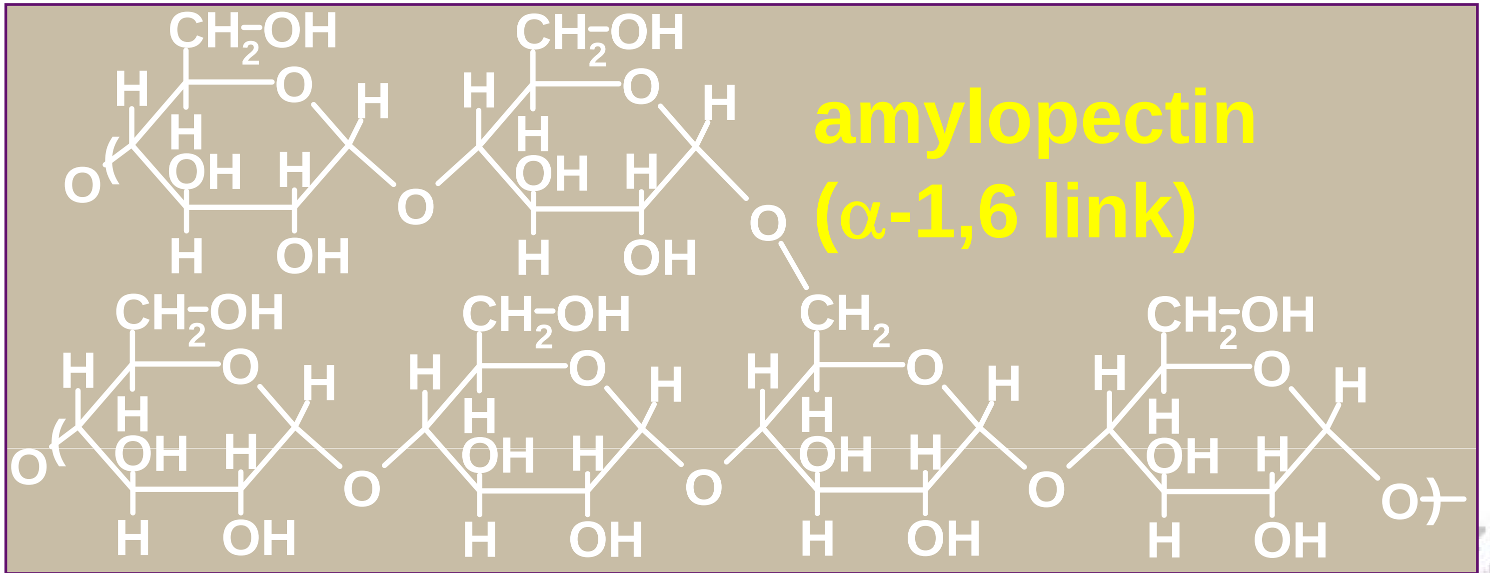
- Starches are storage forms of glucose found in plants
- They are polymers of α linked glucose
- If the links are:
  - Only 1,4 links, the polymer is linear = amylose
    - Amylose usually assumes a helical configuration with six glucose units per turn
    - Comprises about 80% of plant starch
  - Both 1,4 and 1,6 links then, the polymer structure is branched = amylopectin
    - Highly branched with branches of approximately 20-25 glucose units

Structure of Amylose (直鏈澱粉)



Comparison of Amylose to Amylopectin (支鏈澱粉)

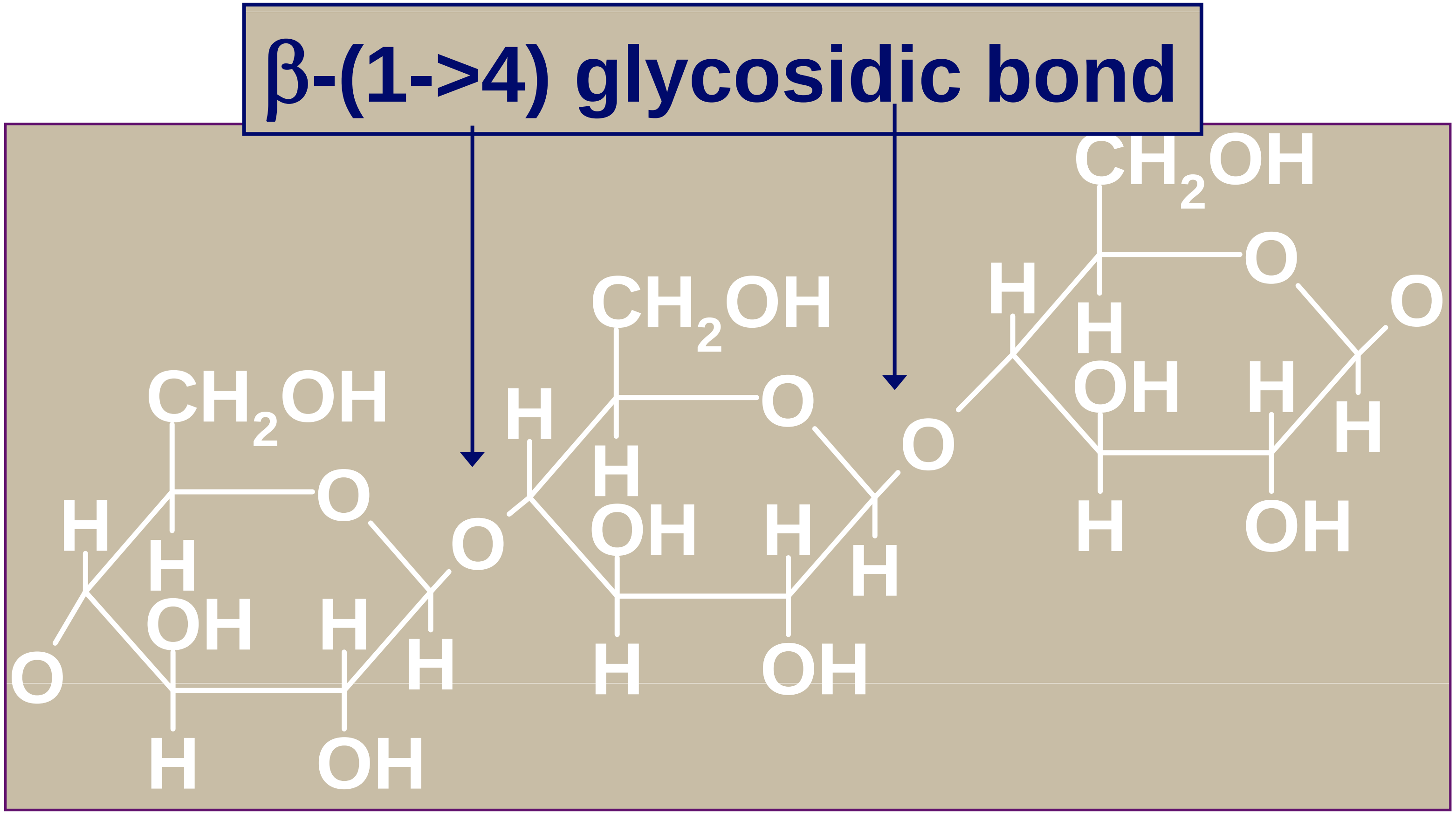




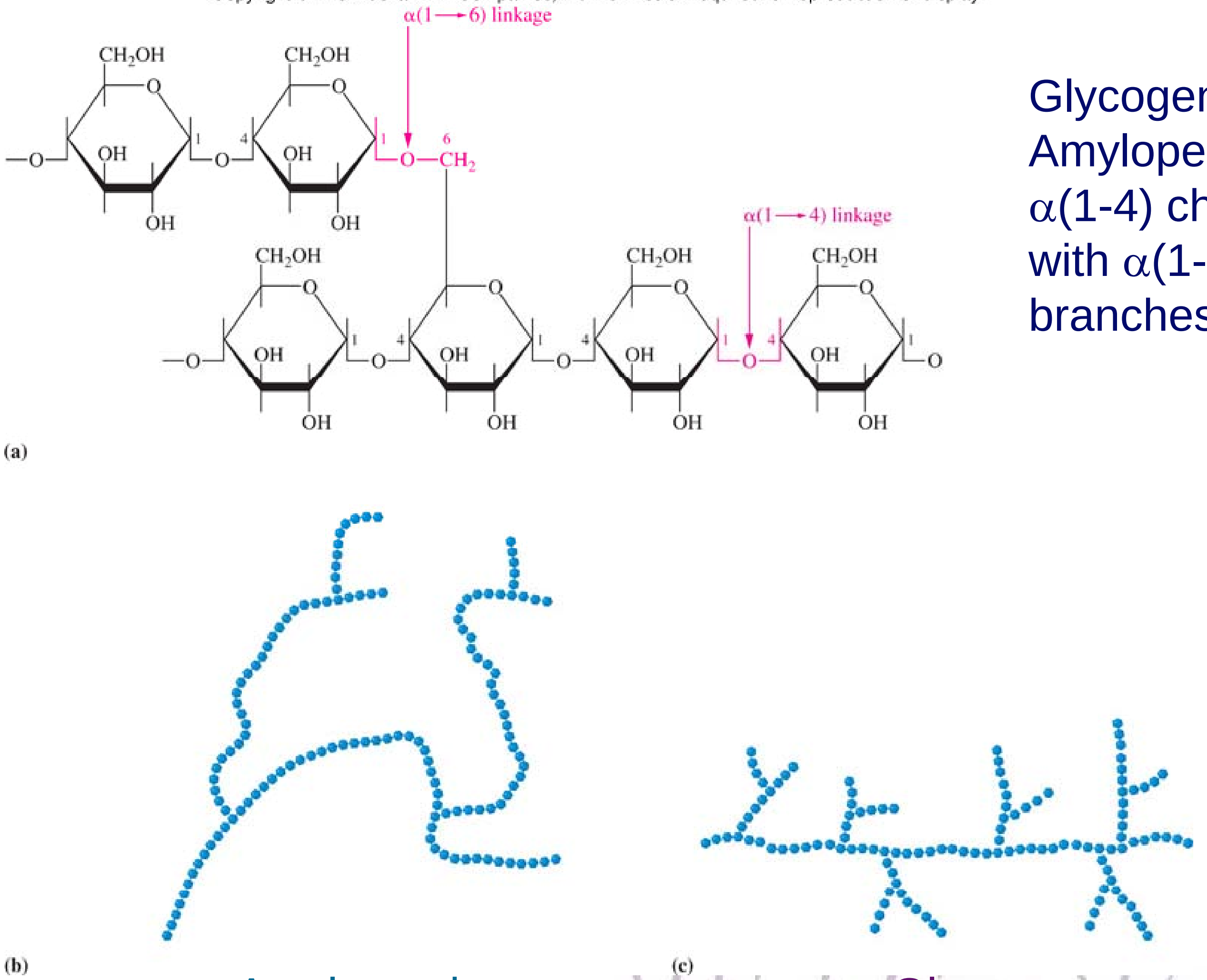
Cellulose (纖維素)

- Cellulose is the major structural polymer in plants
- It is a liner homopolymer composed of β-D-glucose units linked β-1,4
- The repeating disaccharide of cellulose is β-cellobiose
- Animals lack the enzymes necessary to hydrolyze cellulose
- The bacteria in ruminants (*e.g.*, cows) can digest cellulose so that they can eat grass, *etc.*

Structure of Cellulose



Glycogen and Amylopectin Structures



Amylopectin

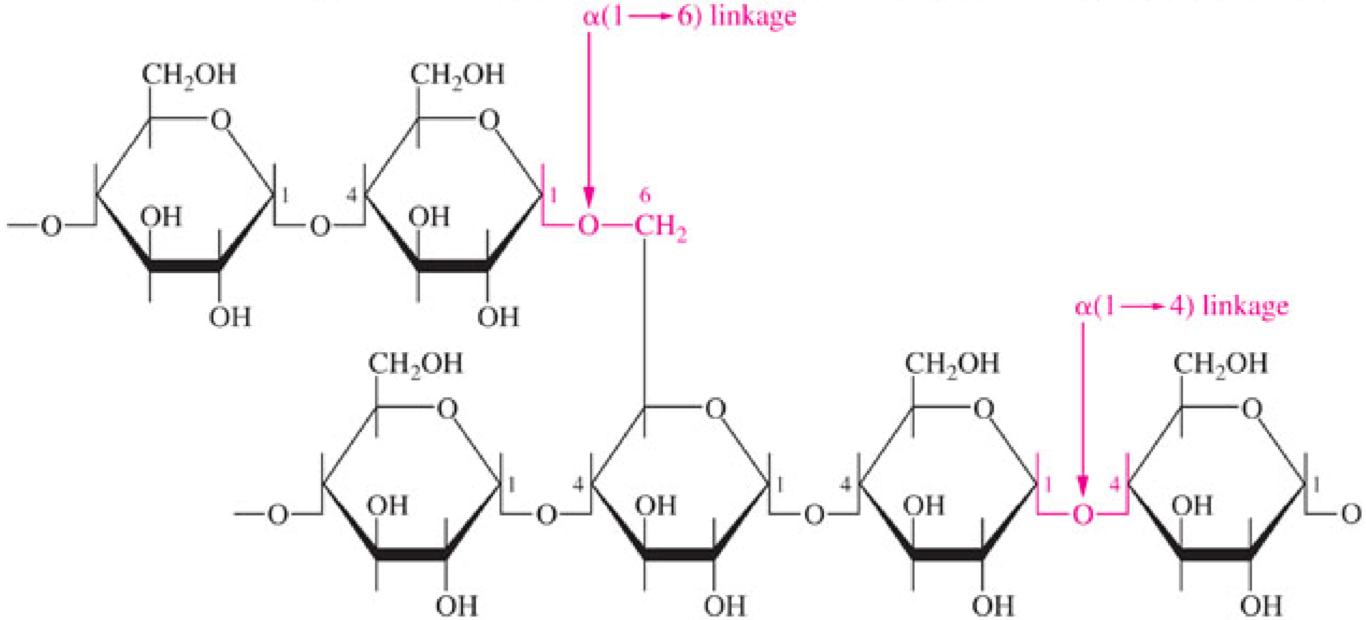
Glycogen

Glycogen and Amylopectin are α(1-4) chains with with α(1-6) branches

Glycogen (肝糖)

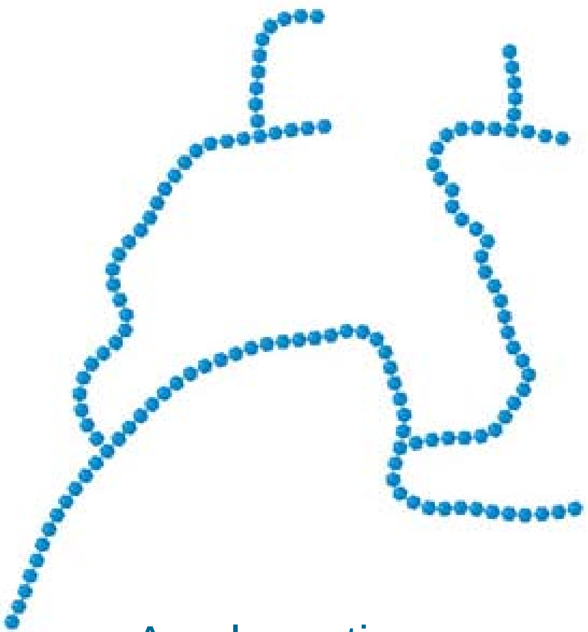
4.1 Carbohydrates

- The major glucose storage carbohydrate in animals is glycogen
- A highly branched chain polymer like amylopectin
  - More frequent branching – 10 monomers
- Glycogen is stored in:
  - Liver
  - Muscle cells

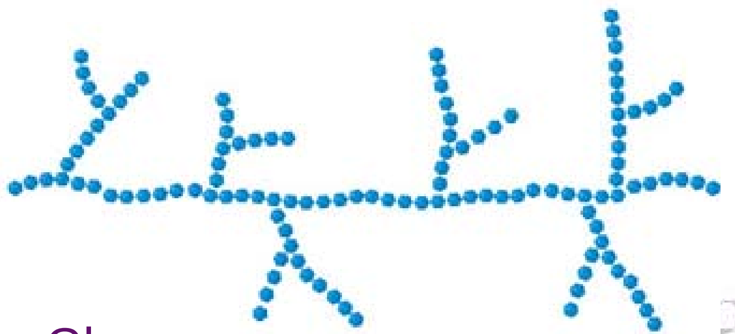


(a)

Glycogen and Amylopectin are α(1-4) chains with with α(1-6) branches



(b) Amylopectin

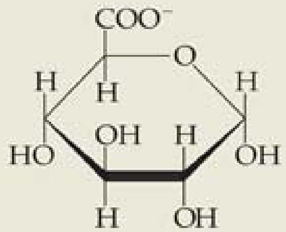


(c) Glycogen

A Medical Perspective

Monosaccharide Derivatives and Heteropolysaccharides of Medical Interest

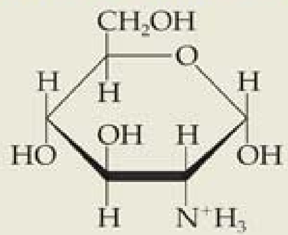
Many of the carbohydrates with important functions in the human body are either derivatives of simple monosaccharides or are complex polymers of monosaccharide derivatives. One type of monosaccharide derivatives, the uronates, is formed when the terminal—CH_2OH group of a monosaccharide is oxidized to a carboxylate group. α-D-Glucuronate is a uronate of glucose:



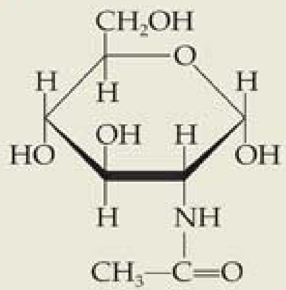
α-D-Glucuronate

In liver cells, α-D-glucuronate is bonded to hydrophobic molecules, such as steroids, to increase their solubility in water. When bonded to the modified sugar, steroids are more readily removed from the body.

Amino sugars are a second important group of monosaccharide derivatives. In amino sugars one of the hydroxyl groups (usually on carbon-2) is replaced by an amino group. Often these are found in complex oligosaccharides that are attached to cellular proteins and lipids. The most common amino sugars, D-glucosamine and D-galactosamine, are often found in the *N*-acetyl form. *N*-acetylglucosamine is a component of bacterial cell walls and *N*-acetylgalactosamine is a component of the A, B, O blood group antigens (see preceding, A Human Perspective: Blood Transfusions and the Blood Group Antigens).

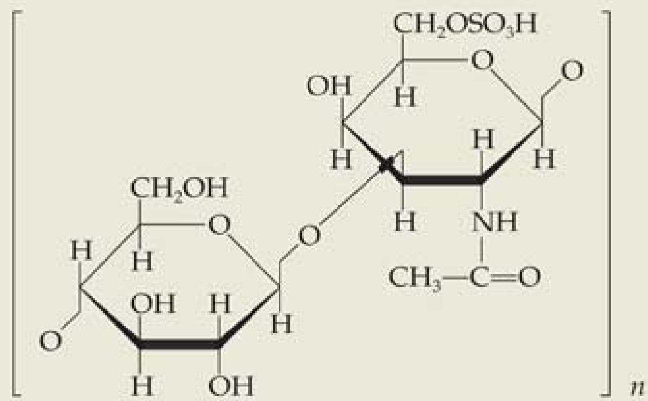


α-D-Glucosamine



α-D-*N*-Acetylglucosamine

Heteropolysaccharides are long-chain polymers that contain more than one type of monosaccharide, many of which are amino sugars. These *glycosaminoglycans* include chondroitin sulfate, hyaluronic acid, and heparin. Hyaluronic acid is abundant in the fluid of joints and in the vitreous humor of the eye. Chondroitin sulfate is an important component of cartilage; and heparin has anticoagulant function. The structures of the repeat units of these polymers are shown below.

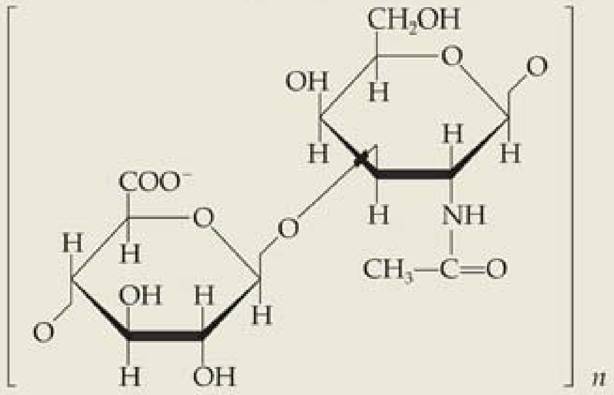


Repeat unit of chondroitin sulfate

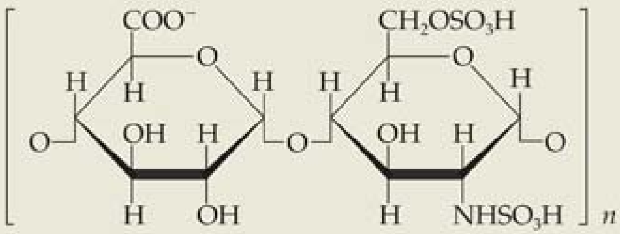
A Medical Perspective

continued

Monosaccharide Derivatives and Heteropolysaccharides of Medical Interest



Repeat unit of hyaluronic acid



Repeat unit of heparin

Two of these molecules have been studied as potential treatments for osteoarthritis, a painful, degenerative disease of the joints. The amino sugar D-glucosamine is thought to stimulate the production of collagen. Collagen is one of the main components of articular cartilage, which is the shock-absorbing cushion within the joints. With aging, some of the D-glucosamine is lost, leading to a reduced cartilage layer and to the onset and progression of arthritis. It has been suggested that ingestion of D-glucosamine can actually "jump-start" production of cartilage and help repair eroded cartilage in arthritic joints.

It has also been suggested that chondroitin sulfate can protect existing cartilage from premature breakdown. It absorbs large amounts of water, which is thought to facilitate diffusion of nutrients into the cartilage, providing precursors for the synthesis of new cartilage. The increased fluid also acts as a shock absorber.

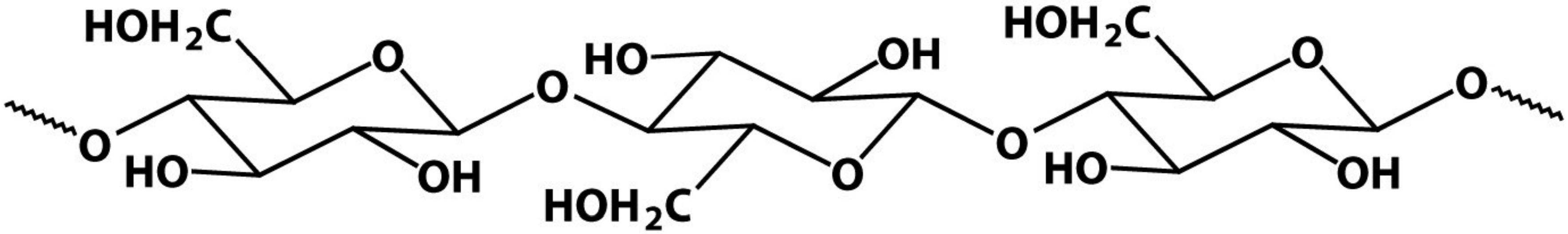
Studies continue on the effects that D-glucosamine and chondroitin sulfate have on degenerative joint disease. To date the studies are inconclusive because a large placebo effect is observed with sufferers of osteoarthritis. Many people in the control groups of these studies also experience relief of symptoms when they receive treatment with a placebo, such as a sugar pill.

Capsules containing D-glucosamine and chondroitin sulfate are available over the counter, and many sufferers of osteoarthritis prefer to take this nutritional supplement as an alternative to any nonsteroidal anti-inflammatory drugs (NSAID), such as ibuprofen. Although NSAIDs can reduce inflammation and pain, long-term use of NSAIDs can result in stomach ulcers, damage to auditory nerves, and kidney damage.

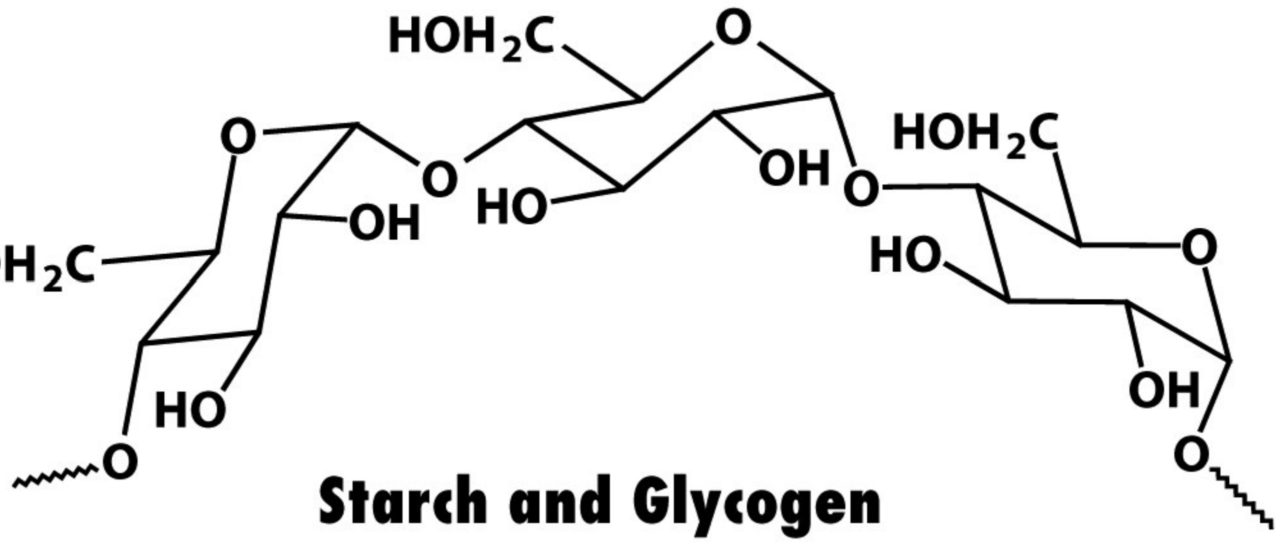
For Further Understanding

In Chapter 15 we learned that nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, are analgesics used to treat pain, such as that associated with osteoarthritis. Why do many people prefer to treat osteoarthritis with D-glucosamine and chondroitin sulfate rather than NSAIDs?

Explain why attaching a molecule such as α-D-glucuronate to a steroid molecule would increase its water solubility.

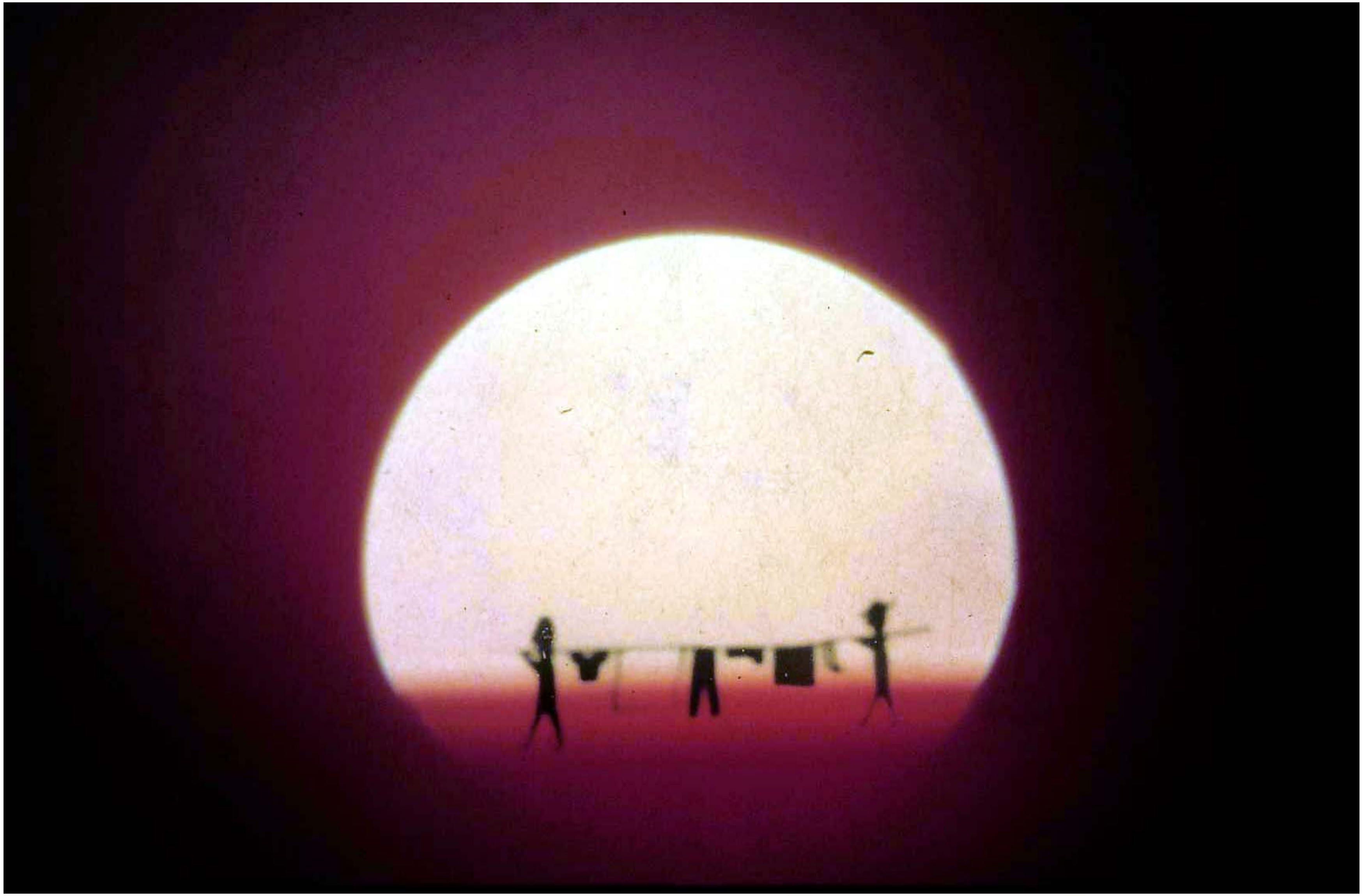


Cellulose
(β-1,4 linkages)



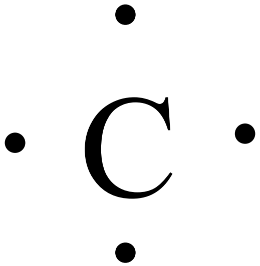
Starch and Glycogen
(α-1,4 linkages)

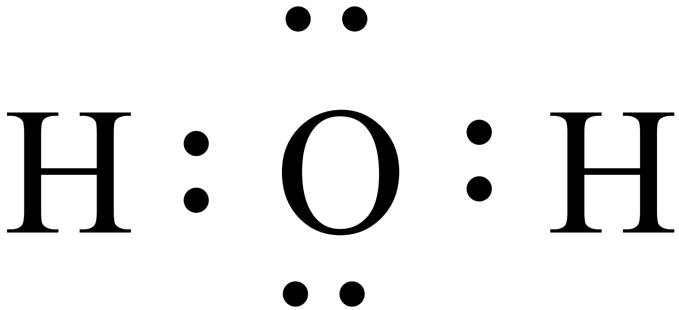
Figure 11-14
Biochemistry, Sixth Edition



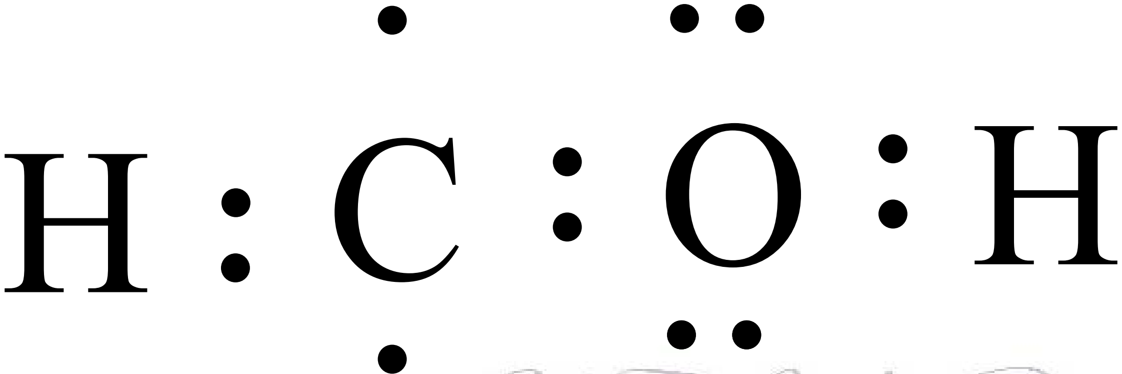
Y.T.Lin's Presentation

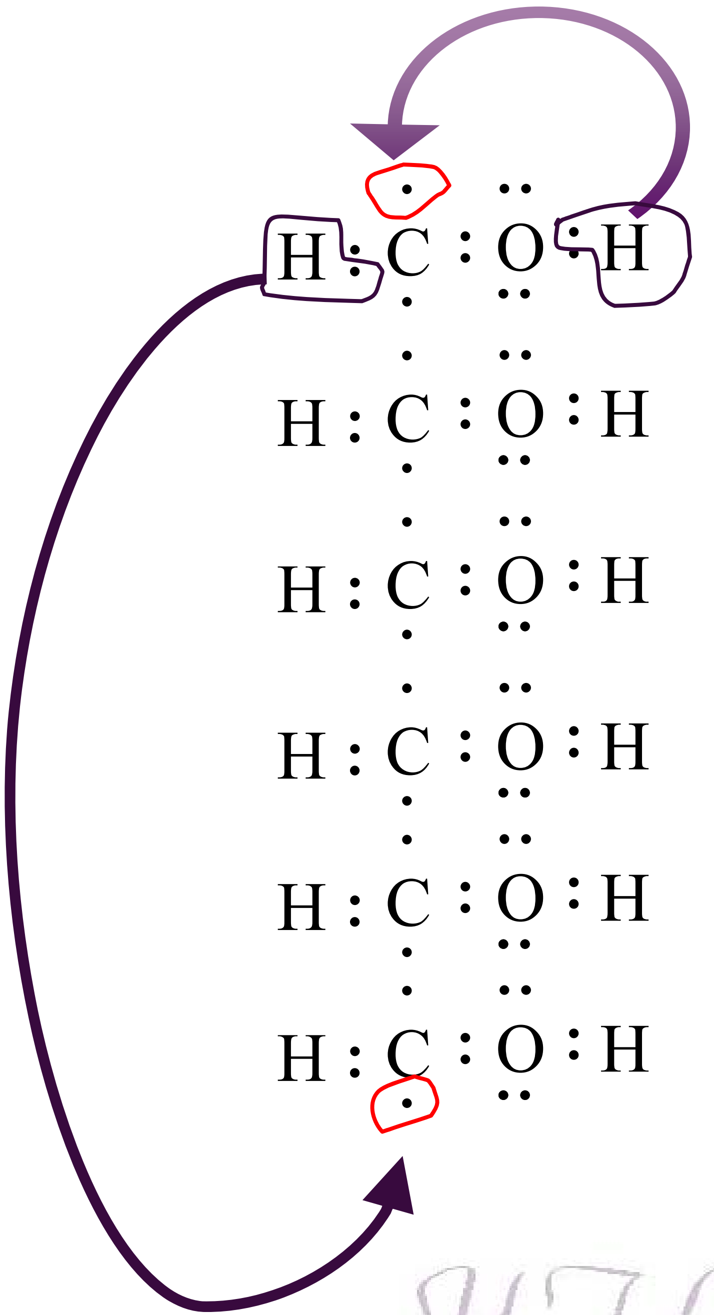
How to store the sunlight energy?





photosynthesis

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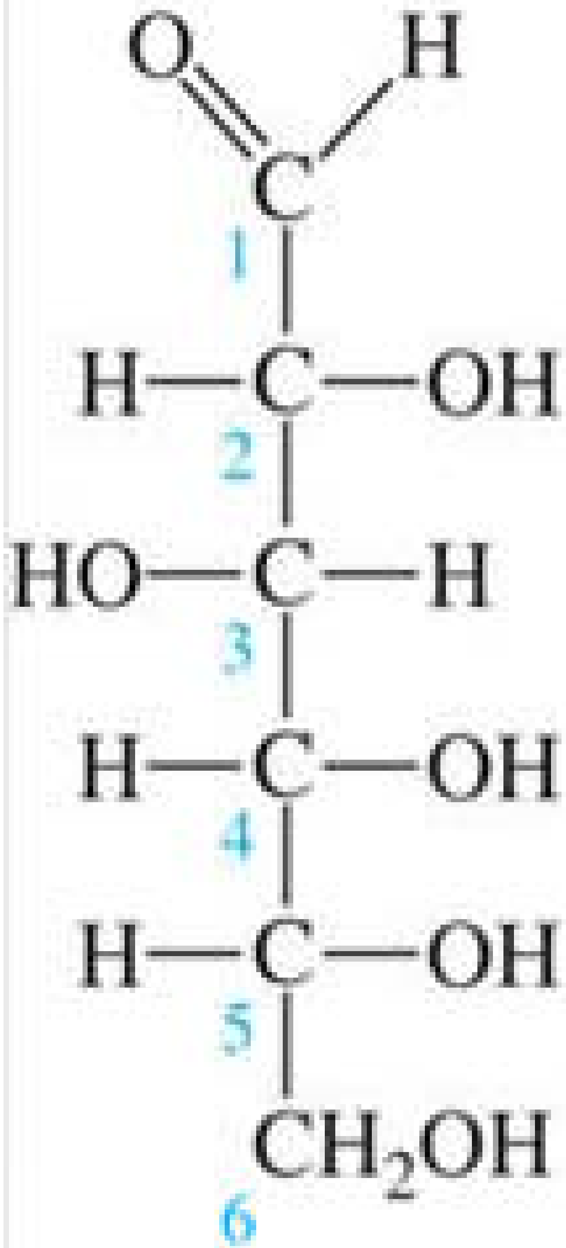


aldose

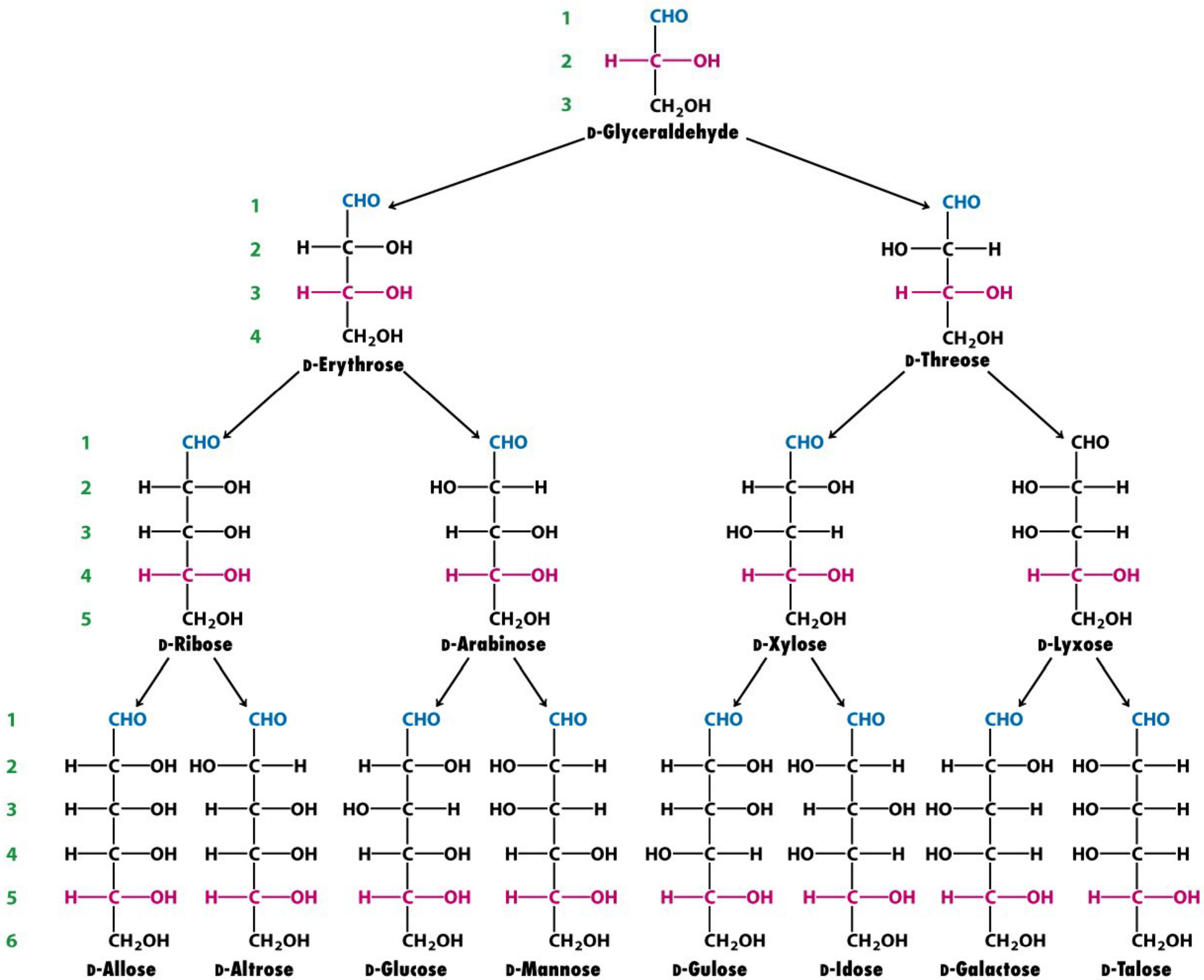
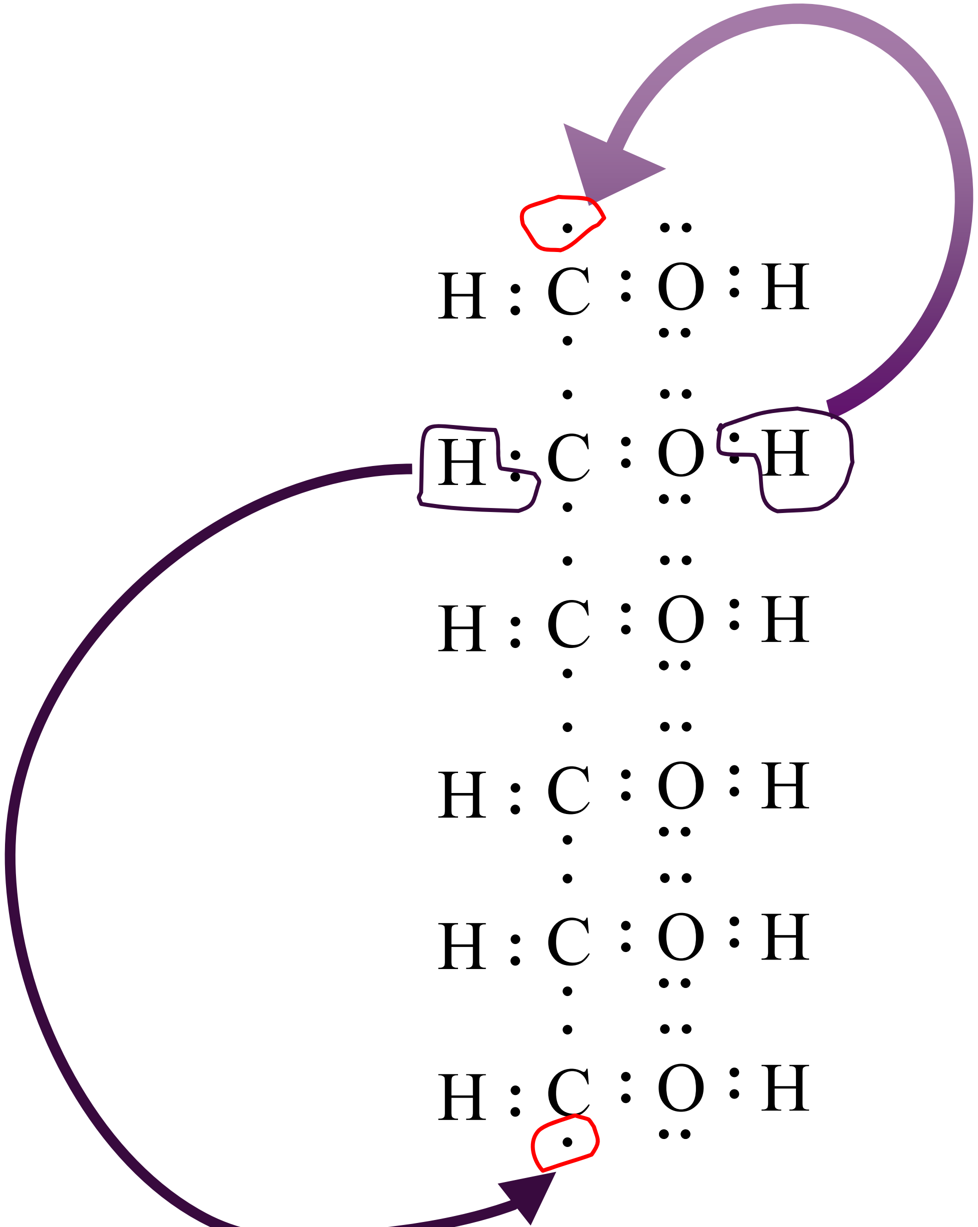
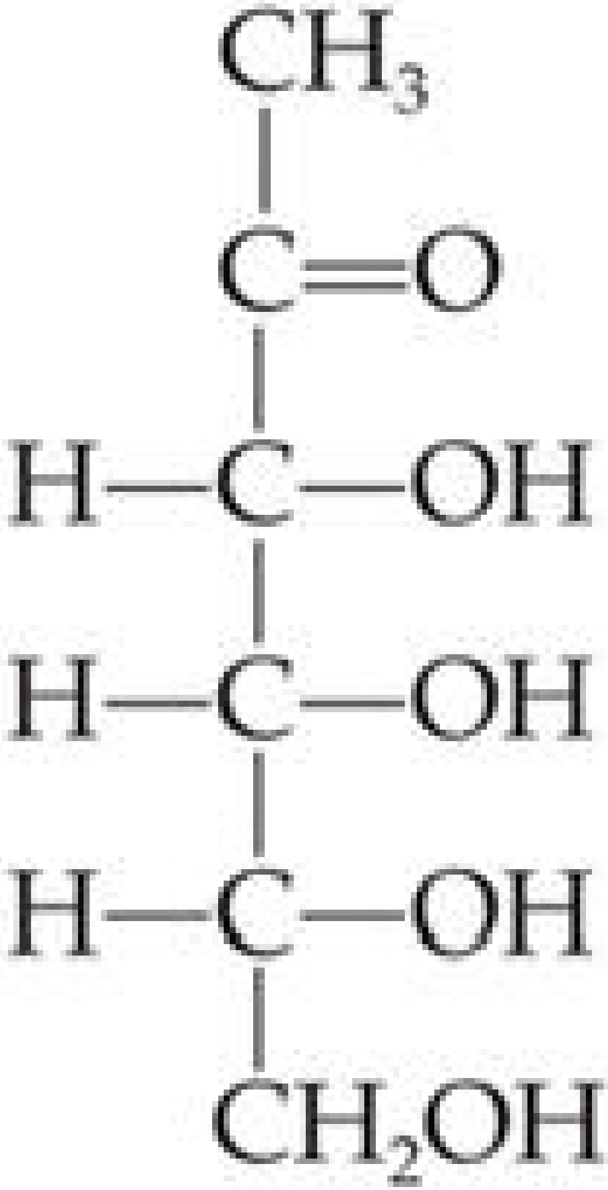


Figure 11-2
Biochemistry, Sixth Edition





ketose

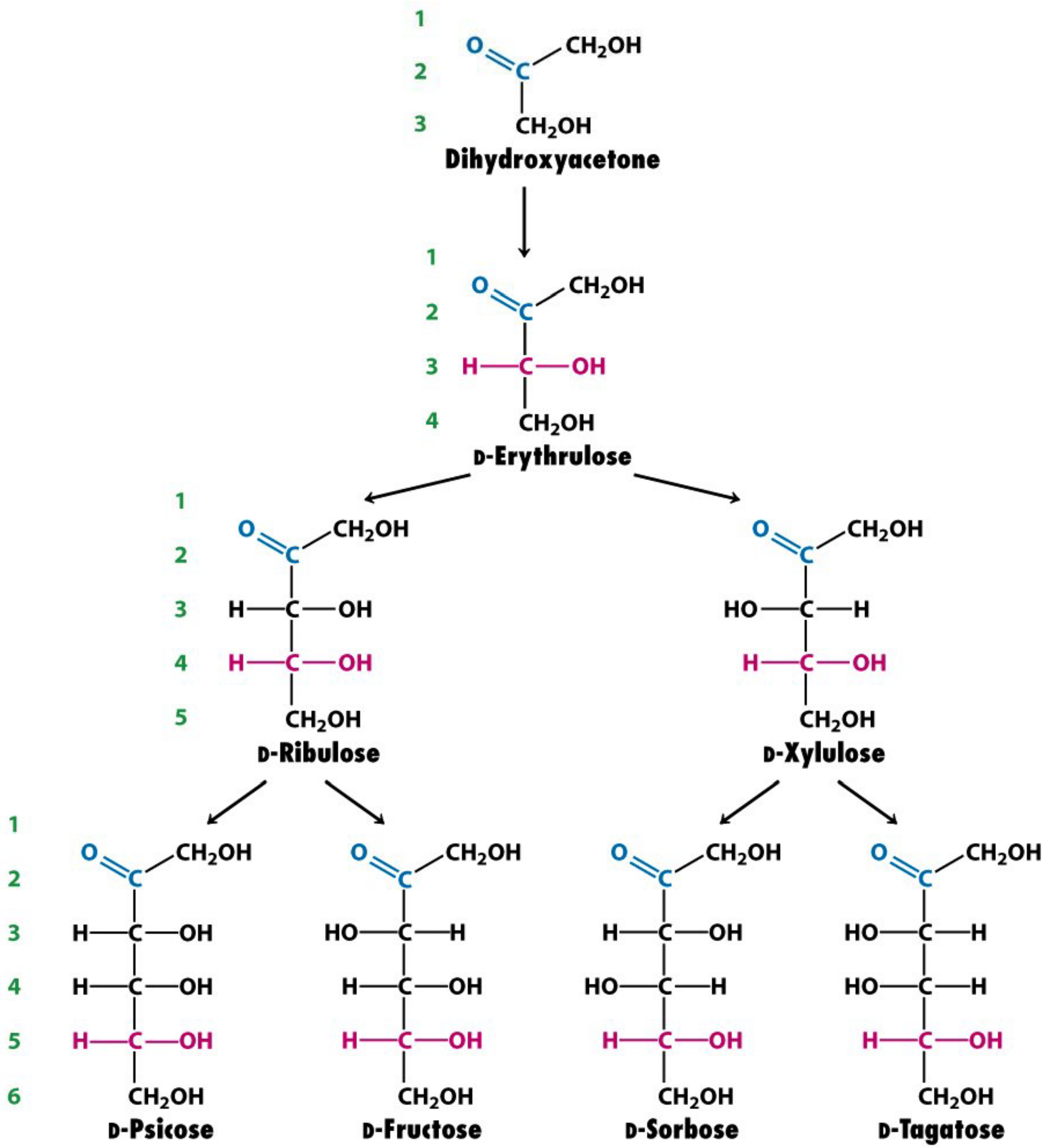


Figure 11-3
Biochemistry, Sixth Edition

3.2 Naming Compounds and Writing Formulas of Compounds

Stock and Common Names for Iron and Copper Ions

TABLE 3.1 Systemic (Stock) and Common Names for Iron and Copper Ions

For systematic name:

Formula	*+ Ion Charge*	*Cation Name*	*Compound Name*
$FeCl_2$	2+	Iron(II)	Iron(II) chloride
$FeCl_3$	3+	Iron(III)	Iron(III) chloride
Cu_2O	1+	Copper(I)	Copper(I) oxide
CuO	2+	Copper(II)	Copper(II) oxide

For common nomenclature:

Formula	*+ Ion Charge*	*Cation Name*	*Common -ous/ic Name*
$FeCl_2$	2+	Ferr*ous*	Ferrous chloride
$FeCl_3$	3+	Ferr*ic*	Ferric chloride
Cu_2O	1+	Cupr*ous*	Cuprous oxide
CuO	2+	Cupr*ic*	Cupric oxide

3.2 Naming Compounds and Writing Formulas of Compounds

Common Monatomic Cations and Anions

TABLE 3.2 Common Monatomic Cations and Anions

Cation	Name	Anion	Name
H^+	Hydrogen ion	H^-	Hydride ion
Li^+	Lithium ion	F^-	Fluoride ion
Na^+	Sodium ion	Cl^-	Chloride ion
K^+	Potassium ion	Br^-	Bromide ion
Cs^+	Cesium ion	I^-	Iodide ion
Be^{2+}	Beryllium ion	O^{2-}	Oxide ion
Mg^{2+}	Magnesium ion	S^{2-}	Sulfide ion
Ca^{2+}	Calcium ion	N^{3-}	Nitride ion
Ba^{2+}	Barium ion	P^{3-}	Phosphide ion
Al^{3+}	Aluminum ion		
Ag^+	Silver ion		

Note: The ions of principal importance are highlighted in magenta.

- **Monatomic ions** - ions consisting of a single charged atom

Polyatomic Ions

- **Polyatomic ions** - ions composed of 2 or more atoms bonded together with an overall positive or negative charge
  - Within the ion itself, the atoms are bonded using covalent bonds
  - The positive and negative ions will be bonded to each other with ionic bonds
- Examples:
  - NH_4^+ ammonium ion
  - SO_4^{2-} sulfate ion

Common Polyatomic Cations and Anions

TABLE 3.3 Common Polyatomic Cations and Anions

Ion	Name
NH_4^+	Ammonium
NO_2^-	Nitrite
NO_3^-	Nitrate
SO_3^{2-}	Sulfite
SO_4^{2-}	Sulfate
HSO_4^-	Hydrogen sulfate
OH^-	Hydroxide
CN^-	Cyanide
PO_4^{3-}	Phosphate
HPO_4^{2-}	Hydrogen phosphate
$H_2PO_4^-$	Dihydrogen phosphate
CO_3^{2-}	Carbonate
HCO_3^-	Bicarbonate
ClO^-	Hypochlorite
ClO_2^-	Chlorite
ClO_3^-	Chlorate
ClO_4^-	Perchlorate
CH_3COO^- (or $C_2H_3O_2^-$)	Acetate
MnO_4^-	Permanganate
$Cr_2O_7^{2-}$	Dichromate
CrO_4^{2-}	Chromate
O_2^{2-}	Peroxide

Note: The most commonly encountered ions are highlighted in magenta.

TABLE 18.2 The Essential and Nonessential Amino Acids

Essential Amino Acids	Nonessential Amino Acids
Isoleucine	Alanine
Leucine	Arginine[1]
Lysine	Asparagine
Methionine	Aspartate
Phenylalanine	Cysteine[2]
Threonine	Glutamate
Tryptophan	Glutamine
Valine	Glycine
	Histidine[1]
	Proline
	Serine
	Tyrosine[2]

[1]Histidine and arginine are essential amino acids for infants but not for healthy adults.

[2]Cysteine and tyrosine are considered to be semiessential amino acids. They are required by premature infants and adults who are ill.

End of Lecture

Three abstract factors of biology

- Material
- Energy
- Information

Slide Downloading

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