PEARSON

Chapter 4 Nucleic Acids

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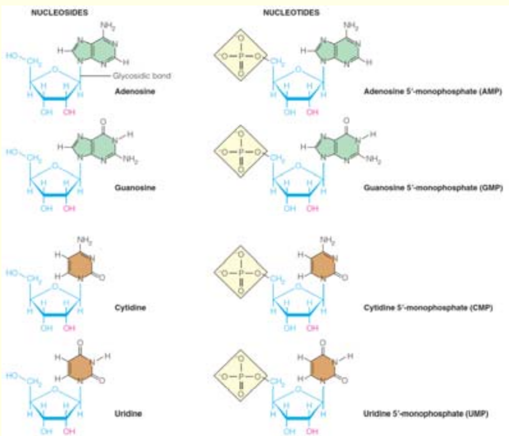
Functions of Nucleotides and Nucleic Acids

- Nucleotide Functions:
  - Energy for metabolism (ATP, GTP)
  - Enzyme cofactors (NAD^+, FAD)
  - Signal transduction (cAMP)
- Nucleic Acid Functions:
  - Storage of genetic info (DNA)
  - Transmission of genetic info (mRNA)
  - Processing of genetic information (ribozymes)
  - Protein synthesis (tRNA and rRNA)
  - Regulation (micro-RNA, long non-coding (lnc)RNA)

The Nature of Nucleic Acids

Nucleo<u>sides</u> are a nitrogenous base with a ribose.

Nucleo<u>tides</u> are a nitrogenous base, a ribose and a phosphate.



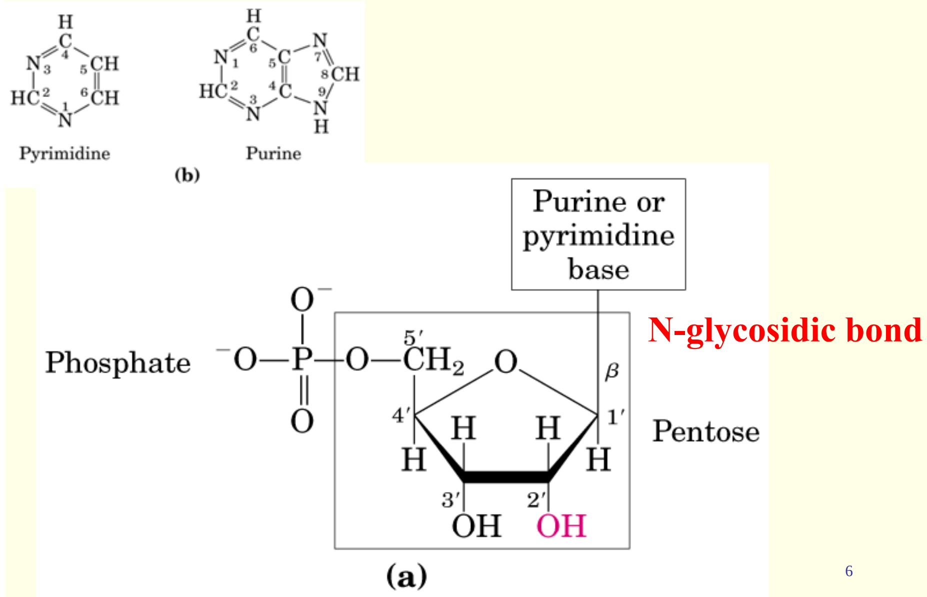
Nucleotides and Nucleosides

- **Nucleotide =**
  - Nitrogeneous base
  - Pentose
  - Phosphate
- **Nucleoside =**
  - Nitrogeneous base
  - Pentose
- **Nucleobase =**
  - Nitrogeneous base

β–*N*-Glycosidic Bond

- In nucleotides the pentose ring is attached to the nucleobase via *N*-glycosidic bond.
- The bond is formed
  - to position N1 in pyrimidines
  - to position N9 in purines
- This bond is quite stable toward hydrolysis, esp. in pyrimidines
- Bond cleavage is catalyzed by acid (purine)

Structure of nucleotides



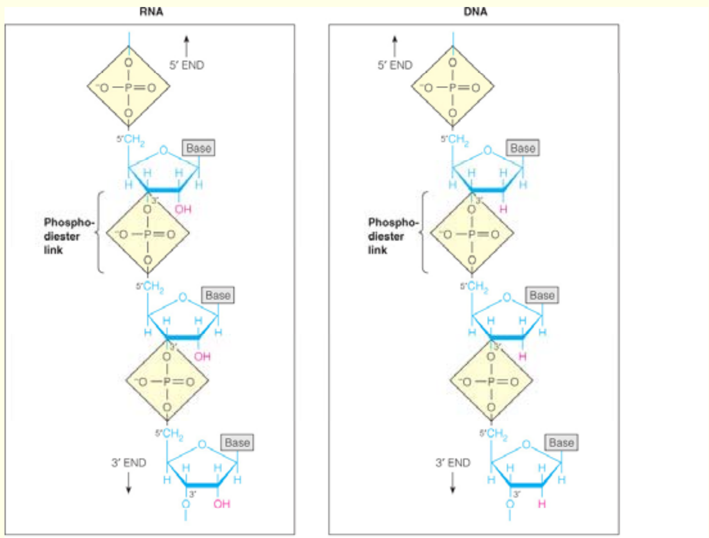
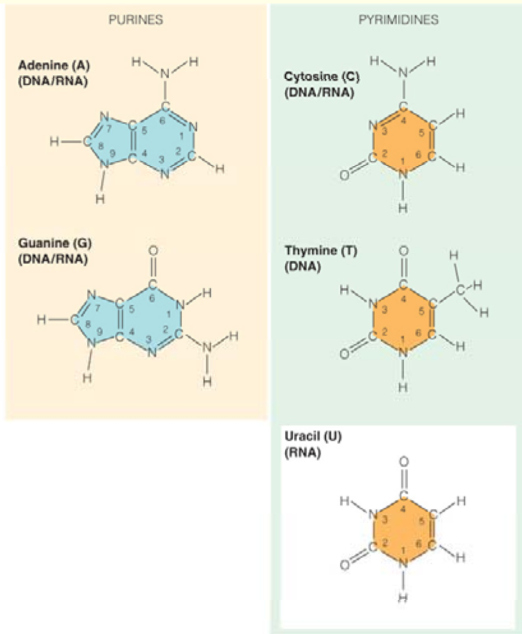


FIGURE 4.1

Chemical structures of ribonucleic acid (RNA) and deoxyribonucleic acid (DNA). The ribose–phosphate or deoxyribose–phosphate backbone of each chain is shown in detail. The bases shown schematically here are detailed in Figure 4.2.

FIGURE 4.2

Purine and pyrimidine bases found in DNA and RNA. DNA always contains the bases A, G, C, T, whereas RNA always contains A, G, C, U. Thymine is simply 5-methyluracil.



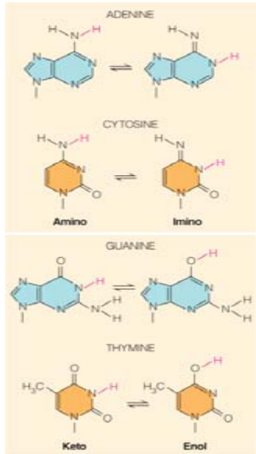


FIGURE 4.4

Tautomerization of the bases. The most stable (and therefore common) forms are shown at the left. The less common imino and enol forms, shown on the right, are found in some special base interactions. Still other tautomers (not shown here) are possible.

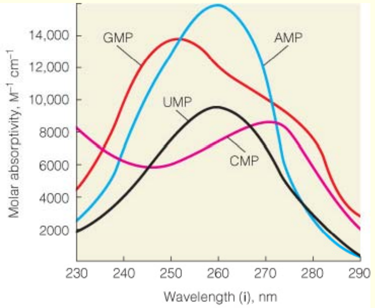


FIGURE 4.5

Ultraviolet absorption spectra of ribonucleotides. The dimensions of the absorption coefficients are $M^{-1}cm^{-1}$. Thus a 10^{-4} solution of UMP would have an absorbance of 0.95 at 260 mm in a 1-cm-thick cuvette. (Absorbance = molar absorptivity × light path in cm × molar concentration; see Tools of Biochemistry 6A).

Data from *Principles of Biochemistry*, 2nd ed., A. L. Lehninger, D. L. Nelson, and M. M. Cox. © 1993, 1982, Worth Publishers, Inc., New York.

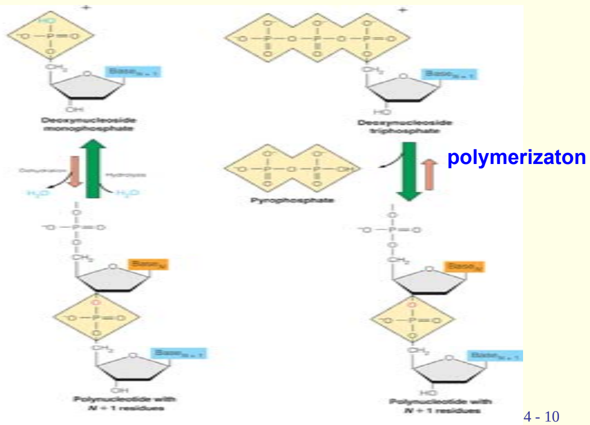
FIGURE 4.6 (*left*)

Formation of a polynucleotide by a hypothetical dehydration reaction. We might imagine that a polynucleotide could be formed directly from nucleoside monophosphates by removal of water, as shown here, but the dehydration reaction is thermodynamically unfavorable. The reverse reaction, hydrolysis, is favored. Note that in this and subsequent figures we adopt a somewhat more compact way of representing the sugar-phosphate backbone.

FIGURE 4.7 (right)

How polynucleotides are actually formed. In this reaction, each monomer is presented as a nucleoside triphosphate to be added to the chain. Cleavage of the nucleoside triphosphate provides the free energy that makes the reaction thermodynamically favorable. The enzymes catalyzing such reactions are called **polymerases.**

hydrolysis



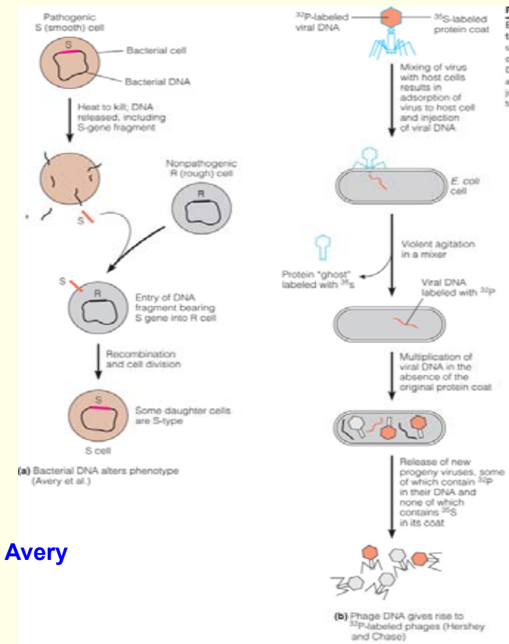


FIGURE 4.8

Experiments that showed DNA to be the genetic substance. (a) Avery et al. showed that nonpathogenic pneumococci could be made pathogenic by transfer of DNA from a pathogenic strain. **(b)** Hershey and Chase showed that it is the transfer of just the viral DNA from a virus to a bacterium that gives rise to new viruses.

Genetic material?

Hershey/Chase

Avery

X-ray diffraction

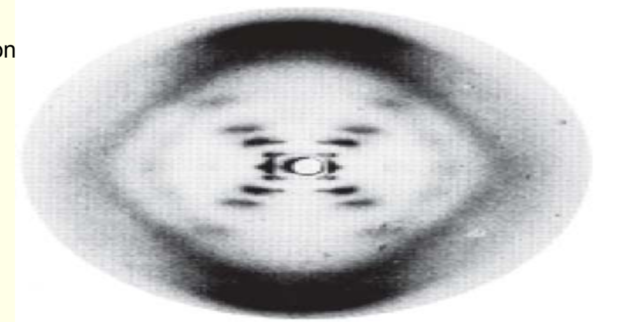


FIGURE 4.9

Evidence for the structure of DNA. This photograph, taken by Rosalind Franklin, shows the X-ray diffraction pattern produced by wet DNA fibers. It played a key role in the elucidation of DNA structure. The cross pattern indicates a helical structure, and the strong spots at top and bottom correspond to a helical rise of 0.34 nm. The layer line spacing is one-tenth of the distance from the center to either of these spots, showing that there are 10 base pairs per repeat.

Reprinted by permission from Macmillan Publishers Ltd. *Nature* 171:740–741, R. E. Franklin and R. Gosling, Molecular configuration in sodium thymonucleate. © 1953.

Rosalind Franklin, 1920–1958

Maurice Wilkins, 1916–2004

Unnumbered 8 p278
Lehninger Principles of Biochemistry, Fifth Edition

Road to the Double Helix

- Watson and Crick:
  - –alternating pattern (major & minor groove)
  - – Hydrogen bonding:
    A pairs with T
    G pairs with C
  - Double helix fits the data!
- Franklin and Wilkins:
  - –"Cross" means helix
  - –"Diamonds" mean that the phosphate-sugar backbone is outside

→Chargaff's rules
A+G=T+C

Watson, Crick, and Wilkins shared
1962 Nobel Prize
Franklin died in 1958

James D. Watson

Francis Crick, 1916–2004

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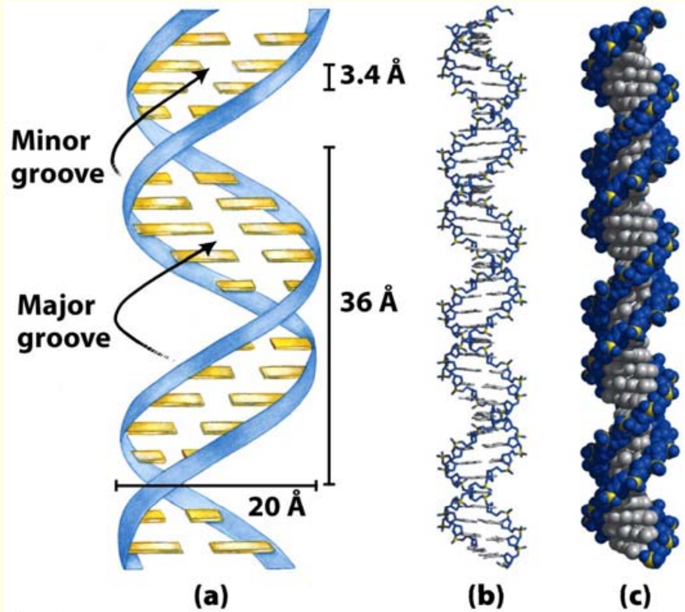

Figure 8-13
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TABLE 4.3 Parameters of polynucleotide helices	A Form	B Form	Z Form
Direction of helix rotation	Right	Right	Left
Number of residues per turn (n)	11	10	12 (6 dimers)
Rotation per residue ($= 360°/n$)	33°	36°	−60° per dimer; ~−30° per residue
Rise[a] in helix per residue (h)	0.255 nm	0.34 nm	0.37 nm
Pitch[a] of helix ($= nh$)	2.8 nm	3.4 nm	4.5 nm

[a]For definitions of *rise* and *pitch* of a helix, see Tools of Biochemistry 4A.

	A form	B form	Z form
Helical sense	Right handed	Right handed	Left handed
Diameter	~26 Å	~20 Å	~18 Å
Base pairs per helical turn	11	10.5	12
Helix rise per base pair	2.6 Å	3.4 Å	3.7 Å
Base tilt normal to the helix axis	20°	6°	7°
Sugar pucker conformation	C-3′ endo	C-2′ endo	C-2′ endo for pyrimidines; C-3′ endo for purines
Glycosyl bond conformation	Anti	Anti	Anti for pyrimidines; syn for purines

Figure 8-17 part 2
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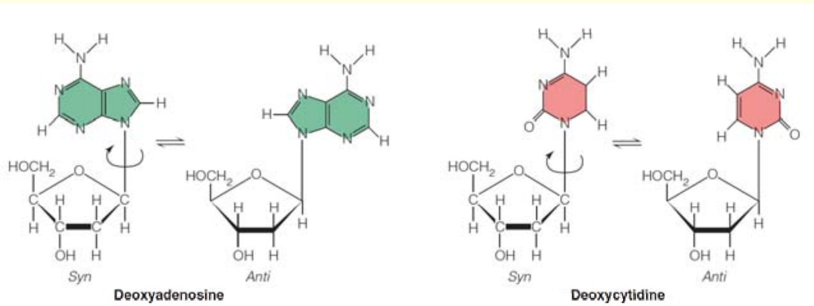
Plasticity of Secondary and Tertiary DNA Structure

Nucleic acid bases can exist in *syn or anti* conformations.



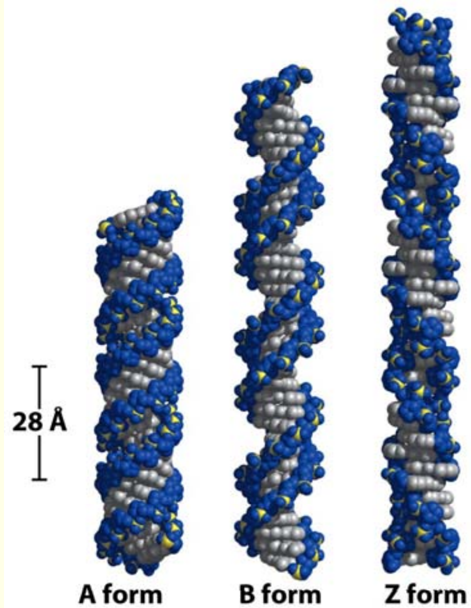


Figure 8-17 part 1
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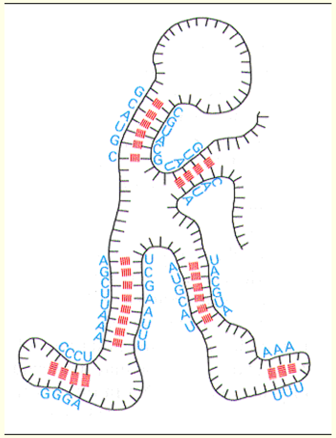
What is RNA?

- Ribonucleic acid
  - Ribonucleotides (Ribose, base, & phosphate)
- Types
  - Coding: messenger RNA (mRNA)
  - Non-coding:
    - Ribosomal RNA (rRNA)
    - Transfer RNA (tRNA)
    - Small nuclear RNA (snRNA)
    - Small nucleolar RNA (snoRNA)
    - Interference RNA (RNAi)
    - Short interfering RNA (siRNA)
    - Micro RNA (miRNA)
    - Long non-coding RNA (lncRNA)



RNA can form :
secondary structures
by internal base-pairing

RNA can also be used:

1. to store genetic information (viruses)
2. for catalytic activity (self-splicing, RNaseP)
3. Regulation (miRNA, siRNA, lncRNA)

MCB 1.6

Messenger RNA:
Code Carrier for the Sequence of Proteins

- Is synthesized using DNA template
- Contains ribose instead of deoxyribose
- Contains uracil instead of thymine
- One mRNA may code for more than one protein (polycistronic)

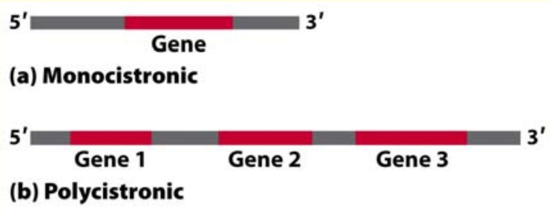


Figure 8-21
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DNA vs RNA

Composition:

*** T in DNA not U to distinguish from T formed by deamination of C**

*** 2' OH in RNA accounts for instability of RNA**

phosphodiester bond Hydrolysis

***RNA:Sensitive to alkaline hydrolysis but resistant to acid hydrolysis**

***DNA:Resistant to alkaline hydrolysis: Depurinates by acid hydrolysis (apurinic base)**

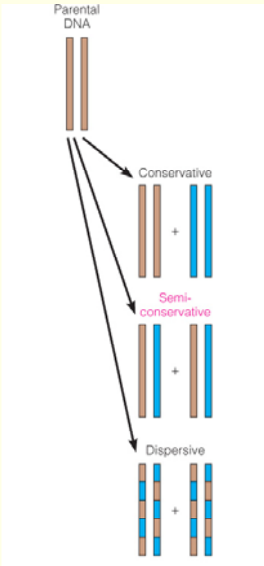

FIGURE 4.13
Three models of DNA replication. Experimental evidence supports the semiconservative model. Brown, parental DNA; blue, new DNA.

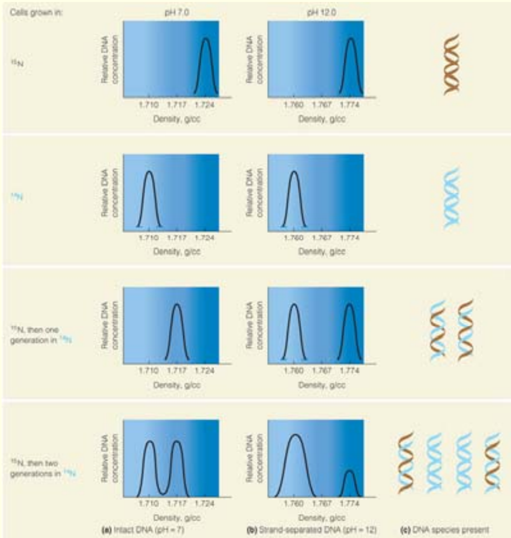

FIGURE 4.14
The Meselson–Stahl experiment proves DNA replicates semiconservatively. The banding patterns shown were obtained in density gradients under two pH conditions. At pH 7, the DNA is double-stranded; at pH 12 the strands are separated, and DNA is in the random-coil configuration.

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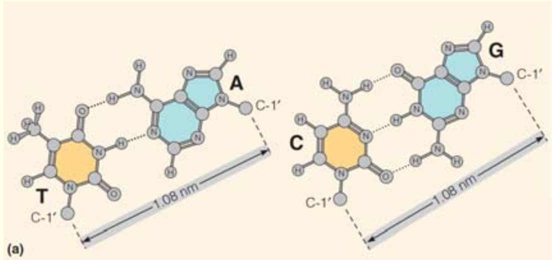
Secondary and Tertiary

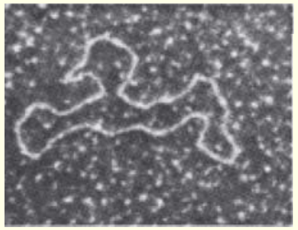
- A-T and G-C are the base pairs in the Watson–Crick model of DNA.
  - o Note the base pairing occurs between the keto tautomers.
  - o The AT pair has two hydrogen bonds.
  - o The GC pair has three hydrogen bonds.



- The complementary, two-strand structure of DNA explains how the genetic material can be replicated.

Secondary and Tertiary

- DNA in cells can differ in size and shape.
- DNA can be from thousands to millions of base pairs in length.
- DNA can be circular or linear.
- DNA can be relaxed or supercoiled

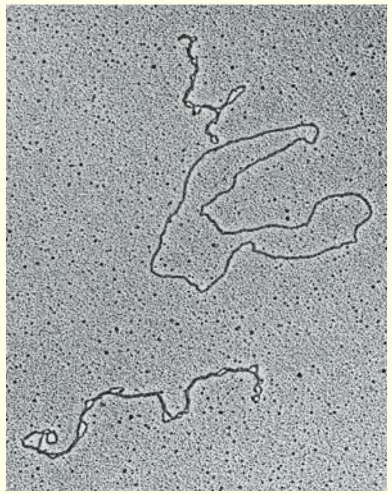


Viral single-strand DNA (circular)

Bacteriophage double-strand DNA (linear)

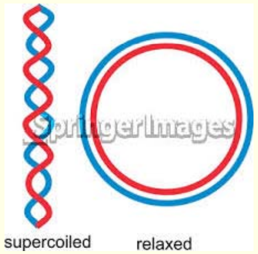
Secondary and Tertiary

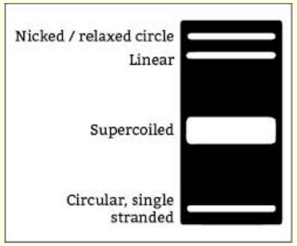
- Relaxed and supercoiled DNA molecules.
- Electron micrograph showing three human mitochondrial DNA molecules.
- All three are of identical sequence and contain 16,569 bp each.
- However, the molecule in the center is relaxed, whereas those at top and bottom are tightly ***supercoiled***.
- Most DNA molecules found *in vivo* are left-handed supercoils.



Secondary and Tertiary

- The DNA or RNA sequence is a ***primary structure***, held together by covalent bonds
- The regular folding patterns observed in the A- and B-DNA double helices are referred to as their ***secondary structures***, held together by non-covalent hydrogen bonds.
- The high-order folding of DNA's secondary structure is called its ***tertiary structure***. These structure are also held together by non-covalent interactions.





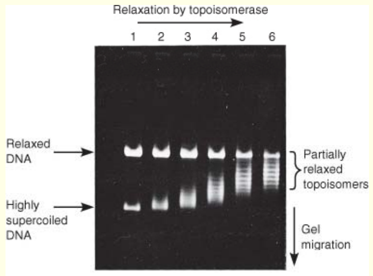


FIGURE 4.26

Gel electrophoresis demonstrating DNA supercoiling. Lane 1: A mixture of relaxed and highly supercoiled DNA. Lanes 2 to 6: The progress of relaxation catalyzed by the enzyme topoisomerase. Samples have been taken at successive times after adding the enzyme. Individual topoisomers are resolved as individual bands on the gel. The highly supercoiled material, which forms a densely packed series of overlapping bands at the bottom, gradually disappears. The DNA species are resolved by electrophoresis in an agarose gel and then visualized by adding the dye ethidium bromide (page 1078) to the gel, a treatment that makes each DNA species fluorescent.

Courtesy of J. C. Wang.

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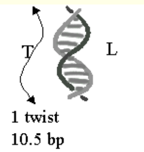
DNA tertiary structure



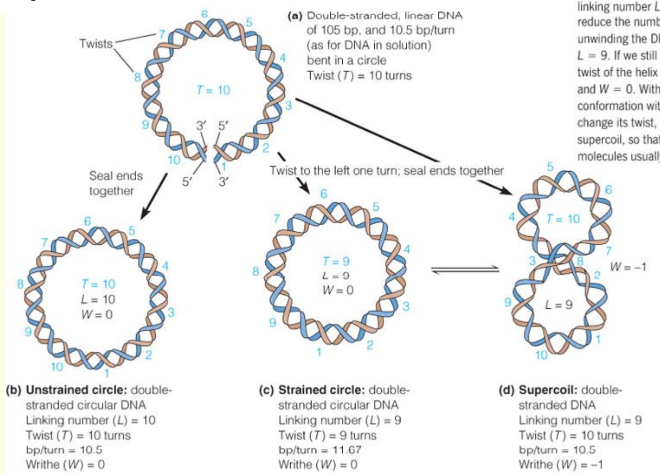


FIGURE 4.25

Forming a DNA supercoil. We can imagine making a linear DNA circular in several ways: **(a)** A linear DNA is laid flat. It has 105 base pairs and 10.5 bp/turn, so there are 10 turns; the twist $T = 10$. **(b)** Because there is an integral number of turns, we can link the 5′ and 3′ ends together without twisting, to form a relaxed circle that lies flat. The linking number $L = 10$ and the writhe $W = 0$. **(c)** If we reduce the number of turns before joining the ends, by unwinding the DNA one turn, the closed circle will have $L = 9$. If we still require the DNA molecule to lie flat, the twist of the helix must change. We now have $L = 9$, $T = 9$, and $W = 0$. With $T = 9$ in 105 bp, the DNA is forced into a conformation with 105/9 = 11.67 bp/turn. **(d)** Rather than change its twist, the strained DNA molecule may writhe, or supercoil, so that $L = 9$, $T = 10$, and $W = 1$. Strained molecules usually supercoil rather than change their twist.

L=T+W

Cutting, twisting, re-joining by topisomerase (DNA gyrase)

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Plasticity of Secondary and Tertiary DNA Structure

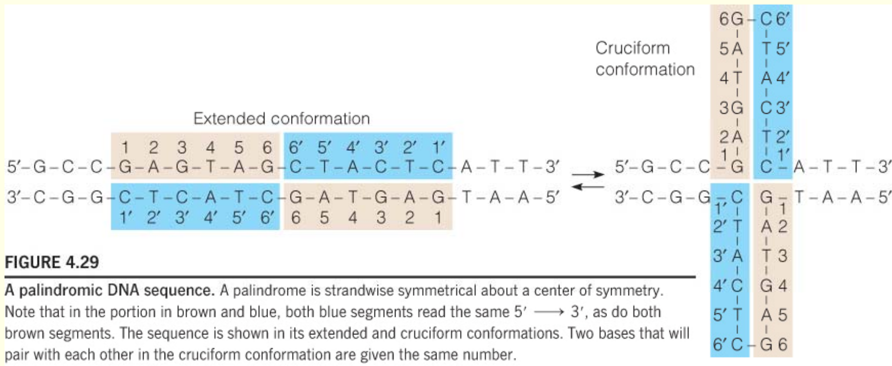


FIGURE 4.29

A palindromic DNA sequence. A palindrome is strandwise symmetrical about a center of symmetry. Note that in the portion in brown and blue, both blue segments read the same 5′ ⟶ 3′, as do both brown segments. The sequence is shown in its extended and cruciform conformations. Two bases that will pair with each other in the cruciform conformation are given the same number.

The critical biological processes of DNA recombination and repair that occur in the cell

DNA Denaturation

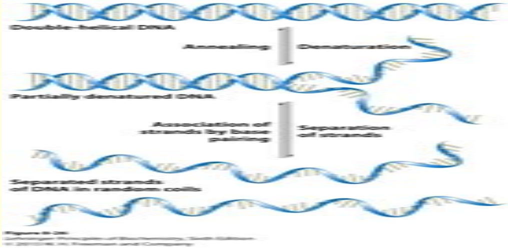
- Covalent bonds remain intact
  - Genetic code remains intact
- Hydrogen bonds are broken
  - Two strands separate
- Base stacking is lost
  - UV absorbance increases---**Hyperchromic shift of UV absorbance upon denaturation**
- **Tm: Midpoint of milting.**

- Denaturation can be induced by high temperature, or change in pH , ionic strength

- Denaturation may be reversible:annealing

Thermal DNA Denaturation (Melting)

- DNA exists as double helix at normal temperatures
- Two DNA strands dissociate at elevated temperatures
- Two strands re-anneal when temperature is lowered
- The reversible thermal denaturation and annealing form basis for the polymerase chain reaction (PCR)
- DNA denaturation is commonly monitored by UV spectrophotometry at 260 nm



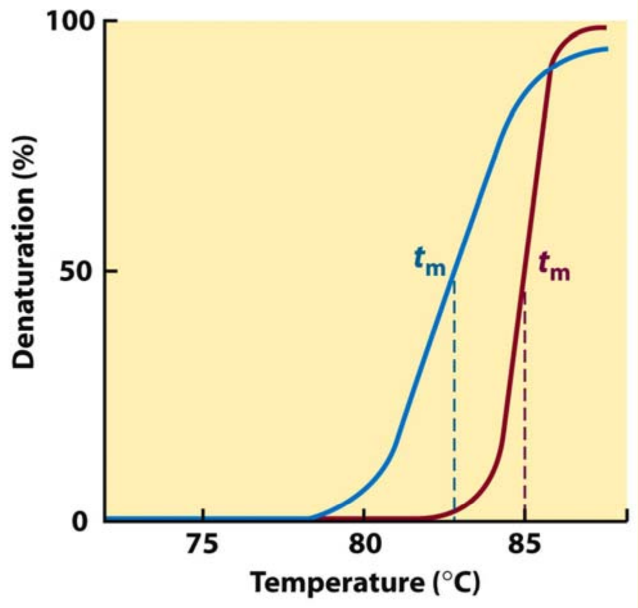


Figure 8-27a
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Factors Affecting DNA Denaturation

- The midpoint of melting (T_m) depends on base composition
  - high CG increases T_m
- T_m depends on DNA length
  - Longer DNA has higher T_m
- T_m depends on pH and ionic strength
  - High salt increases T_m

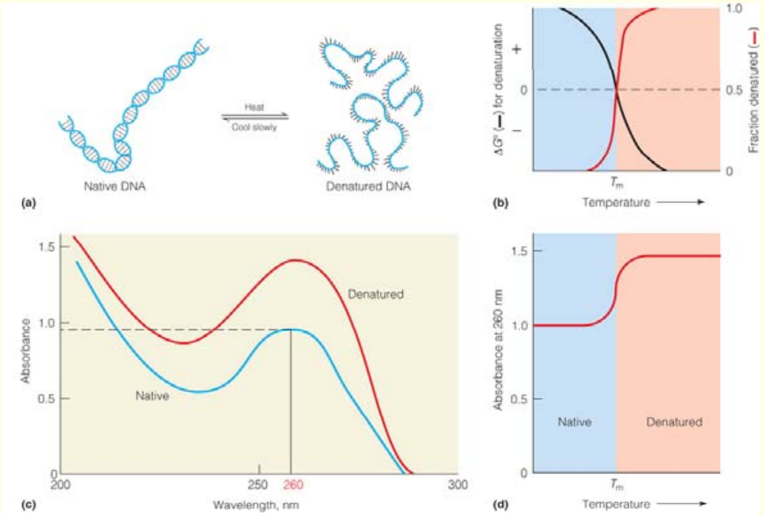

FIGURE 4.34

Denaturation of DNA. (a) When native (double-stranded) DNA is heated above its "melting" temperature, it is denatured (separates into single strands). The two random-coil strands have a higher entropy than the double helix. **(b)** At low T, ΔG is positive and denaturation of DNA is not favored. As T increases, $-T\Delta S$ overcomes ΔH, making ΔG negative and denaturation favorable. The midpoint of the curve marks the "melting" temperature, T_m, of DNA. **(c)** Absorption spectra of native and denatured DNA show that native DNA absorbs less light than denatured DNA, with the maximum difference occurring at a wavelength of 260 nm. This **hypochromicity** of double-stranded DNA can be used to distinguish between native and denatured forms. **(d)** The change in absorbance can be used to follow the denaturation of DNA as temperature increases. An abrupt increase in absorbance, corresponding to the sudden "melting" of DNA, is seen at T_m.

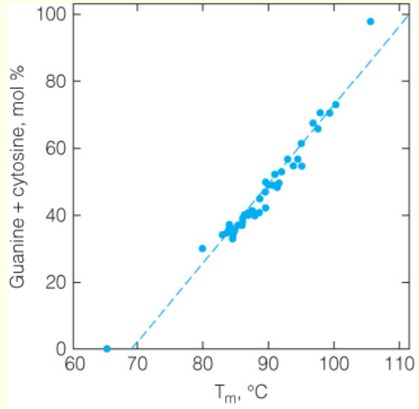

FIGURE 4.35

Effect of base-pair composition on the denaturation temperature of DNA. The graph shows the rise in "melting" temperature of DNA as its percent (G + C) increases.

Data from *Journal of Molecular Biology* (1962) 5:120, J. Marmur and P. Doty.

Depurination: DNA, pH 3, purine base removed

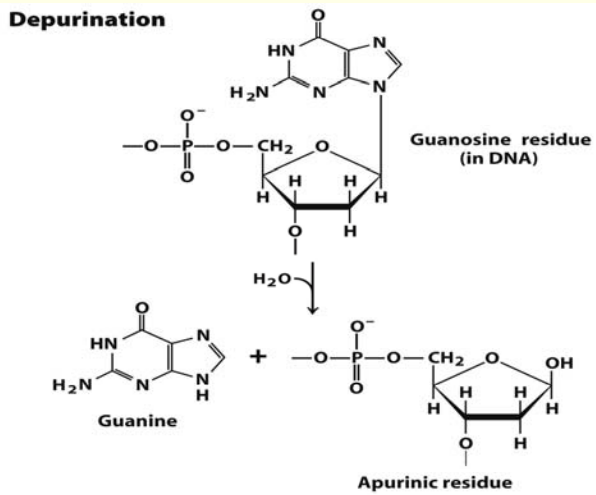

Figure 8-30b
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DNA sequencing

***Chain termination (dideoxynucleotide): Sanger**

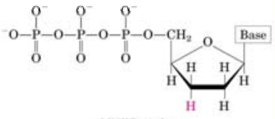
Enzymatic synthesis of DNA using DNA polymerase

Primer extended using dNTPs but terminated using specific ddNTPs (lack 3' hydroxyl)

Four reactions produce four sets of products

Analyze products by electrophoresis

*** Automatic DNA sequencing: End-label DNA with dideoxynucleotides with fluorescent dyes of different colors**



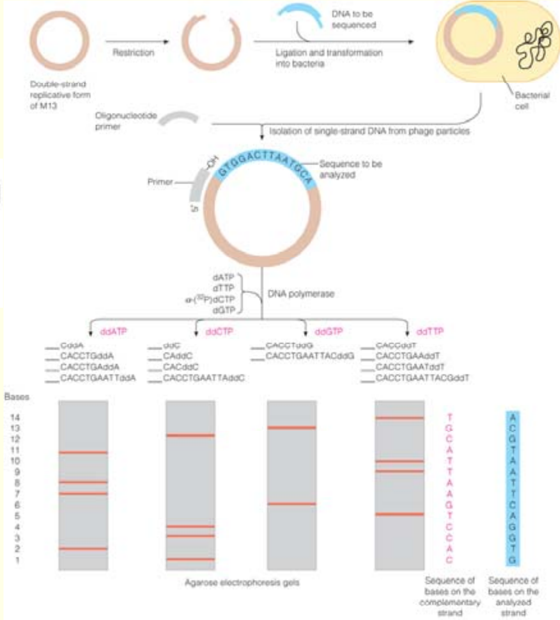


FIGURE 4B.6
Cloning into M13 and sequencing by the Sanger method.

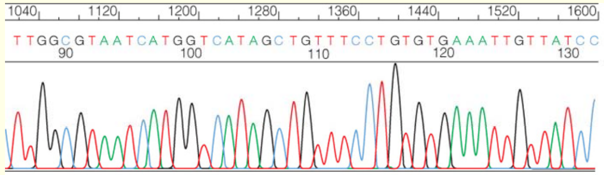


FIGURE 4B.7
Data from a DNA sequencing gel.
Courtesy of Dr. Robert H. Lyons, The University of Michigan's DNA Sequencing Core.

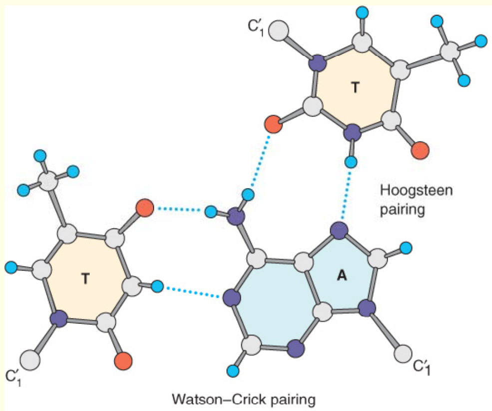
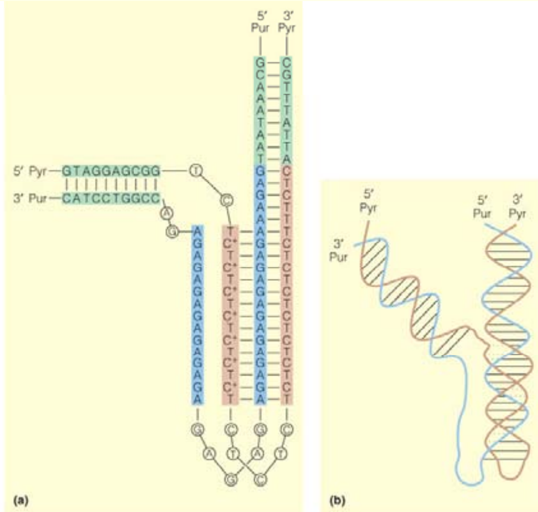


FIGURE 4.30
Base-pairing in one type of DNA triple helix. Both normal Watson–Crick pairing and the unusual Hoogsteen pairing occur on the same A residue.

FIGURE 4.31
H-DNA. An H-DNA region has one all-purine (blue) and one all-pyrimidine (brown) strand, allowing it to form a triple-stranded helix by doubling back. Some segments contain both purines and pyrimidines (green). **(a)** The nucleotide sequence shown here is one that could give rise to H-DNA. A segment of the purine strand is shown bonded to two different segments of the pyrimidine strand. **(b)** The bonding shown in (a) gives rise to a triple-stranded helix, shown schematically here.



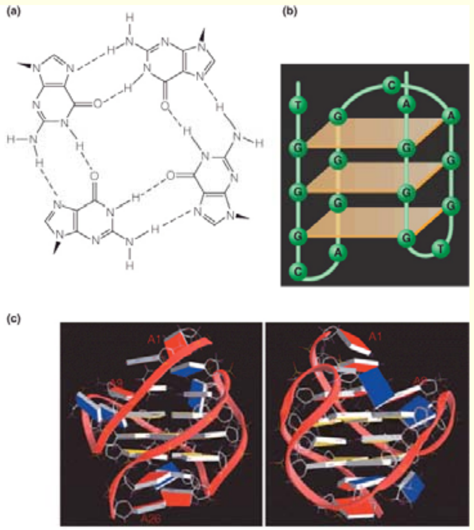


FIGURE 4.32

G-quartets and quadruplexes. (a) Arrangement of bases in a G-quartet, with four Hoogsteen-bonded guanines surrounding a central metal ion (not shown); **(b)** Folding of a single DNA strand to give a G-quadruplex, consisting in this example of three planar G-quartets. **(c)** Two views of the G-quadruplex formed by the DNA sequence in human telomeres. Yellow, guanine; red, adenine; blue, thymine.

Primary structure:
Sequence of nucleotide chains.

Secondary structure:
It is a double helix structureIt was postulated by Watson and Crick, based on X-ray diffraction that Franklin and Wilkins had been made, and the equivalence of bases Chargaff

It is a double strand, right-handed or left-handed, depending on the DNA.
There are three models of DNA. The DNA of type B is the most abundant and is discovered by Watson and Crick.

Tertiary structure:
Refers to how DNA is stored in a confined space to form the chromosomes. Varies depending on whether the organisms prokaryotes and eukaryotes:

In prokaryotes the DNA is folded like a super-helix, usually in circular shape and associated with a small amount of protein.

In eukaryotes since the amount of DNA from each chromosome is very large, the packing must be more complex and compact, this requires the presence of proteins such as histones and other proteins of non-histone

CHAPTER 10 Lipids

Lipids

Key topics:

– Biological roles of lipids
– Structure and properties of storage lipids
– Structure and properties of membrane lipids
– Structure and properties of signaling lipids

Lipids: Structurally Diverse Class

- Low solubility in water
- Good solubility in nonpolar solvents

Biological Functions of Lipids

- Storage of energy
  - Reduced compounds: lots of available energy
- Insulation from environment
  - Low thermal conductivity
  - High heat capacity (can “absorb” heat)
  - Mechanical protection (can absorb shocks)
- Water repellant
  - Hydrophobic nature: keeps surface of the organism dry
    - Prevents excessive wetting (birds)
    - Prevents loss of water via evaporation
- Membrane Structure
  - Main structure of cell membranes

More Functions

- Cofactors for enzymes
  - Vitamin K: blood clot formation
  - Coenzyme Q: ATP synthesis in mitochondria
- Signaling molecules
  - Paracrine hormones (act locally)
  - Steroid hormones (act body-wide)
  - Growth factors
  - Vitamins A and D (hormone precursors)
- Pigments
  - Color of tomatoes, carrots, pumpkins, some birds
- Antioxidants
  - Vitamin E

Classification of Lipids

- Based on the structure and function
  - Lipids that do not contain fatty acids: cholesterol, terpenes, CH2=C(CH3)-CH=CH2 …(C_5H_8) (Vit A)
  - those that are based on **isoprene** , a five-carbon chain. Terpenes are derived biosynthetically from units of isoprene,
  - Terpenes and terpenoids are the primary constituents of the **essential oils** of many types of plants and flowers.
  - Lipids that contain fatty acids
    – Storage lipids and membrane lipids

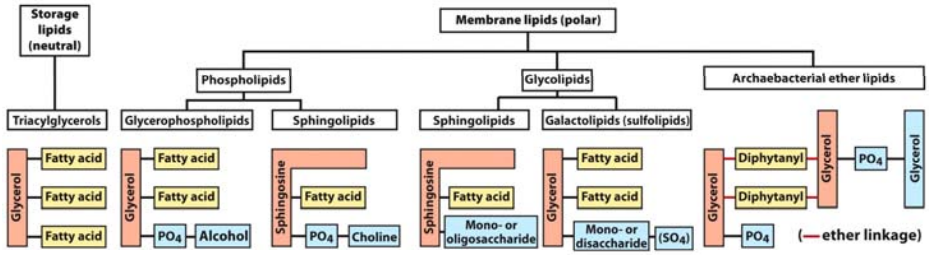


Figure 10-7
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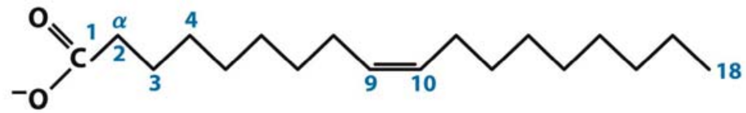
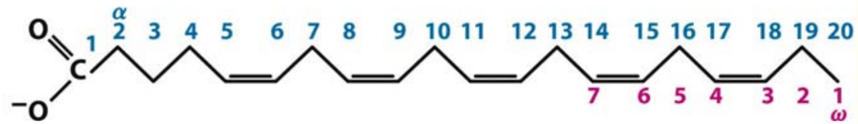
Fatty Acids

- Carboxylic acids with hydrocarbon chains containing from 4 to 36 carbons
- Almost all natural fatty acids have an even number of carbons
- Most natural fatty acids are unbranched
- Saturated: no double bonds between carbons in the chain
- Monounsaturated: one double bond between carbons in the alkyl chain
- Polyunsaturated: more than one double bond in the alkyl chain



(a) 18:1(Δ^9) *cis*-9-Octadecenoic acid



(b) 20:5($\Delta^{5,8,11,14,17}$) Eicosapentaenoic acid (EPA), an omega-3 fatty acid

Figure 10-1
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TABLE 10–1 Some Naturally Occurring Fatty Acids: Structure, Properties, and Nomenclature

Carbon skeleton	Structure*	Systematic name†	Common name (derivation)	Melting point (°C)	Solubility at 30 °C (mg/g solvent) Water	Benzene
12:0	$CH_3(CH_2)_{10}COOH$	*n*-Dodecanoic acid	Lauric acid 月桂酸 (Latin *laurus*, "laurel plant")	44.2	0.063	2,600
14:0	$CH_3(CH_2)_{12}COOH$	*n*-Tetradecanoic acid	Myristic acid 豆蔻酸 (Latin *Myristica*, nutmeg genus)	53.9	0.024	874
16:0	$CH_3(CH_2)_{14}COOH$	*n*-Hexadecanoic acid	Palmitic acid (Latin *palma*, "palm tree")	63.1	0.0083	348
18:0	$CH_3(CH_2)_{16}COOH$	*n*-Octadecanoic acid	Stearic acid (Greek *stear*, "hard fat")	69.6	0.0034	124
20:0	$CH_3(CH_2)_{18}COOH$	*n*-Eicosanoic acid	Arachidic acid (Latin *Arachis*, legume genus)	76.5 花生酸		
24:0	$CH_3(CH_2)_{22}COOH$	*n*-Tetracosanoic acid	Lignoceric acid (Latin *lignum*, "wood" + *cera*, "wax")	86.0		
16:1(Δ^9)	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$	*cis*-9-Hexadecenoic acid	Palmitoleic acid	1 to –0.5		
18:1(Δ^9)	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$	*cis*-9-Octadecenoic acid	Oleic acid (Latin *oleum*, "oil")	13.4		
18:2($\Delta^{9,12}$)	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$	*cis*-,*cis*-9,12-Octadecadienoic acid	Linoleic acid (Greek *linon*, "flax")	1–5		
18:3($\Delta^{9,12,15}$)	$CH_3CH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$	*cis*-,*cis*-,*cis*-9,12,15-Octadecatrienoic acid	α-Linolenic acid	–11		
20:4($\Delta^{5,8,11,14}$)	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_3COOH$	*cis*-,*cis*-,*cis*-,*cis*-5,8,11,14-Icosatetraenoic acid	Arachidonic acid	–49.5		

*All acids are shown in their nonionized form. At pH 7, all free fatty acids have an ionized carboxylate. Note that numbering of carbon atoms begins at the carboxyl carbon.

†The prefix *n*- indicates the "normal" unbranched structure. For instance, "dodecanoic" simply indicates 12 carbon atoms, which could be arranged in a variety of branched forms; "*n*-dodecanoic" specifies the linear, unbranched form. For unsaturated fatty acids, the configuration of each double bond is indicated; in biological fatty acids the configuration is almost always cis.

Table 10-1
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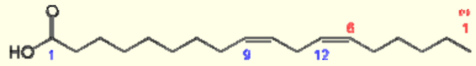
Fatty Acid Nomenclature

Conformation of Fatty Acids

- The saturated chain tends to adopt extended conformations
- The double bonds in natural unsaturated fatty acids are commonly in cis configuration

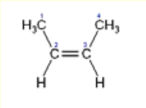
ω-3系列的脂肪酸:
EPA（Eicosapentaenoic Acid）20:5
DHA（Docosahexaenoic Acid）22:6
ALA（α- linoleic acid；**α-**亞麻油酸）18:3

ω-6系列的脂肪酸:
LA（linoleic acid；亞麻油酸） 18:2
GLA (Gamma linoleic acid；**γ-**亞麻油酸) 18:3
AA 花生烯酸 (Arachidonic acid) 20:4

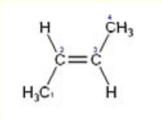


Trans Fatty Acids

- Trans fatty acids form by partial dehydrogenation of unsaturated fatty acids
- Trans fatty acids can pack more regularly, and show higher melting points than cis forms



cis



trans

Consuming trans fats increases risk of cardiovascular disease

Avoid deep-frying partially hydrogenated vegetable oils
Current trend: reduce trans fats in foods (fast food)

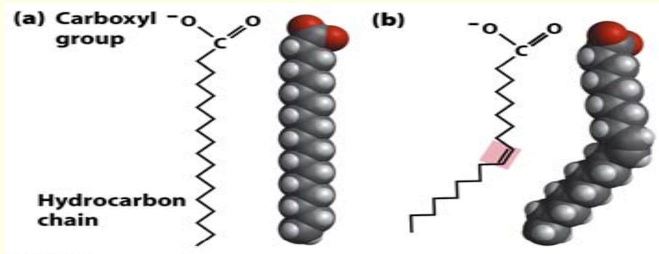


Figure 10-2ab

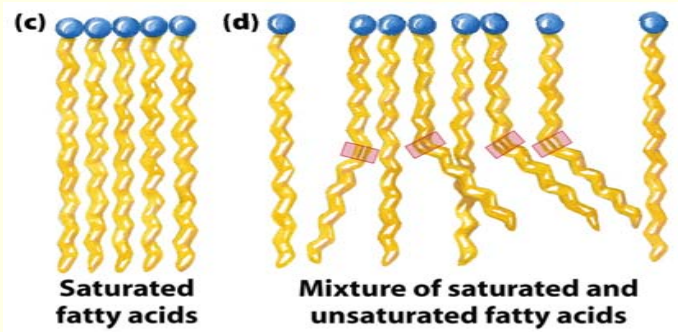


Figure 10-2cd

Triacylglycerols (fats and oils)

- Majority of fatty acids in biological systems are found in the form of triacylglycerols
- Solid ones are called fats
- Liquid ones are called oils
- Triacylglycerols are the primary storage form of lipids (body fat)
- Triacylglycerols are less soluble in water than fatty acids due to the lack of charged carboxylate group
- Triacylglycerols are less dense than water: fats and oils float

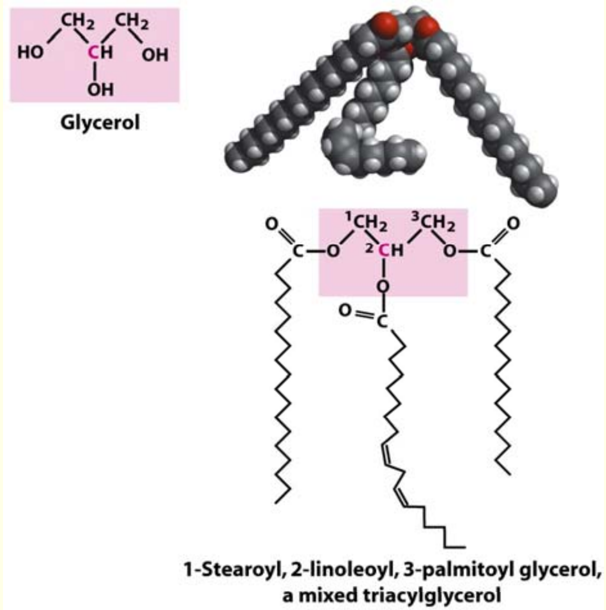


Figure 10-3
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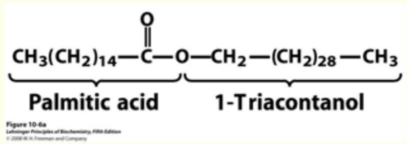
Fats Provide Efficient Fuel Storage

- The advantage of fats over polysaccharides:
  - Fatty acid carry more energy per carbon because they are more reduced
  - Fatty acids carry less water along because they are nonpolar
- Glucose and glycogen are for short-term energy needs, quick delivery
- Fats are for long term (months) energy needs, good storage, slow delivery

Waxes

- Waxes are esters of long-chain saturated and unsaturated fatty acids with long-chain alcohols
- Insoluble and have high melting points
- Variety of functions:
  - Storage of metabolic fuel in plankton(浮游生物)
  - Protection and pliability (柔軟) for hair and skin in vertebrates
  - Waterproofing of feathers in birds
  - Protection from evaporation in tropical plants
  - Used by people in lotions, ointments, and polishes



Biological Wax

Simple Lipid:

Triacylglycerides (Triacylglycerols): provide stored energy and insulation.

Glycerol esterified with three fatty acids.

Such as: Fats, oils and waxes.

Complex Lipids:membrane lipid

- **Phospholipids:**
  - **→Glycerophospholipids (Glycerol+2FA+PO4)**
  - **→ Sphingolipids (Sphingosine+FA+PO4)**
- **Glycolipids:**
  - **→ Sphingolipids (Sphingosine+FA+sugar)**
  - **→ Galactolipids (Glycerol+2FA+sugar)**

Glycerophospholipids:

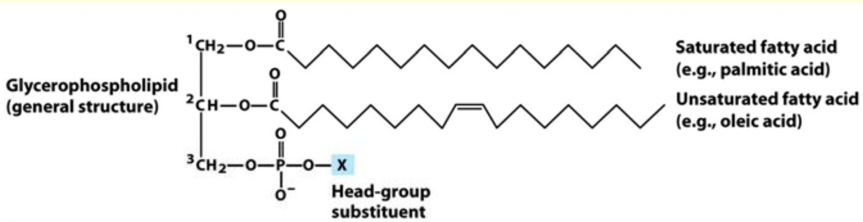


Figure 10-9 part 1
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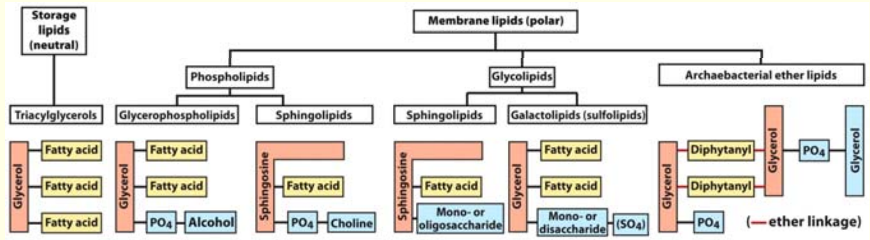

Figure 10-7
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Examples of Glycerophospholipids

- The properties of head groups determine the surface properties of cell membranes
- Different organisms have different membrane lipid head group compositions
- Different tissues have different membrane lipid head group compositions

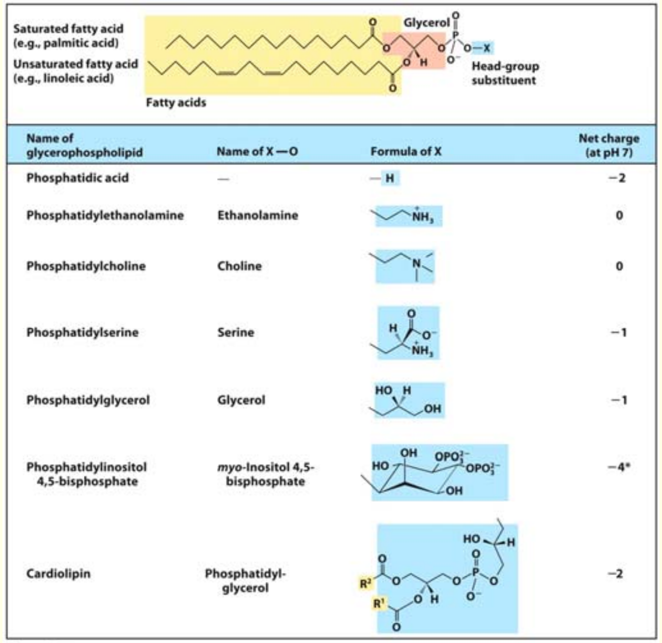

Figure 10-9
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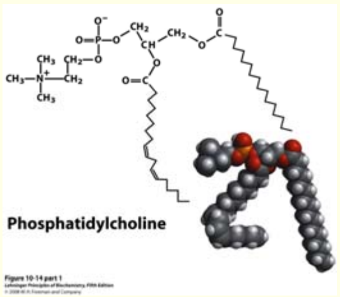
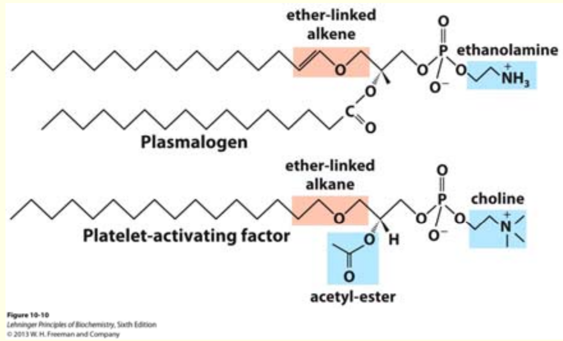
Phosphatidylcholine

- Phosphatidylcholine is the major component of most eukaryotic cell membranes
- Many prokaryotes, including *E. coli* cannot synthesize this lipid; their membranes do not contain phosphatidylcholine



Ether Lipids: Plasmalogen

- Common in vertebrate heart tissue
- Also found in some protozoa and anaerobic bacteria
- Function is not well understood



Ether Lipids: Platelets-Activating Factor

- Aliphatic（脂肪）ether analog of phosphatidylcholine
- Acetic acid has esterified position C2
- First signaling lipid to be identified
- Stimulates aggregation of blood platelets
- Plays role in mediation of inflammation

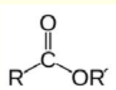
(D) 5.支氣管哮喘症(Bronchial asthma)的早期變化約在暴露於過敏原後30分鐘內發生，其致病機轉與下列物質有關，何者除外?
A.Histamine
B.Leukotrienes
C.Prostaglandins
D.Dopamine
E.PAF(platelet-activating factor)

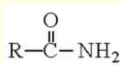
Sphingolipids:

Backbone of sphingosine: 18-Carbon amino alcohol with C-C trans double bond. Sphingolipids are derivatives of Sphingosine. (Fig 10-13)

Sphingolipids

- The backbone of sphingolipids is NOT glycerol
- The backbone of sphingolipids is a long-chain amino alcohol sphingosine
- A fatty acid is joined to sphingosine via an amide linkage rather than an ester linkage as usually seen in lipids
- A polar head group is connected to sphingosine by a glycosidic or phosphodiester linkage
- The sugar-containing glycosphingolipids are found largely in the outer face of plasma membranes


ester linkage


amide linkage

cerebroside:
ceramide + monosaccharide

an important constituent of brain cell membranes.

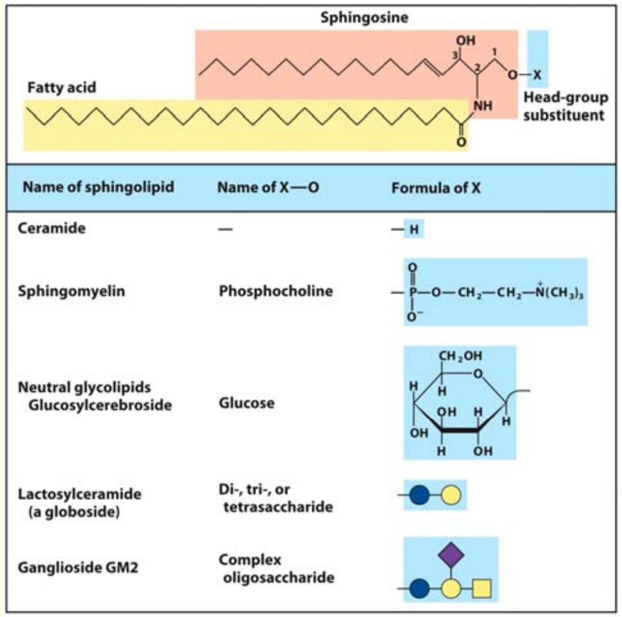


Figure 10-13
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Sphingomyelins:

1. In plasma membrane
2. A membranous sheath in some neurons

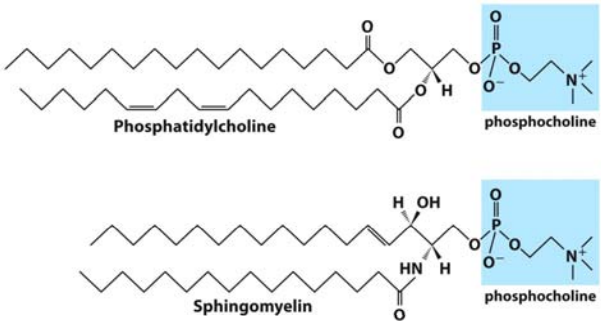

Figure 10-14
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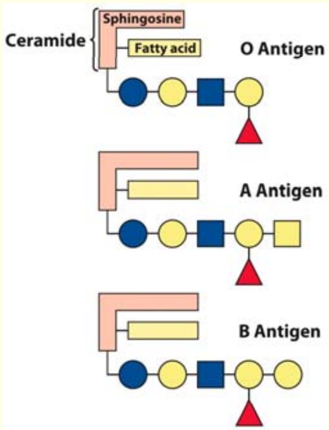
Glycosphingolipids and Blood Groups

- The blood groups are determined in part by the type of sugars located on the head groups in glycosphingolipids.
- The structure of sugar is determined by a expression of specific glycosyltransferases
  - Individuals with no active glycosyltransferase will have the **O antigen**
  - Individuals with a glycosyltransferase that transfers an N-acetylgalactosamine group have **A blood group**
  - Individuals with a glycosyltransferase that transfers a galactose group to phosphate will have **B blood group**

Glycosphingolipids at cell surfaces are sites of biological recognition: (Fig 10-15)

Blood A, B, O.

glycosyltransferases



N-acetylgalactosamine

galactose

Figure 10-15
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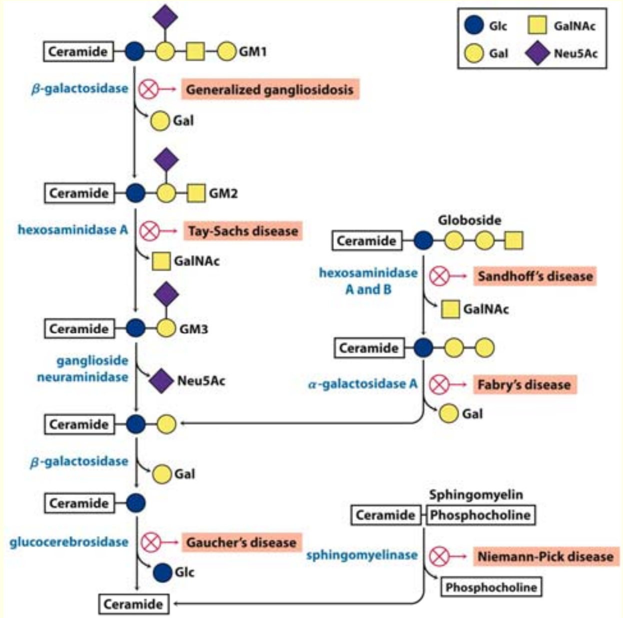

Box 10-1 figure 1
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Niemann-PicK disease

1. Sphingomyelin accumulates in brain, spleen and liver
2. Mental retardation, early death

Tay-Sachs disease

1. Ganglioside GM2 accumulates in brain, spleen.
2. Progressive retardation in development, paralysis, blindness, death 3, or 4y.

Lipids as signals, cofactors, and pigments

Membrane lipid: 5-10% of cells

Storage lipids: >80% of adipocyte.

Phosphatidylinositols act as intracellular signals

Fig 11-15. 1,4,5-triphosphate (IP3)—Ca^{++} release.

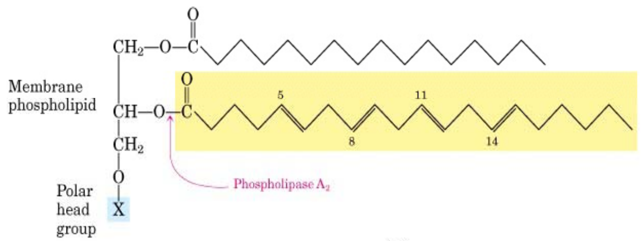
Ceramids and sphingomyelin are potent regulators of protein kinases.

Signaling Lipids

- Paracrine lipid hormones are are present in small amounts but play vital roles as signaling molecules between nearby cells
- Enzymatic oxidation of arachidonic acid yields
  - prostaglandins,
  - thromboxanes, and
  - leukotrienes

Arachidonic Acid : Derivatives as Signaling Lipids (20:4 (Δ5,8,11,14) 花生四烯酸) Omega-6 fatty acids

- Variety of functions:
  - Inflammation and fever (prostaglandins)
  - Formation of blood clots (thromboxanes)
  - Smooth muscle contraction in lungs (leukotrienes)
  - Smooth muscle contraction in uterus (prostaglandins)



(a)

Eicosanoids carry messages to nearby cells

paracrine hormone involved in:

reproductive function

inflammation function

formation blood clot, regulation blood pressure derived from 20-carbon polyunsaturated fatty acid arachidonic acids 20:4 (Δ5,8,11,14).

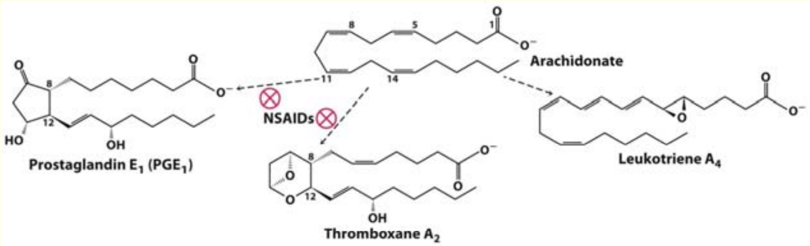


Figure 10-18
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Eicosanoids, 3 classes

A. Prostaglandins:

1 regulate cAMP.

2 stimulate contraction of smooth muscle of uterus, pain for MC and Labor.

3 affect blood flow. 4 affect wake-sleep cycle. 5 elevate body temp.

B. Thromboxanes:

1. produced by platelets. Act in formation of blood clots, reduction blood flow.

2. NSAIDs (non-steroidal anti- inflammatory drugs): aspirin, ibuprofen, acetaminophen.

C. Leukotrienes:

Derived from leukocytes. Induces contraction of muscle lining of the lung—asthmatic attacks or anaphylactic shock.

Prednisone-anti-asthmatic, anti-rheumatoid arthritis drugs.

Lipids Summary

In this chapter, we learned that:

- lipids are a structurally and functionally diverse class of molecules that are poorly soluble in water
- triacylglycerols are the main storage lipids
- phospholipids are the main constituents of membranes
- sphingolipids play roles in cell recognition
- cholesterol is both a membrane lipid and the precursor for steroid hormones
- some lipids carry signals from cell to cell and from tissue to tissue