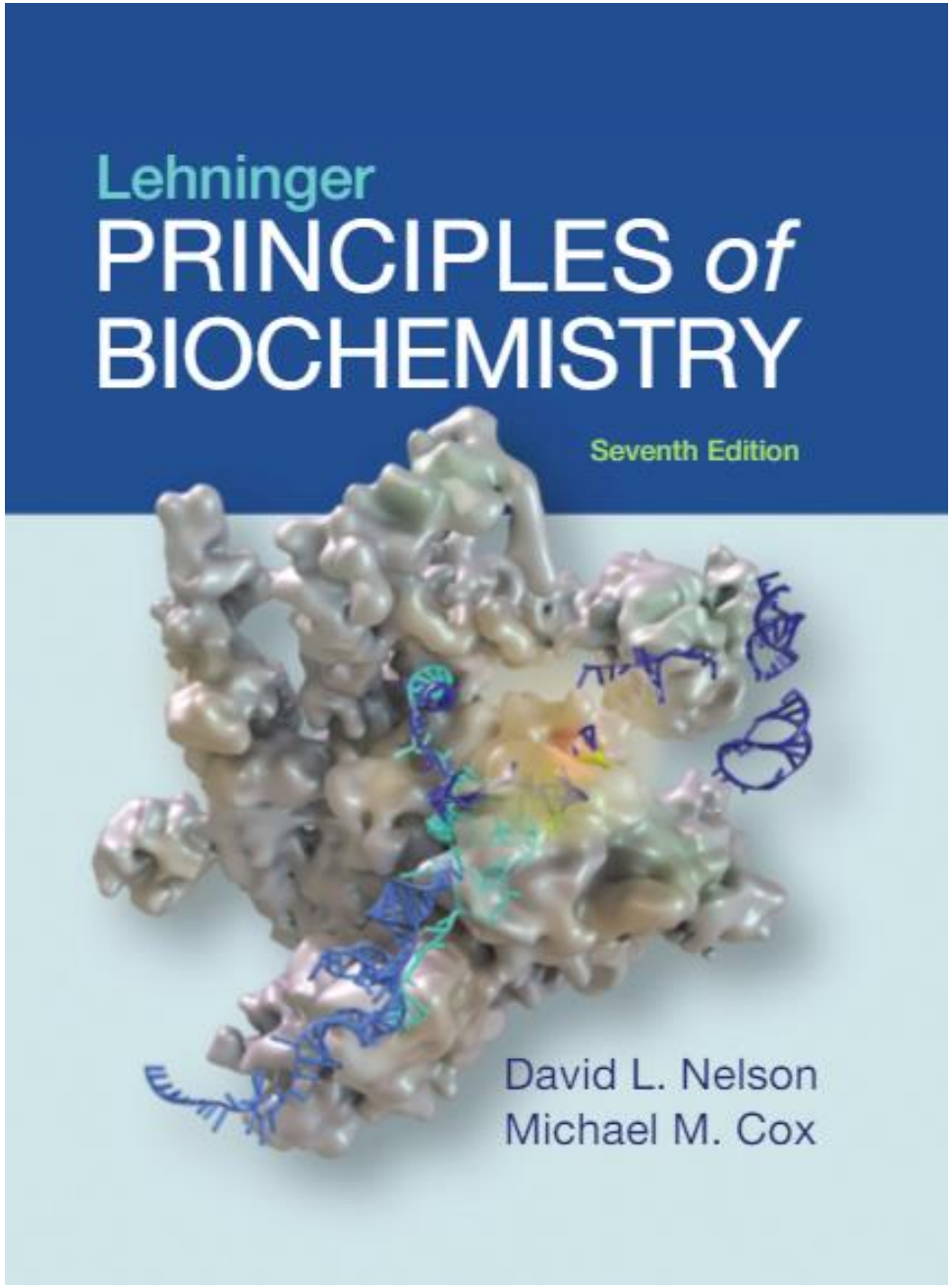
8| Nucleotides and Nucleic Acids



CHAPTER 8
Nucleotides and Nucleic Acids

Learning goals:

- Biological function of nucleotides and nucleic acids
- Structures of common nucleotides
- Structure of double-stranded DNA
- Structures of ribonucleic acids
- Denaturation and annealing of DNA
- Chemistry of nucleic acids; mutagenesis

8.1 Some Basics

- **Gene:** a segment of a DNA molecule that contains information required for the synthesis of a functional biological product (protein or RNA)

- The only known function of DNA is to *store and transmit biological information*

RNAs

- RNAs have broader range of functions:

  - **Ribosomal RNAs (rRNAs)** – components of ribosomes

  - **Messenger RNAs (mRNAs)** – carry genetic information from genes to a ribosome

  - **Transfer RNAs (tRNAs)** – adapter molecules that translate the information in mRNA into specific aa sequence

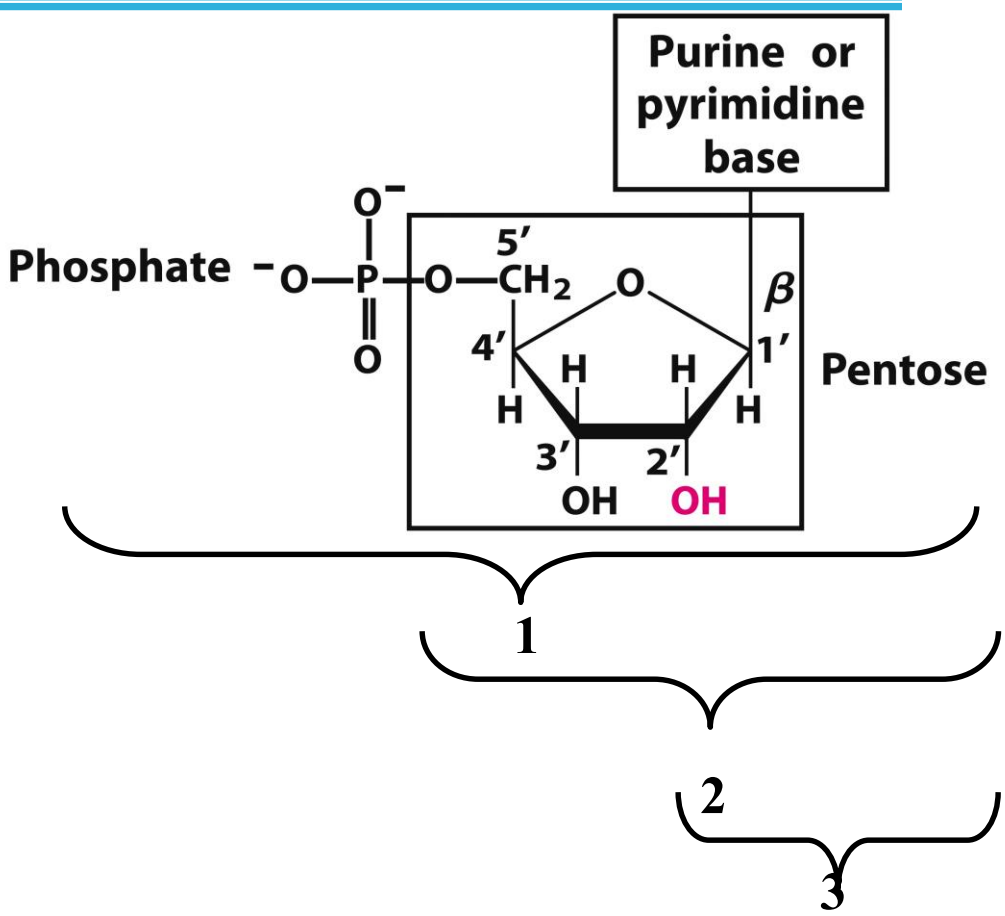
  - Many other forms of RNA are present *in vivo*

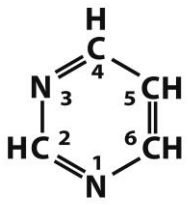
Functions of Nucleotides and Nucleic Acids

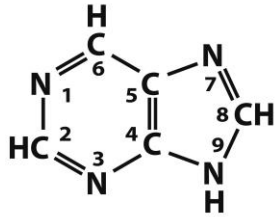
- *Nucleic acids* are polymers of nucleotides used for:
  - storage of genetic info (DNA)
  - transmission of genetic info (mRNA)
  - processing of genetic information (ribozymes)
  - protein synthesis (tRNA and rRNA)
- *Nucleotides* are also used in the monomer form for cellular functions:
  - energy for metabolism (ATP)
  - enzyme cofactors (NAD^+)
  - signal transduction (cAMP)

Nucleotides and Nucleosides

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





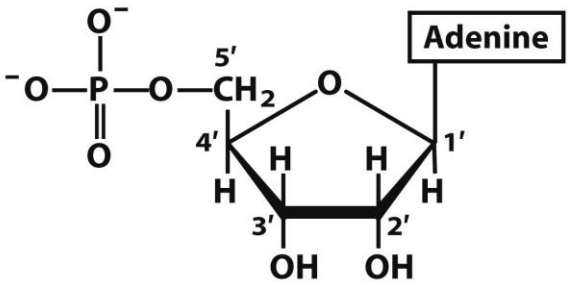


- *Carbon AND nitrogen atoms on the nitrogenous base are numbered in cyclic format.*
- *Carbons of the pentose are designated N' to alleviate confusion.*

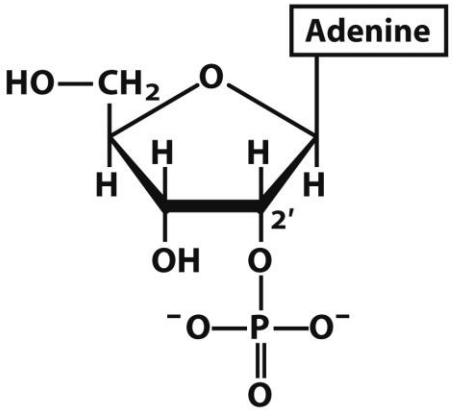
Phosphate Group

- Negatively charged at neutral pH
- Typically attached to 5’ position
  - Nucleic acids are built using 5’-triphosphates
    - ATP, GTP, TTP, CTP
  - Nucleic acids contain one phosphate moiety per nucleotide
- May be attached to other positions for specialized functions

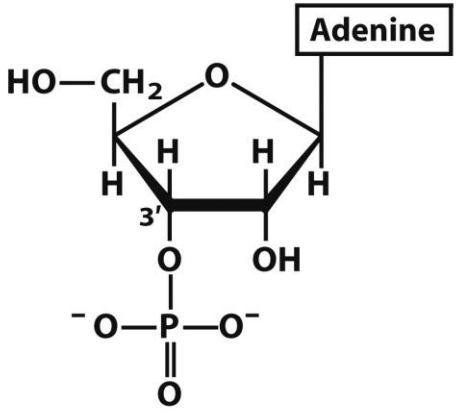
Other Nucleotides: Monophosphate Group in Different Positions



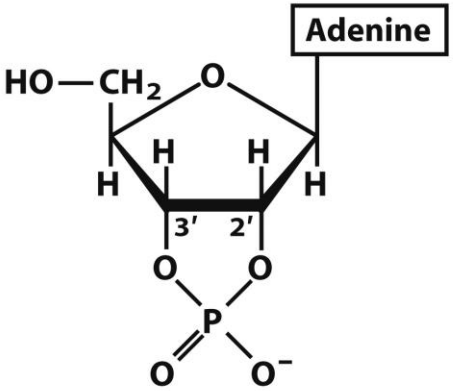
Adenosine 5′-monophosphate



Adenosine 2′-monophosphate



Adenosine 3′-monophosphate

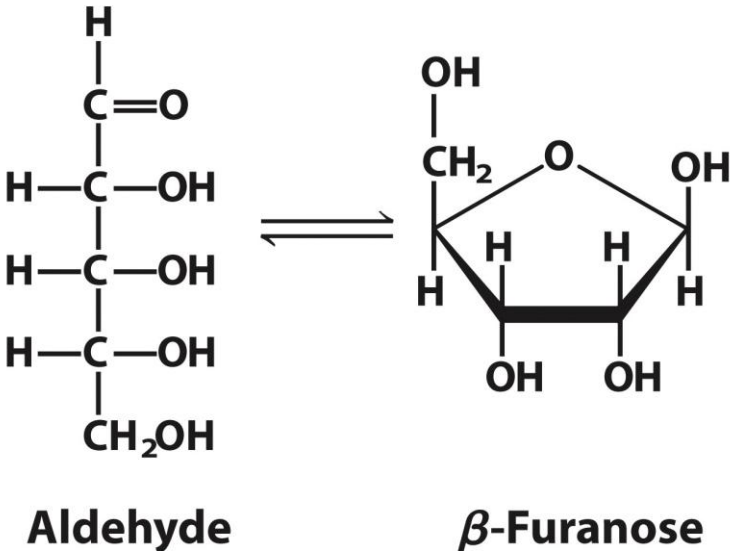


Adenosine 2′,3′-cyclic monophosphate

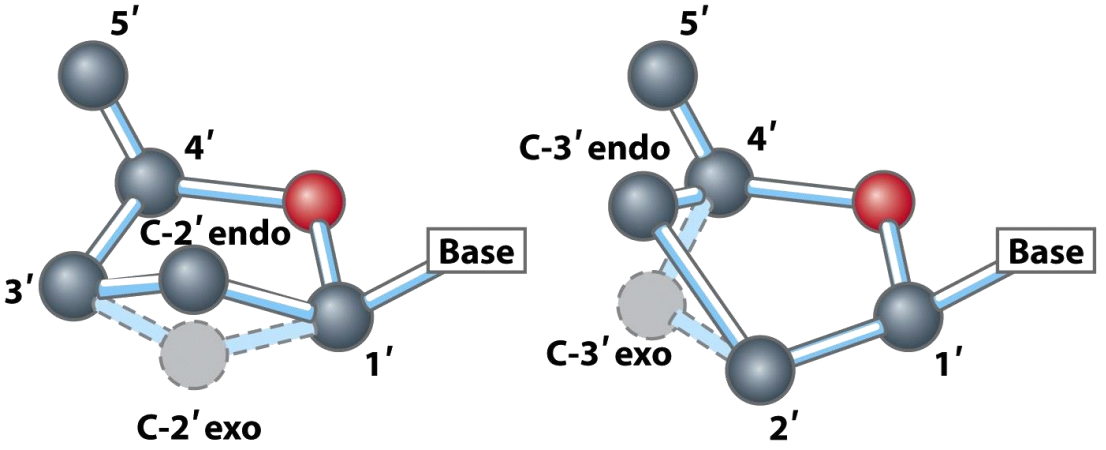
Figure 8-6
Lehninger Principles of Biochemistry, Sixth Edition

Pentose in Nucleotides

- β-D-ribofuranose in RNA
- β-2′-deoxy-D-ribofuranose in DNA

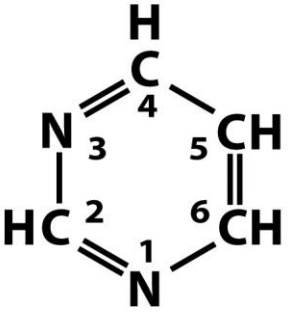


- The pentose ring is not planar: Different "puckered" conformations of the sugar ring are possible

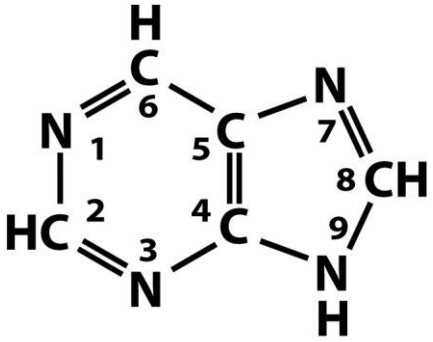


Nucleobases

- Derivatives of pyrimidine or purine
- Nitrogen-containing heteroaromatic molecules



Pyrimidine



Purine

- Planar or almost planar structures
- Absorb UV light around 250-270 nm

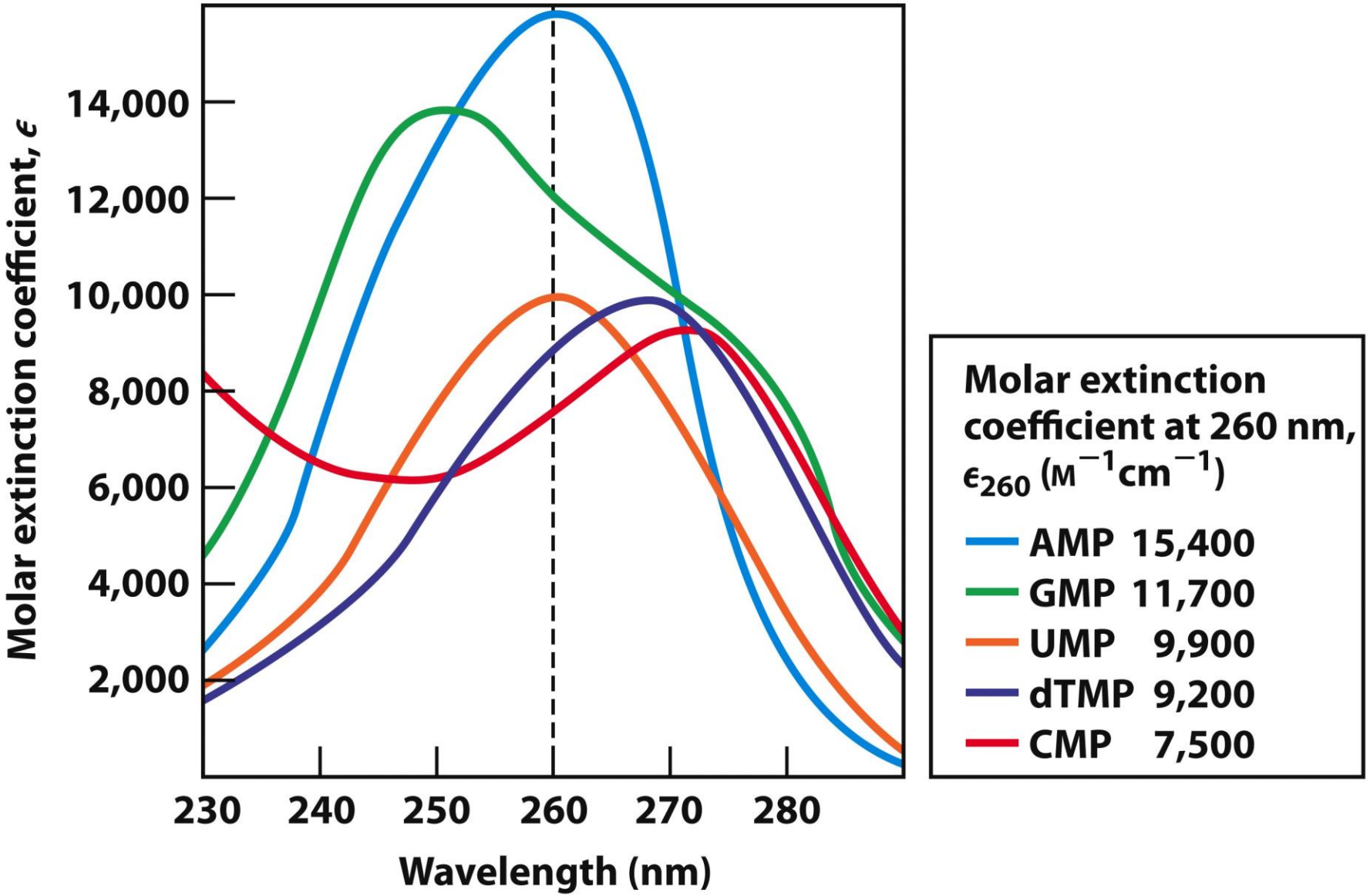
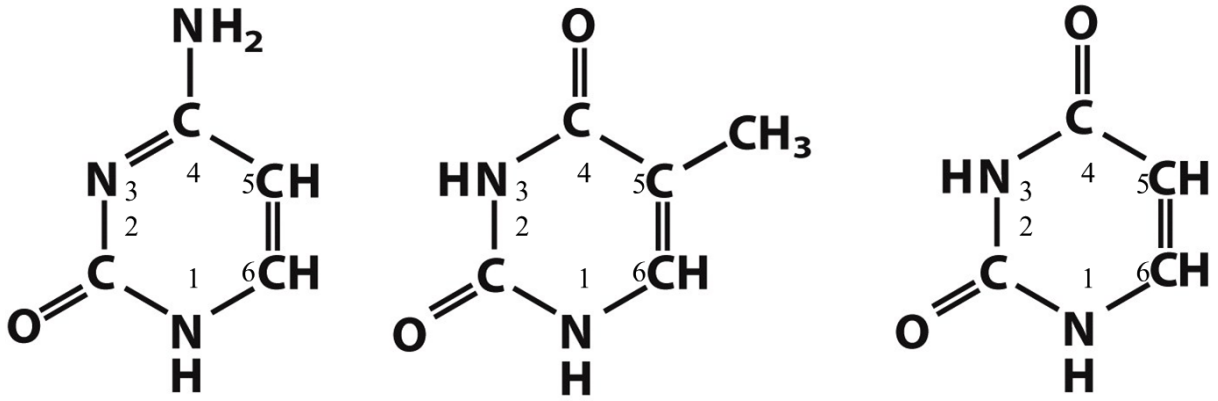


Figure 8-10
Lehninger Principles of Biochemistry, Sixth Edition

Pyrimidine Bases

- Cytosine is found in both DNA and RNA
- Thymine is found only in DNA
- Uracil is found only in RNA (very rarely in DNA)
- All are good H-bond donors and acceptors
- Neutral molecules at pH 7



Cytosine

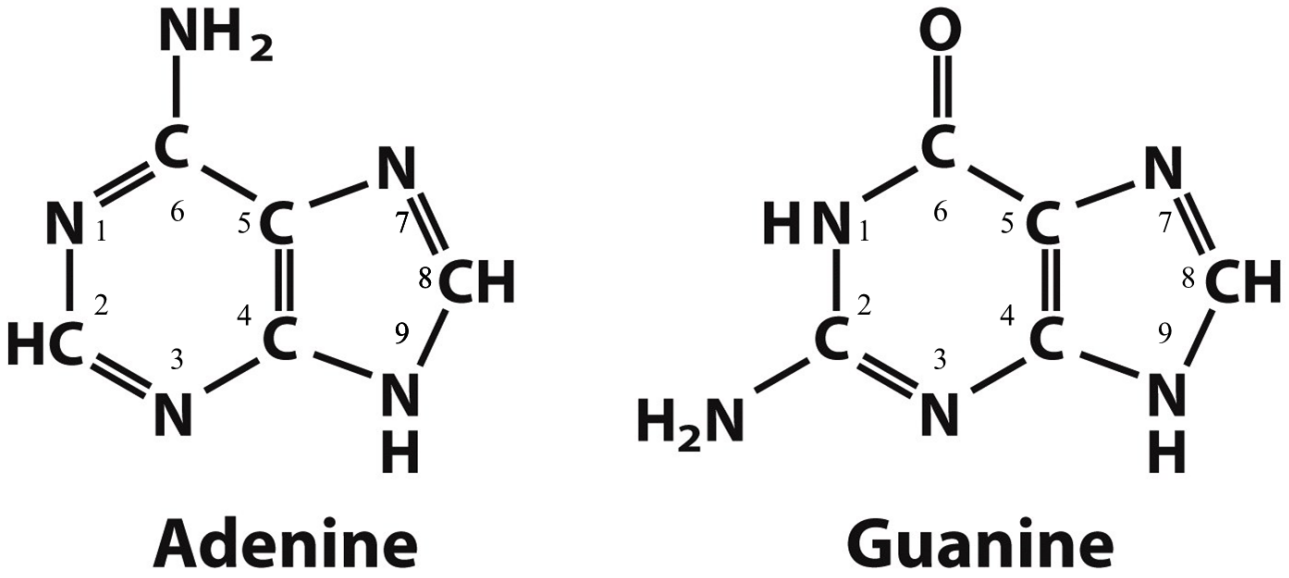
Thymine (DNA)

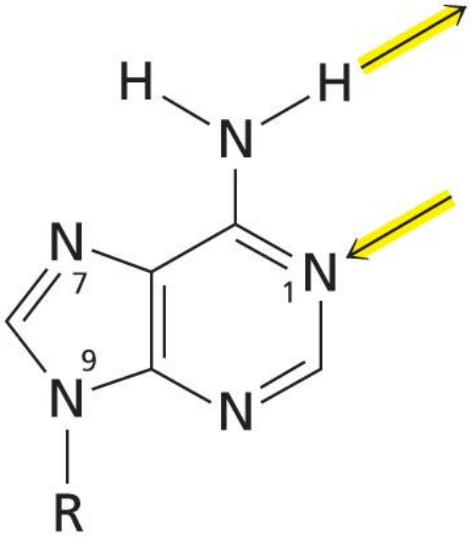
Uracil (RNA)

Pyrimidines

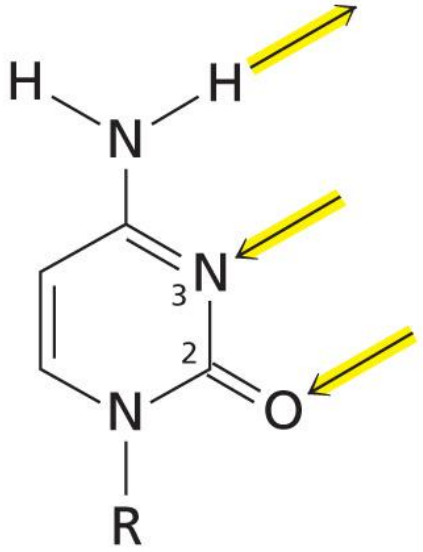
Purine Bases

- Adenine and guanine are found in in both RNA and DNA
- Good H-bond donors and acceptors
- Neutral molecules at pH 7



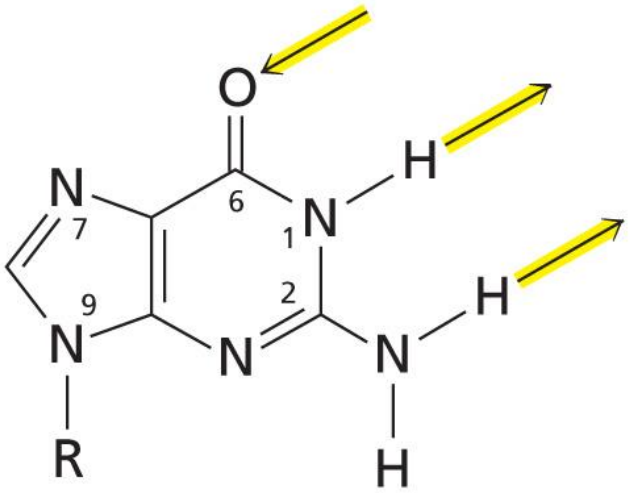


(Deoxy)Adenosine

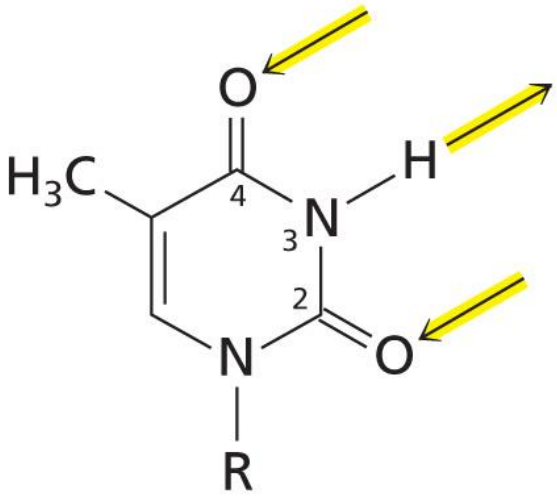


(Deoxy)Cytidine

Good H-bond donors and acceptors



(Deoxy)Guanosine



(Deoxy)Thymidine

Tautomerism of Nucleobases

- Prototropic tautomers are structural isomers that differ in the location of protons
- Keto-enol tautomerism is common in ketones
- Lactam-lactim tautomerism occurs in some heterocycles
- Both tautomers exist in solution but the lactam forms are predominant at neutral pH

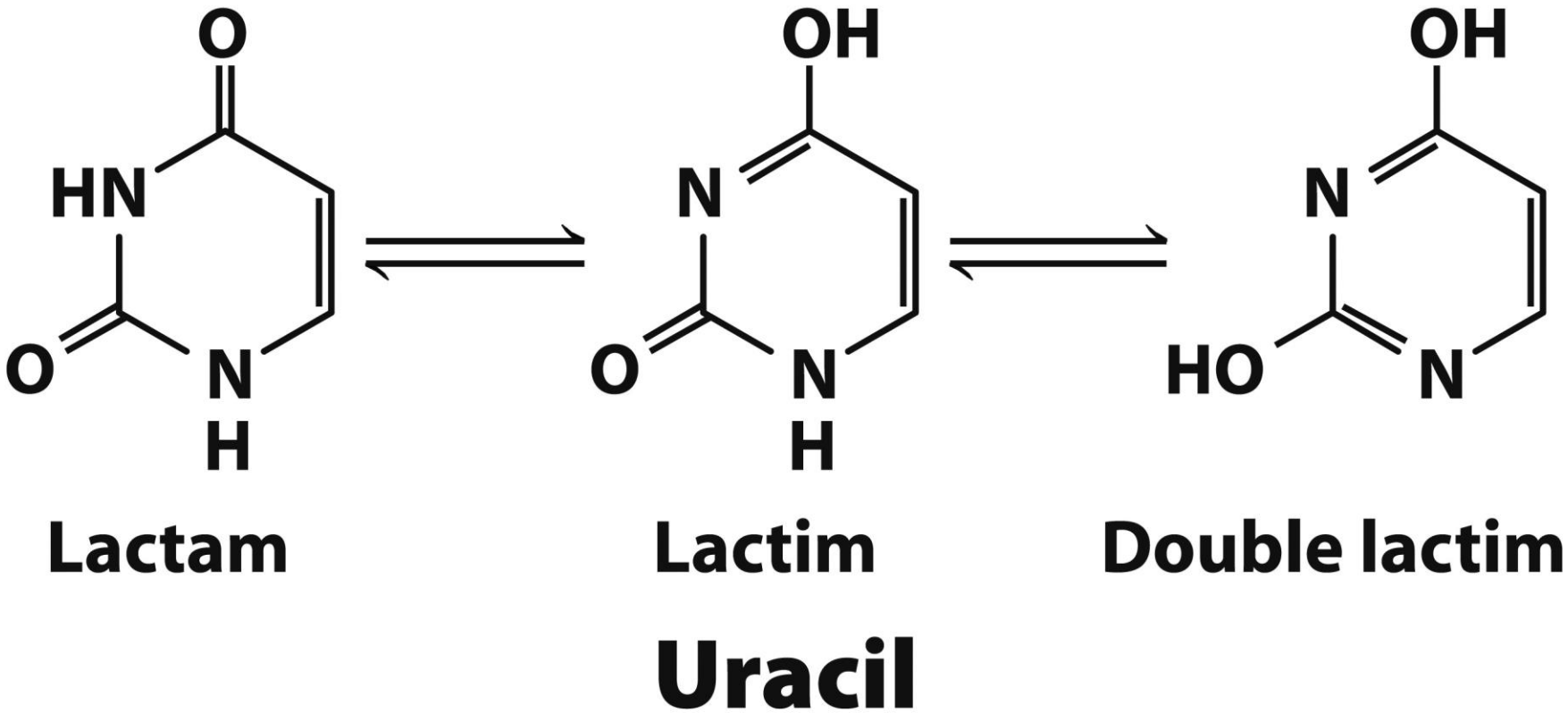


Figure 8-9
Lehninger Principles of Biochemistry, Sixth Edition

β–*N*-Glycosidic Bond

- In nucleotides the pentose ring is attached to the nucleobase via *N*-glycosidic bond
- The bond is formed to the anomeric carbon of the sugar in β configuration
- The bond is formed:
  - to position N1 in pyrimidines
  - to position N9 in purines
- This bond is quite stable toward hydrolysis, especially in pyrimidines
- Bond cleavage is catalyzed by acid

Conformation around *N*-Glycosidic Bond

- Relatively free rotation can occur around the *N*-glycosidic bond in free nucleotides.

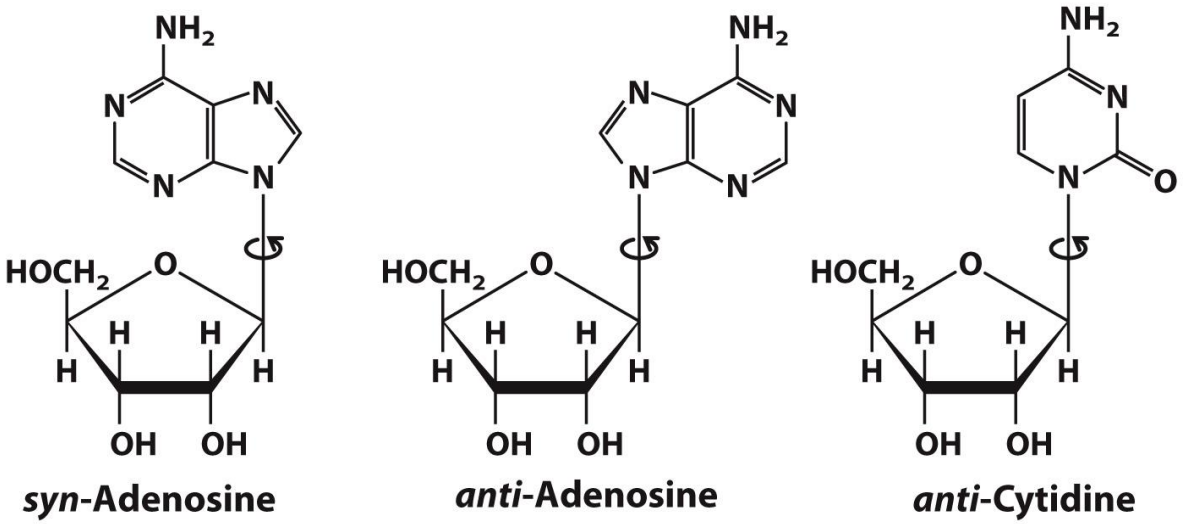


Figure 8-16b
Lehninger Principles of Biochemistry, Seventh Edition

- The sequence of atoms chosen to define this angle is O4'-C1'-N9-C4 for purine, and O4'-C1'-N1-C2 for pyrimidine derivatives.
- Angle near 0° corresponds to *syn* conformation.
- Angle near 180° corresponds to *anti* conformation.
- Anticonformation is found in normal B-DNA.

Nomenclature

TABLE 8–1 Nucleotide and Nucleic Acid Nomenclature

Base	Nucleoside	Nucleotide	Nucleic acid
Purines			
Adenine	Adenosine	Adenylate	RNA
	Deoxyadenosine	Deoxyadenylate	DNA
Guanine	Guanosine	Guanylate	RNA
	Deoxyguanosine	Deoxyguanylate	DNA
Pyrimidines			
Cytosine	Cytidine	Cytidylate	RNA
	Deoxycytidine	Deoxycytidylate	DNA
Thymine	Thymidine or deoxythymidine	Thymidylate or deoxythymidylate	DNA
Uracil	Uridine	Uridylate	RNA

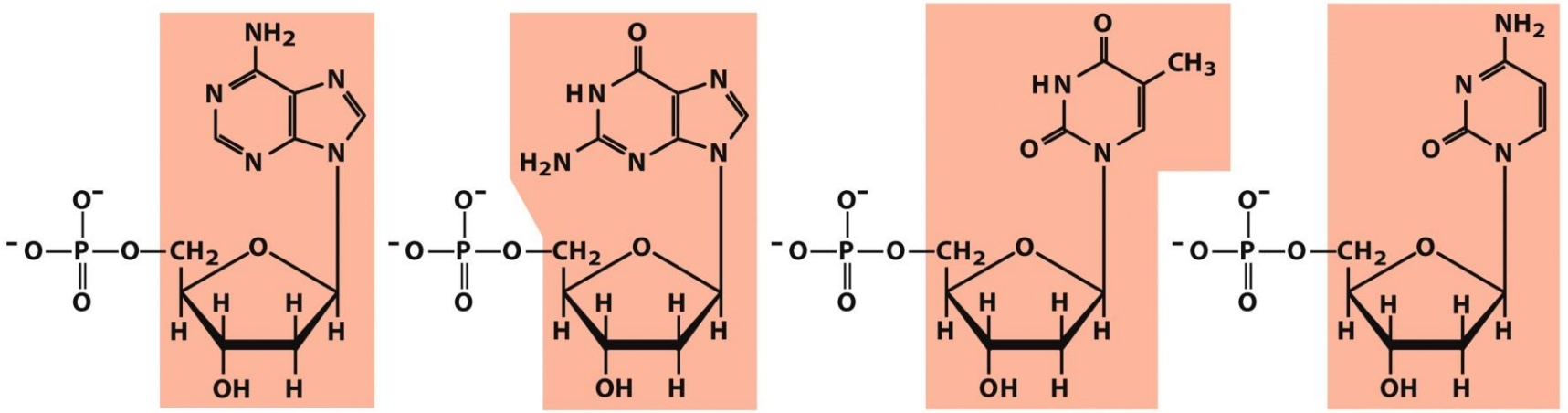
Note: "Nucleoside" and "nucleotide" are generic terms that include both ribo- and deoxyribo- forms. Also, ribonucleosides and ribonucleotides are here designated simply as nucleosides and nucleotides (e.g., riboadenosine as adenosine), and deoxyribonucleosides and deoxyribonucleotides as deoxynucleosides and deoxynucleotides (e.g., deoxyriboadenosine as deoxyadenosine). Both forms of naming are acceptable, but the shortened names are more commonly used. Thymine is an exception; "ribothymidine" is used to describe its unusual occurrence in RNA.

Table 8-1

Lehninger Principles of Biochemistry, Sixth Edition

Nomenclature: Deoxyribonucleotides

You need to know structures, names, and symbols (four-letter (dAMP) codes)



	Deoxyadenylate (deoxyadenosine 5′-monophosphate)	Deoxyguanylate (deoxyguanosine 5′-monophosphate)	Deoxythymidylate (deoxythymidine 5′-monophosphate)	Deoxycytidylate (deoxycytidine 5′-monophosphate)
Nucleotide:				
Symbols:	A, dA, dAMP	G, dG, dGMP	T, dT, dTMP	C, dC, dCMP
Nucleoside:	Deoxyadenosine	Deoxyguanosine	Deoxythymidine	Deoxycytidine

Deoxyribonucleotides

Figure 8-4a
Lehninger Principles of Biochemistry, Sixth Edition

Nomenclature: Ribonucleotides

You need to know structures, names, and symbols (three-letter codes)

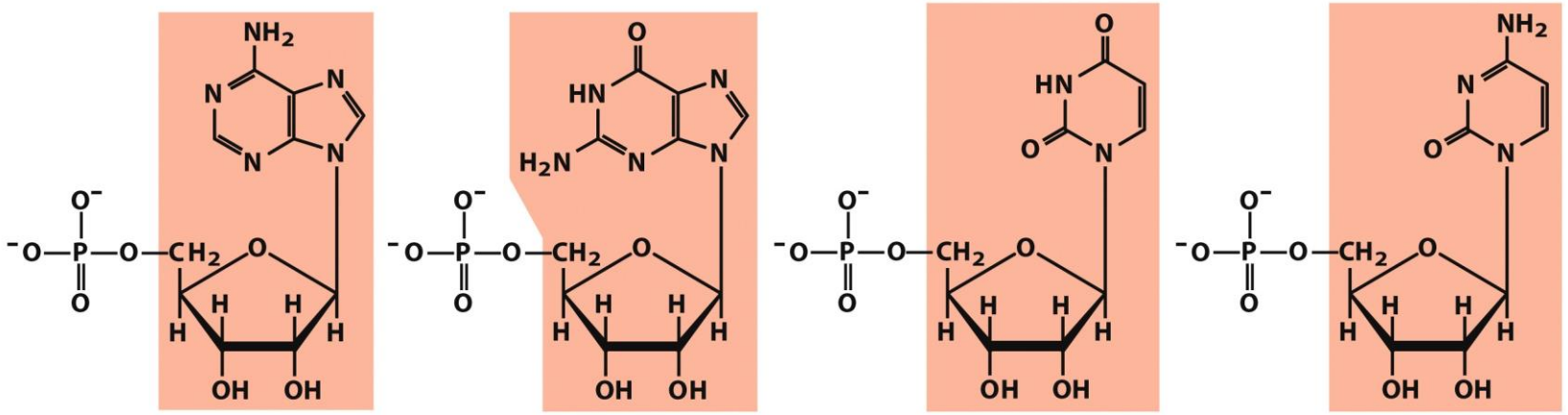
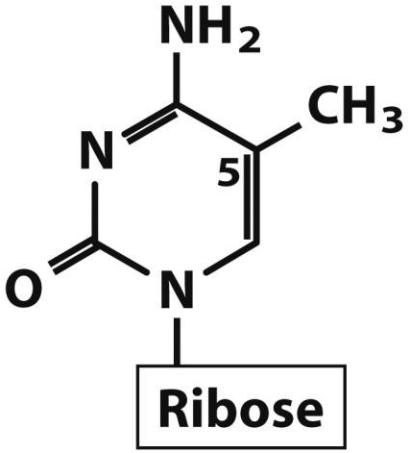


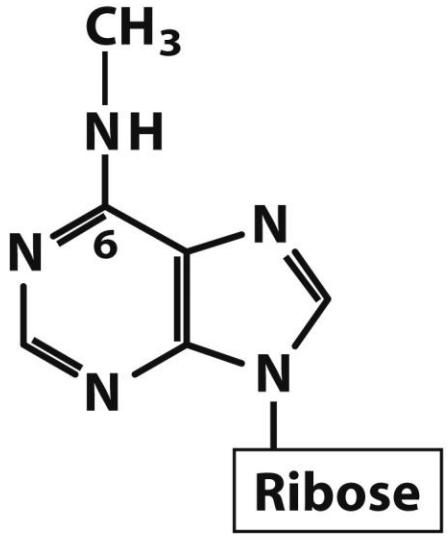
Figure 8-4b
Lehninger Principles of Biochemistry, Sixth Edition

Minor Nucleosides in DNA

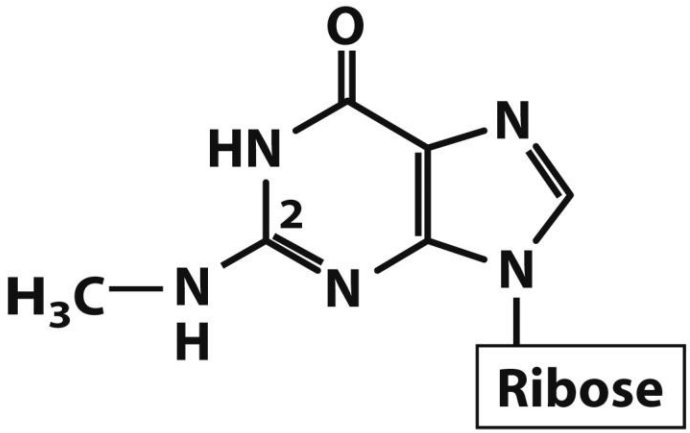
- Modification is done after DNA synthesis
- 5-Methylcytosine is common in eukaryotes, also found in bacteria
- N^6-Methyladenosine is common in bacteria, not found in eukaryotes
- Epigenetic marker
  - Way to mark own DNA so that cells can degrade foreign DNA (prokaryotes)
  - Way to mark which genes should be active (eukaryotes)
  - Could the environment turn genes on and off in an inheritable manner?



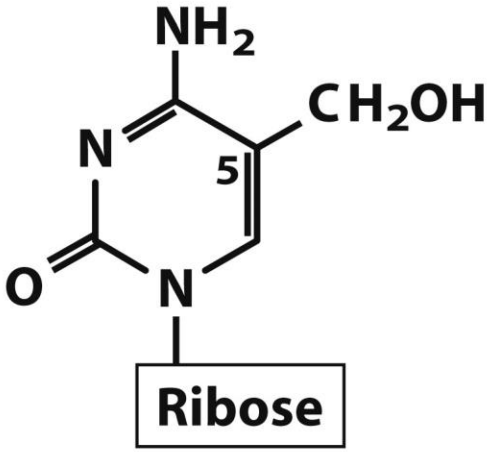
5-Methylcytidine



N^6-Methyladenosine



N^2-Methylguanosine



5-Hydroxymethylcytidine

Figure 8-5a
Lehninger Principles of Biochemistry, Sixth Edition

Minor Nucleosides in RNA

- Inosine sometimes found in the "wobble position" of the anticodon in tRNA
  - Made by de-aminating adenosine
  - Provides richer genetic code

- Pseudouridine (Ψ) found widely in tRNA and rRNA
  - More common in eukaryotes but found also in eubacteria
  - Made from uridine by enzymatic isomerization after RNA synthesis
  - May stabilize the structure of tRNA
  - May help in folding of rRNA

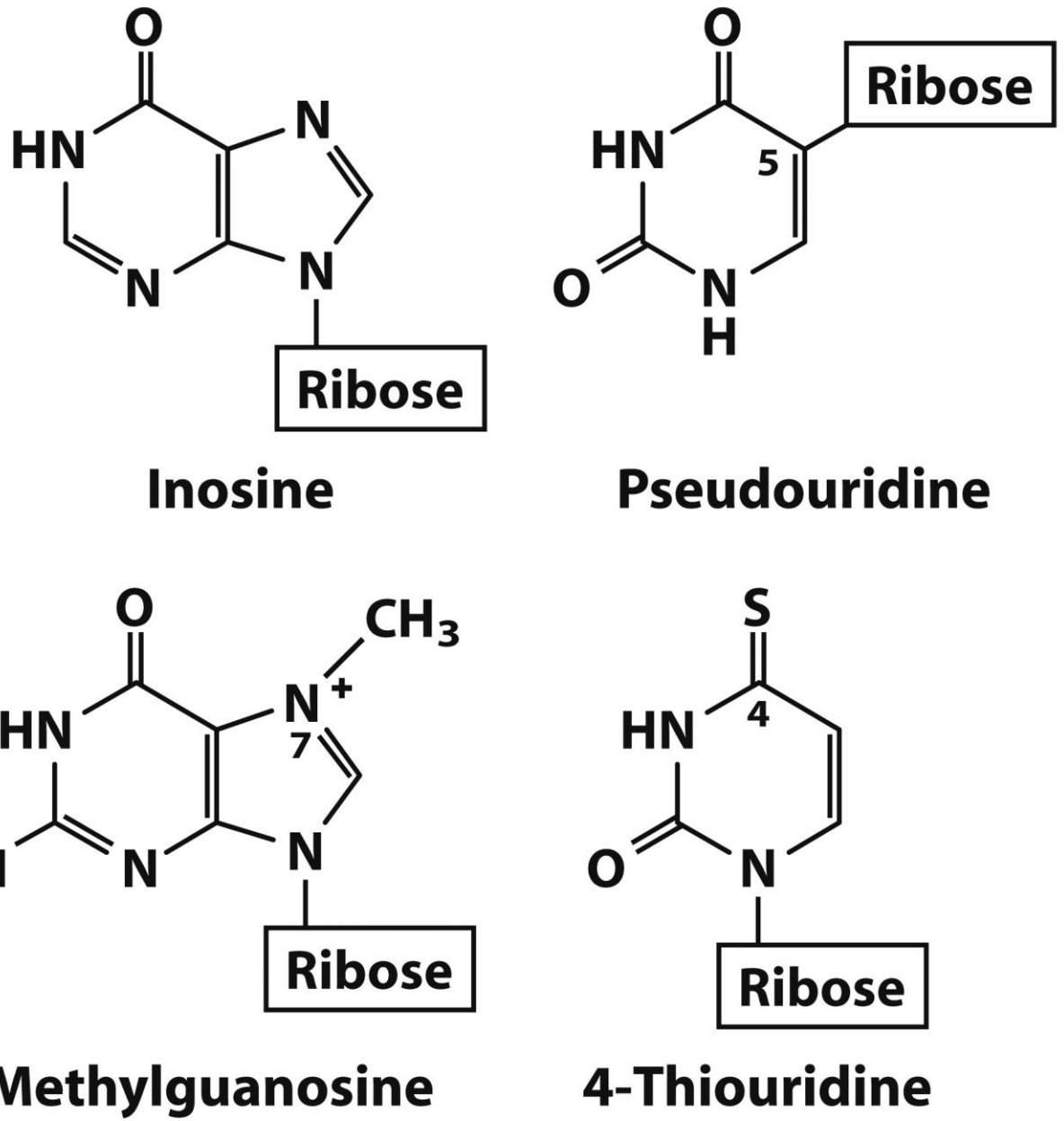
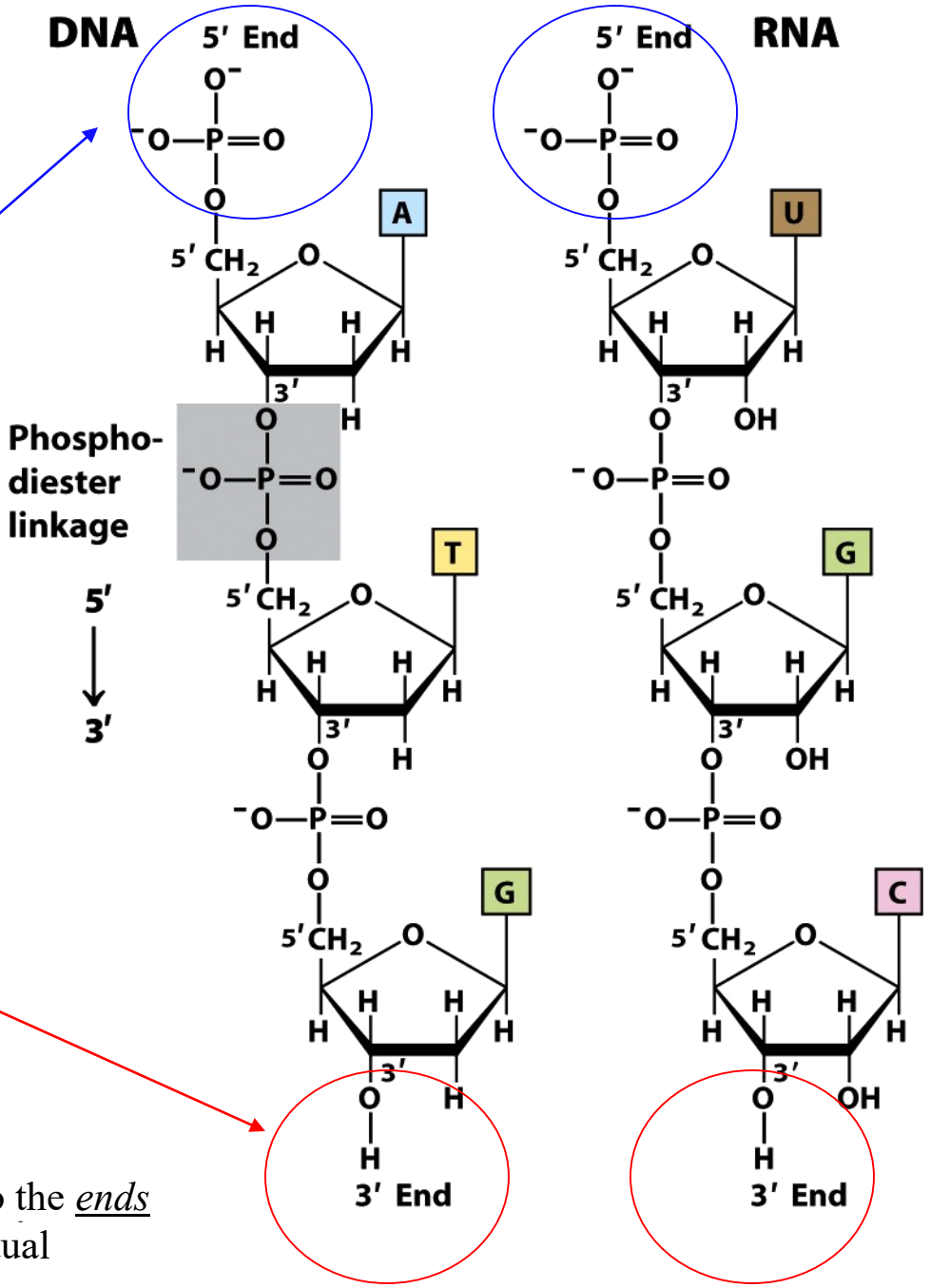


Figure 8-5b
Lehninger Principles of Biochemistry, Sixth Edition

Polynucleotides

- Covalent bonds formed via phosphodiester linkages
  - negatively charged backbone
  - Nucleic acid backbone consists of alternating phosphate and pentose residues with nitrogenous bases as side groups occurring at regular intervals
- DNA backbone is fairly stable
  - DNA from mammoths?
  - Hydrolysis accelerated by enzymes (DNases)
- RNA backbone is relatively unstable
  - In water, RNA can last for a few years
  - In cells, mRNA is degraded in few hours
- Linear polymers
  - No branching or cross-links
- Directionality
  - 5’ end is different from 3’ end
  - We read the sequence from 5’ to 3’

Phosphodiester linkages in the covalent backbone of DNA and RNA



The **5′ end** of the macromolecule does not have a nucleotide at the 5′ position.

The **3′ end** does not have a nucleotide at the 3′ position.

Important: The 5′ → 3′ orientation refers to the *ends* of the strand, NOT the orientation of individual phosphodiester bonds.

Representations of polynucleotides

- Can be represented by their nitrogenous bases:

  E.g.

  5′ pA-T-G-C-A_{OH} 3′

  or 5′ pApTpGpCpA 3′

  or 5’ ATGCA 3′

Hydrolysis of RNA

- RNA is unstable under alkaline conditions (*while DNA is not – why?*)
- Hydrolysis is also catalyzed by enzymes (RNases)
- RNase enzymes are abundant around us:
  - S-RNase in plants prevents inbreeding
  - RNase P is a ribozyme (enzyme made of RNA) that processes tRNA precursors
  - Dicer is an enzyme that cleaves double-stranded RNA into oligonucleotides
    - protection from viral genomes
    - RNA interference technology

Mechanism of Base-catalyzed RNA Hydrolysis

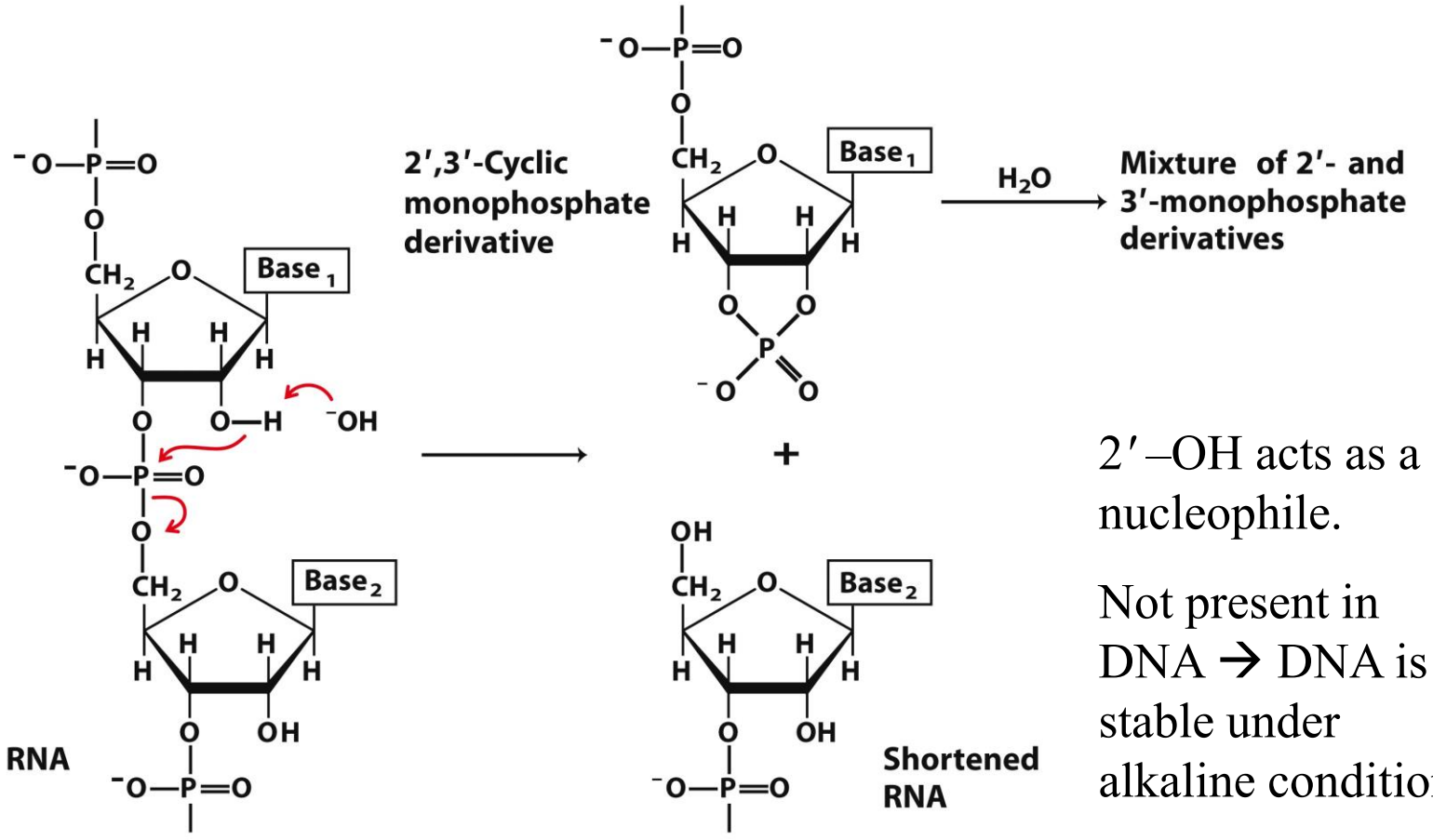


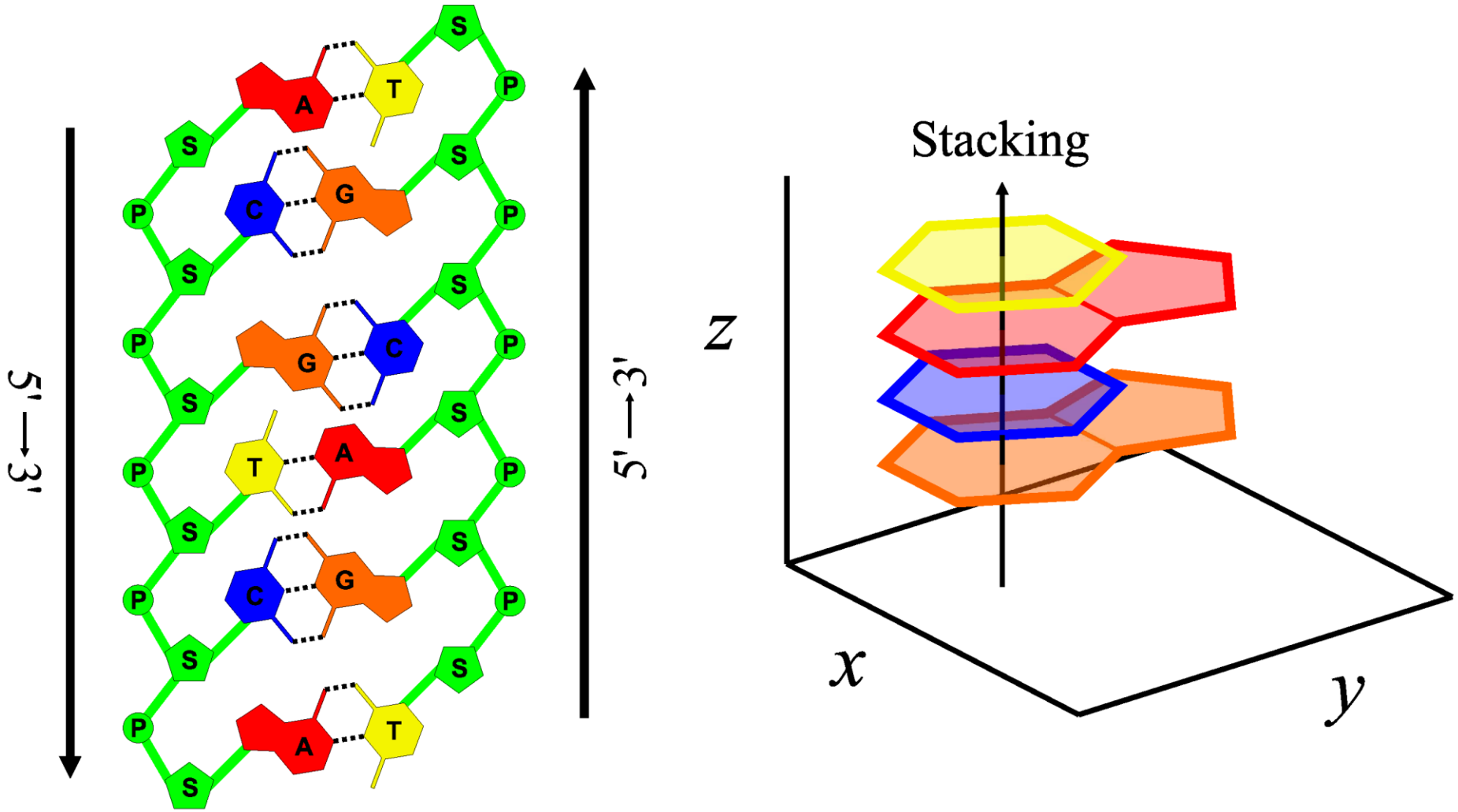
Figure 8-8
Lehninger Principles of Biochemistry, Sixth Edition

2′–OH acts as a nucleophile.

Not present in DNA → DNA is stable under alkaline conditions.

Nitrogenous Base Interactions

- Nucleotides are hydrophobic
- At pH 7, nucleotides are essentially water insoluble (become more soluble at more acidic or basic pH)
- To minimize contact of bases with water, base stacking occurs
- Hydrophobic stacking interactions; van der Waal's interactions; dipole-dipole interactions
- Very important in stabilizing 3D shape of nucleic acids


5'—3'
5'—3'
S
P
A
T
C
G
Stacking
z
x
y

8.2 Nucleic Acid Structure

- Levels of structural complexity:

1) **Primary structure** – covalent structure and nucleotide sequence
2) **Secondary structure** – any regular and stable structure made by some or all the nucleotides
3) **Tertiary structure** – complex folding of large chromosomes within eukaryotic chromatin

Hydrogen-Bonding Interactions

- Two bases can hydrogen bond to form a **base pair**
- For monomers, large number of base pairs is possible
- In polynucleotide, only few possibilities exist
- **Watson-Crick base pairs** predominate in double-stranded DNA
- A pairs with T
- C pairs with G
- (Purine pairs with pyrimidine)

AT and GC Base Pairs

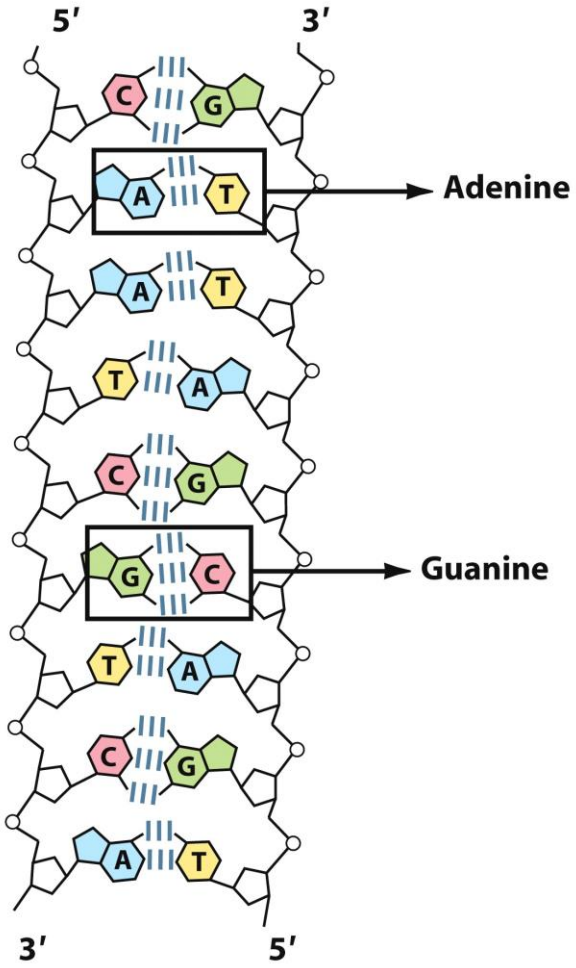
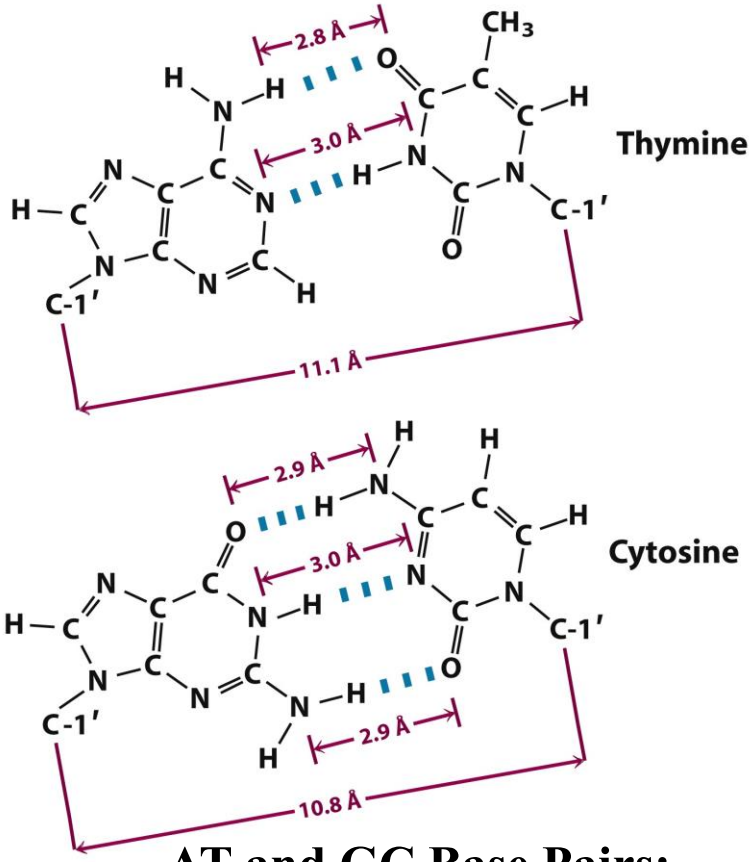
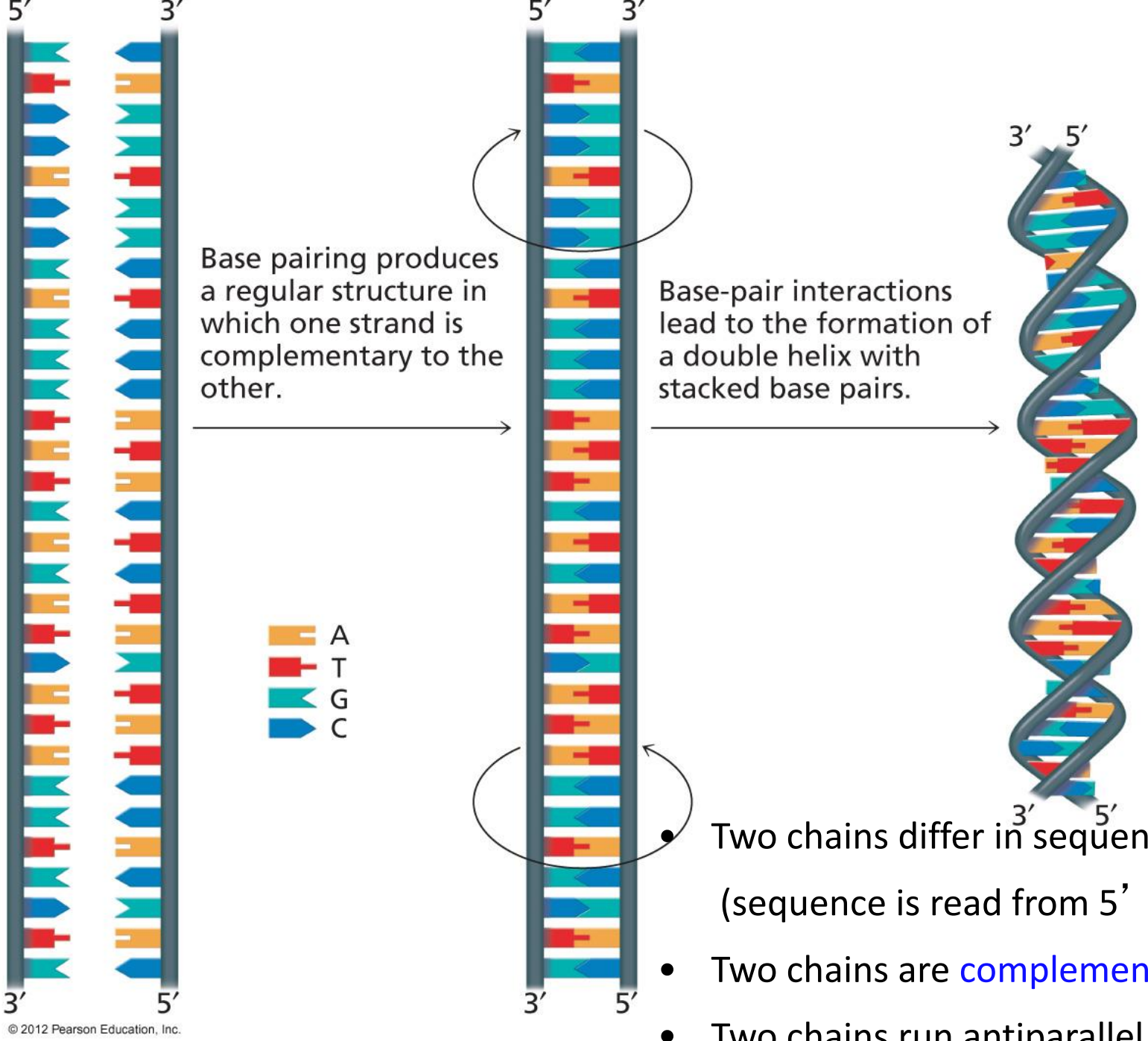


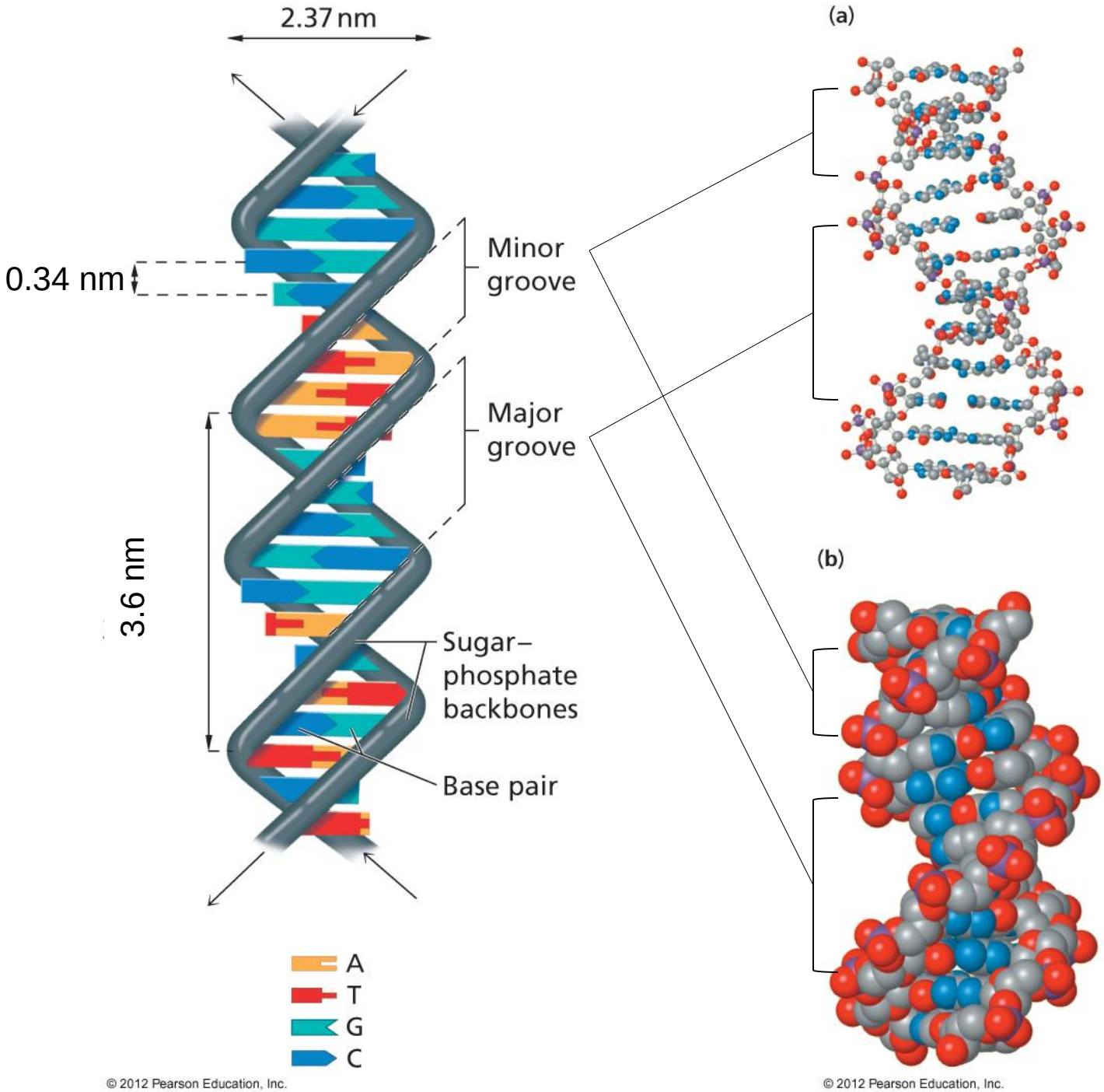
Figure 8-11
Lehninger Principles of Biochemistry, Sixth Edition



AT and GC Base Pairs:
Separation of paired DNA strands is more difficult when GC:AT ratio is high
GC have higher T_m than AT



- Two chains differ in sequence (sequence is read from 5’ to 3’)
- Two chains are complementary
- Two chains run antiparallel



© 2012 Pearson Education, Inc.

DNA is a Double Helix that Stores Genetic Information

- **Chargaff's rules:** Put together by Erwin Chargaff

1) DNA base composition is different between species
2) DNA from different tissues of the same organism have the same base composition
3) DNA base composition in an organism does not change with age, environment or nutritional state
4) In all cellular DNA, in any species, A = T and C = G
5) Purines = pyrimidines (A+G = T+C)

Worked Example

In samples of DNA isolated from 2 bacteria species (X and Y), adenine makes 32% and 17%, respectively, of the total bases. What relative proportions of A, T, C and G would you expect to find in these 2 samples? What assumptions have you made? One of these species was isolated from a hot spring. Which one and why?

For any DNA double helix, A=T and C=G and A+G = C+T
X → A= 32% and T= 32%; G=C= 36%/2= 18% each
Y → A= 17% and T= 17%; G=C= 66%/2= 33% each

This is based on the assumption that both DNA molecules are double-stranded

The higher the GC content the higher its melting temperature → Y is most likely thermophilic because its DNA has higher melting temperature (more stable at high temperatures)

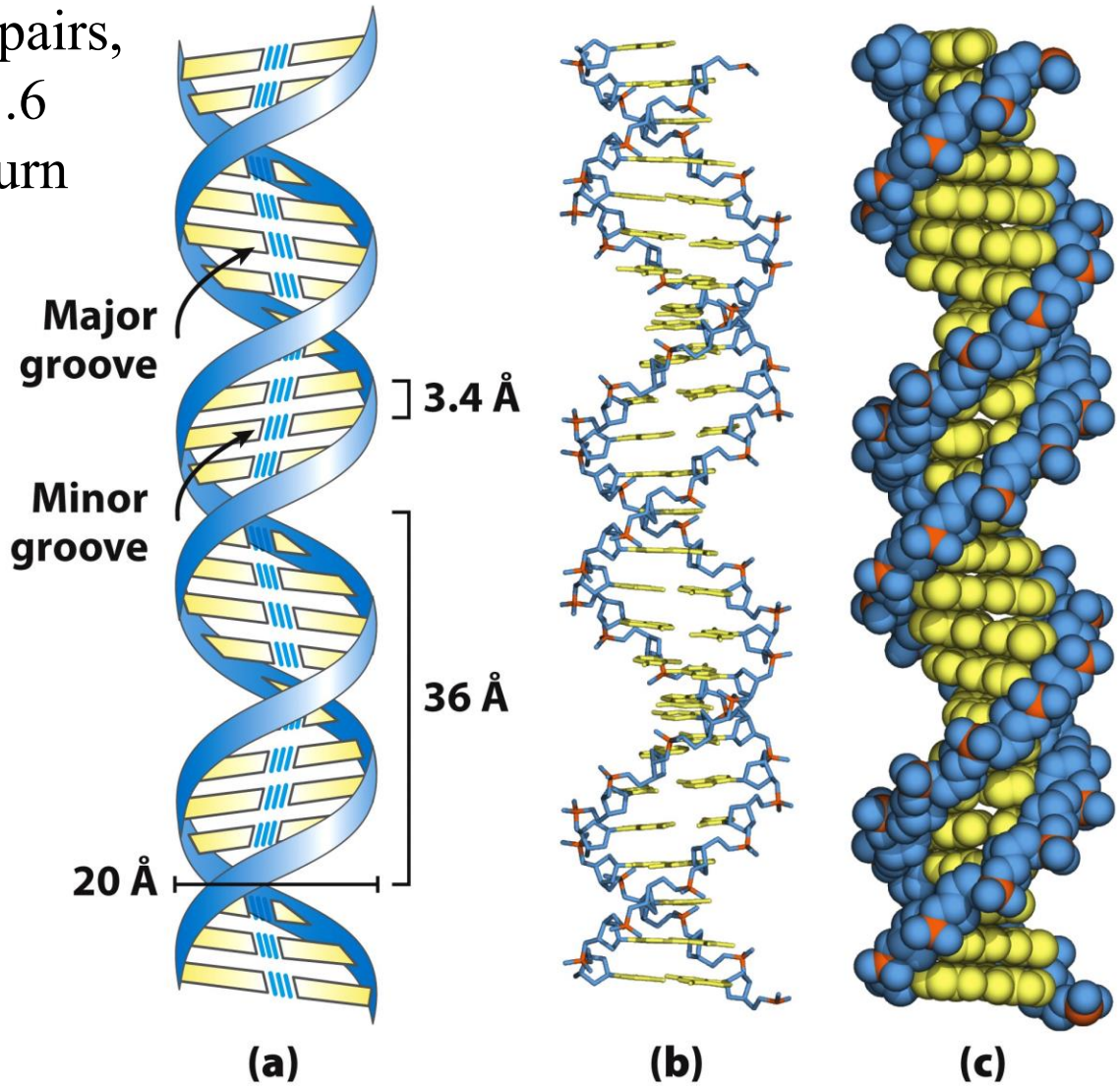
Table 19.2 Base composition of DNA (mole %) and ratios of bases

Source	A	G	C	T	A/T[a]	G/C[a]	(G + C)	Purine/ pyrimidine[a]
Escherichia coli	26.0	24.9	25.2	23.9	1.09	0.99	50.1	1.04
Mycobacterium tuberculosis	15.1	34.9	35.4	14.6	1.03	0.99	70.3	1.00
Yeast	31.7	18.3	17.4	32.6	0.97	1.05	35.7	1.00
Cow	29.0	21.2	21.2	28.7	1.01	1.00	42.4	1.01
Pig	29.8	20.7	20.7	29.1	1.02	1.00	41.4	1.01
Human	30.4	19.9	19.9	30.1	1.01	1.00	39.8	1.01

[a]Deviations from a 1:1 ratio are due to experimental variations.

Watson-Crick Model of B-DNA

10.5 base pairs, or 36 Å (3.6 nm), per turn



James D. Watson

Francis Crick, 1916–2004

Figure 8-13
Lehninger Principles of Biochemistry, Sixth Edition

Other Forms of DNA

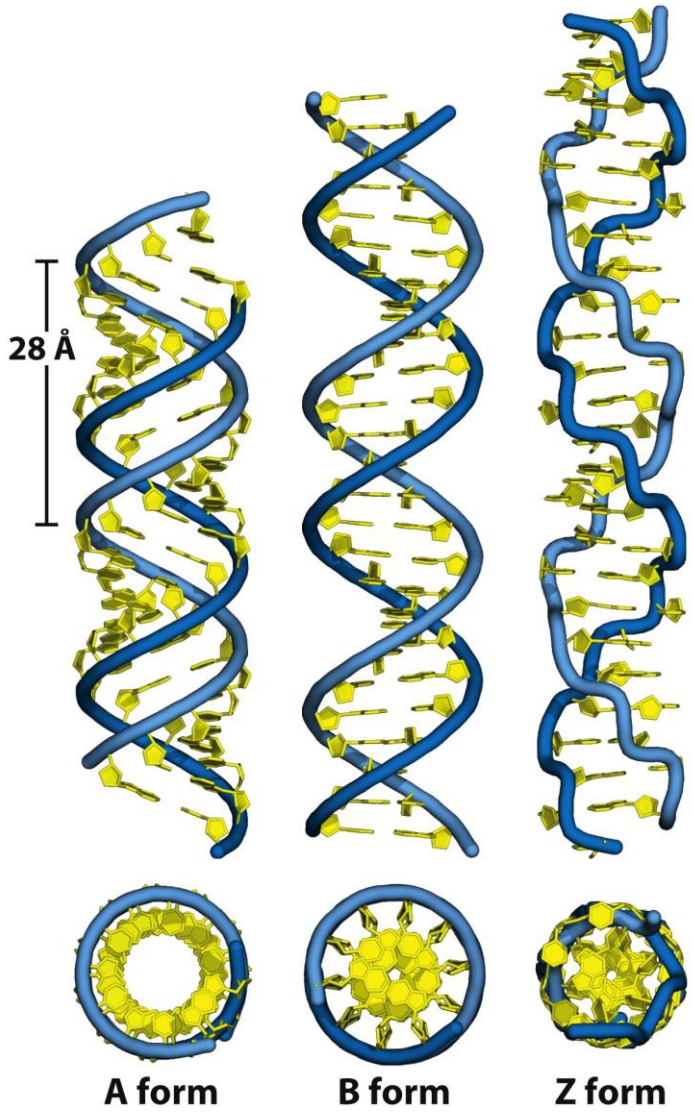


Figure 8-17 part 1
Lehninger Principles of Biochemistry, Sixth Edition

	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
Lehninger Principles of Biochemistry, Sixth Edition

Replication of Genetic Code

- Strand separation occurs first (DNA helicases)
- Each strand serves as a template for the synthesis of a new strand
- Synthesis is catalyzed by DNA polymerases
- Newly made DNA molecule has one daughter strand and one parent strand.

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

—Watson and Crick, *Nature,* 1953

Replication of Genetic Code

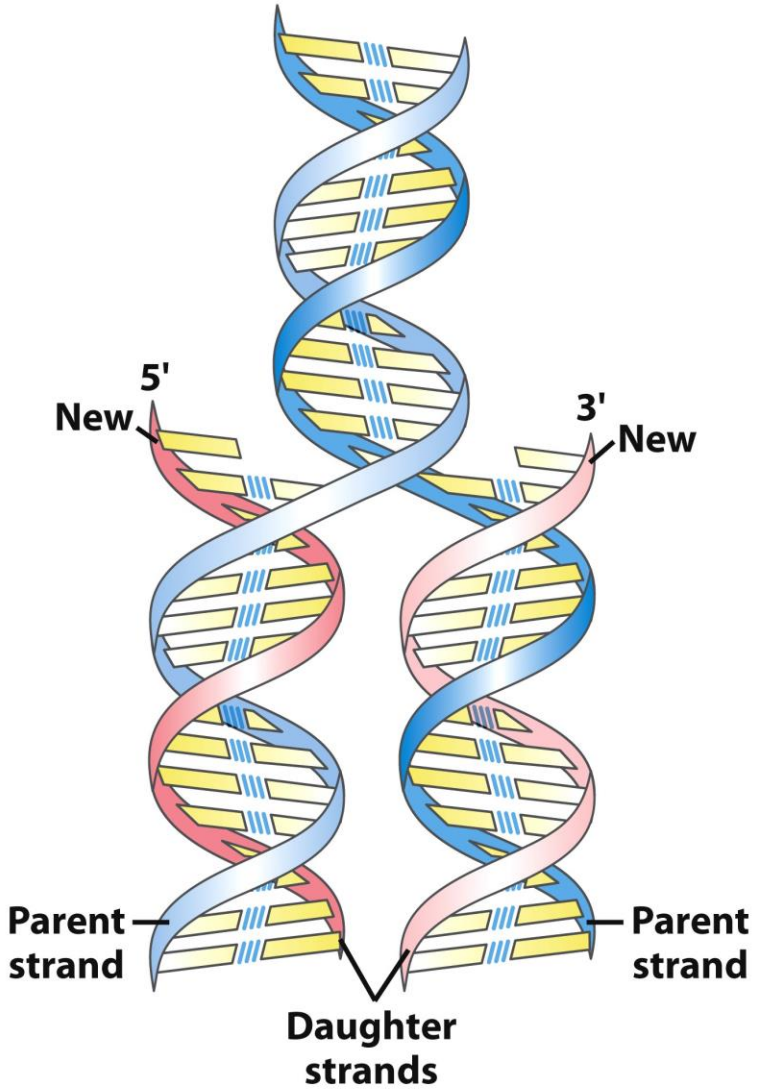


Figure 8-15
Lehninger Principles of Biochemistry, Sixth Edition

Palindromic Sequences can form Hairpins and Cruciforms

Palindromes: words or phases that are the same when read backward or forward: (القلب المستوى)

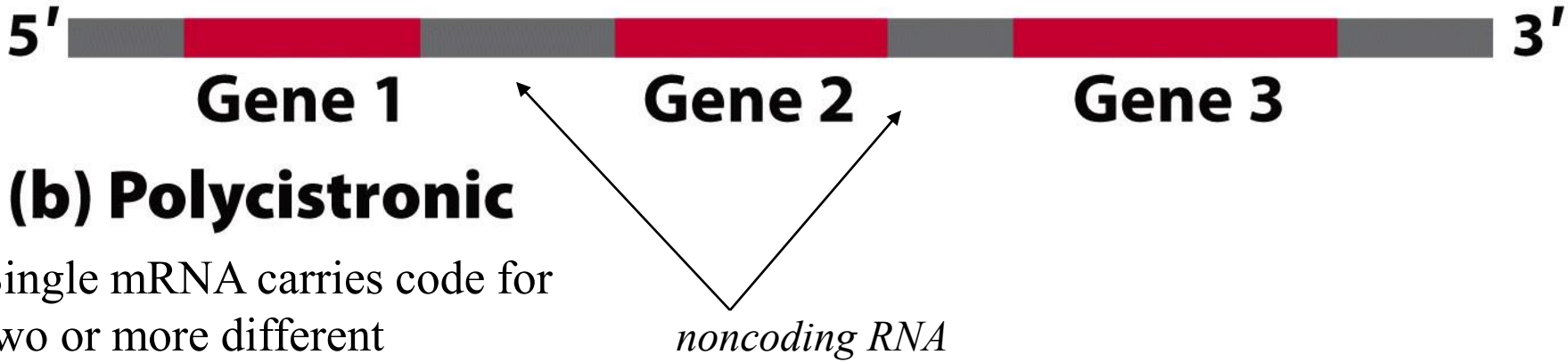
Nurses run
Never odd or even
A Toyota! Race fast... safe car: a Toyota

بلح تعلق تحت قلعة حلب
مودته تدوم لكل هول – وهل كل مودته تدوم

Messenger RNA: Code Carrier for the Sequence of Proteins

- Is synthesized using DNA template
- Generally occurs as a single strand
- Contains ribose instead of deoxyribose
- Contains uracil instead of thymine
- One mRNA may code for more than one protein
- Together with transfer RNA (tRNA) transfers genetic information from DNA to proteins

(a) Monocistronic Single mRNA carries code for only one polypeptide



(b) Polycistronic

Single mRNA carries code for two or more different polypeptide

noncoding RNA

- In eukaryotic cells, most mRNAs are monocistronic
- The minimum length of mRNA depends on the protein it encodes (a 100 aa protein must have mRNA with at least 300 bp). mRNA transcribed from DNA is always longer (noncoding RNA)

Typical right-handed stacking pattern of single-stranded RNA

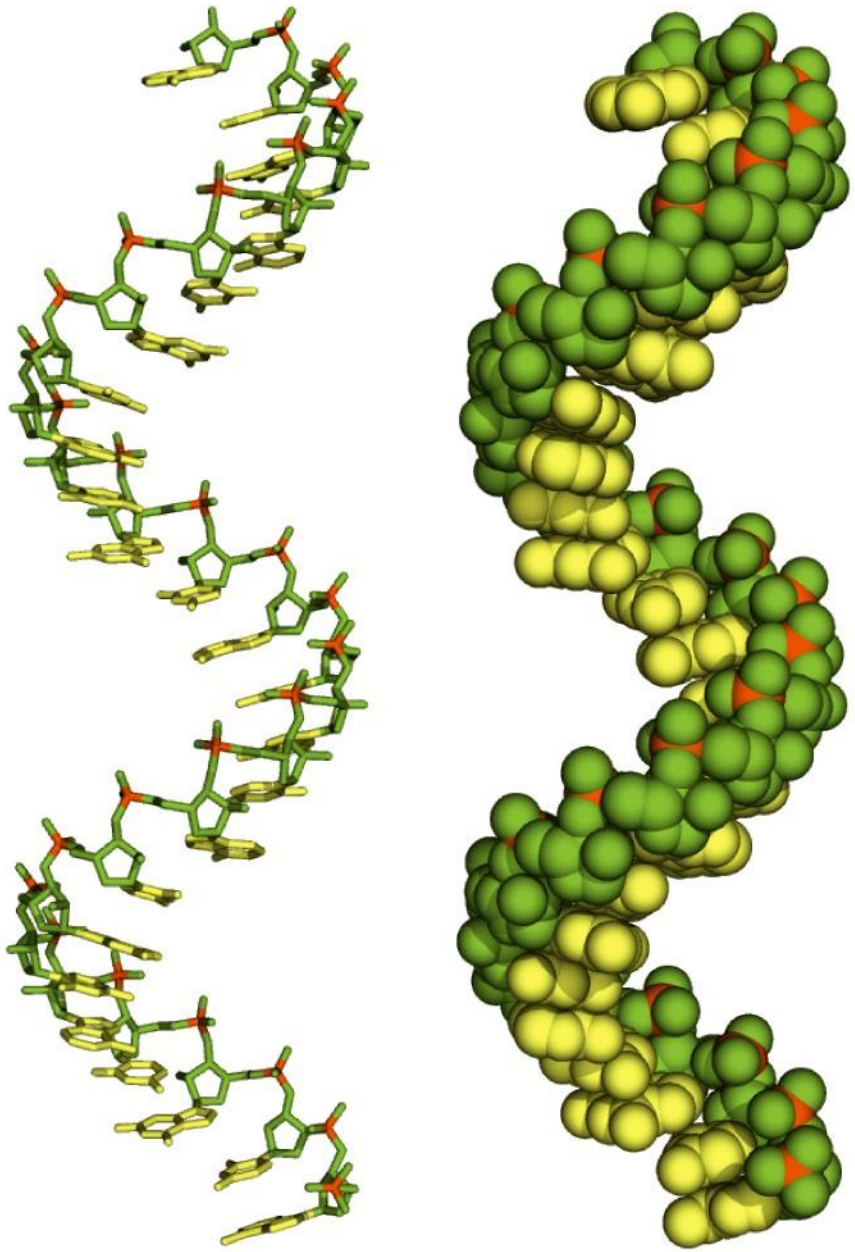


Figure 8-22
Lehninger Principles of Biochemistry, Sixth Edition

Structure is dominated by base stacking interactions (strongest between 2 purines, weakest between 2 pyrimidines)

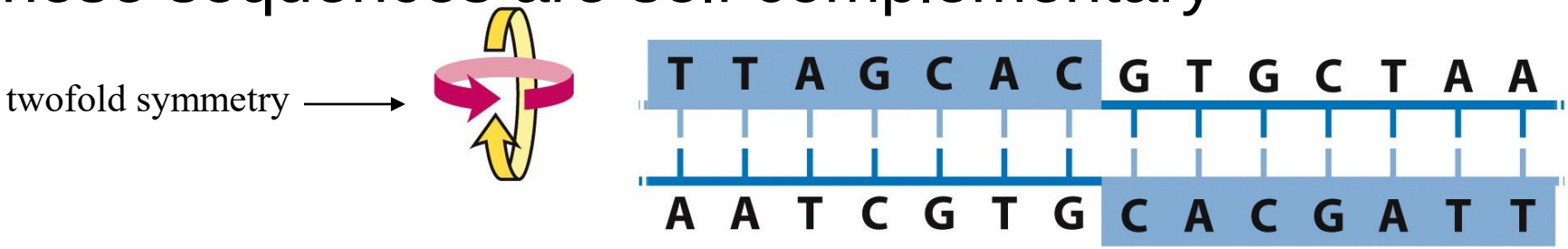
RNA can base pair (G with C and A with U)

Note that G and U base pairs are common in RNA

No simple, regular secondary structure available, it depends on RNA molecule. Complex in nature (like proteins)

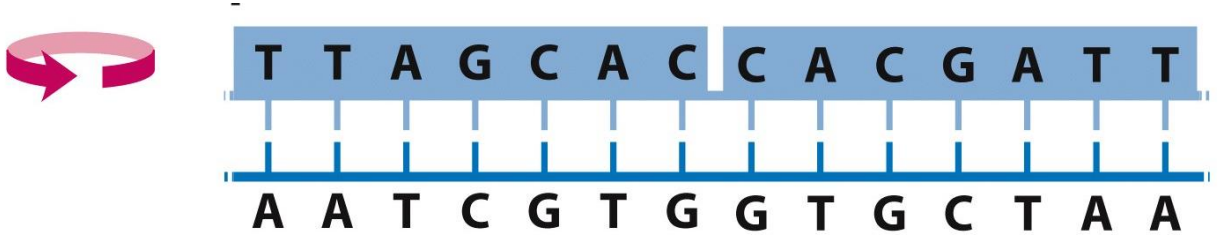
Palindromes in DNA: regions of DNA with **inverted repeats** of base sequence having twofold symmetry over two strands of DNA

* These sequences are self complementary



➔Can form **hairpin** or **cruciform** structures

Mirror repeats: when the inverted repeat are in one strand only → cannot form hairpins or cruciforms



When only one DNA (or RNA) strand is involved, the structure is a hairpin

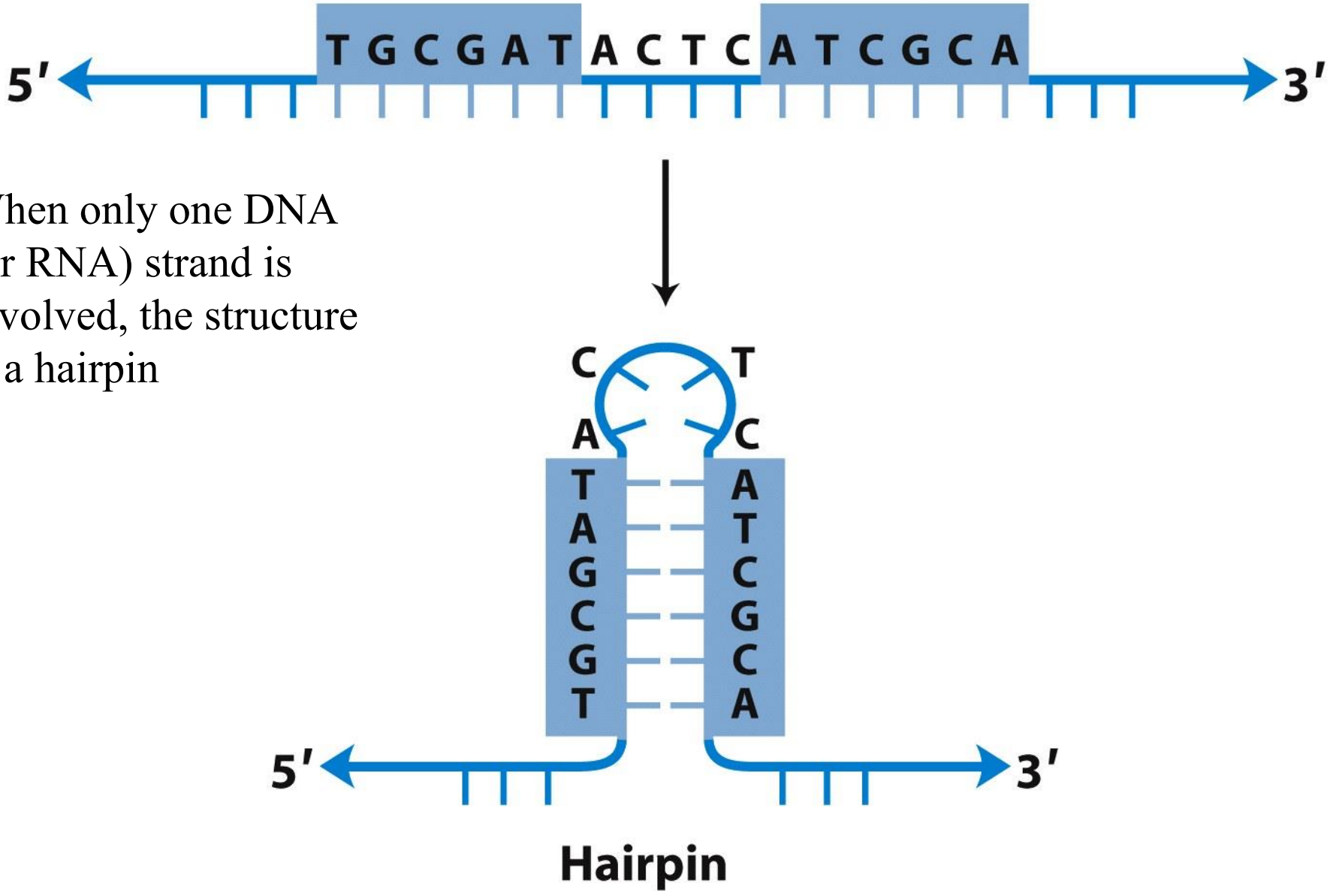
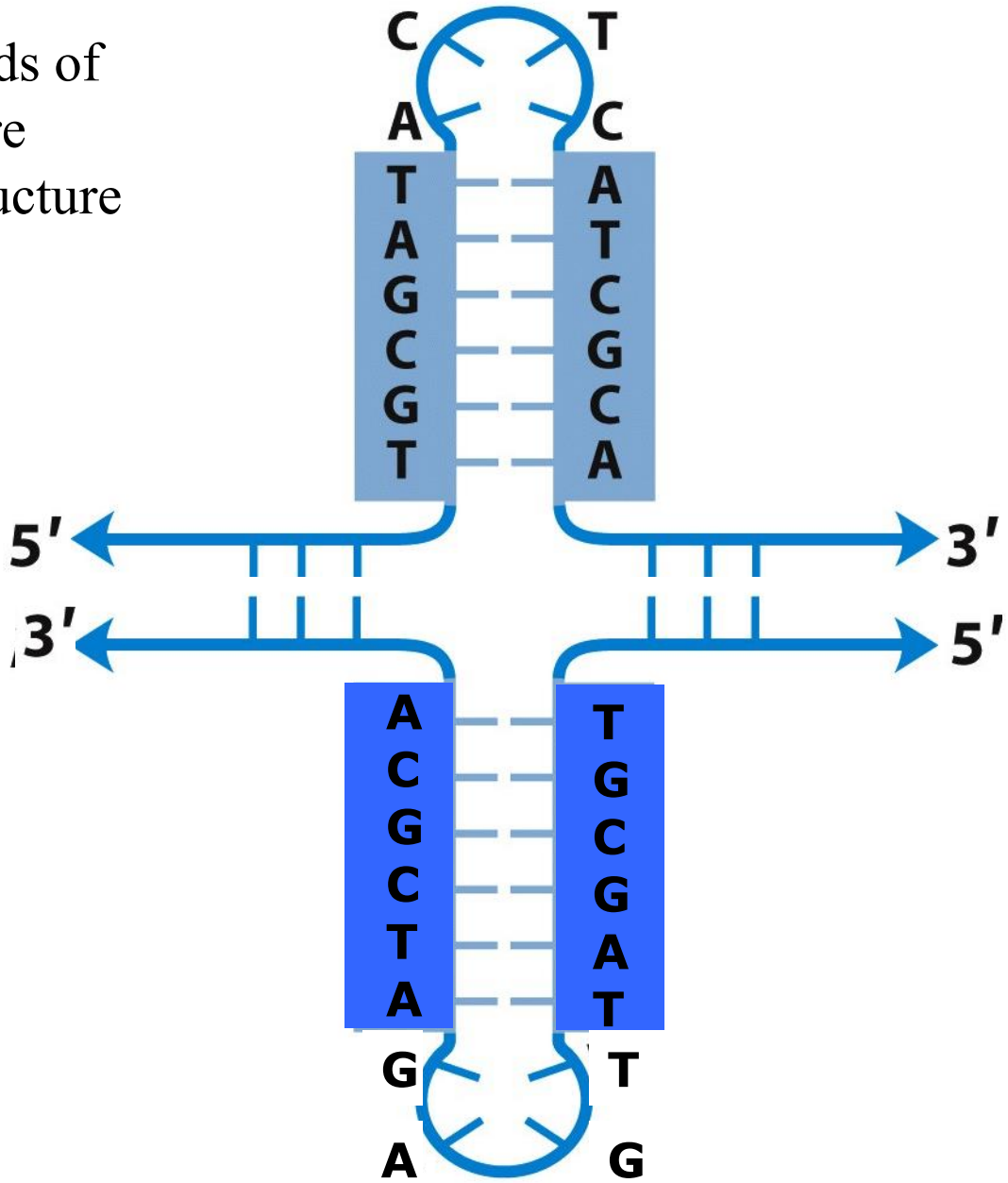


Figure 8-19a
Lehninger Principles of Biochemistry, Fifth Edition

When both strands of a duplex DNA are involved, the structure is a cruciform

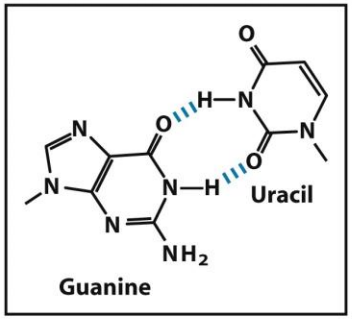


RNA molecules have quite complex structures

Base-paired helical structures in an RNA.

Possible secondary structure of an RNA

Note that G=U base pairs are allowed only when presynthesized strands of RNA fold up or anneal with each other. There are no RNA polymerases (the enzymes that synthesize RNAs on a DNA template) that insert a U opposite a template G, or vice versa, during RNA synthesis.



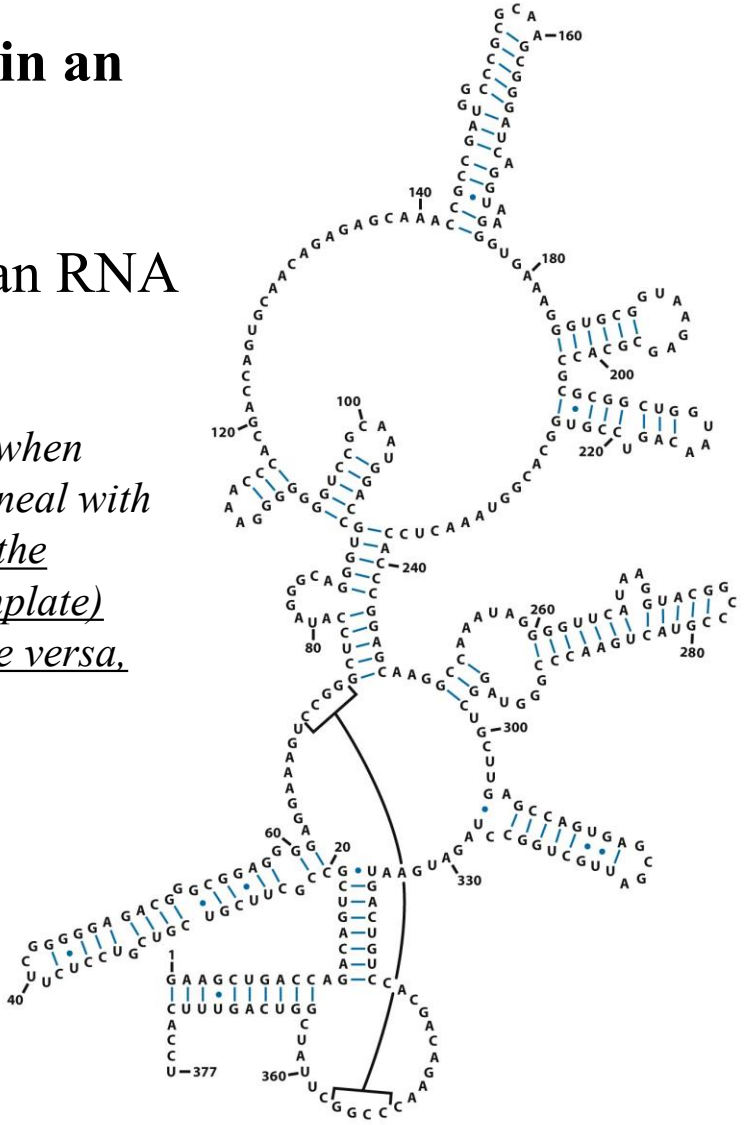
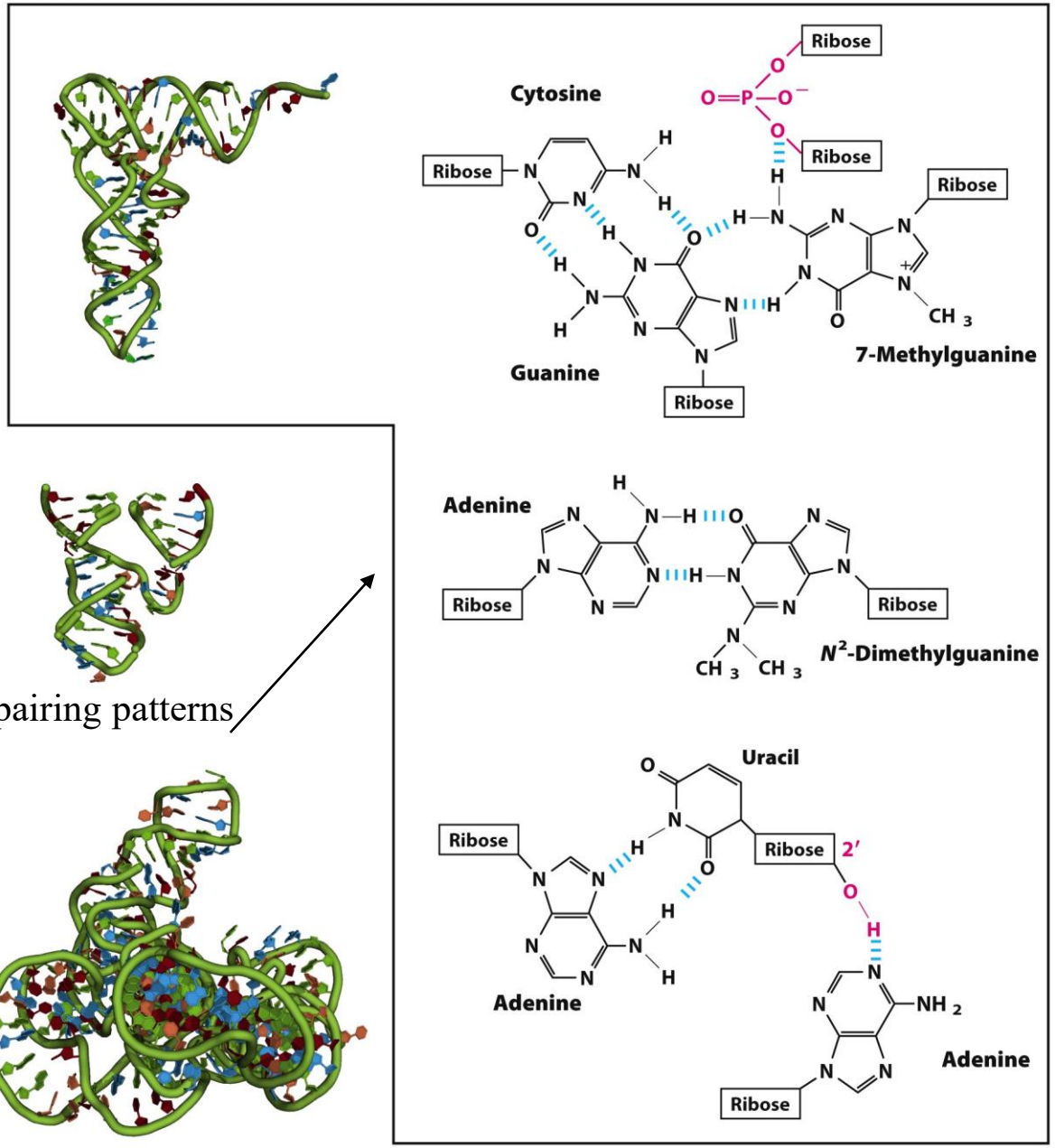


Figure 8-24
Lehninger Principles of Biochemistry, Sixth Edition

Transfer RNA: Matching Amino Acids with the mRNA Code

- tRNA molecules also have quite complex structures
- tRNA are adapter molecules covalently linked to aa at one end and the other end pairs with incoming mRNA in such a way that aa are joined together to a growing polypeptide in the correct sequence
- Stabilized by Non-Watson-Crick Base-Pair Interactions



Some unusual base-pairing patterns found in this tRNA

Figure 8-25
Lehninger Principles of Biochemistry, Sixth Edition

8.3 Nucleic Acid Chemistry

- DNA is very stable (that's why it is used as informational storage molecules)

- Chemical transformations need enzyme catalysts to occur

- However, even small and slow changes can be physiologically significant
  - carcinogenesis
  - aging

- Slowly accumulating irreversible DNA changes may lead to diseases

DNA Denaturation

- Covalent bonds remain intact.
  - Genetic code remains intact.
- Hydrogen bonds are broken.
  - Two strands separate.
- Base stacking is lost
  - UV absorbance increases.

Denaturation can be induced by high temperature, or change in pH.

Denaturation may be reversible: annealing. - spontaneous rewinding of a denatured DNA molecule when >12 bp are still in a helix

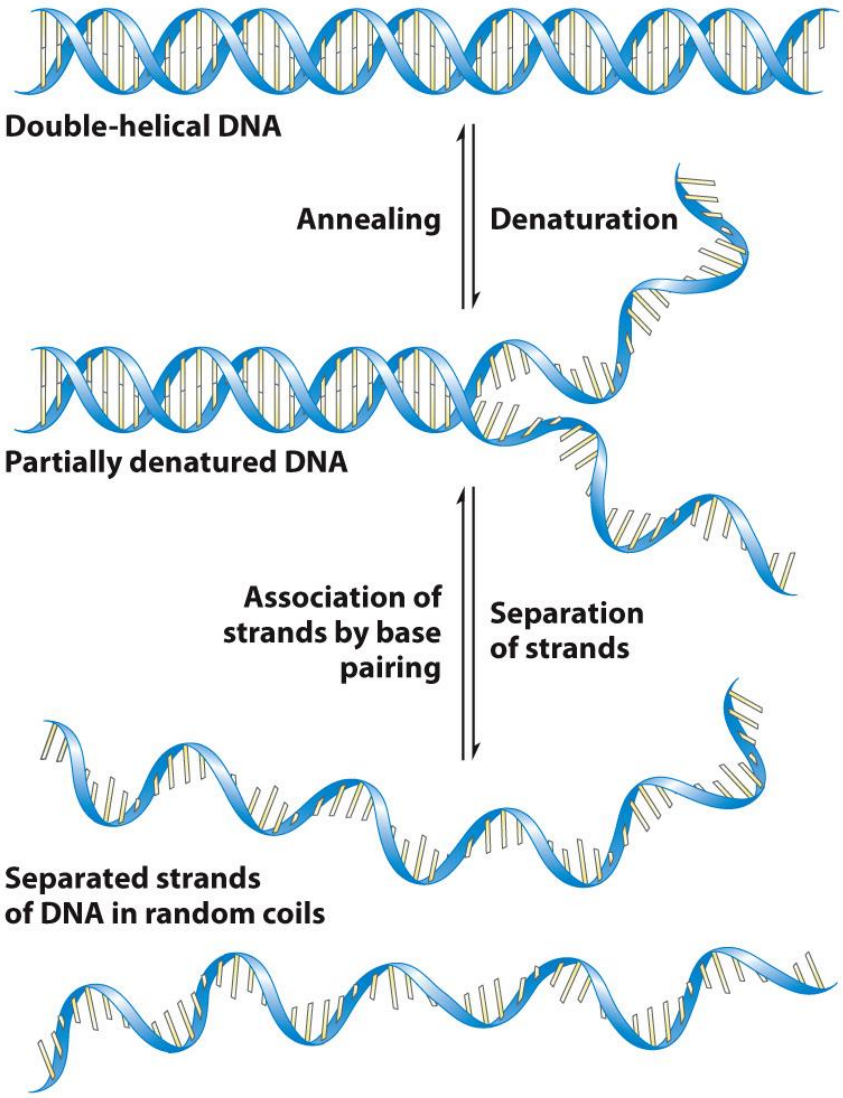


Figure 8-26
Lehninger Principles of Biochemistry, Seventh Edition

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
- DNA denaturation is commonly monitored by UV spectrophotometry at 260 nm

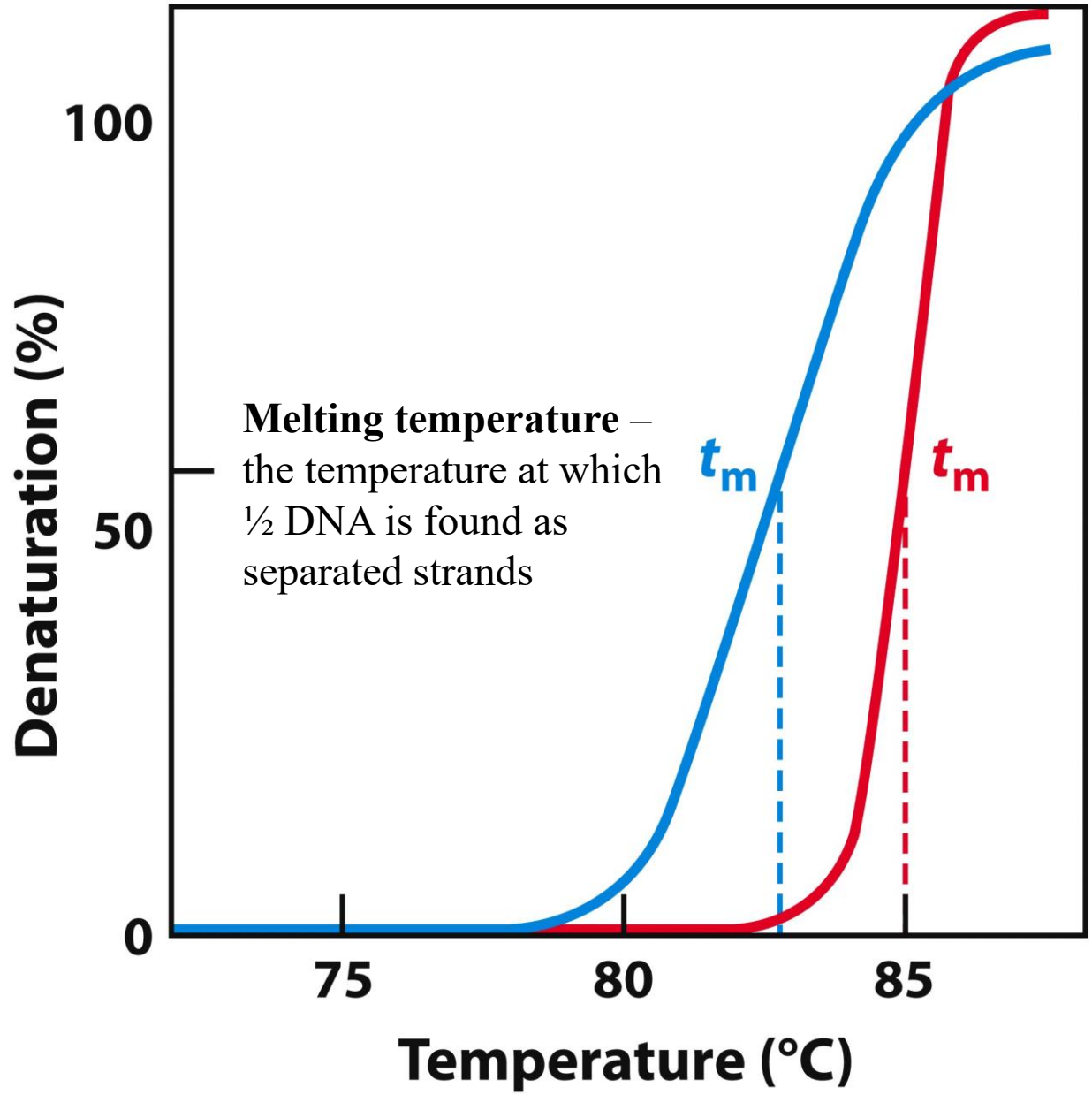
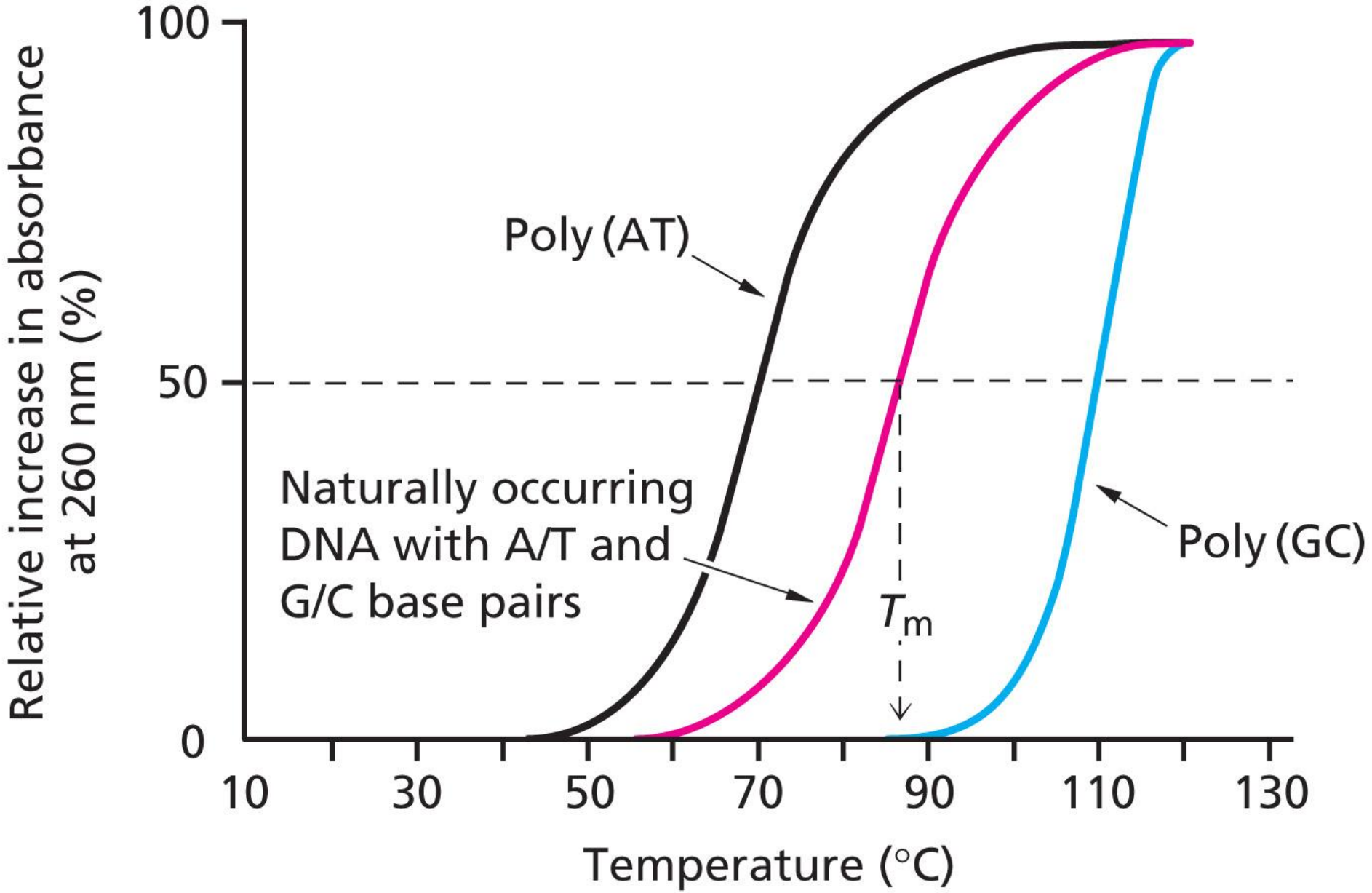


Figure 8-27a
Lehninger Principles of Biochemistry, Sixth Edition

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
  - Important for short DNA
- T_m depends on pH and ionic strength
  - High salt increases T_m



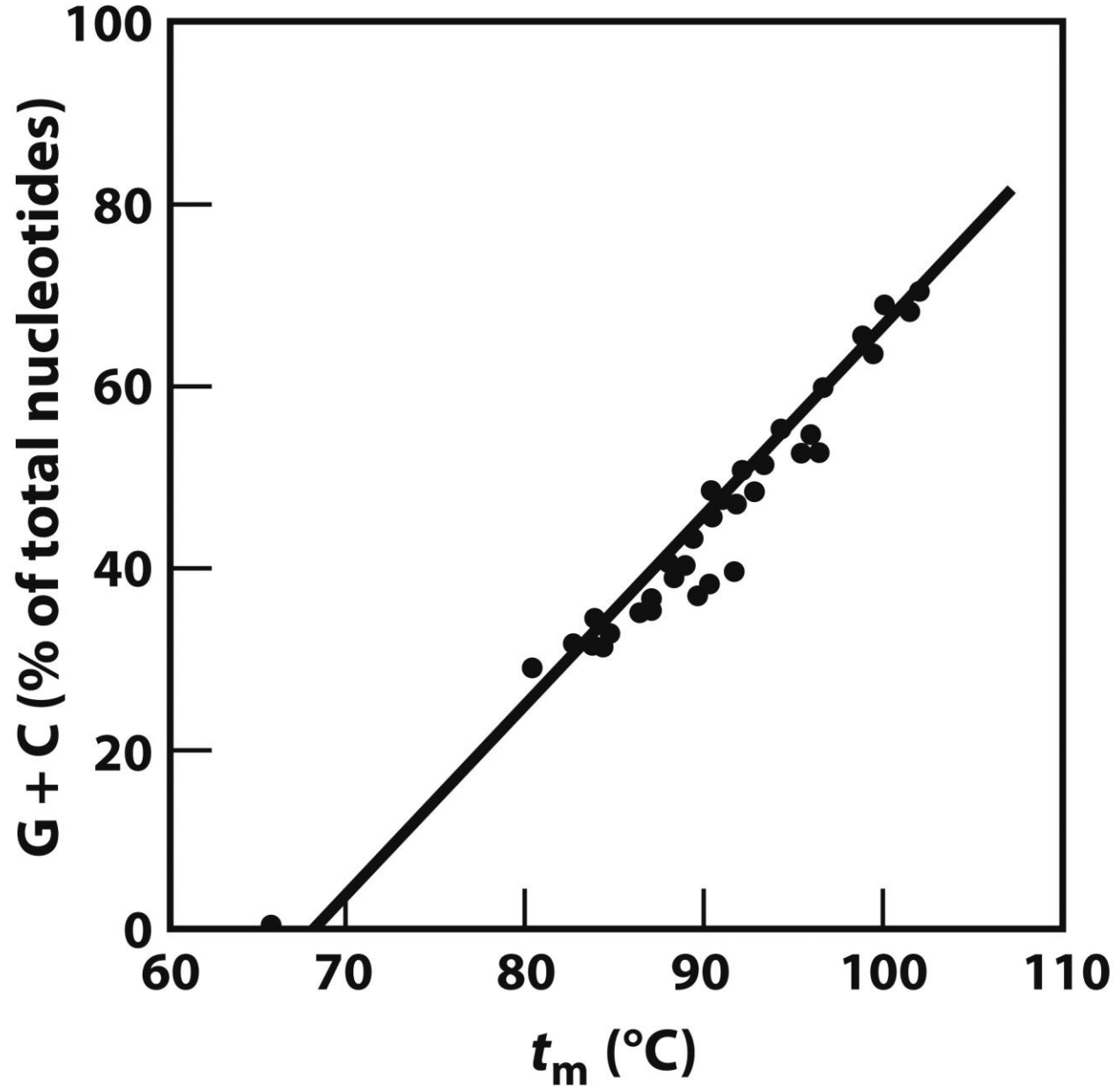


Figure 8-27b
Lehninger Principles of Biochemistry, Sixth Edition

Denaturation of large DNA molecules is not uniform

AT rich regions melt at a lower temperature than GC-rich regions

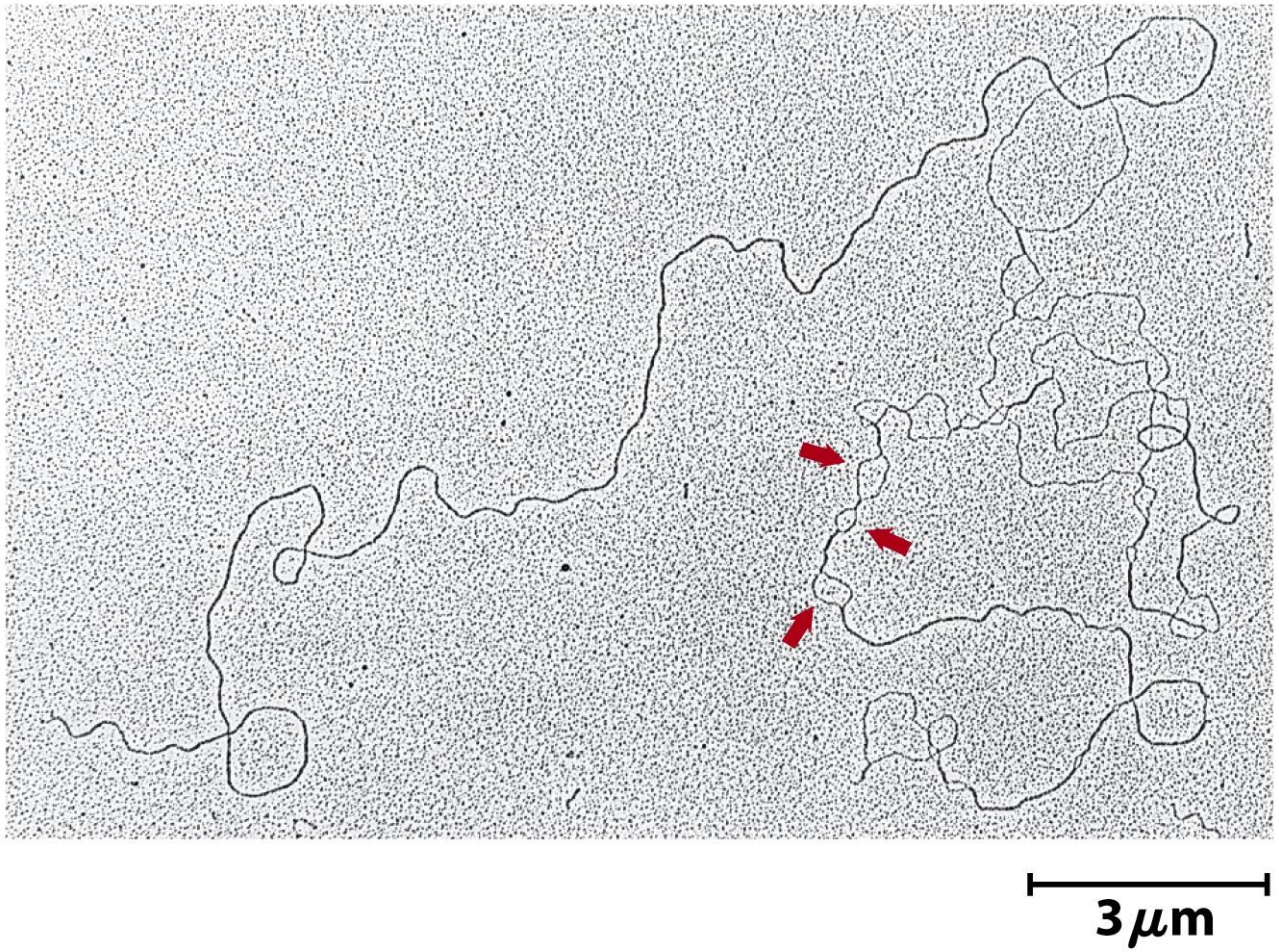


Figure 8-28
Lehninger Principles of Biochemistry, Sixth Edition

Nucleotides and Nucleic Acids Undergo Nonenzymatic Transformations

- **Mutations** - Changes in DNA structure that produce permanent changes in genetic information

- Mutations can happen in response to changes in environment

- Spontaneous (nonenzymatic) covalent changes occur in some nucleobases

- Cells have mechanisms to correct most of these modifications.

Molecular Mechanisms of Spontaneous Mutagenesis

- Deamination
  - Very slow reactions
  - Large number of residues
  - The net effect is significant: 100 C $\rightarrow$ U events/day in a mammalian cell
- Depurination
  - N-glycosidic bond is hydrolyzed
  - Significant for purines: 10,000 purines lost/day in a mammalian cell
- Cells have mechanisms to correct most of these modifications

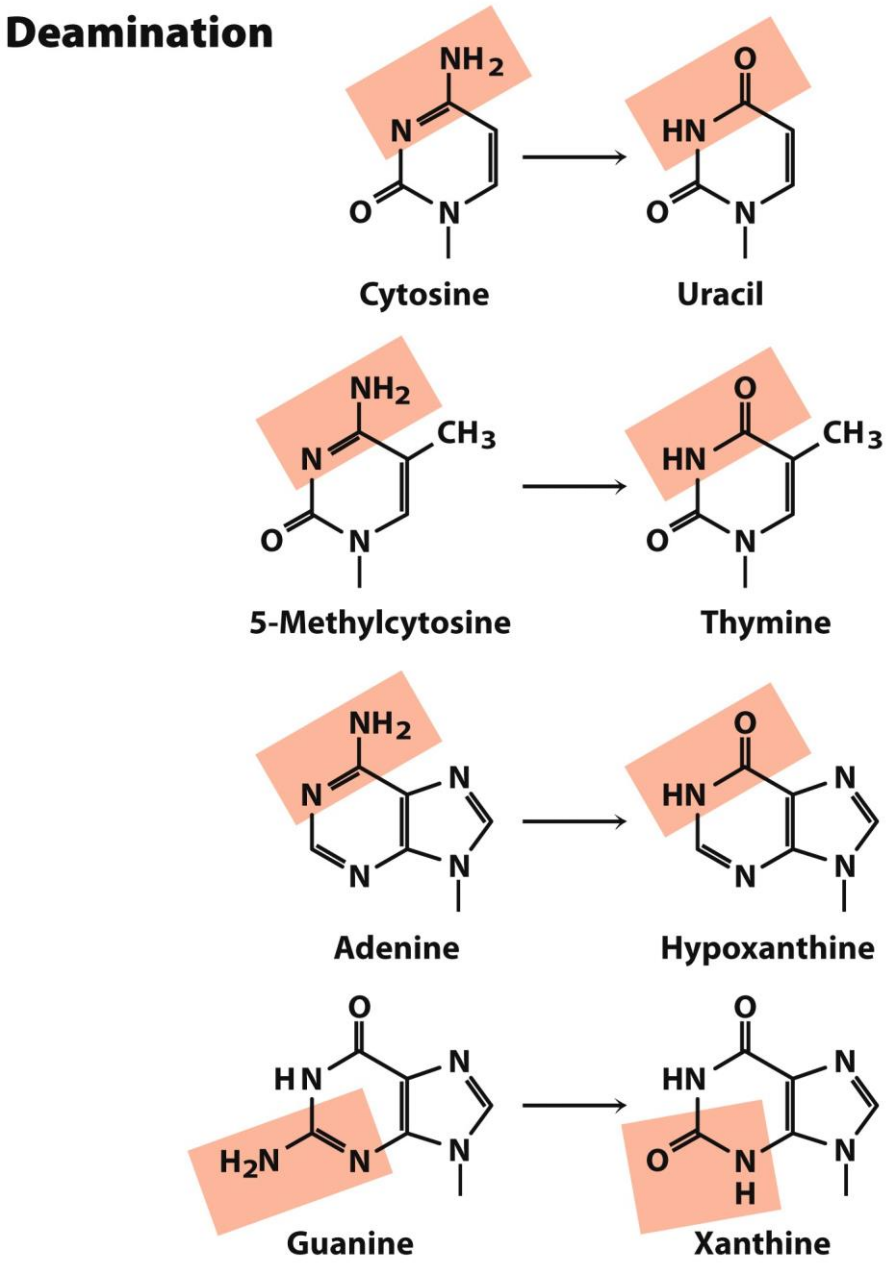
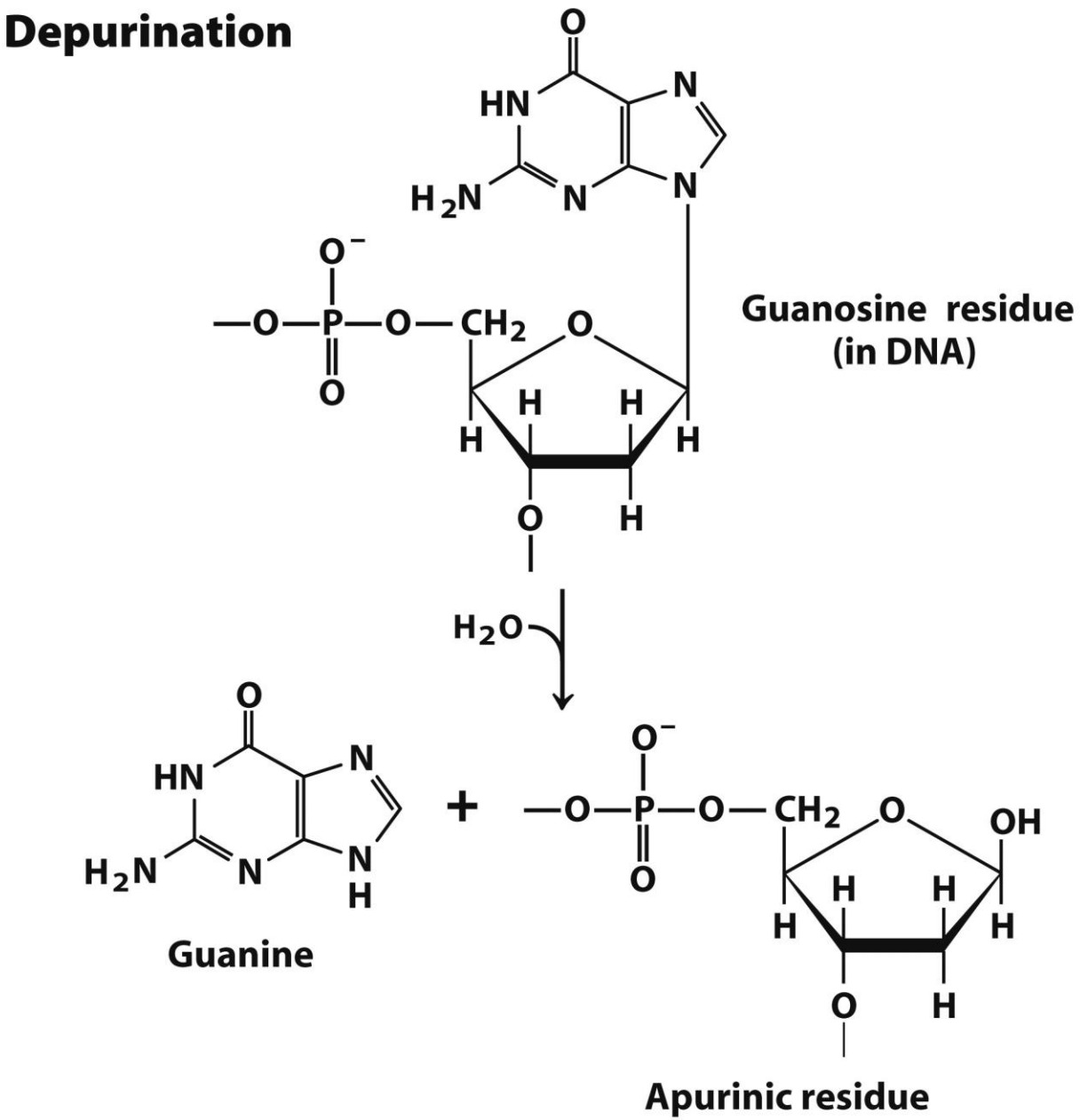


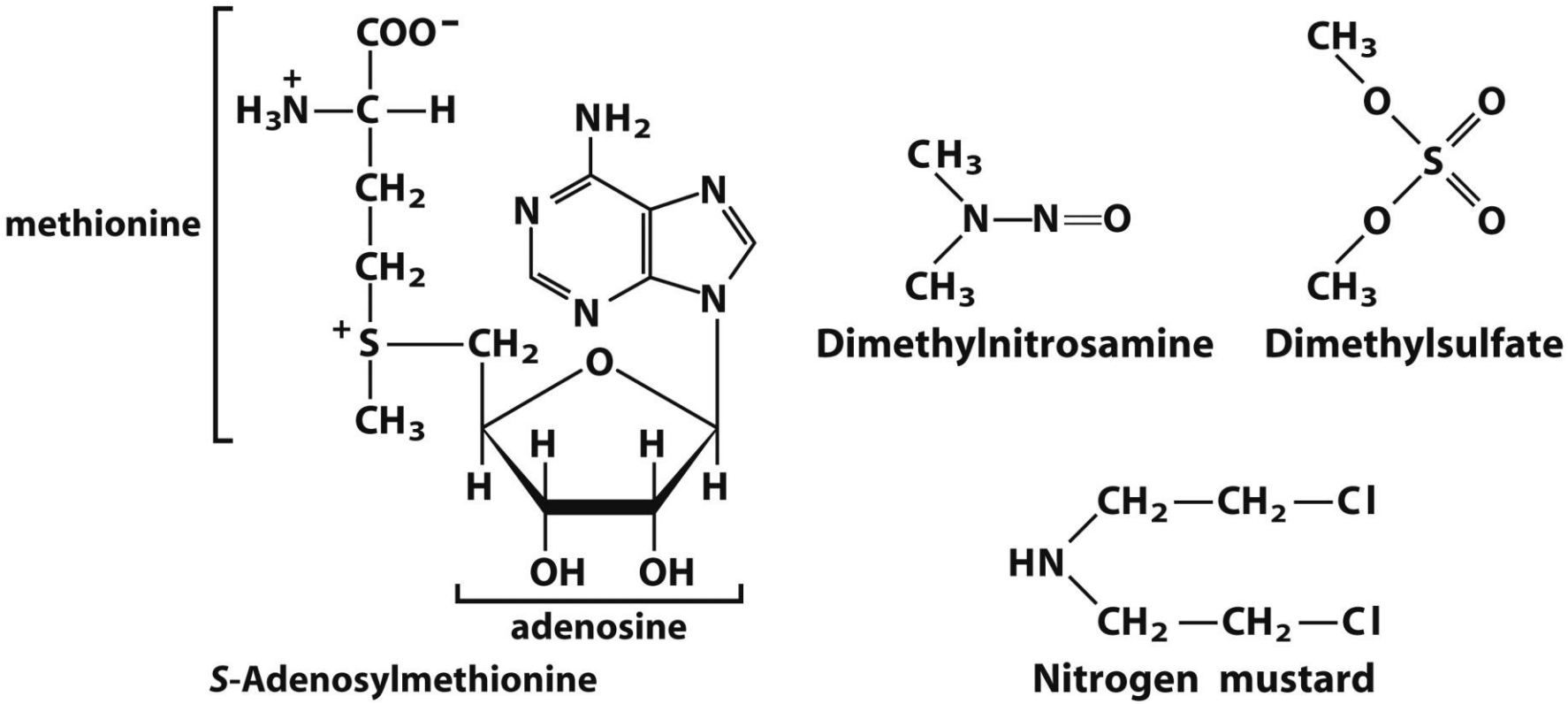
Figure 8-30a
Lehninger Principles of Biochemistry, Sixth Edition



The deoxyribose remaining after depurination is readily converted from the β-furanose to the aldehyde form, further destabilizing the DNA at this position

Molecular Mechanisms of Oxidative and Chemical Mutagenesis

- Oxidative damage
  - Hydroxylation of guanine
  - Mitochondrial DNA is most susceptible
- Chemical alkylation
  - Methylation of guanine
- Cells have mechanisms to correct most of these modifications



Alkylating agents

Figure 8-32b
Lehninger Principles of Biochemistry, Sixth Edition

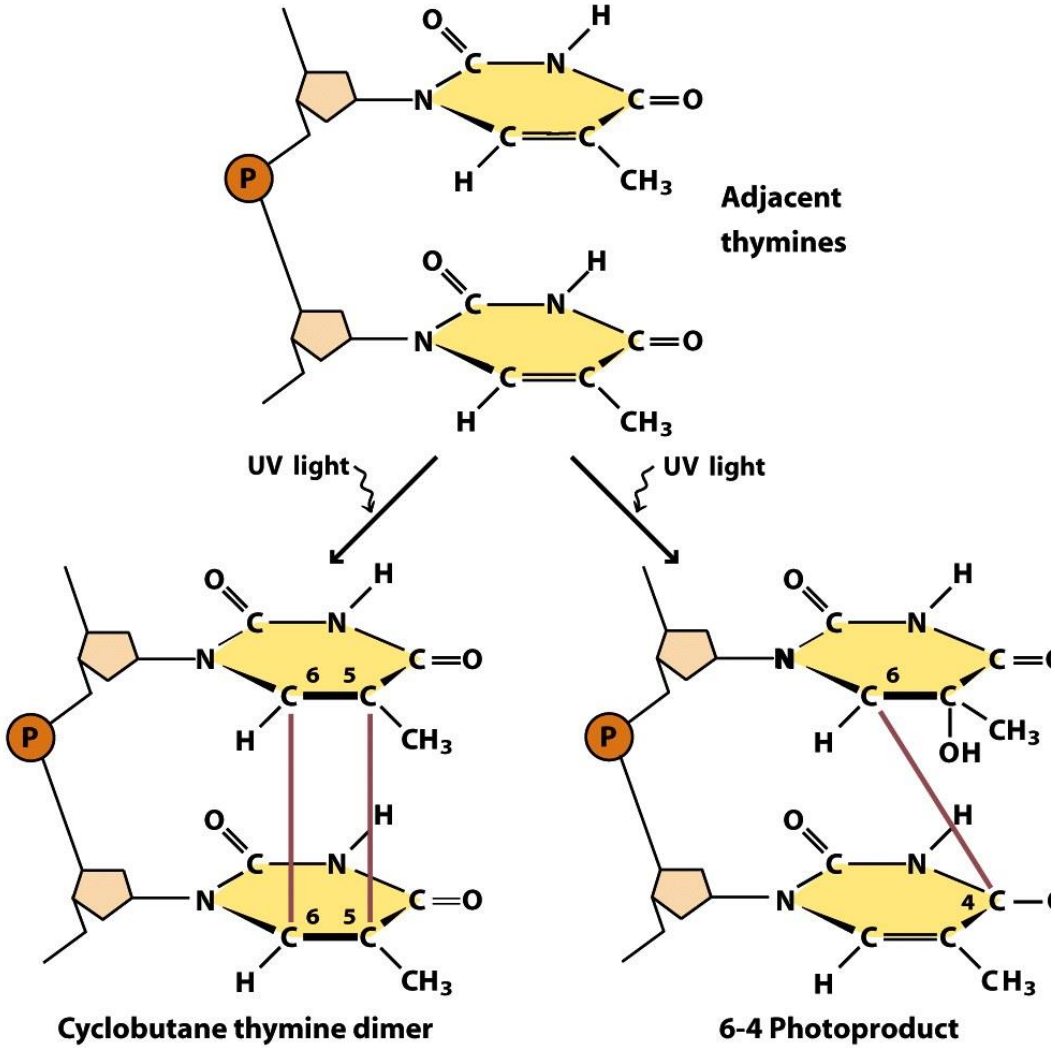
Molecular Mechanisms of Radiation-Induced Mutagenesis

- UV light induces dimerization of pyrimidines; this may be the main mechanism for skin cancers.

- Ionizing radiation (X-rays and γ-rays) causes ring opening and strand breaking .
    - These are difficult to fix.

- Cells can repair some of these modifications, but others cause mutations. Accumulation of mutations is linked to aging and carcinogenesis.

Formation of pyrimidine dimers induced by UV light



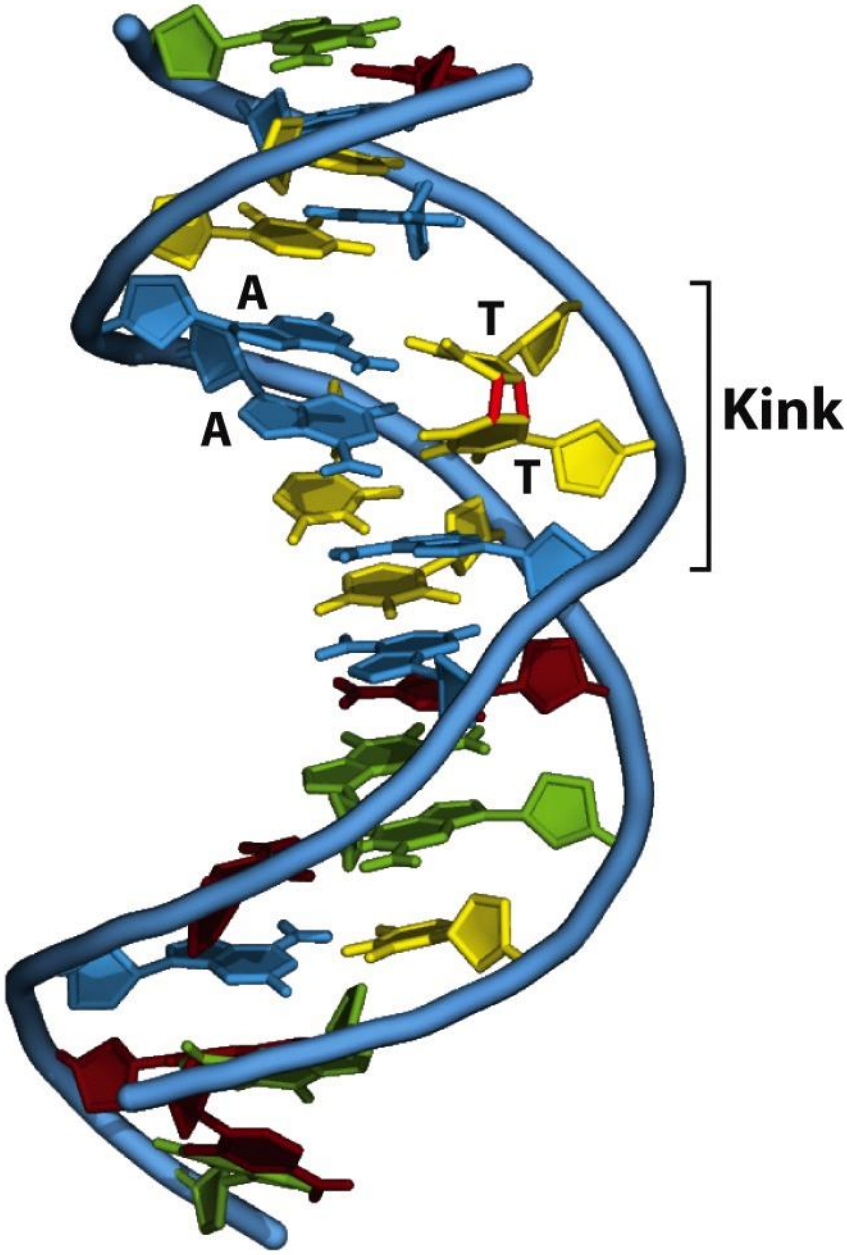


Figure 8-31b
Lehninger Principles of Biochemistry, Sixth Edition

Ch 24 DNA Packing into Nucleosomes

- Chromatin - DNA and proteins (equal by mass) randomly dispersed in the nucleus in interphase
- Chromosomes - DNA and proteins condensed together during mitotic phase
- Histones - the proteins on which the DNA is tightly wrapped
- Nucleosomes consist of DNA wrapped around positively charged histone proteins

Regularly spaced nucleosomes consist of histone complexes bound to DNA.

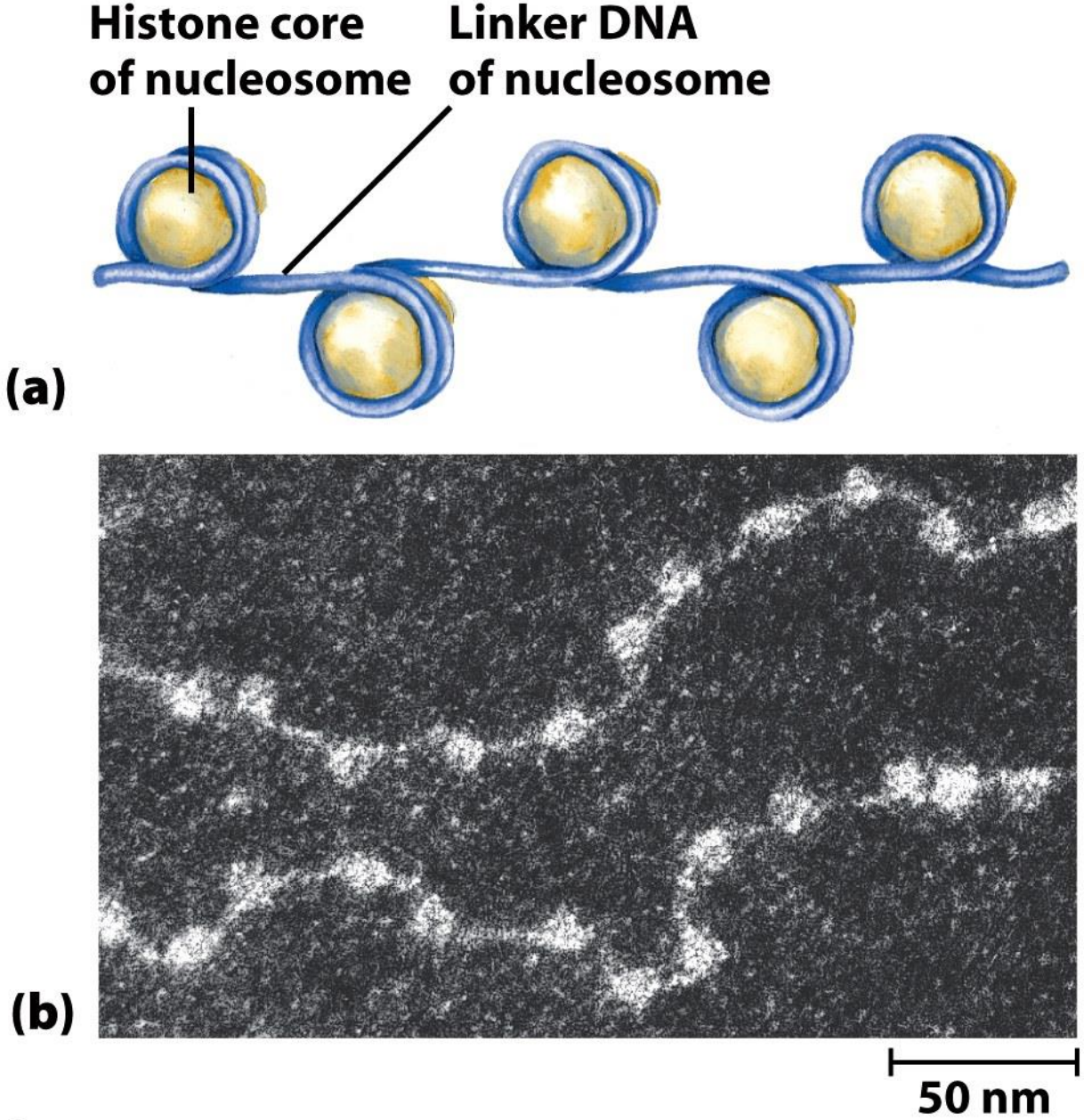


Figure 24-26
Lehninger Principles of Biochemistry, Fifth Edition

Histones Are Small, Basic Protein

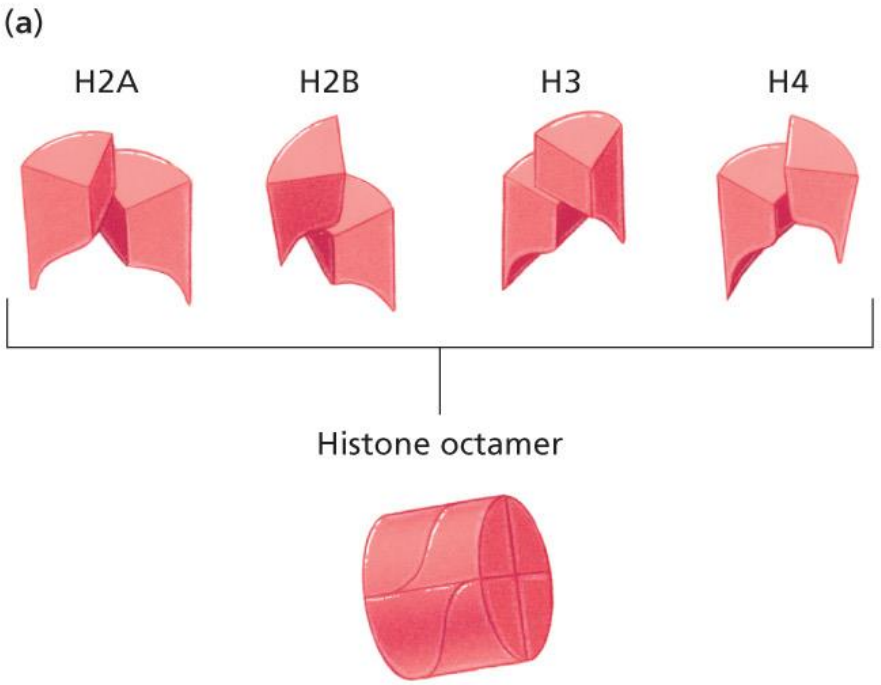
- Found in chromatins of all eukaryotic cells
- MW ~ 11000 – 21000
- Very rich in basic (+ve) aa, Lys and Arg
- 5 major classes:
  H1, H2A, H2B, H3 and H4 (differ in MW and aa composition)
- Each type of histone can be enzymatically modified (methylation, acetylation, glycosylation, phosphorylation, etc.)

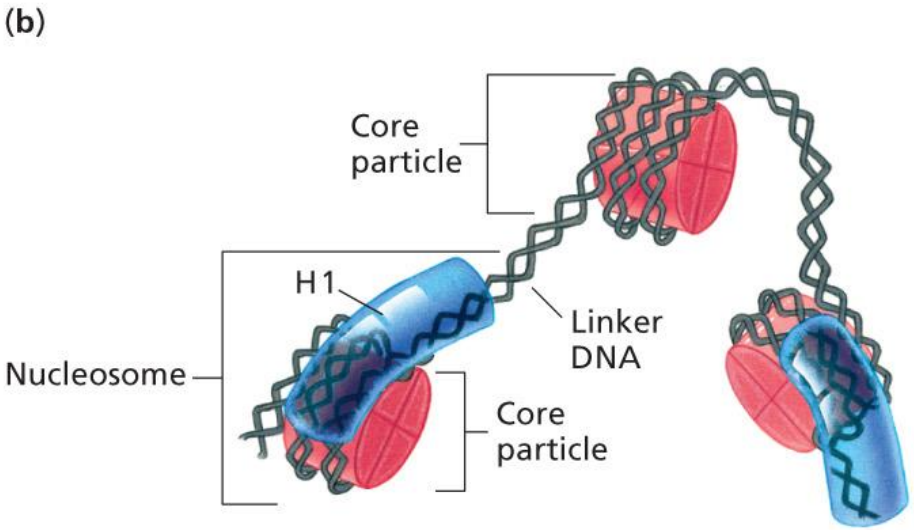
Table 19.4 Basic and acidic residues in mammalian histones

Type	Molecular weight	Number of residues	Number of basic residues	Number of acidic residues
Rabbit thymus H1	21,000	213	65	10
Calf thymus H2A	14,000	129	30	9
Calf thymus H2B	13,800	125	31	10
Calf thymus H3	15,300	135	33	11
Calf thymus H4	11,300	102	27	7

Nucleosomes Are the Fundamental Organizational Units of Chromatin

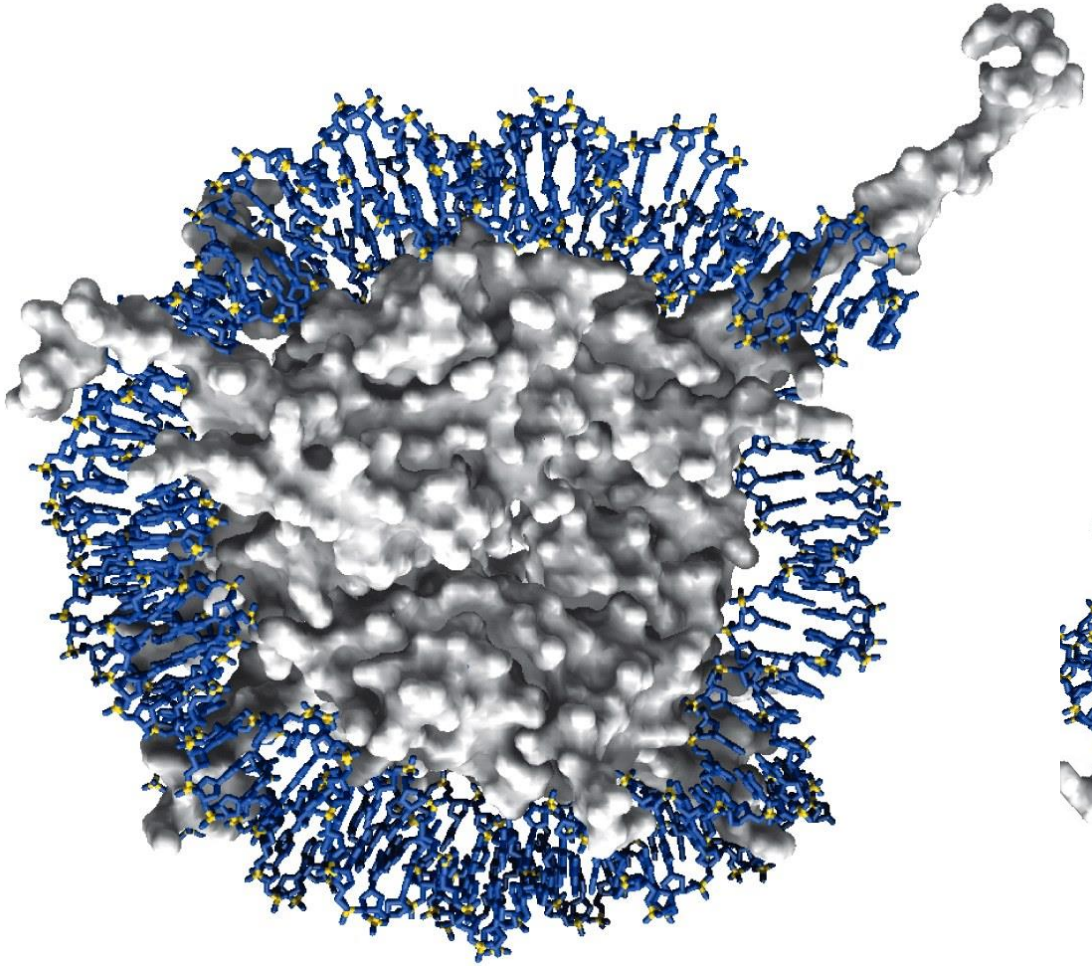
- Compacting DNA into a shorter structure
- Beads-on-a-string arrangement (beads are complex histones, strings are DNA)
- The bead + the connecting DNA that leads to the next bead = the nucleosome
- Each bead contains 8 histones (2x H2A, H2B, H3, H4). H1 binds to linker DNA

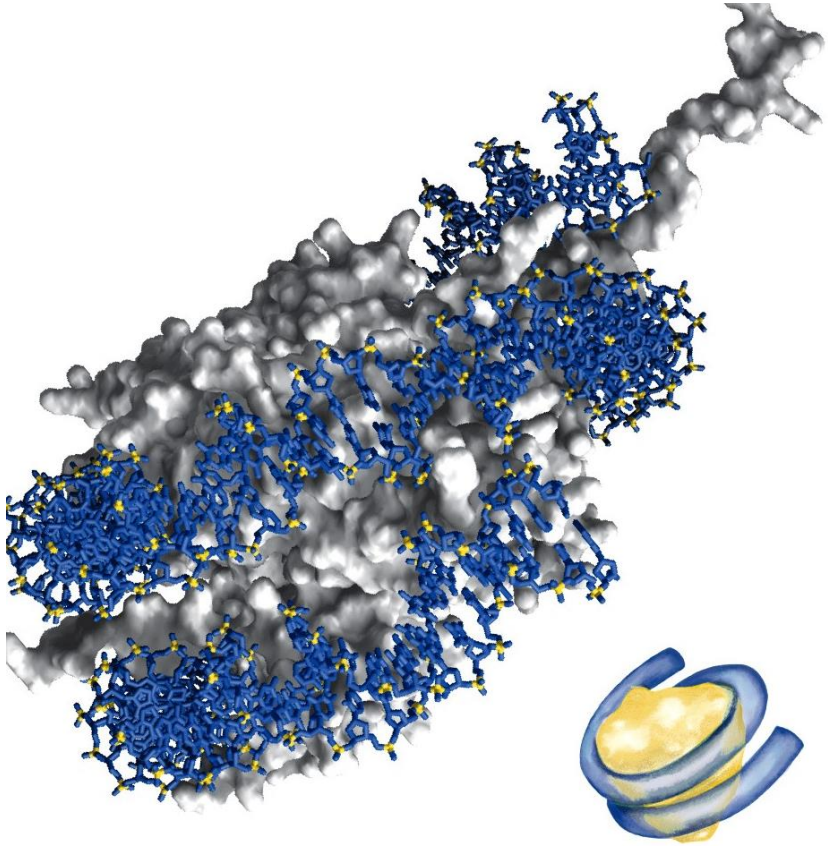




Top view

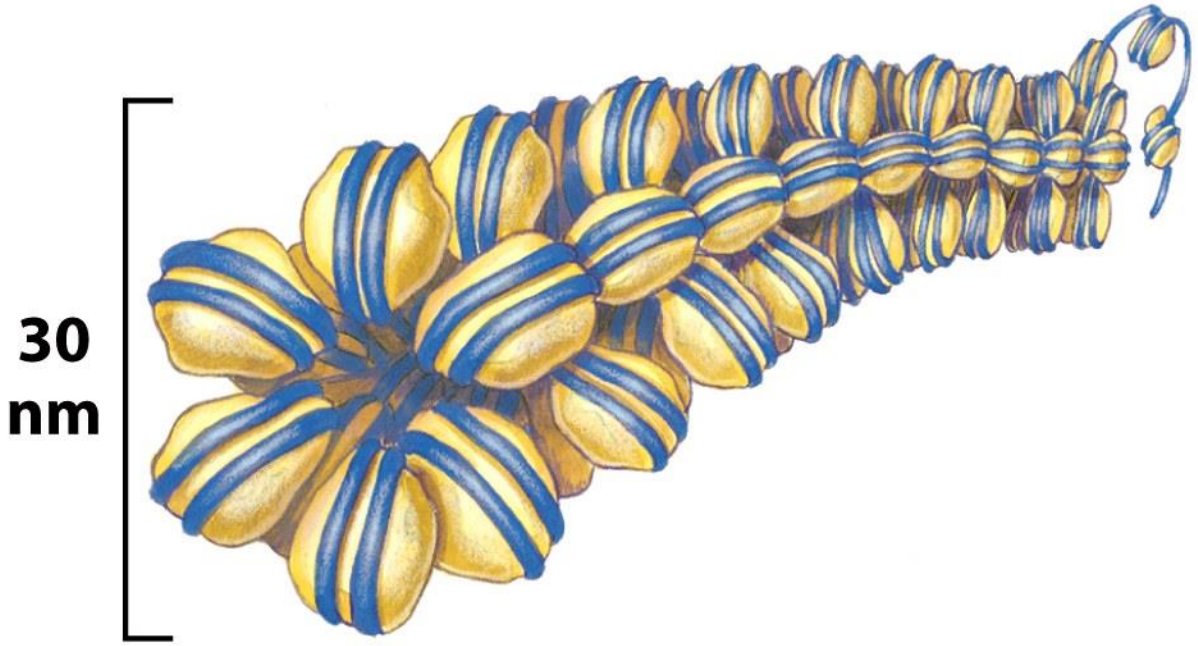
Side view



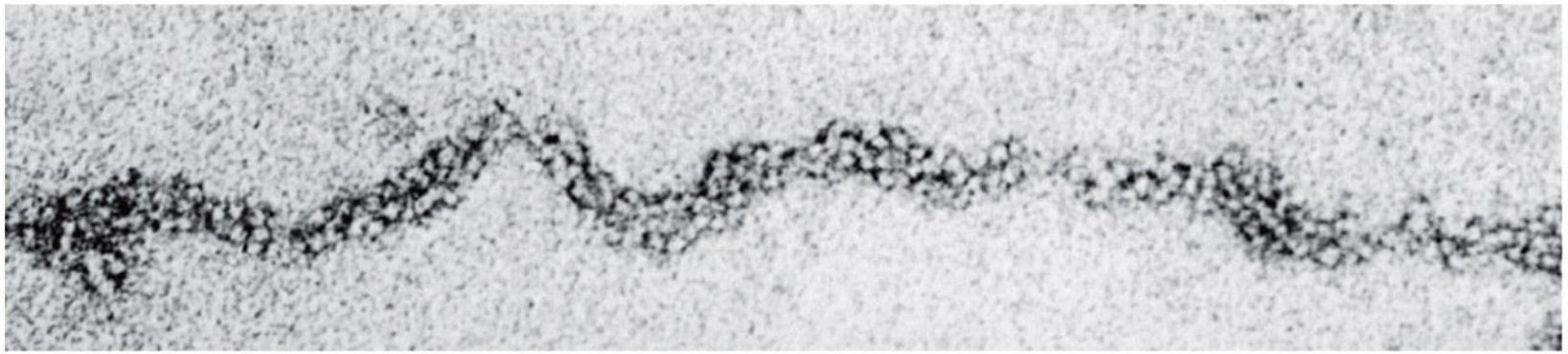


Nucleosomes Are Packed into Successively Higher-Order Structures

- When isolated gently, nucleosome cores can be seen as structures organized into a **30 nm fiber**
- Histone H1 is thought to stabilize the 30 nm fiber because one H1 molecule is necessary per nucleosome core
- Not in the entire chromosome
- Regions with genes that are transcribed are less ordered → little or no H1



(a)



(b)

Figure 24-30
Lehninger Principles of Biochemistry, Fifth Edition

Higher Levels of Chromatin Structure are Poorly Understood

- A nuclear scaffold anchors DNA loops and regulates access to information in DNA

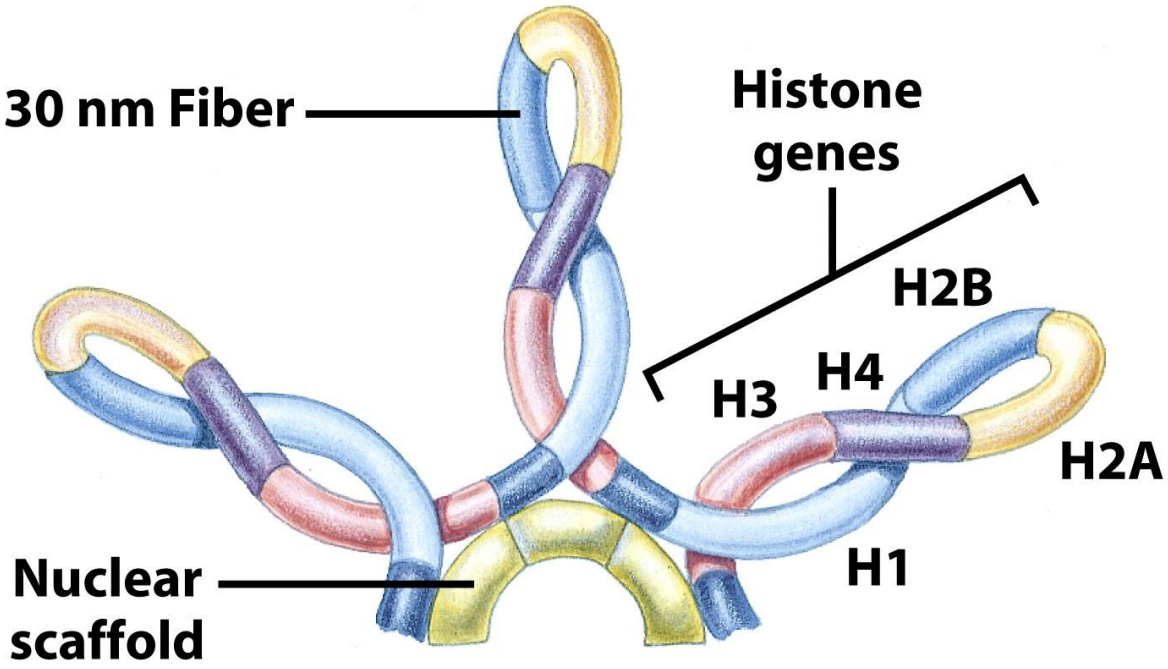


Figure 24-32
Lehninger Principles of Biochemistry, Fifth Edition

Compaction of DNA in a eukaryotic chromosome:

This *model* shows the levels of organization that could provide the observed degree of DNA compaction in the chromosomes of eukaryotes.

The levels take the form of coils upon coils.

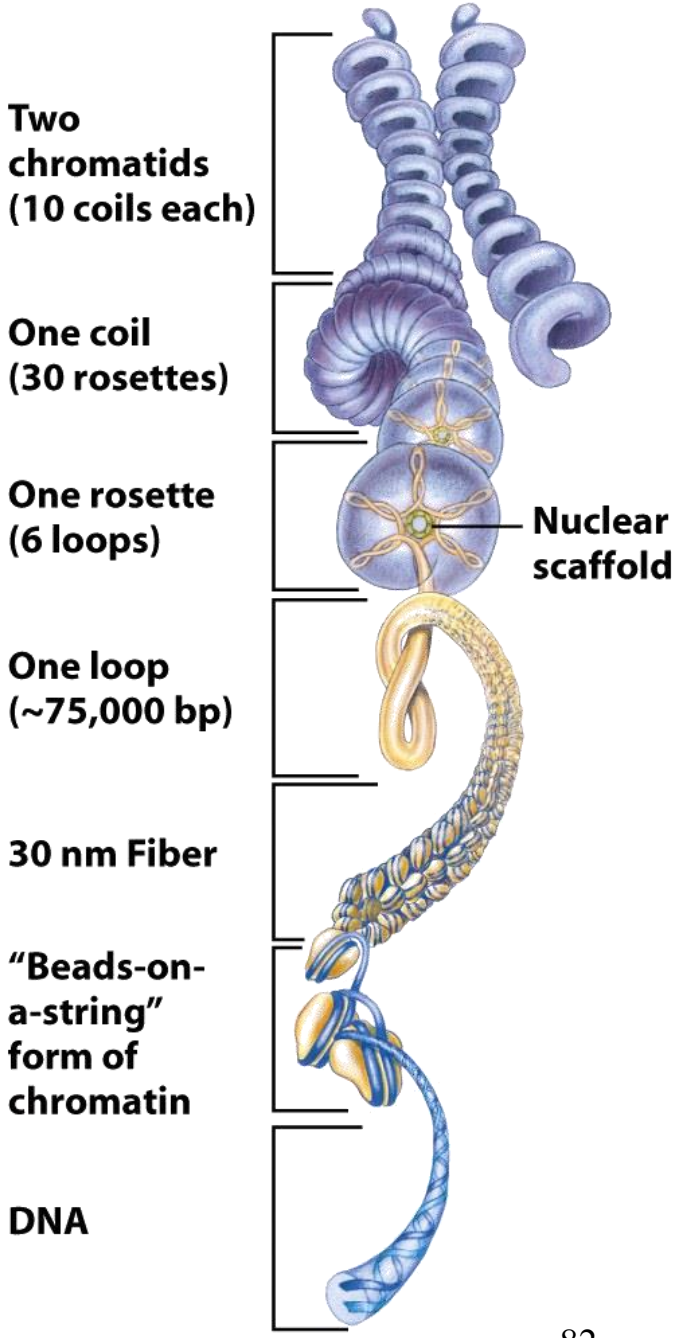


Figure 24-33
Lehninger Principles of Biochemistry, Fifth Edition