Donald Voet • Judith G. Voet • Charlotte W. Pratt

# Fundamentals of Biochemistry

## Second Edition

## Chapter 3:

## Nucleotides, Nucleic Acids, and Genetic Information

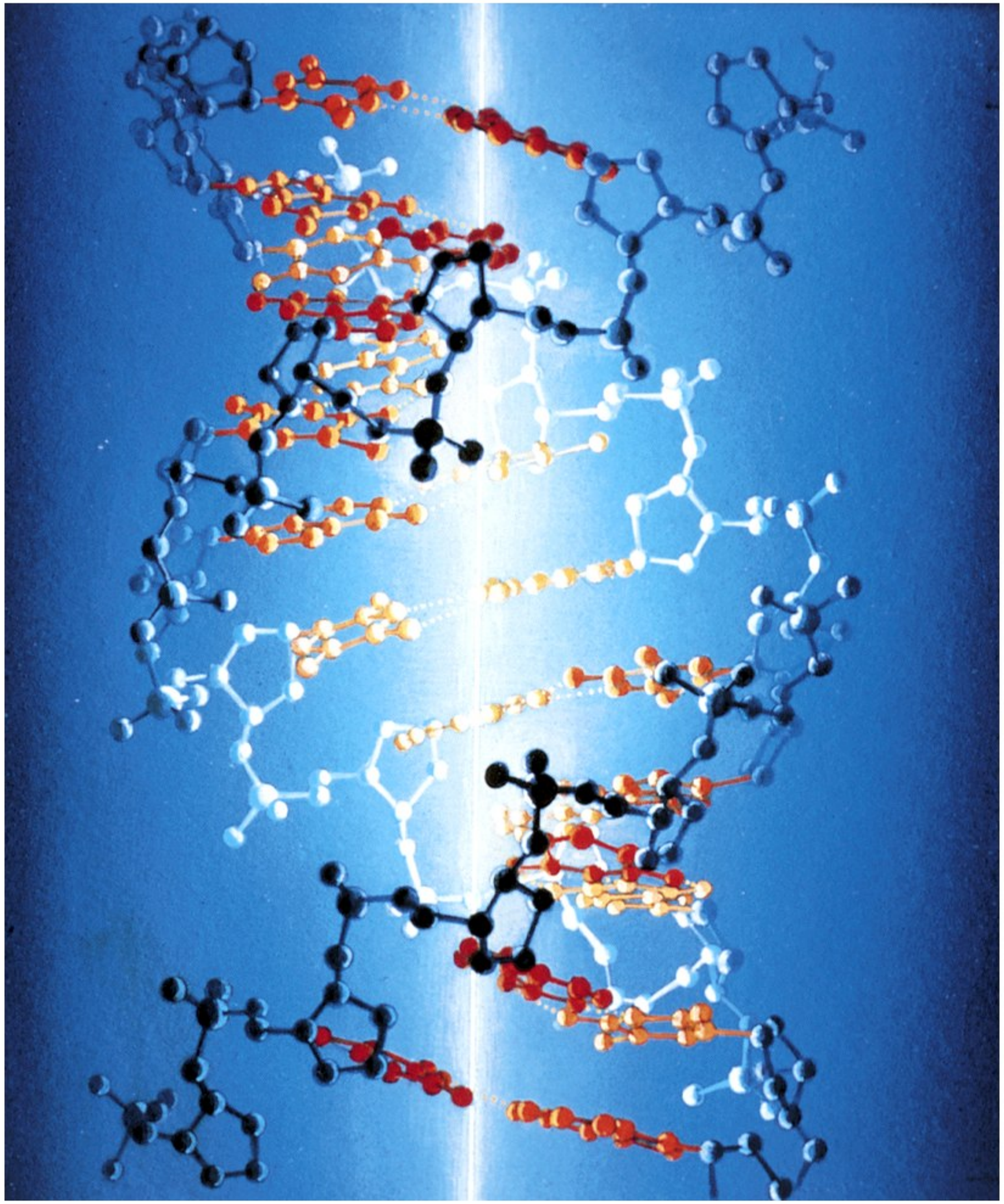
Nucleic acids

↓

DNA, RNA
(consists of nucleotides)

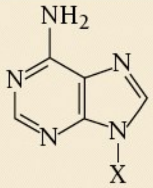
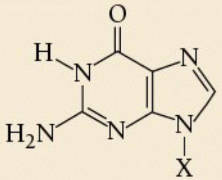
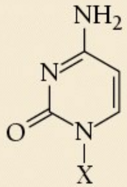
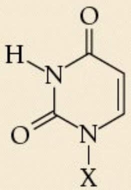
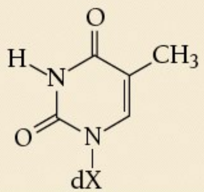
↓

Bases
Sugars
Phosphates



Chapter 3 Opener Fundamentals of Biochemistry, 2/e

**Table 3-1 Names and Abbreviations of Nucleic Acid Bases, Nucleosides, and Nucleotides**

| Base Formula | Base (X = H) | Nucleoside (X = ribose[a]) | Nucleotide[b] (X = ribose phosphate[a]) |
|---|---|---|---|
|  | Adenine<br>Ade<br>A | Adenosine<br>Ado<br>A | Adenylic acid<br>Adenosine monophosphate<br>AMP |
|  | Guanine<br>Gua<br>G | Guanosine<br>Guo<br>G | Guanylic acid<br>Guanosine monophosphate<br>GMP |
|  | Cytosine<br>Cyt<br>C | Cytidine<br>Cyd<br>C | Cytidylic acid<br>Cytidine monophosphate<br>CMP |
|  | Uracil<br>Ura<br>U | Uridine<br>Urd<br>U | Uridylic acid<br>Uridine monophosphate<br>UMP |
|  | Thymine<br>Thy<br>T | Deoxythymidine<br>dThd<br>dT | Deoxythymidylic acid<br>Deoxythymidine monophosphate<br>dTMP |

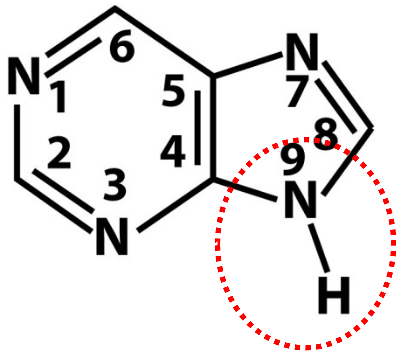
[a]The presence of a 2′-deoxyribose unit in place of ribose, as occurs in DNA, is implied by the prefixes "deoxy" or "d." For example, the deoxynucleoside of adenine is deoxyadenosine or dA. However, for thymine-containing residues, which rarely occur in RNA, the prefix is redundant and may be dropped. The presence of a ribose unit may be explicitly implied by the prefix "ribo."

[b]The position of the phosphate group in a nucleotide may be explicitly specified as in, for example, 3′-AMP and 5′-GMP.

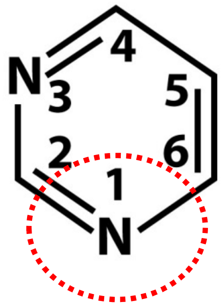
**Table 3-1 Fundamentals of Biochemistry, 2/e**

# The bases of nucleotides

planar, aromatic, heterocyclic molecules




**Purine**




**Pyrimidine**

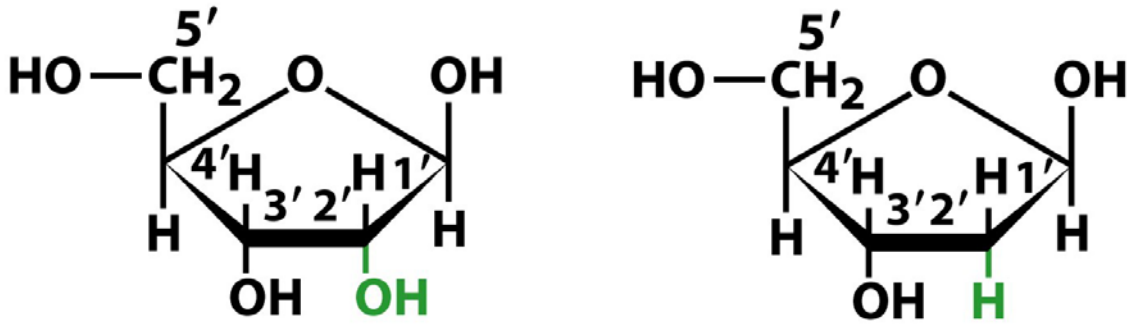
Unnumbered figure pg 41 Fundamentals of Biochemistry, 2/e


Adenine
Guanine

Cytosine
Uracil
Thymine

## Sugars

Primed numbers
Dexoyribonucleic acid (DNA)
Ribonucleic acid (RNA)



Ribose　　Deoxyribose

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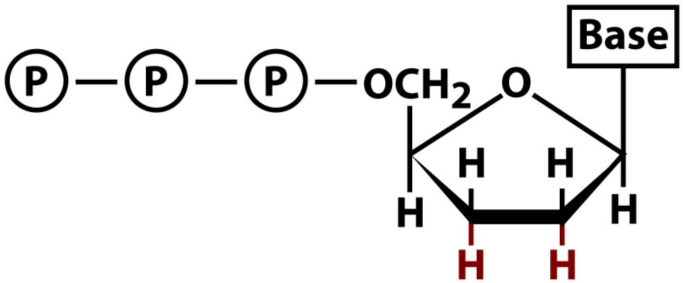
# Dideoxynucleotide for DNA sequencing




**2′,3′-Dideoxynucleoside triphosphate**

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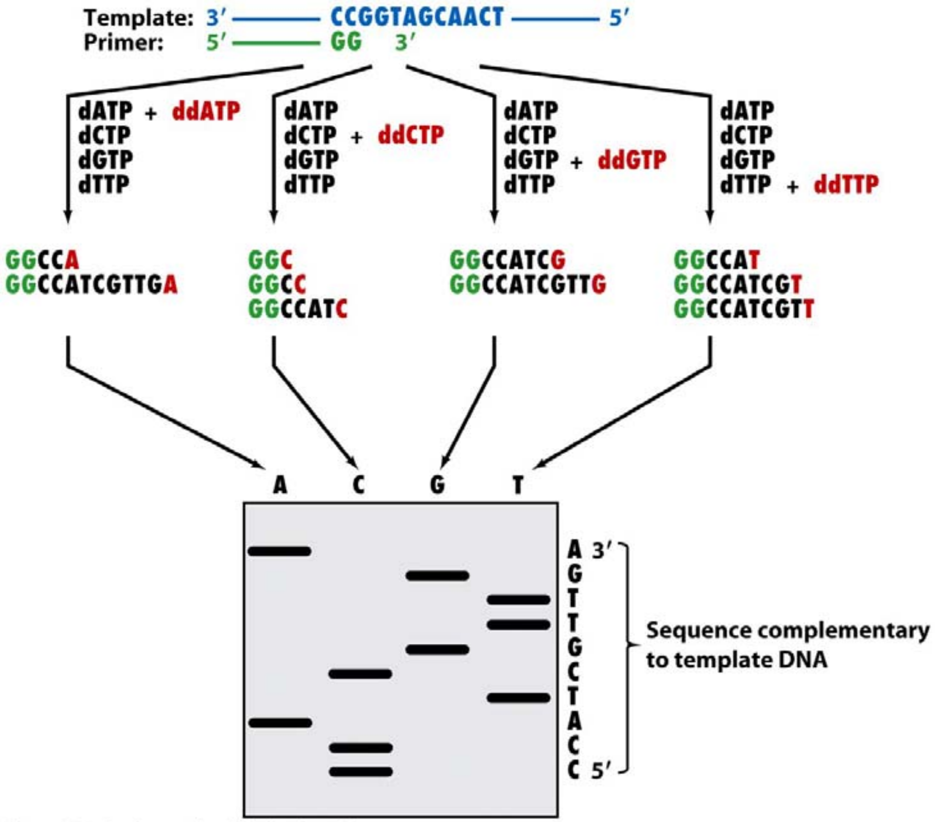



Figure 3-21 Fundamentals of Biochemistry, 2/e

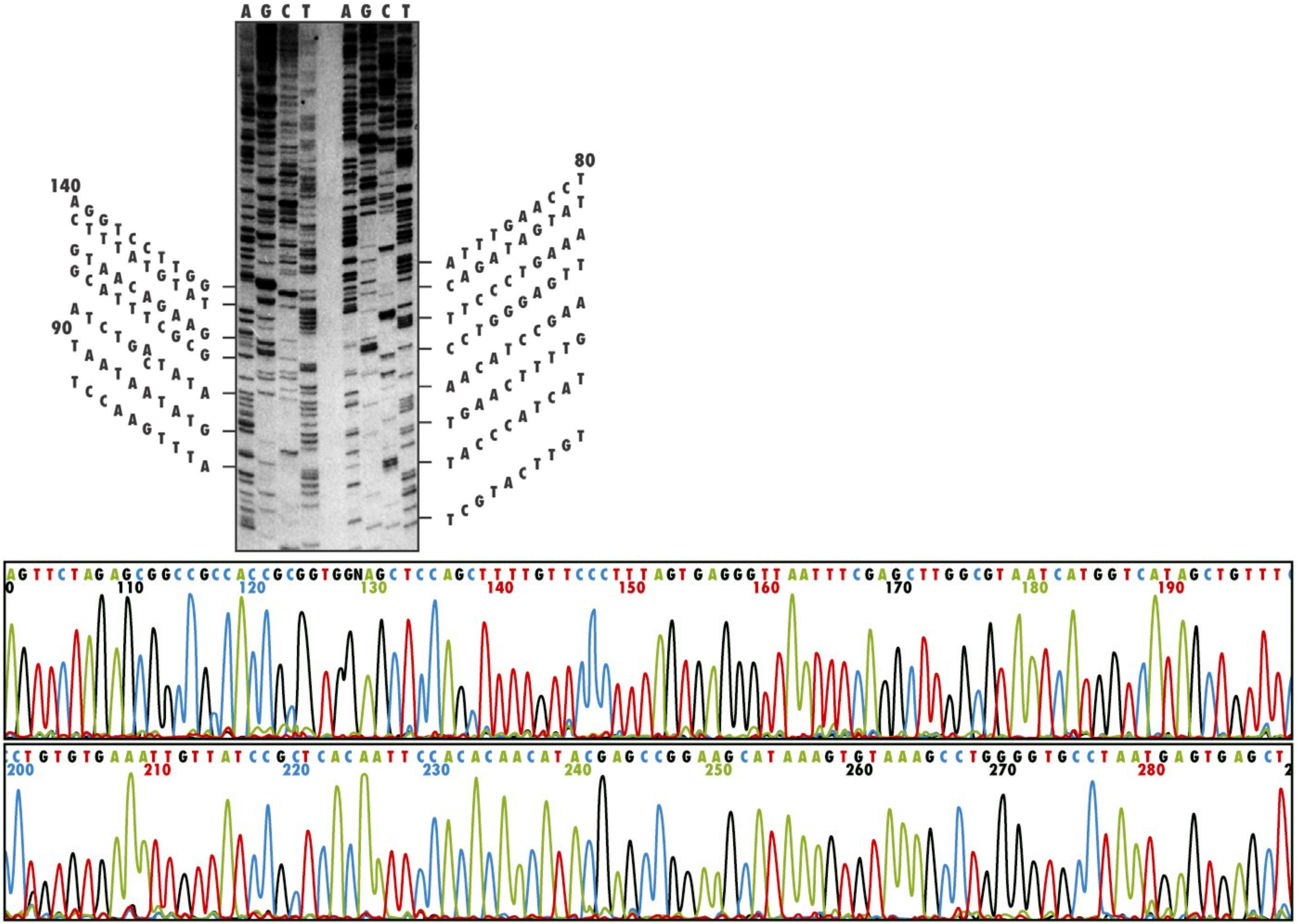



Figure 3-23 Fundamentals of Biochemistry, 2/e

Nucleosides: base + sugar

Nucleotides: base + sugar + phosphate

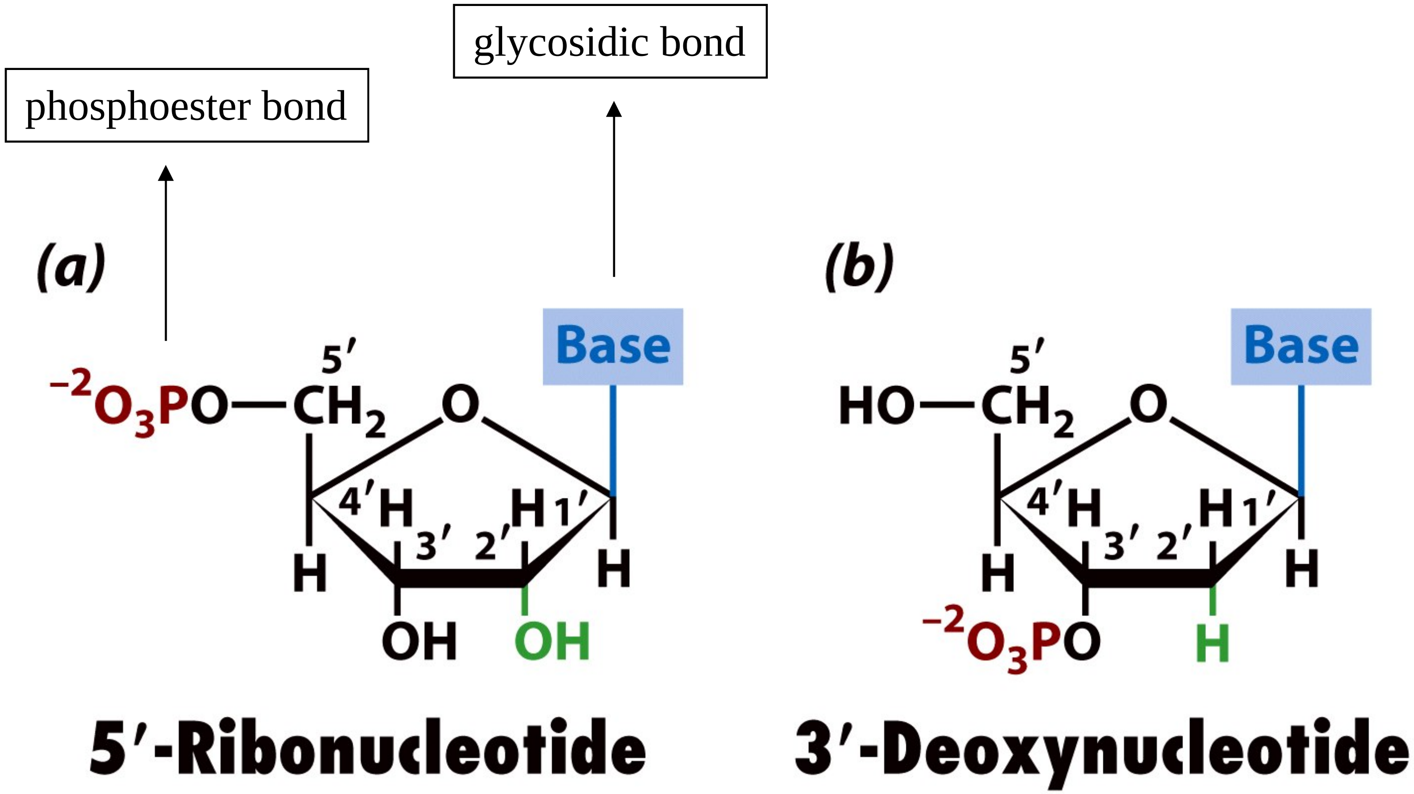
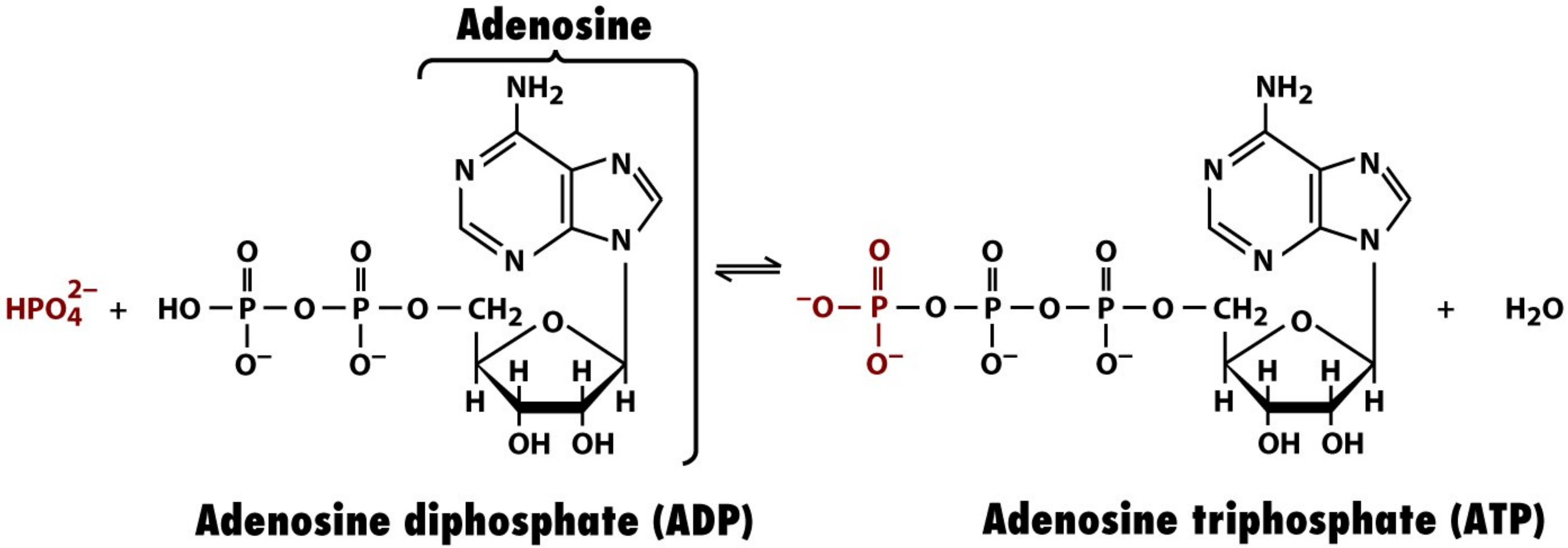



Figure 3-1 Fundamentals of Biochemistry, 2/e

The best known nucleotide

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# Nucleic acid structure

Polynucleotides: mono-, di-, oligo-
Phosphodiester bond
Direction: 5’-, 3’-ends

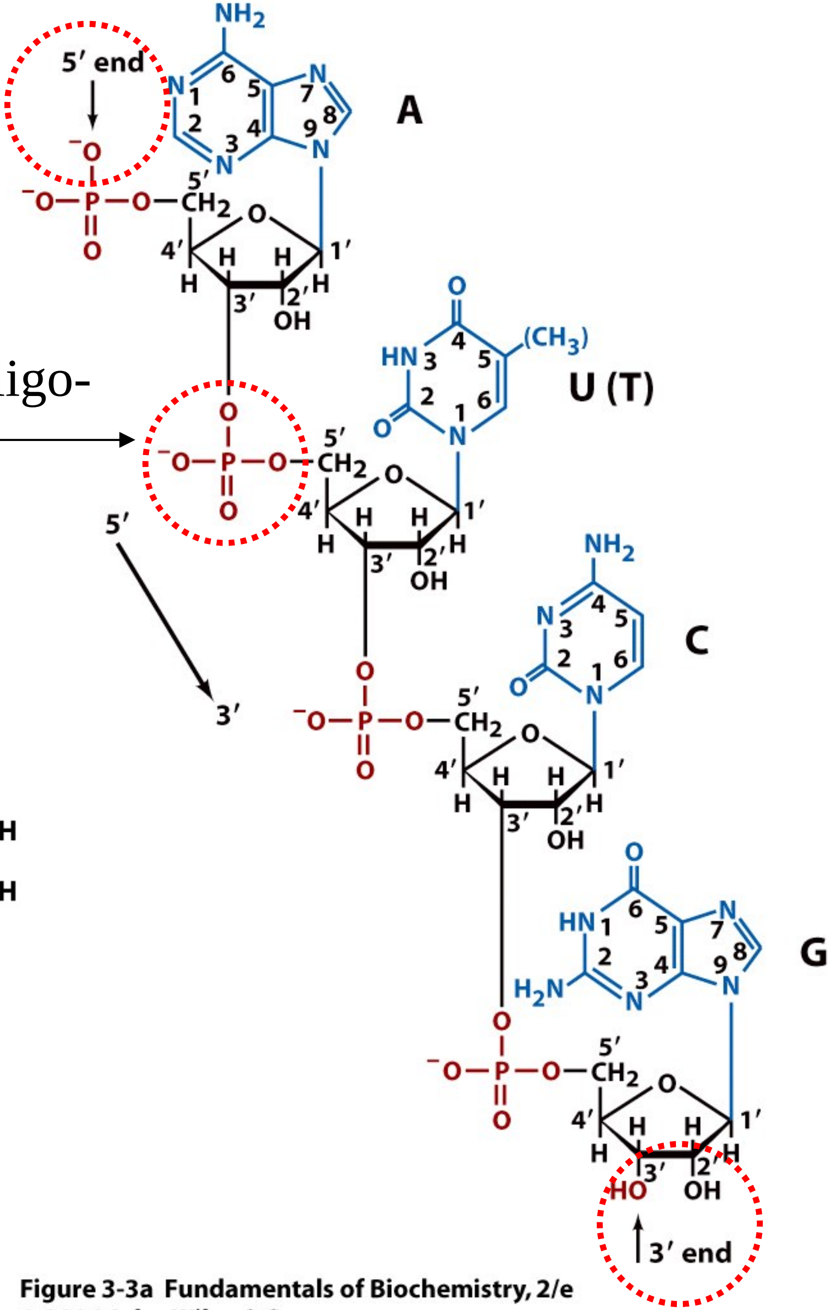



Figure 3-3a Fundamentals of Biochemistry, 2/e

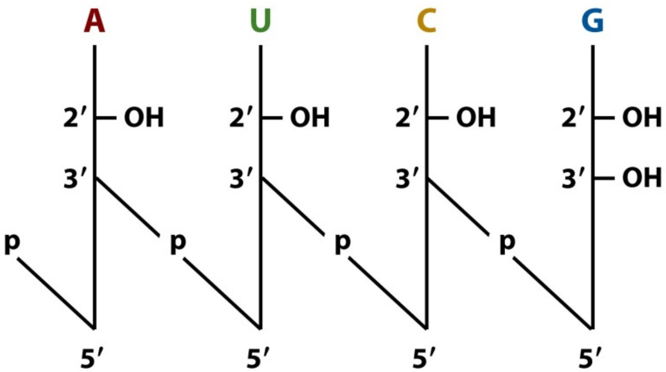




Figure 3-3b Fundamentals of Biochemistry, 2/e


5’-AUCG-3’
pAUCG
AUCG

# DNA double helix

1. Chargaff's rules
   A=T, G=C
   GC ratio

2. Bases in tautomeric forms

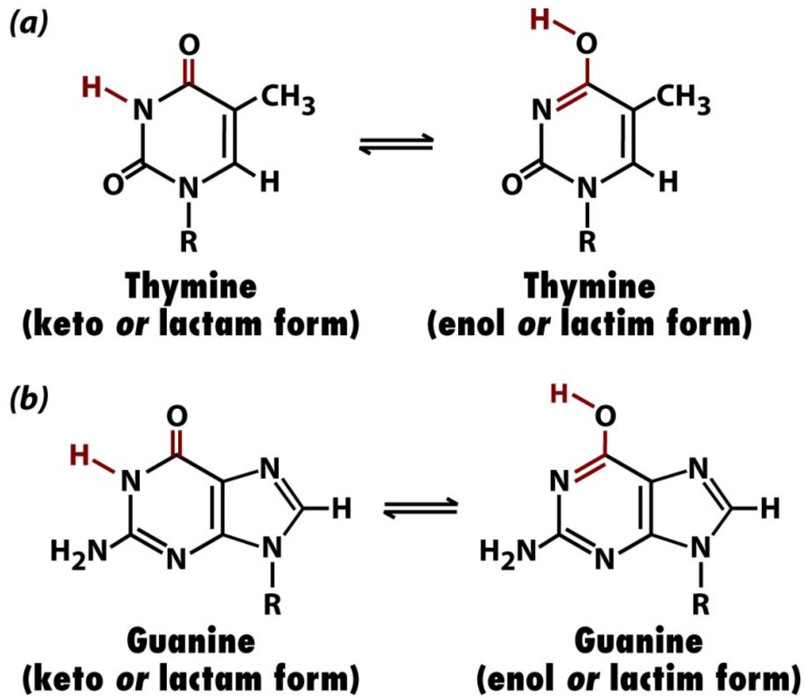



Figure 3-4 Fundamentals of Biochemistry, 2/e

3. DNA is a helical molecule

provided by Rosalind Franklin (p822-823)

X-ray diffraction photograph of DNA fiber

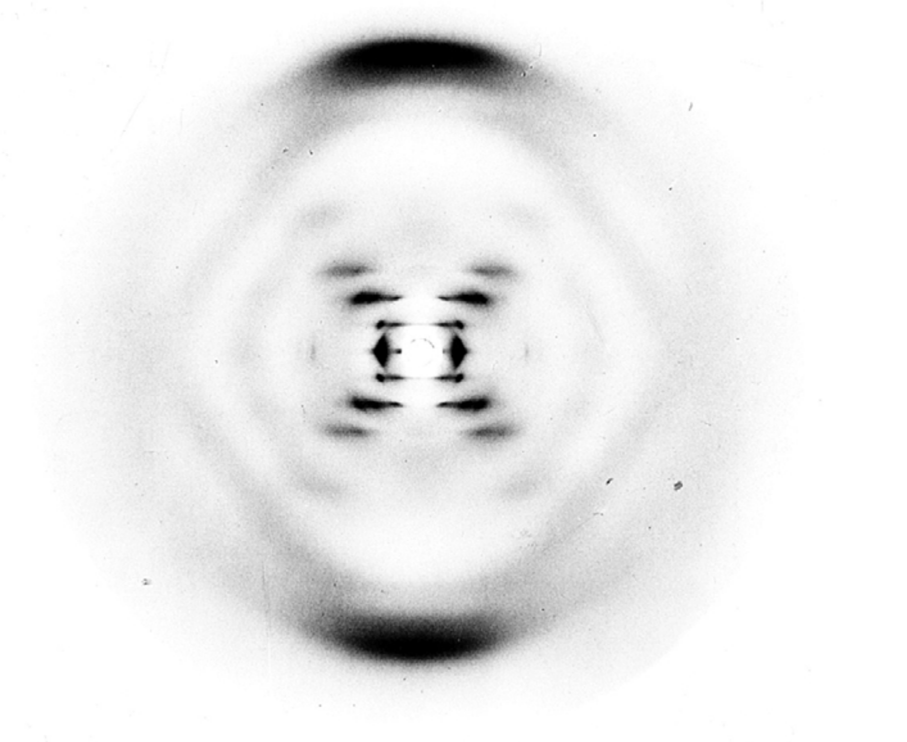


Figure 3-5 Fundamentals of Biochemistry, 2/e

# Watson-Crick model of double helix
## 3D-structure

two polynucleotide chains forming a double helix
Antiparallel forming right handed helix
Bases occupy the core:sugar-phosphate chain in the periphery
 minimizing repulsion between the charged groups
 minor and major grooves
Hydrogen bonded base pairs
 complementary base pairing

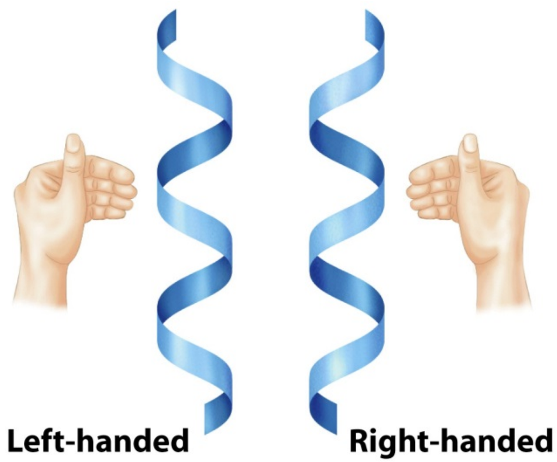



Figure 3-7 Fundamentals of Biochemistry, 2/e

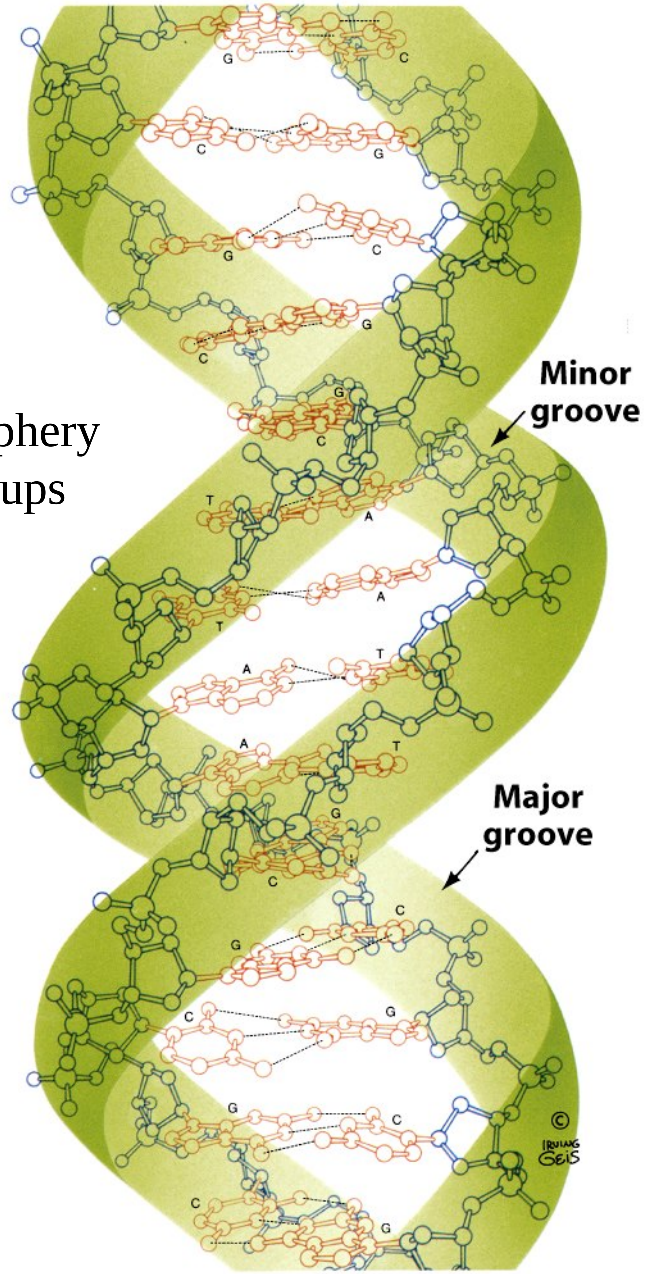




Figure 3-6 Fundamentals of Biochemistry, 2/e

Complementary

↓

Template in replication

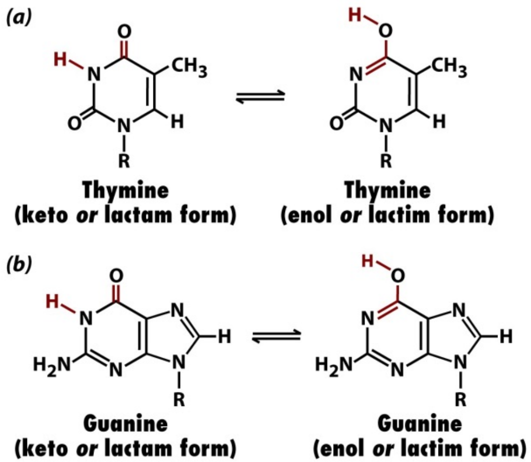



Figure 3-4 Fundamentals of Biochemistry, 2/e

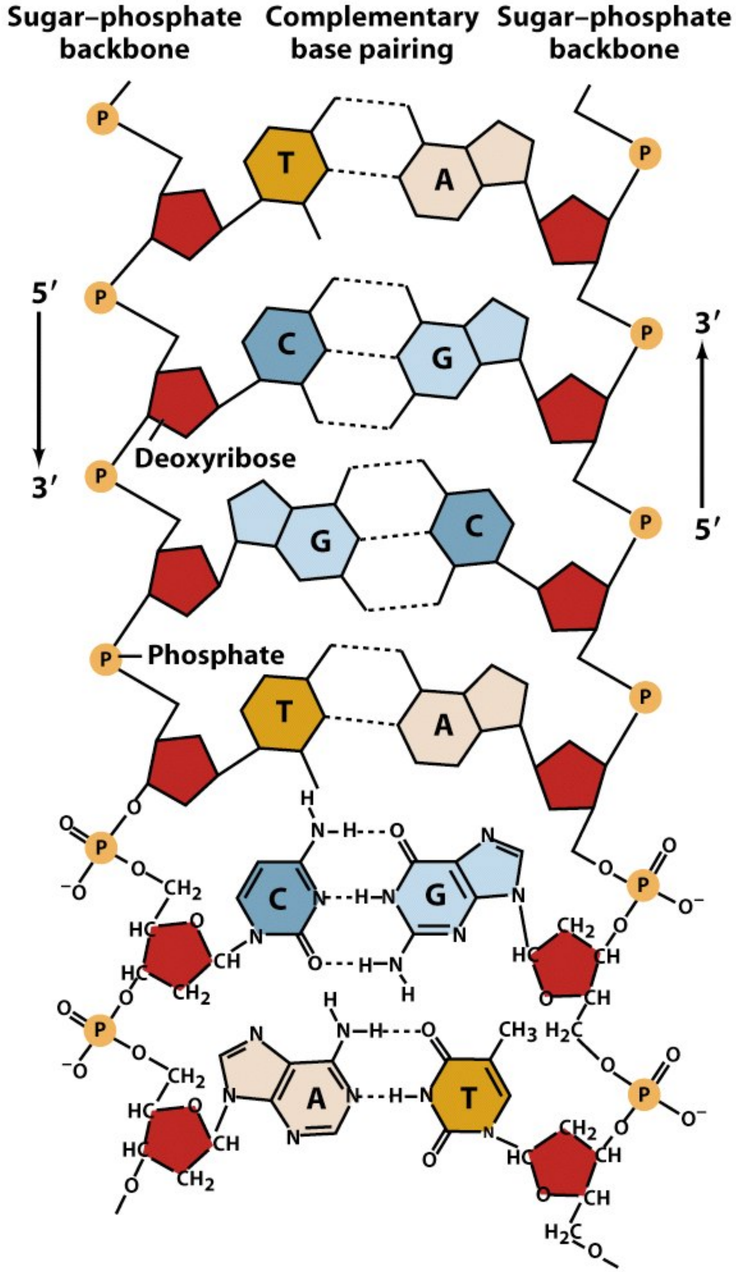




Figure 3-8 Fundamentals of Biochemistry, 2/e

Chromosome
Genome
Gene
Diploid
Haploid
Base pairs (bp)
Kilobase pairs (kb)

**Table 3-3 Some Sequenced Genomes**

| Organism | Genome Size (kb) | Number of Chromosomes |
|---|---|---|
| *Mycoplasma genitalium* (human parasite) | 580 | 1 |
| *Rickettsia prowazekii* (putative relative of mitochondria) | 1,112 | 1 |
| *Methanococcus jannaschii* (thermophilic methanogen) | 1,665 | 1 |
| *Haemophilus influenzae* (human pathogen) | 1,830 | 1 |
| *Synechocystis* sp. (cyanobacterium) | 3,573 | 1 |
| *Escherichia coli* (human symbiont) | 4,639 | 1 |
| *Saccharomyces cerevisiae* (baker's yeast) | 11,700 | 16 |
| *Plasmodium falciparum* (protozoan that causes malaria) | 30,000 | 14 |
| *Caenorhabditis elegans* (nematode) | 97,000 | 6 |
| *Arabidopsis thaliana* (dicotyledonous plant) | 117,000 | 5 |
| *Drosophila melanogaster* (fruit fly) | 137,000 | 4 |
| *Danio rerio* (zebrafish) | 1,700,000 | 25 |
| *Homo sapiens* | 3,200,000 | 23 |

**Table 3-3 Fundamentals of Biochemistry, 2/e**


http://www.ncbi.nlm.nih.gov/Genomes/

# RNA: single stranded molecule

double stranded RNA is possible (p824)

intramolecular base-pairing: 3D structure

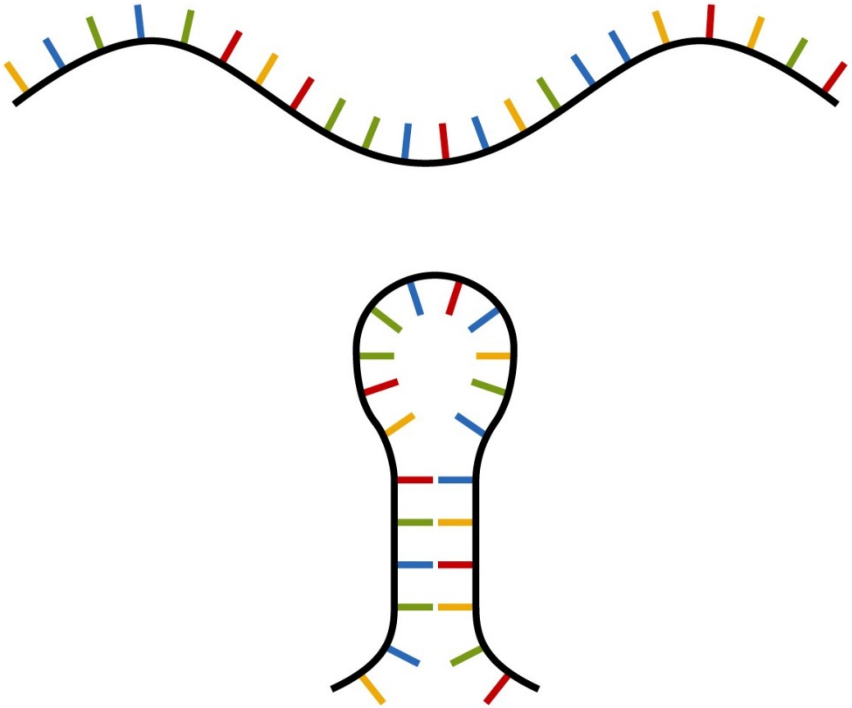


Figure 3-9 Fundamentals of Biochemistry, 2/e

## Structure of yeat $tRNA^{phe}$

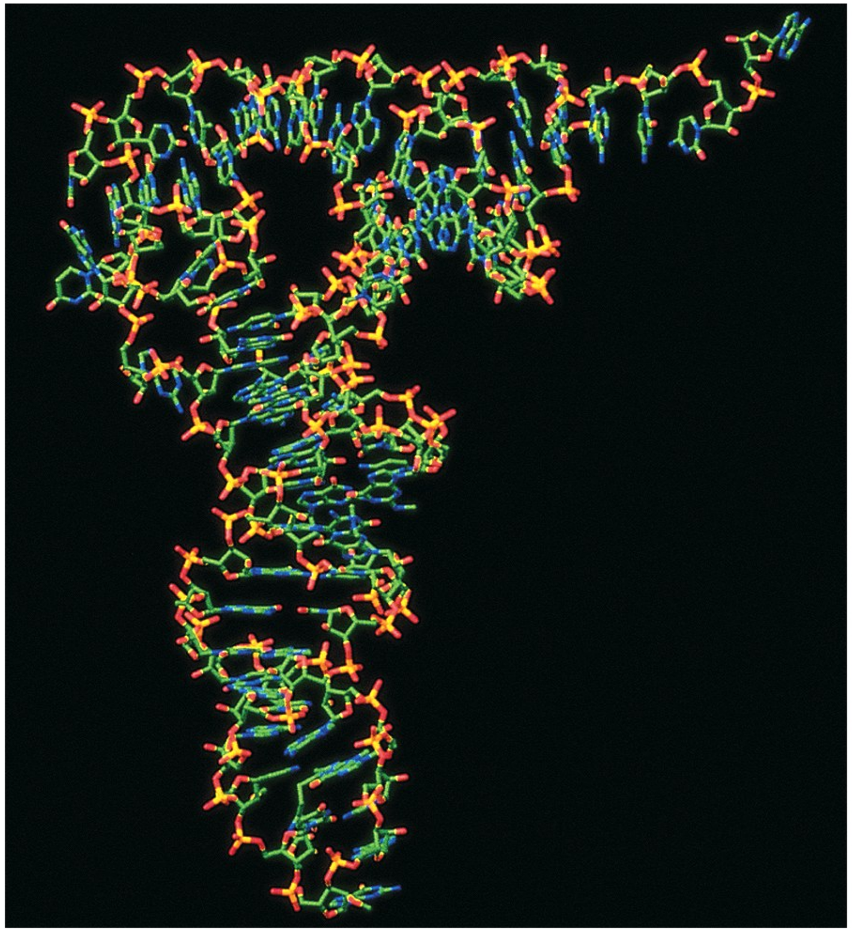


Figure 23-26 Fundamentals of Biochemistry, 2/e

## RNA-DNA hybrid

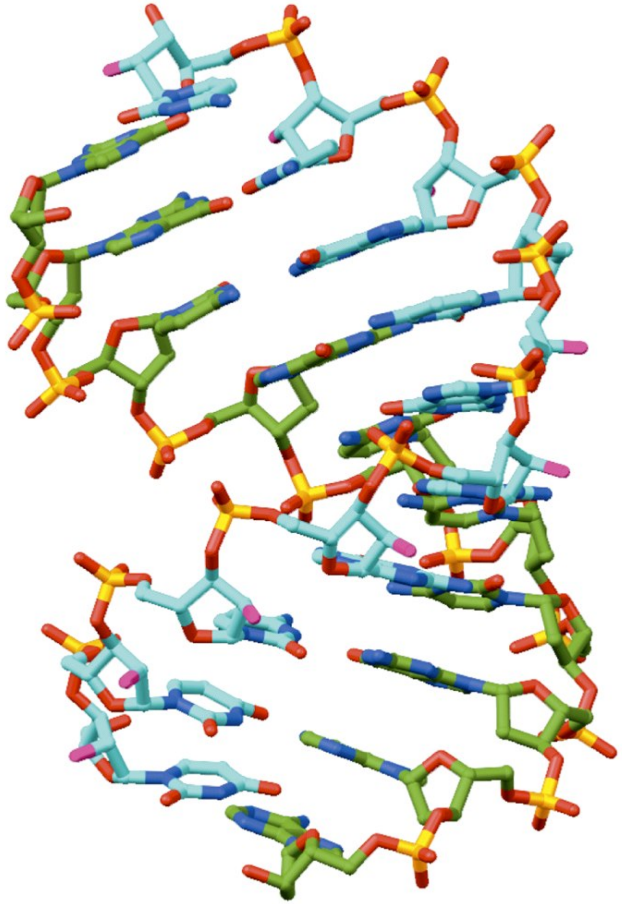


Figure 23-4 Fundamentals of Biochemistry, 2/e

Some RNAs are catalysts: ribozymes

Self cleavage at the scissile bond

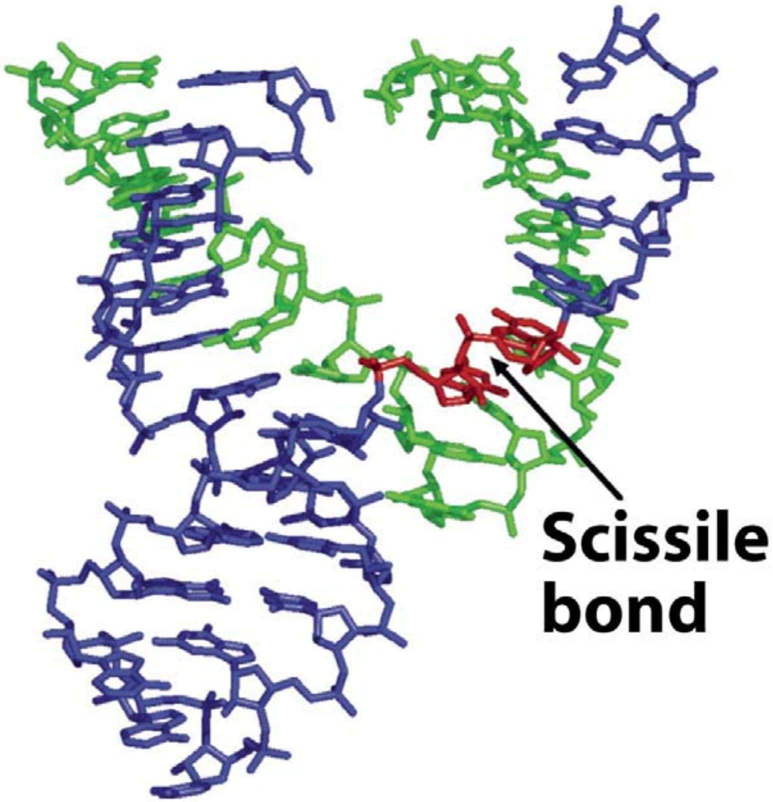
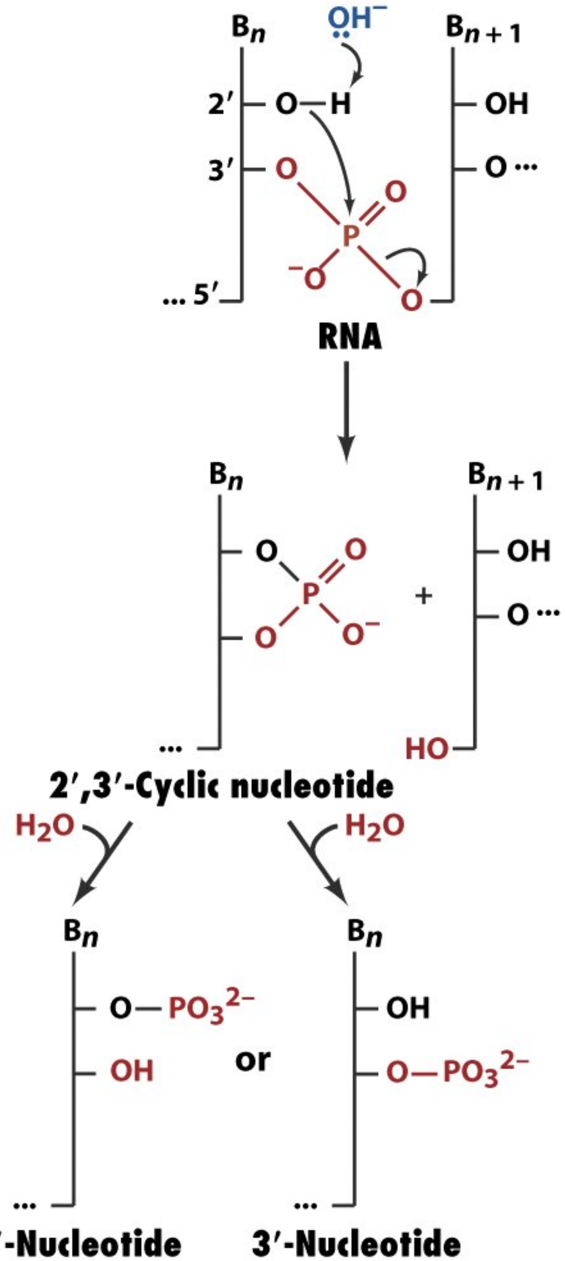



Figure 23-27b Fundamentals of Biochemistry, 2/e

RNA is alkali unstable
DNA is acid unstable




Box 23-3 Fundamentals of Biochemistry, 2/e

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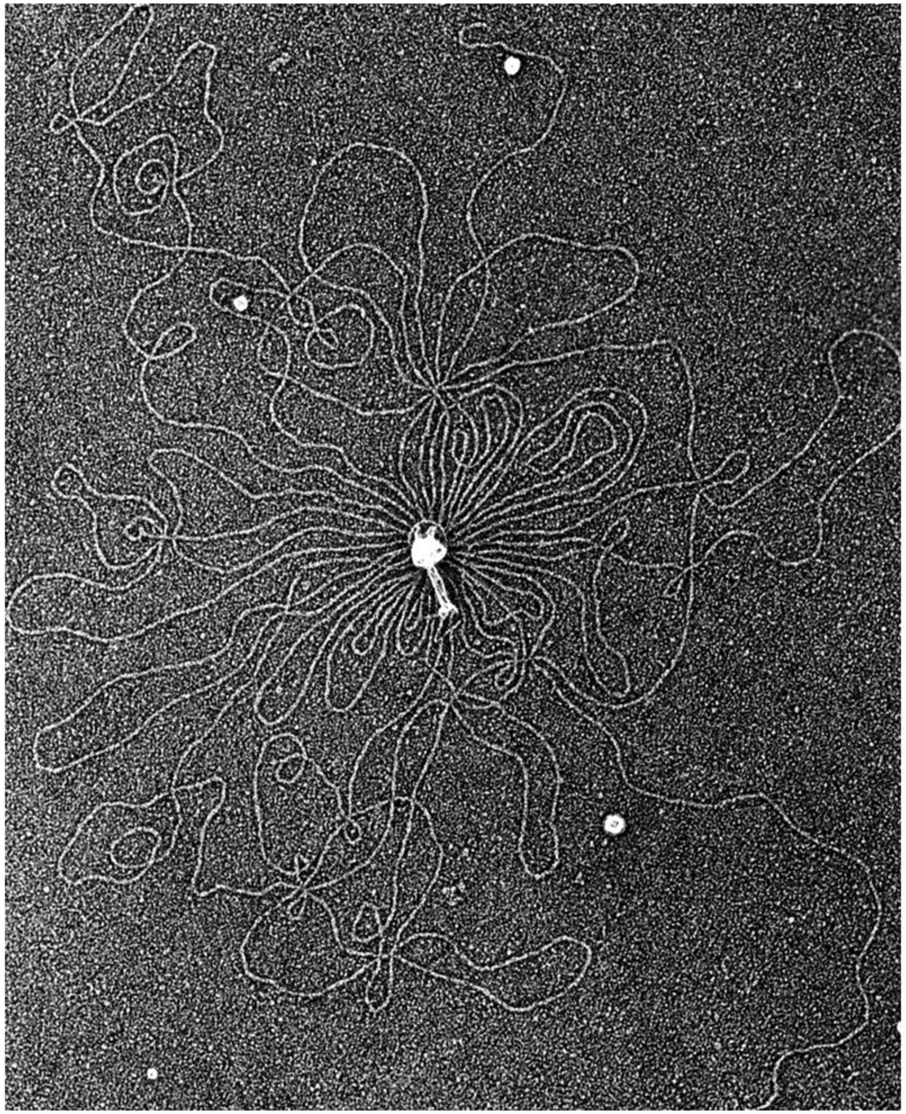
# Fundamentals of Biochemistry

## Second Edition

# Chapter 23:

## Nucleic Acid Structure

Osmotically lysed bacteriophage T2



Chapter 23 Opener Fundamentals of Biochemistry, 2/e

In ideal B DNA

Near perfect two fold symmetry
10 bp per turn
Base planes
perpendicular to the axis
3.4Å van der Waals thickness

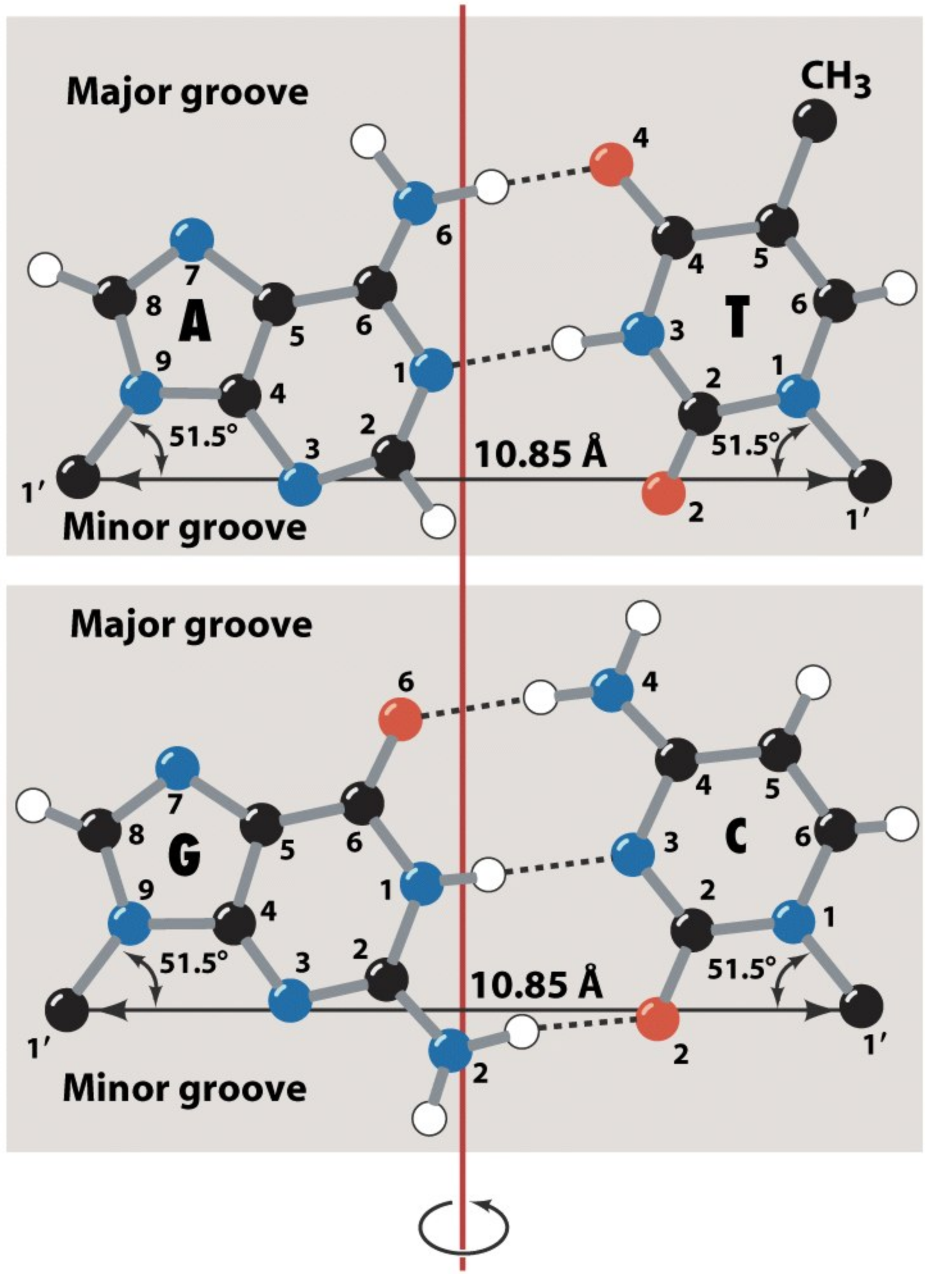



Figure 23-1 Fundamentals of Biochemistry, 2/e

# Several distinct structures

depending on the solvent composition and base sequences

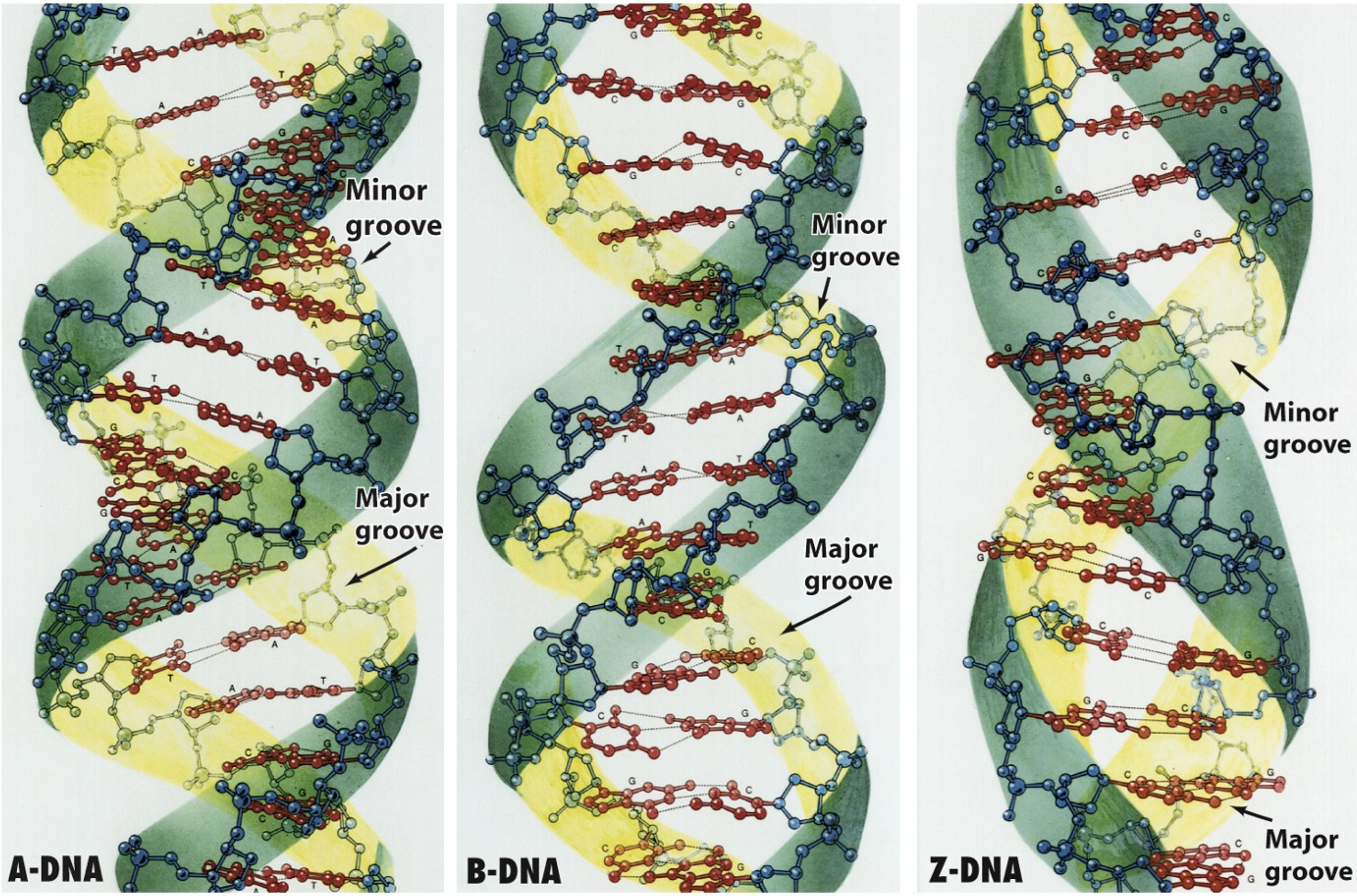
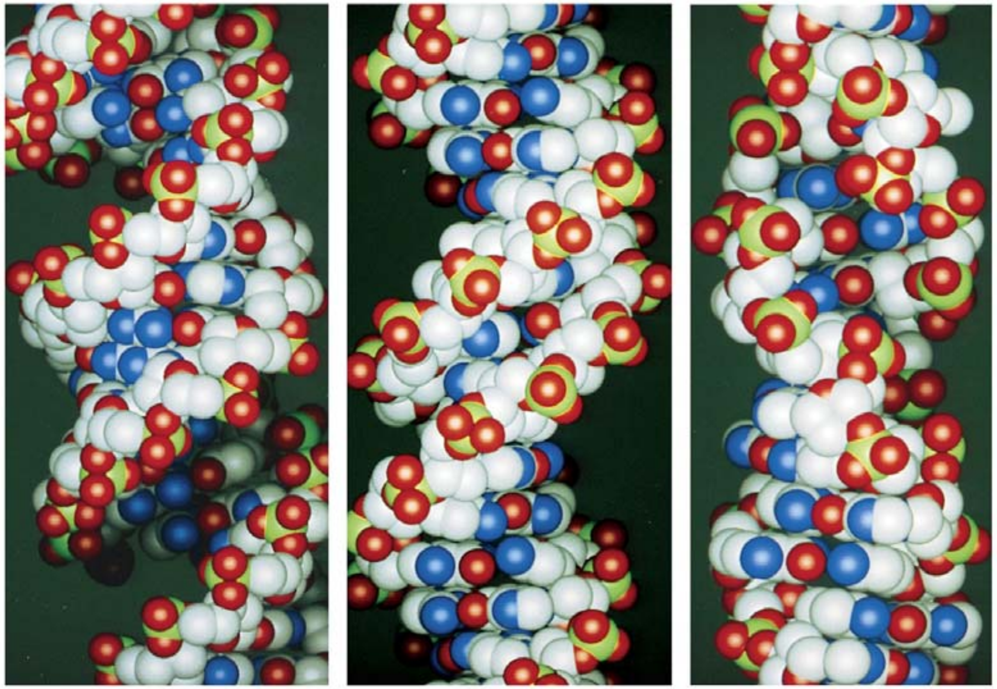



Figure 23-2a Fundamentals of Biochemistry, 2/e

Under dehydrating condition



d(CGCGCG)
Left handed
Z-DNA binding protein

A-DNA B-DNA Z-DNA

Figure 23-2b Fundamentals of Biochemistry, 2/e

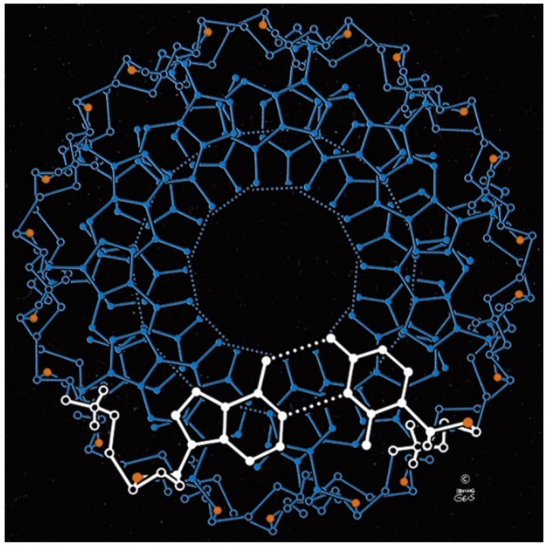


Figure 23-2c part 1 Fundamentals of Biochemistry, 2/e

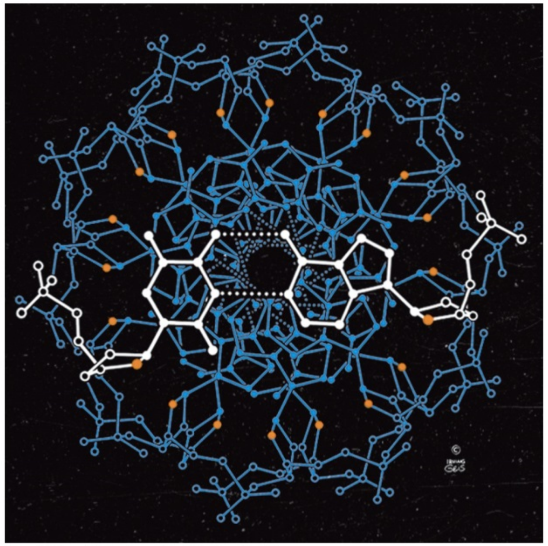


Figure 23-2c part 2 Fundamentals of Biochemistry, 2/e

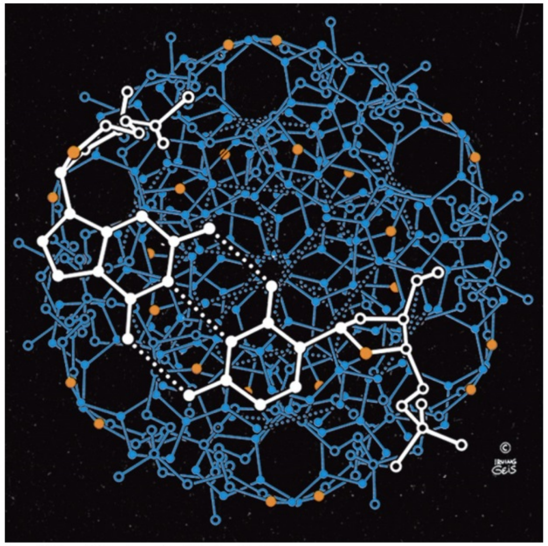


Figure 23-2c part 3 Fundamentals of Biochemistry, 2/e

**Table 23-1** ***Key to Structure.*** **Structural Features of Ideal A-, B-, and Z-DNA**

| | A | B | Z |
|---|---|---|---|
| Helical sense | Right handed | Right handed | Left handed |
| Diameter | ~26 Å | ~20 Å | ~18 Å |
| Base pairs per helical turn | 11.6 | 10 | 12 (6 dimers) |
| Helical twist per base pair | 31° | 36° | 60° (per dimer) |
| Helix pitch (rise per turn) | 34 Å | 34 Å | 44 Å |
| Helix rise per base pair | 2.9 Å | 3.4 Å | 7.4 Å per dimer |
| Base tilt normal to the helix axis | 20° | 6° | 7° |
| Major groove | Narrow and deep | Wide and deep | Flat |
| Minor groove | Wide and shallow | Narrow and deep | Narrow and deep |
| Sugar pucker | C3′-*endo* | C2′-*endo* | C2′-*endo* for pyrimidines; C3′-*endo* for purines |
| Glycosidic bond conformation | Anti | Anti | Anti for pyrimidines; syn for purines |

**Table 23-1 Fundamentals of Biochemistry, 2/e**

# Flexibility of DNA

Each base pair deviates from ideal conformation depending on sequences
Flexible rod, not rigid
More severe distortions by protein binding

However, limited conformational flexibility

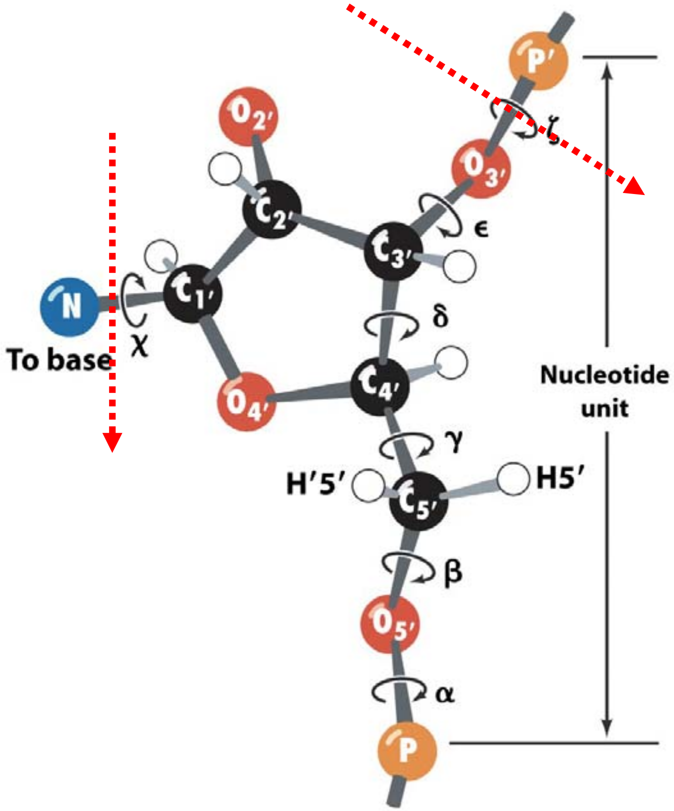



Figure 23-5 Fundamentals of Biochemistry, 2/e


7 torsion angles determining
the conformation of a nucleotide unit

# Glycosidic bond rotation is not free

Purine has two permissible orientations: syn and anti
Pyrimidine is stable with anti-conformation
All bases are in anti in most double helix

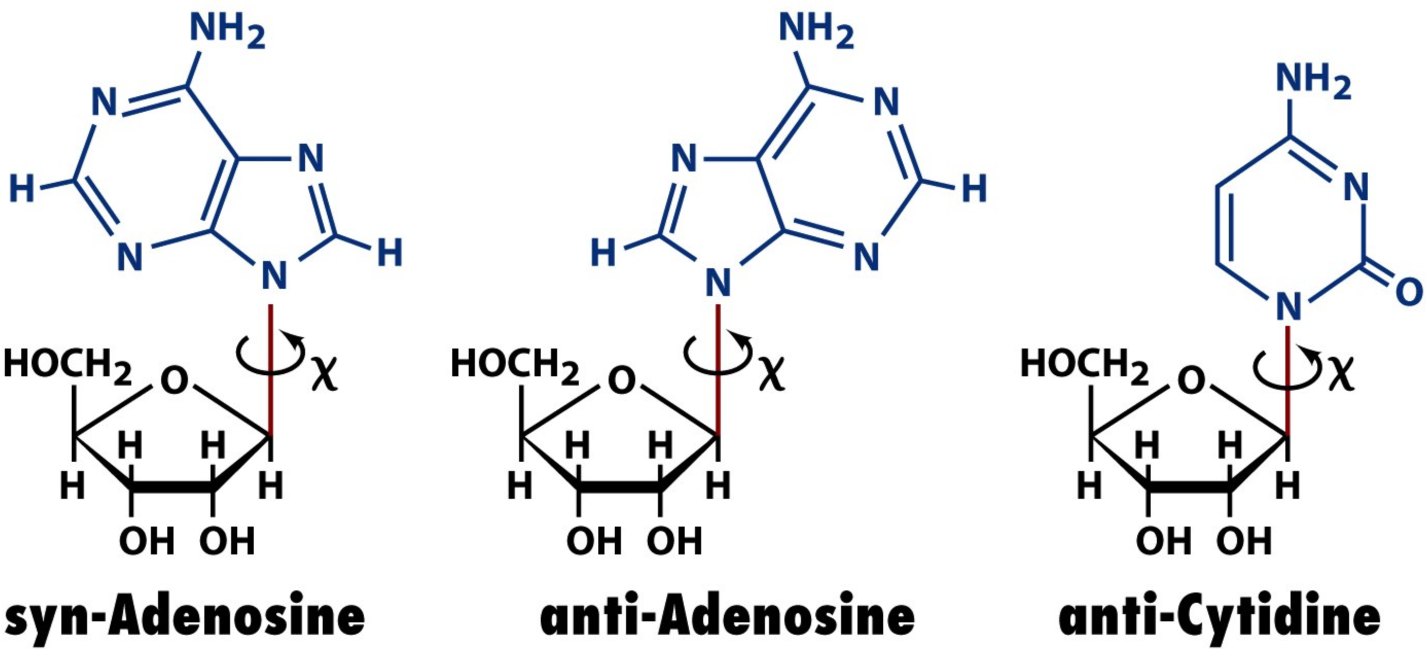
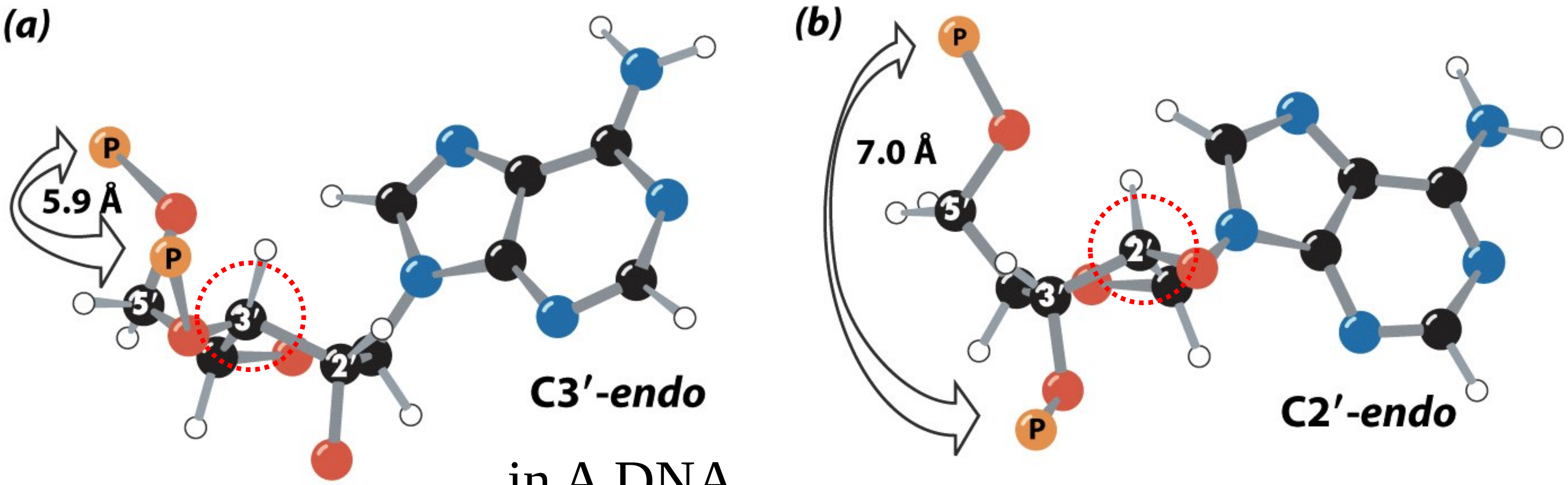



Figure 23-6 Fundamentals of Biochemistry, 2/e

# Ribose ring flexibility

Ribose ring is not planar
Out of plane atoms: C2’ and C3’
C3’-endo, C2’-endo: on the same side of C5’




in A DNA

Figure 23-7 Fundamentals of Biochemistry, 2/e


in B DNA

Sugar-phosphate backbone is constrained

# Supercoiled DNA

No supercoiling → tightly supercoiled

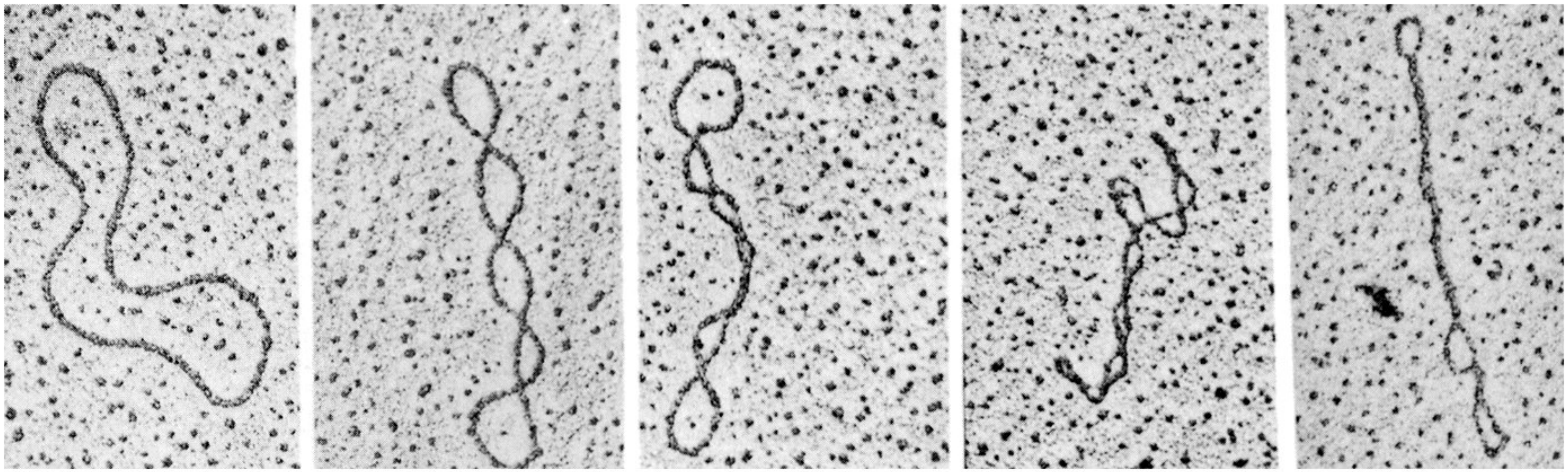


Figure 23-8 Fundamentals of Biochemistry, 2/e

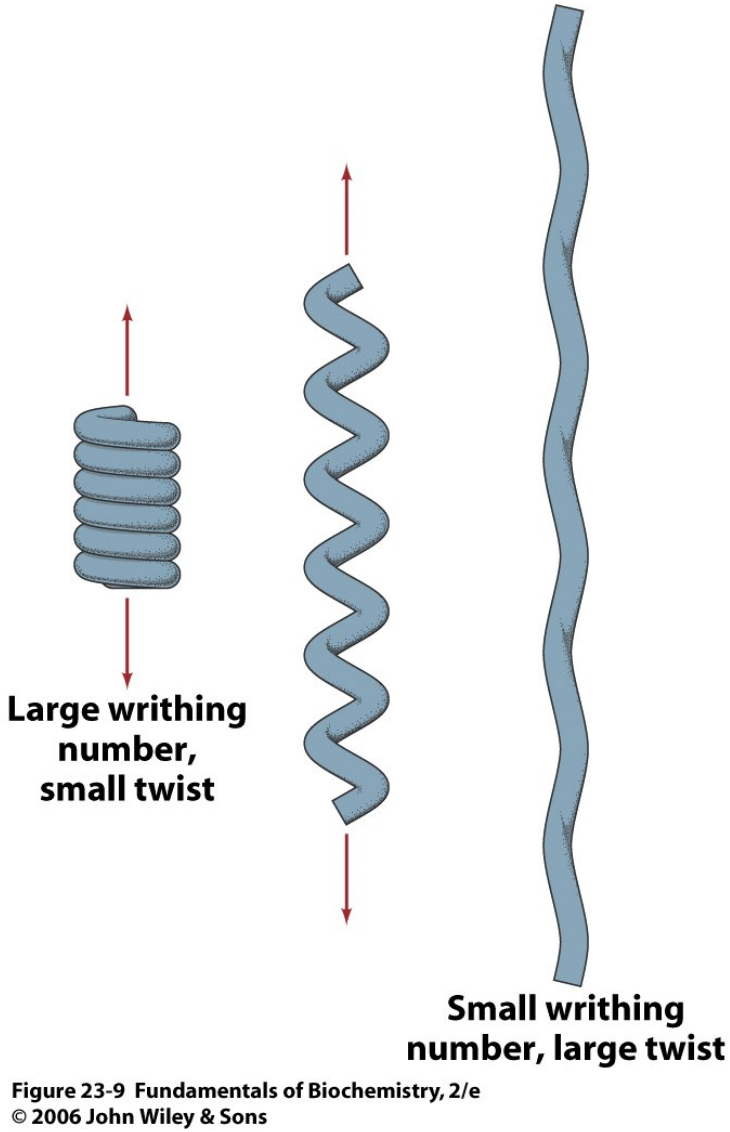
EM of supercoiled DNAs

Supercoiling and superhelicity

Superhelix topology

L = T + W

Linking number
Twist
Writhing number




The difference between writhing and twist

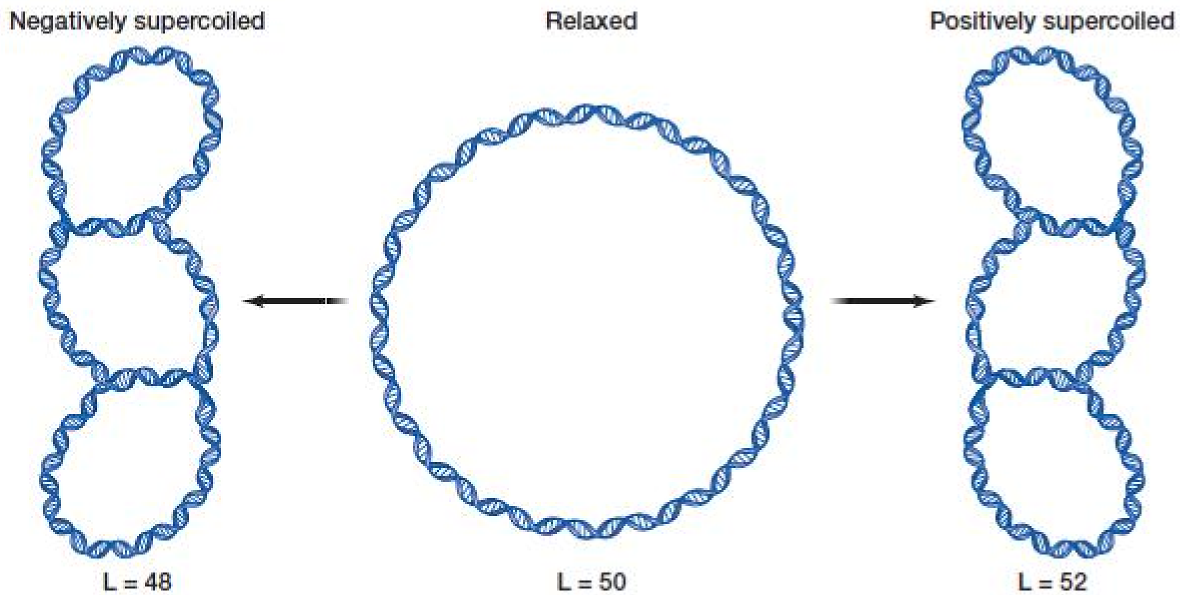



**figure 9.24** Positive and negative supercoils. Enzymes called topoisomerases can take relaxed DNA (center) and add negative (left-handed) or positive (right-handed) supercoils. L is the linkage number.

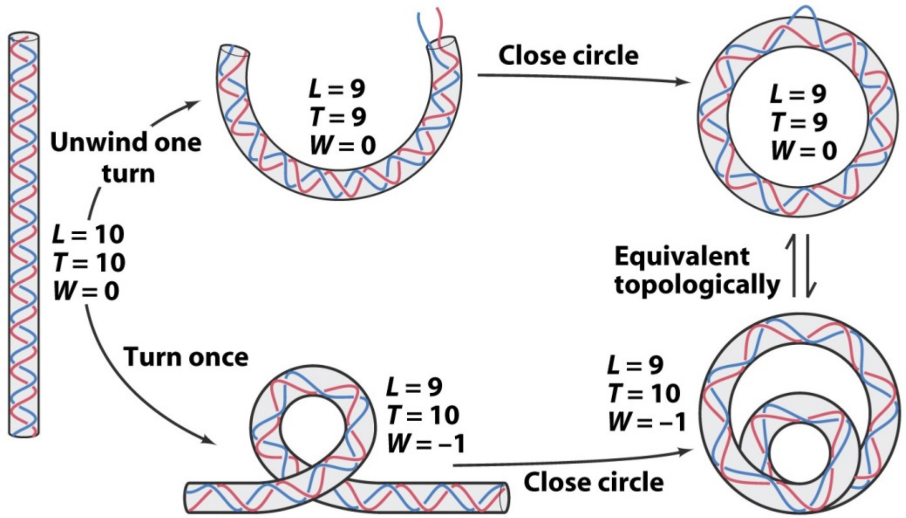



Figure 23-10 Fundamentals of Biochemistry, 2/e

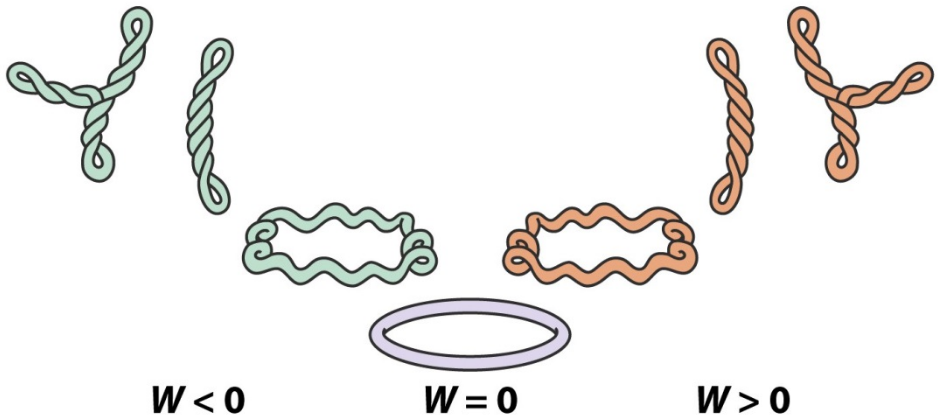




Figure 23-11 Fundamentals of Biochemistry, 2/e

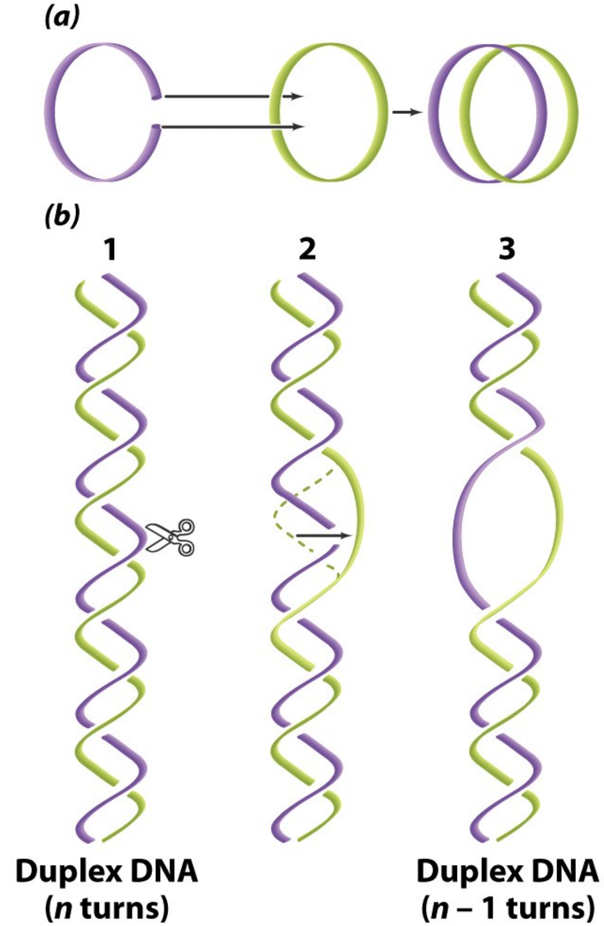




Figure 23-12 Fundamentals of Biochemistry, 2/e

Forces stabilizing nucleic acid structures

Denaturation and renaturation

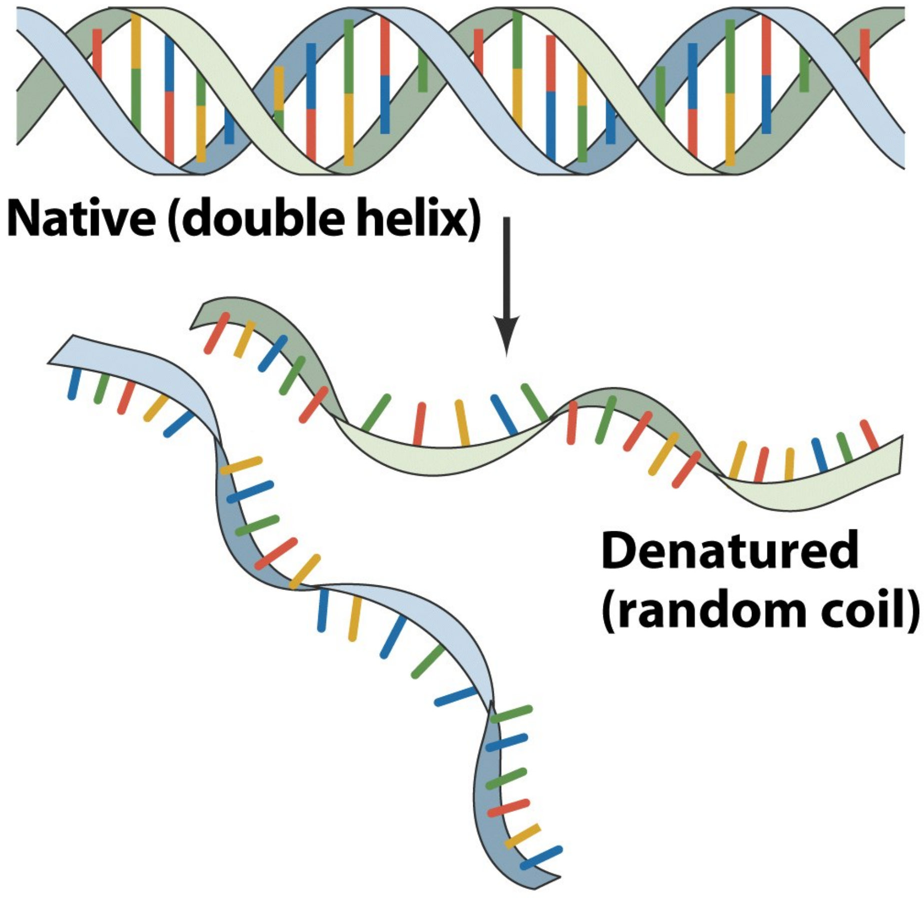



Figure 23-19 Fundamentals of Biochemistry, 2/e

# Hyperchromatic effect

UV absorption increases ~40% upon denaturation

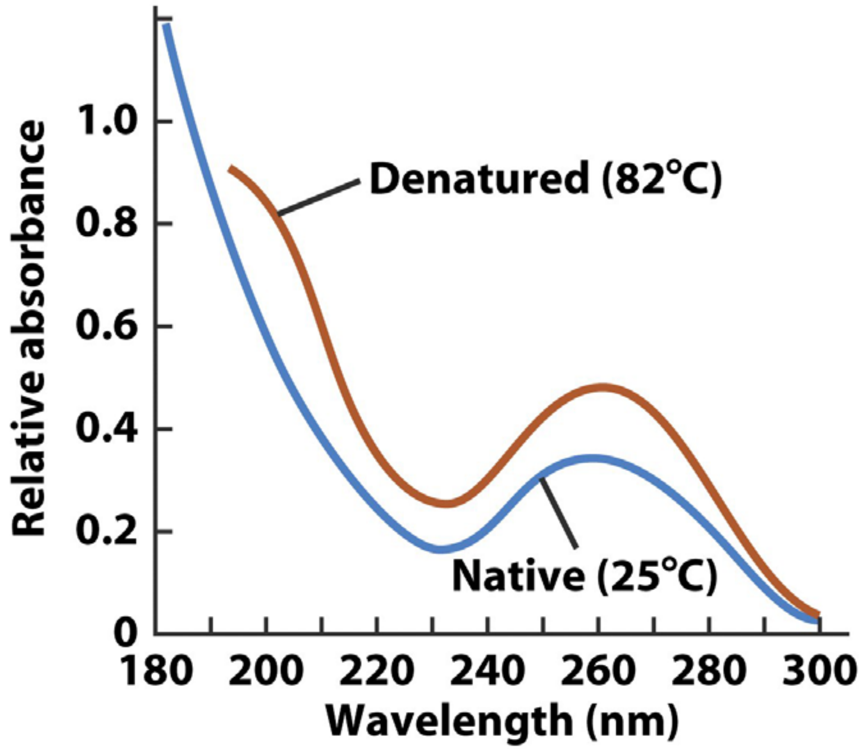



Figure 23-20 Fundamentals of Biochemistry, 2/e

# denaturation & renaturation

incomplete renaturation

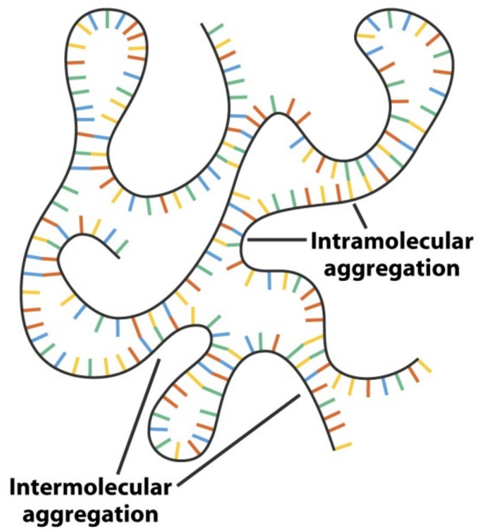



Figure 23-22 Fundamentals of Biochemistry, 2/e


Melting curve of DNA: Tm depends on GC ratio

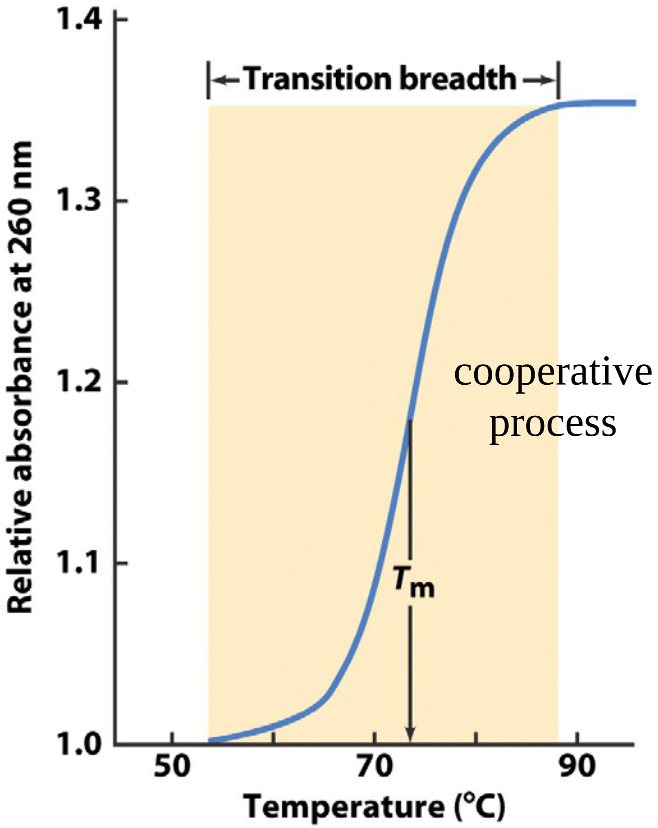



Figure 23-21 Fundamentals of Biochemistry, 2/e


rapid cooling

slow cooling

Complete renaturation

The principle of denaturation and renaturation is important for DNA manipulation

Polymerase Chain Reaction (PCR)

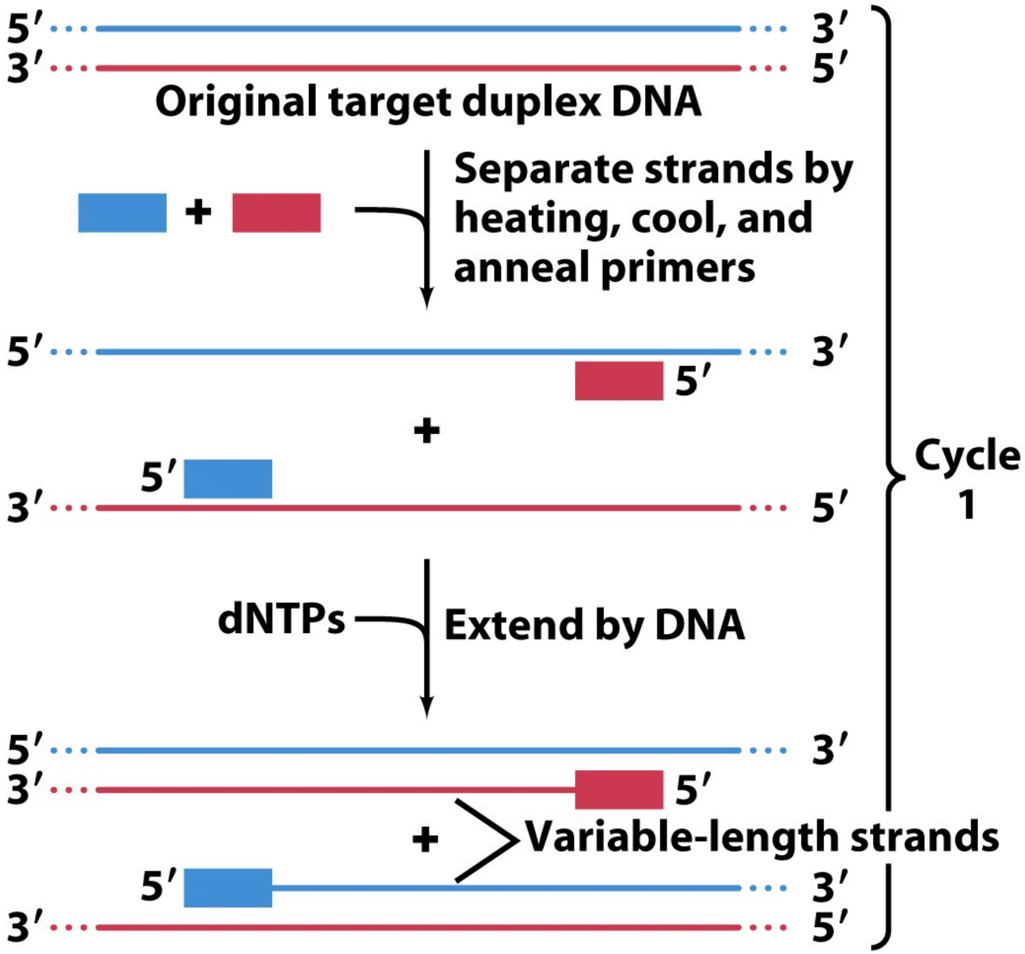



Figure 3-30 part 1 Fundamentals of Biochemistry, 2/e

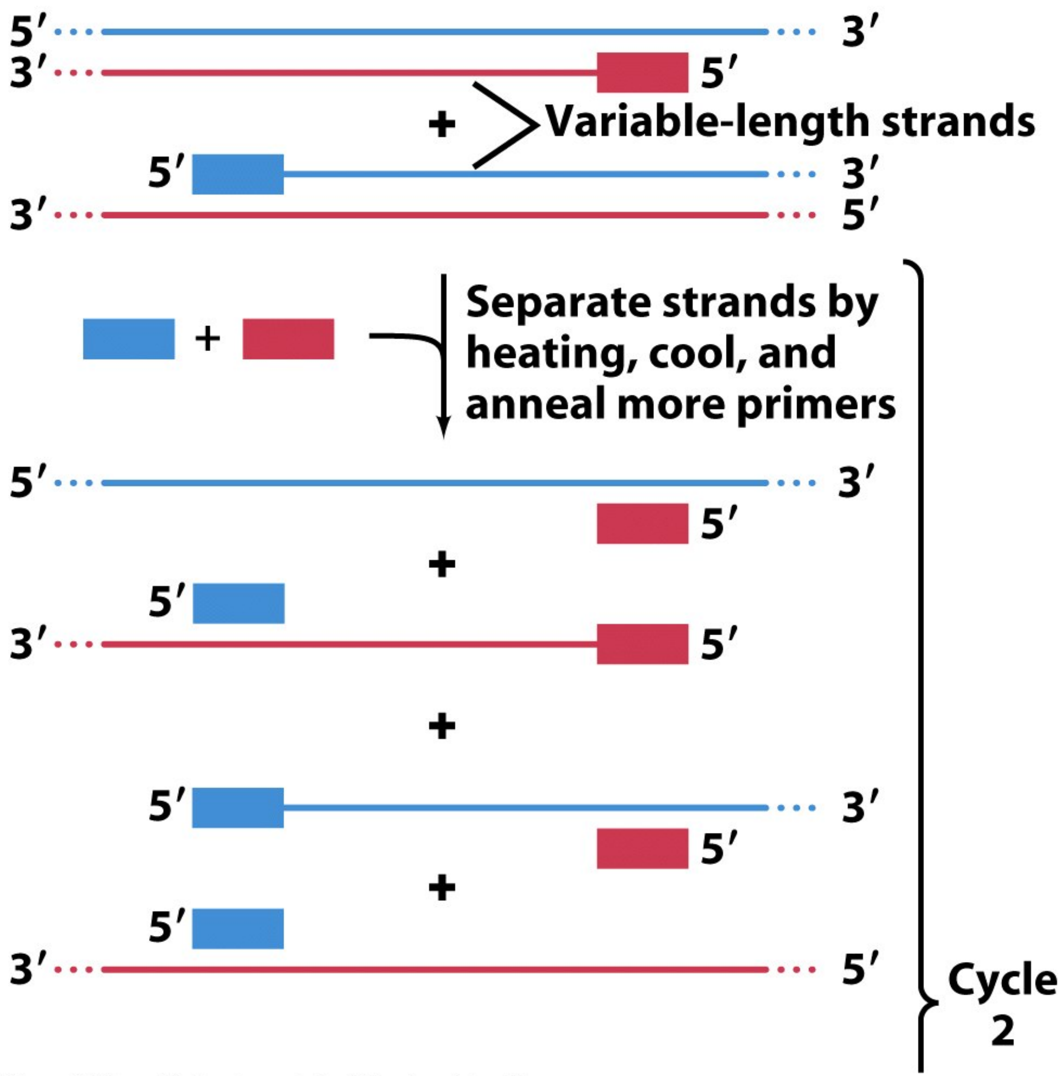



Figure 3-30 part 2 Fundamentals of Biochemistry, 2/e

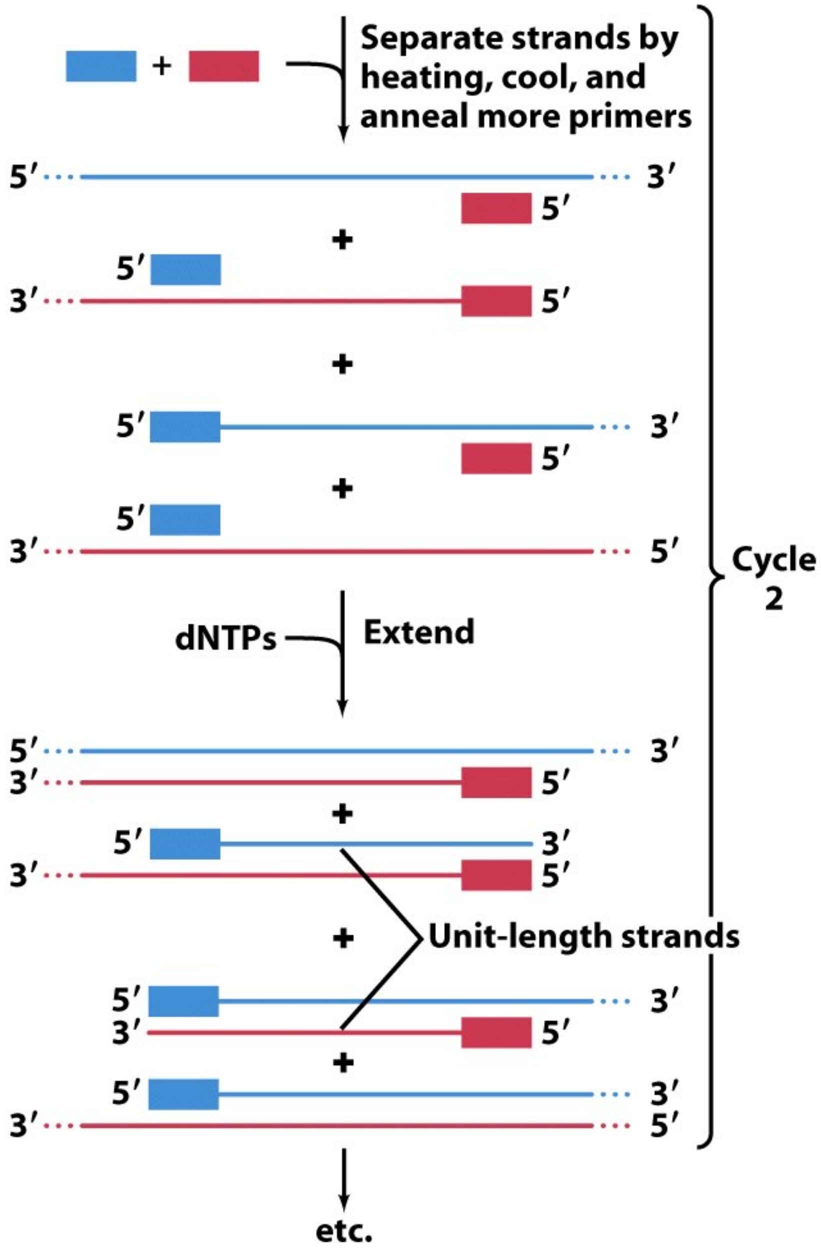



Figure 3-30 part 3  Fundamentals of Biochemistry, 2/e

# Forces stabilizing nucleic acid structures

Base pairing: essential but not enough for helix stability
Base stacking: resulting from hydrophobic interactions
Ionic interactions: melting temp depends on salt conc.

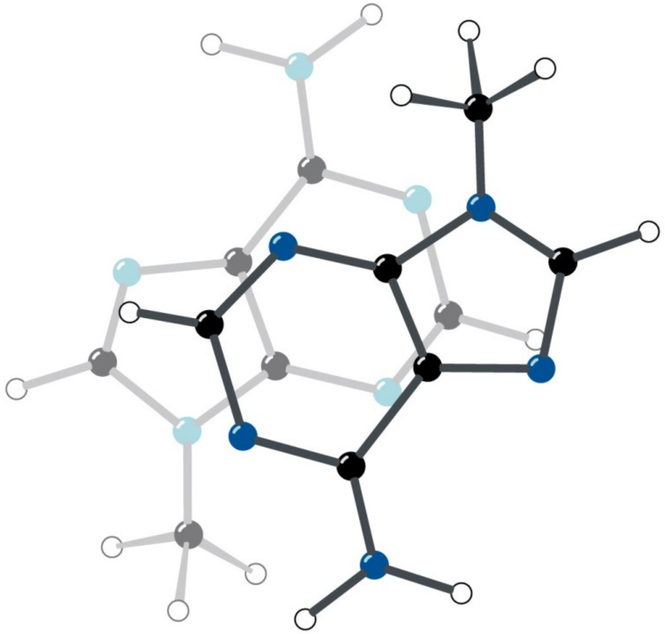


Figure 23-24 Fundamentals of Biochemistry, 2/e


**Table 23-2 Stacking Energies for the Ten Possible Dimers in B-DNA**

| Stacked Dimer | Stacking Energy ($kJ \cdot mol^{-1}$) |
|---|---|
| C·G<br>G·C | −61.0 |
| C·G<br>A·T | −44.0 |
| C·G<br>T·A | −41.0 |
| G·C<br>C·G | −40.5 |
| G·C<br>G·C | −34.6 |
| G·C<br>A·T | −28.4 |
| T·A<br>A·T | −27.5 |
| G·C<br>T·A | −27.5 |
| A·T<br>A·T | −22.5 |
| A·T<br>T·A | −16.0 |

*Source:* Ornstein, R.L., Rein, R., Breen, D.L., and MacElroy, R.D., *Biopolymers* **17,** 2356 (1978).

Table 23-2 Fundamentals of Biochemistry, 2/e

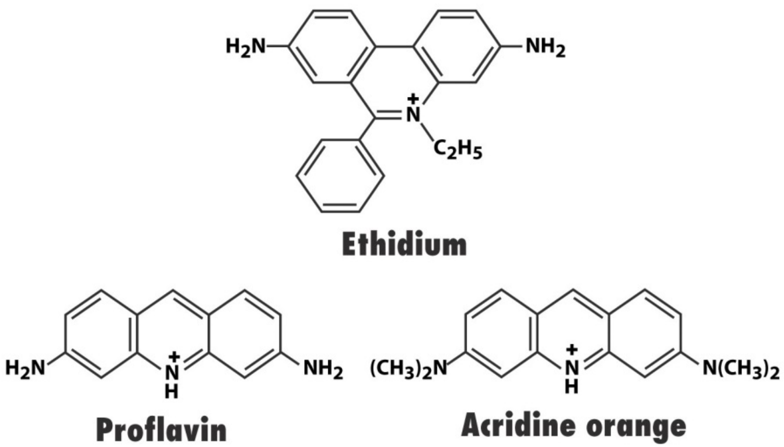
# Ionic interactions

Charged phosphate groups
Monovalent cations
Divalent cations: specific binding to phosphate groups

# Fractionation of nucleic acids

Chromatography
Electrophoresis
Ultracentrifugation

Intercalating agents
for DNA staining




Unnumbered figure pg 843 Fundamentals of Biochemistry, 2/e

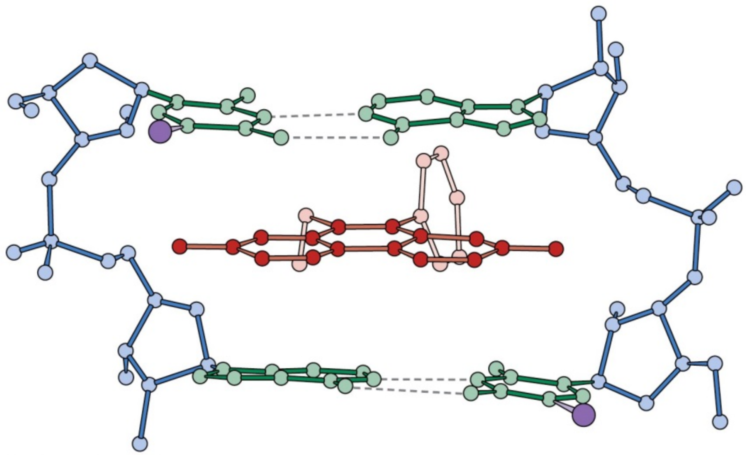



Figure 23-29 Fundamentals of Biochemistry, 2/e

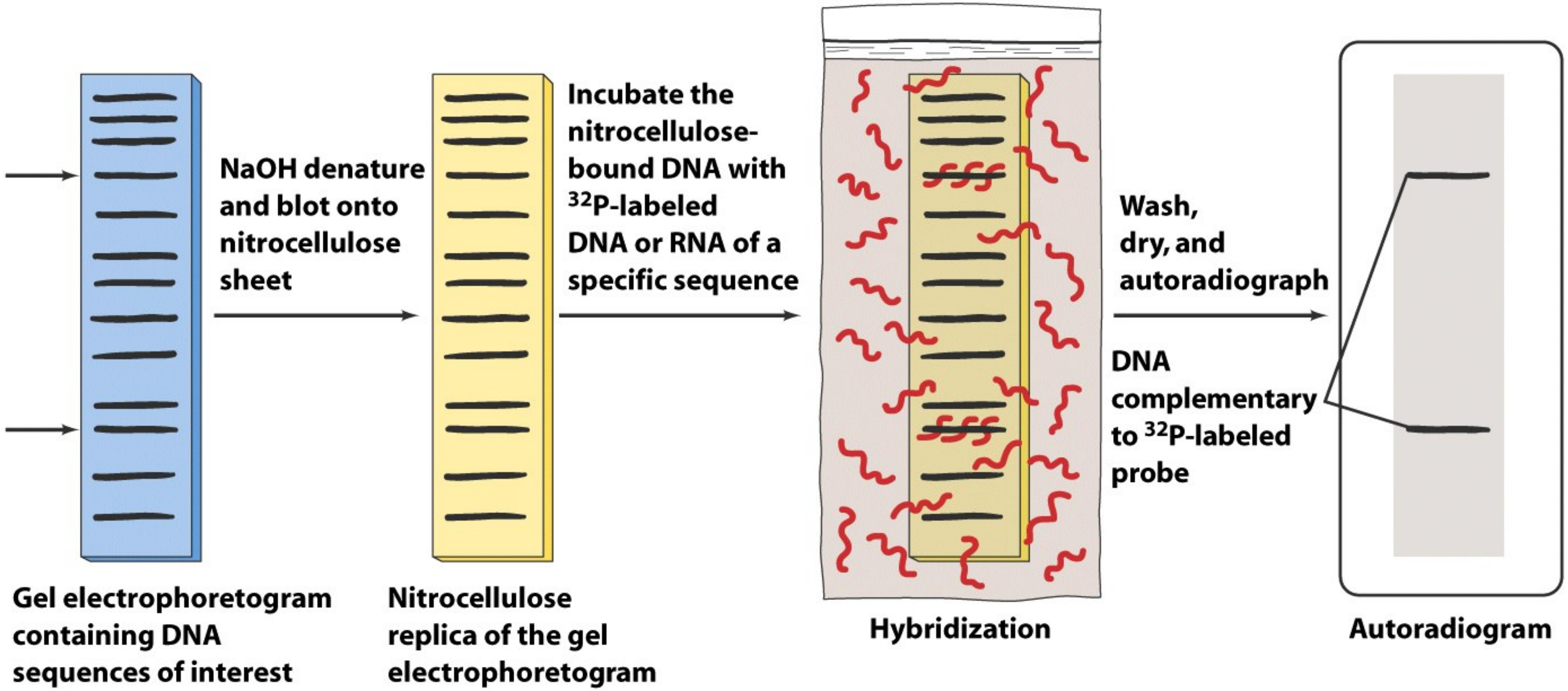



Figure 23-30 Fundamentals of Biochemistry, 2/e

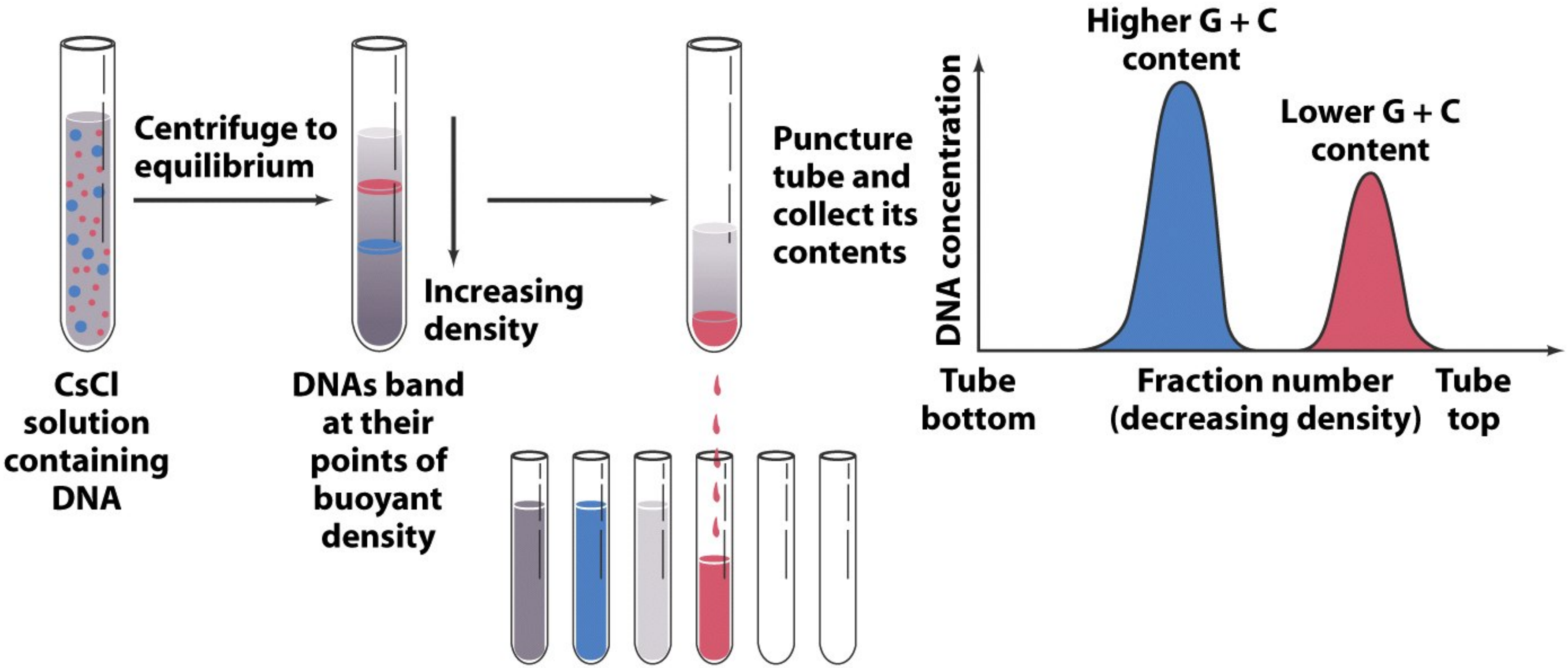



Figure 23-31 Fundamentals of Biochemistry, 2/e

# Eukaryotic chromosome structure

Packaging of chromosomes in a cell
23 human chromosome: 3.2 billion bp x 3.4A = 1 m

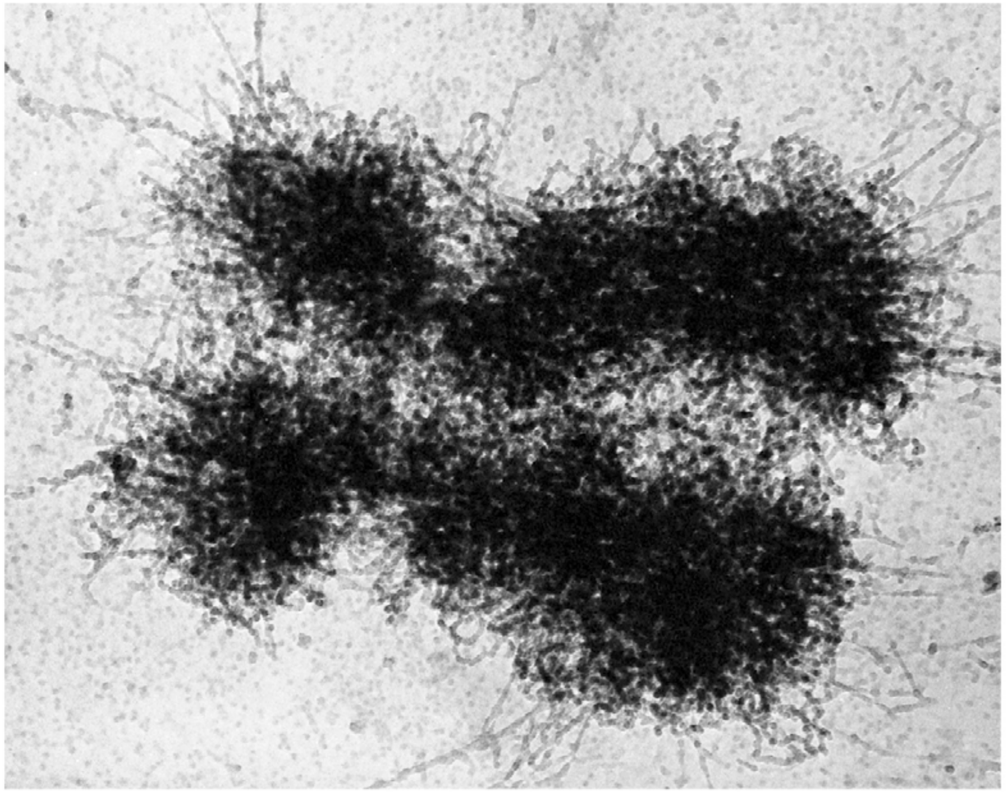


Figure 23-43 Fundamentals of Biochemistry, 2/e

# Nucleosomes: chromatin particles

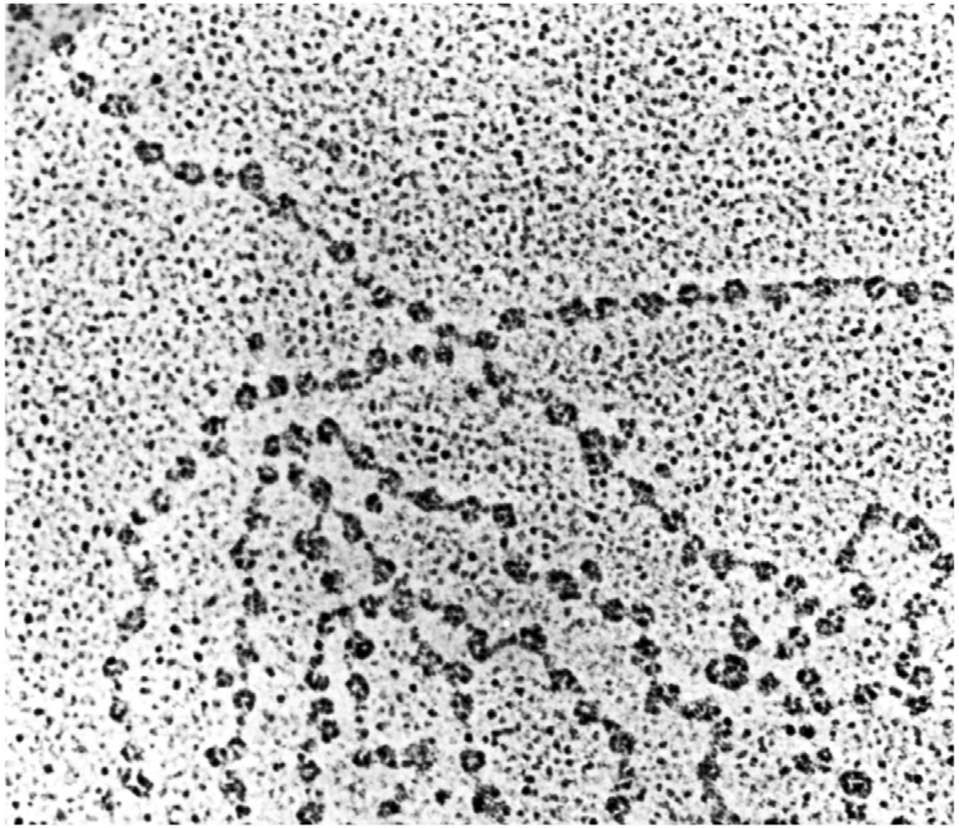


Figure 23-44 Fundamentals of Biochemistry, 2/e

# 166-bp nucleosome: role of H1

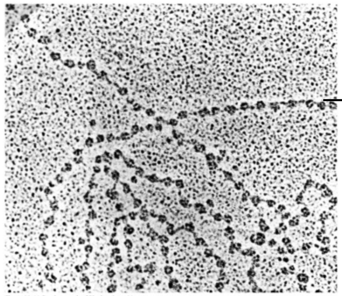


Figure 23-44 Fundamentals of Biochemistry, 2/e

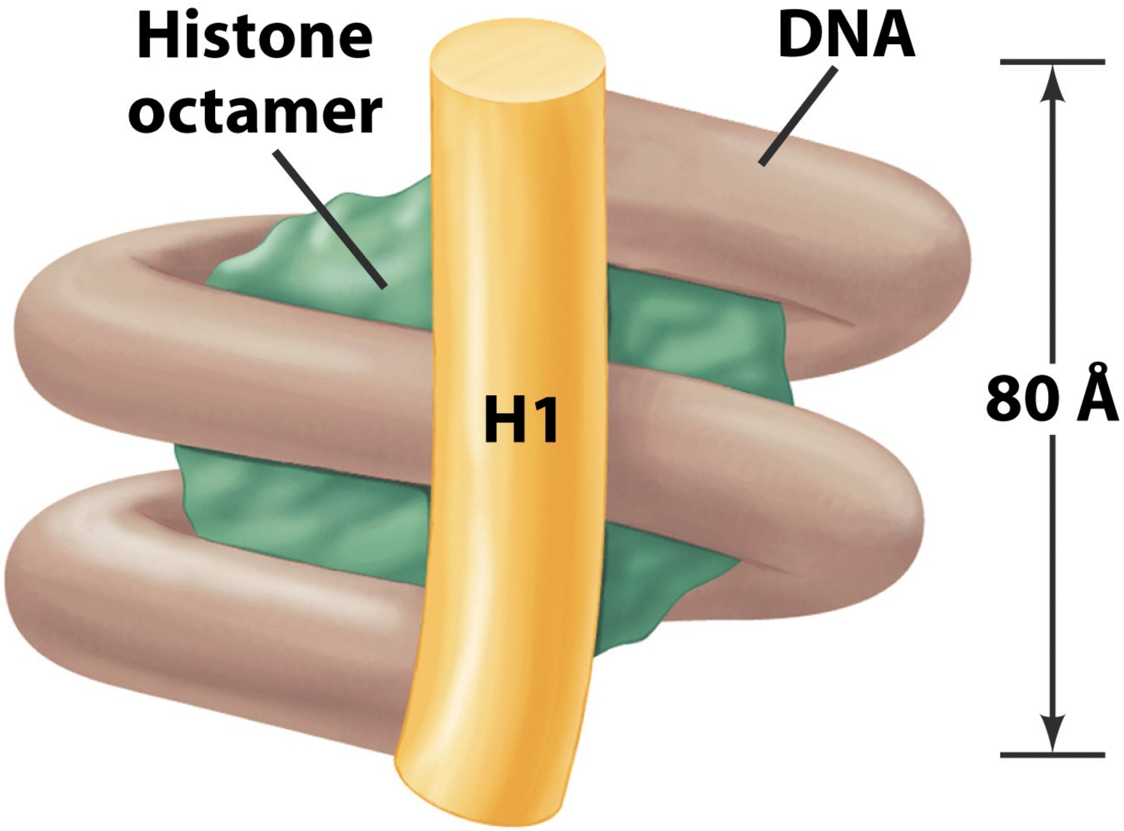



Figure 23-47 Fundamentals of Biochemistry, 2/e

## Table 23-3 Calf Thymus Histones

| Histone | Number of Residues | Mass (kD) | % Arg | % Lys |
|---|---|---|---|---|
| H1 | 215 | 23.0 | 1 | 29 |
| H2A | 129 | 14.0 | 9 | 11 |
| H2B | 125 | 13.8 | 6 | 16 |
| H3 | 135 | 15.3 | 13 | 10 |
| H4 | 102 | 11.3 | 14 | 11 |

Table 23-3 Fundamentals of Biochemistry, 2/e

H1 bound chromatin H1 depleted chromatin

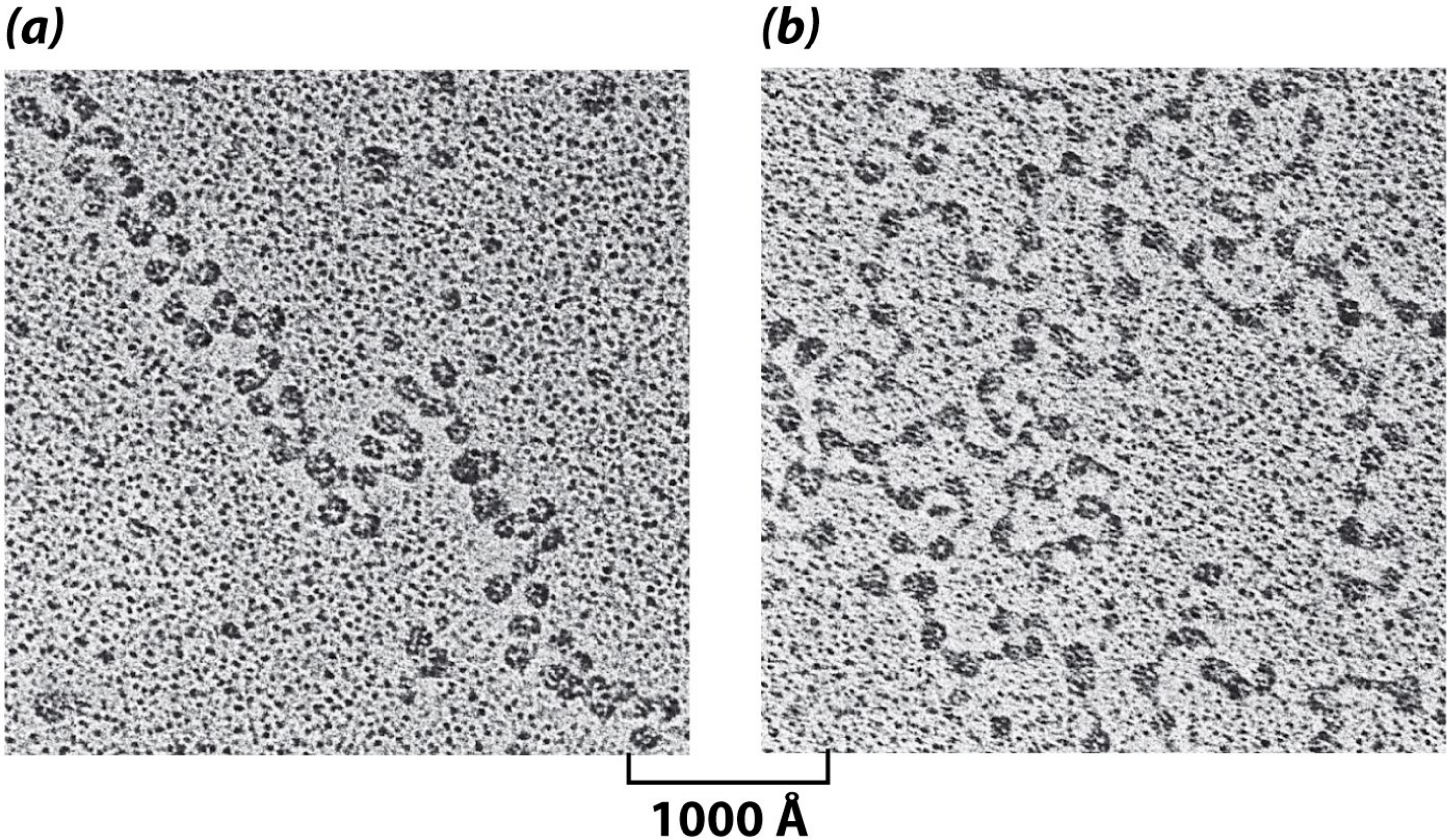



Figure 23-48 Fundamentals of Biochemistry, 2/e

Higher levels of chromatin organization
30 nm diameter chromatin filaments

EM

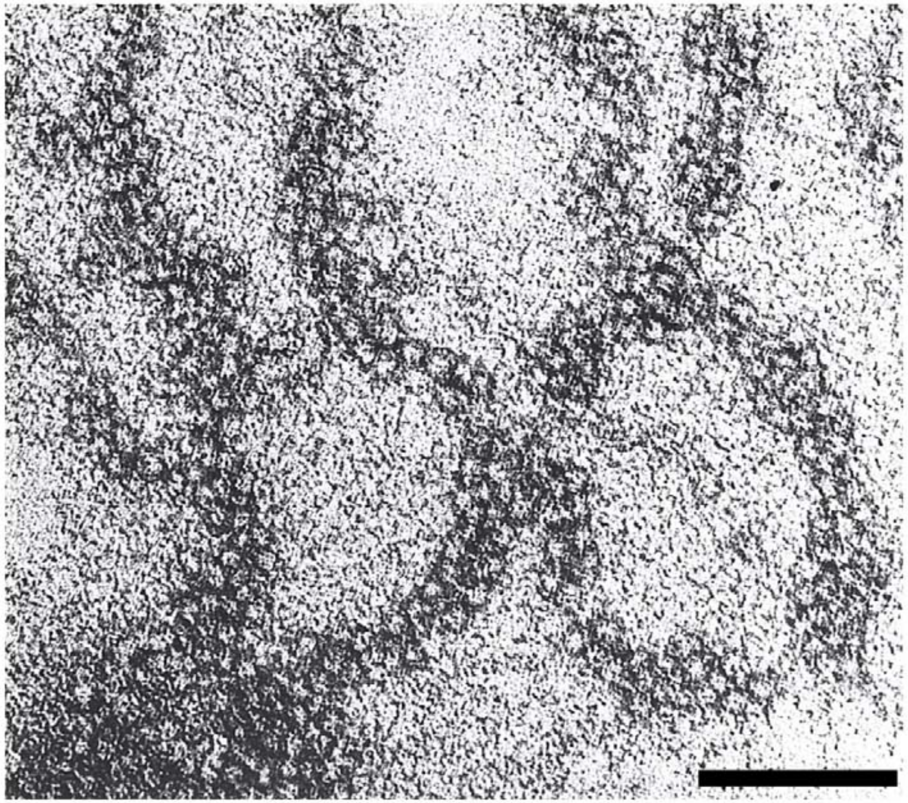


Figure 23-49 Fundamentals of Biochemistry, 2/e

Model building

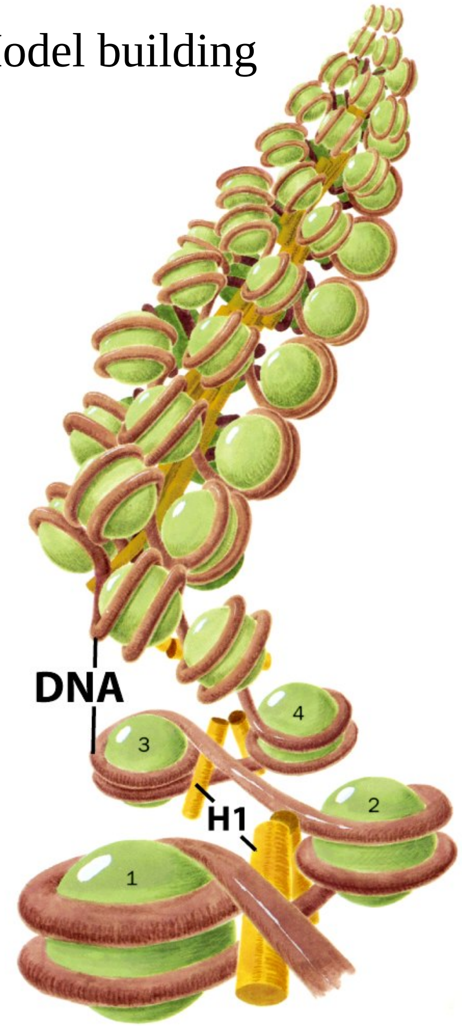



Figure 23-50 Fundamentals of Biochemistry, 2/e

Histone depleted chromosome

Figure 23-51a Fundamentals of Biochemistry, 2/e

Higher magnification

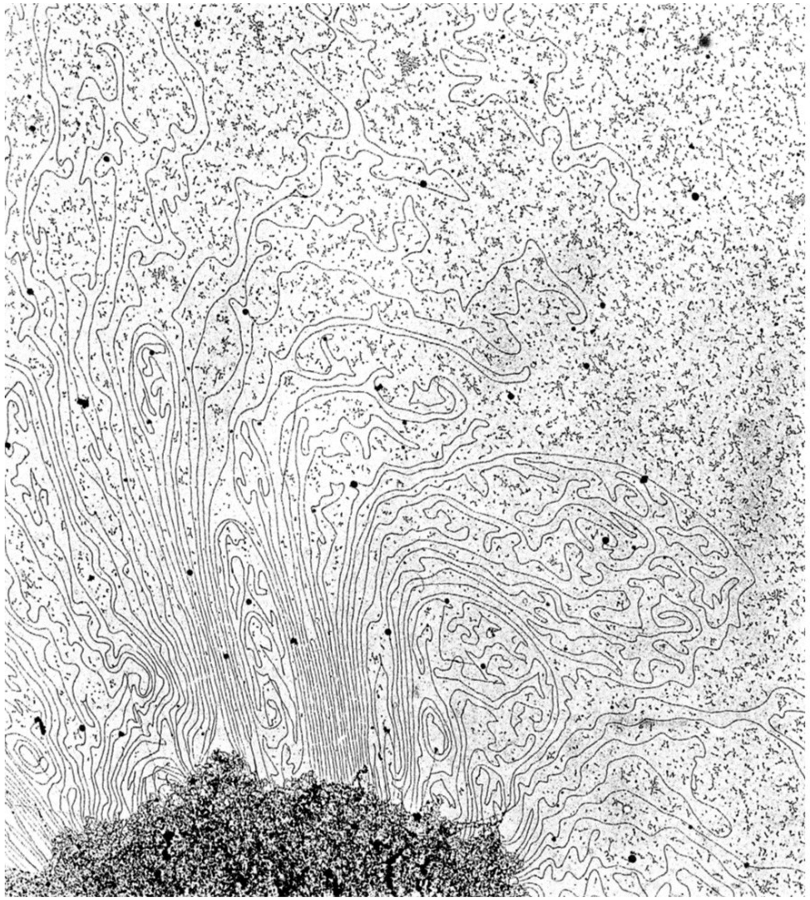


Figure 23-51b Fundamentals of Biochemistry, 2/e

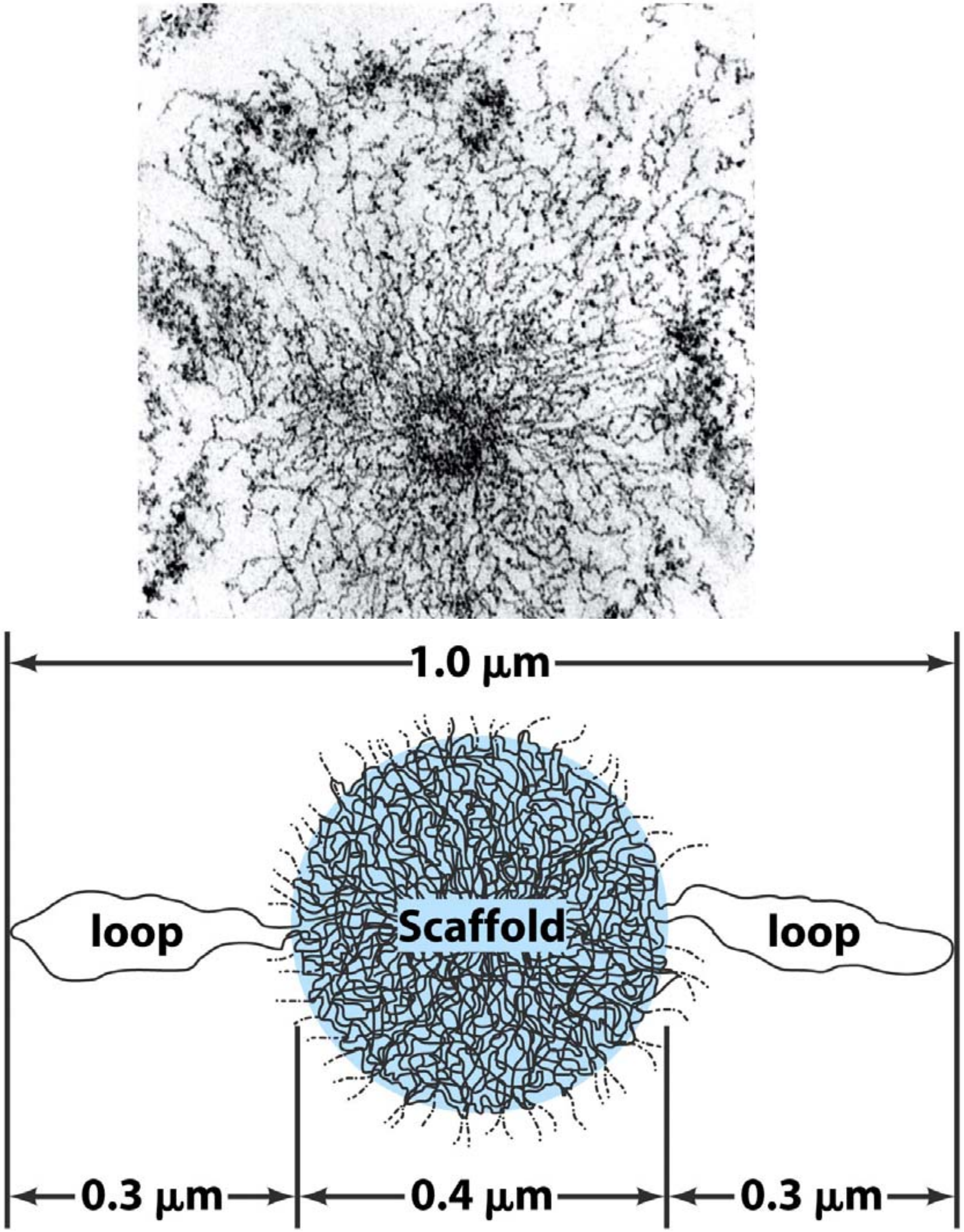



Figure 23-52b Fundamentals of Biochemistry, 2/e