OVERVIEW OF NUCLEIC ACIDS STRUCTURE

Course: Molecular Biology (BIOL 333)

Instructor: Dr. Mahmoud Srour

Textbook:
Watson J, et al. (2014). Molecular Biology of the Gene, 7th ed.
Chap 2 & 4

The Central Dogma in Biology

Proposed by F. Crick in 1958

Processes

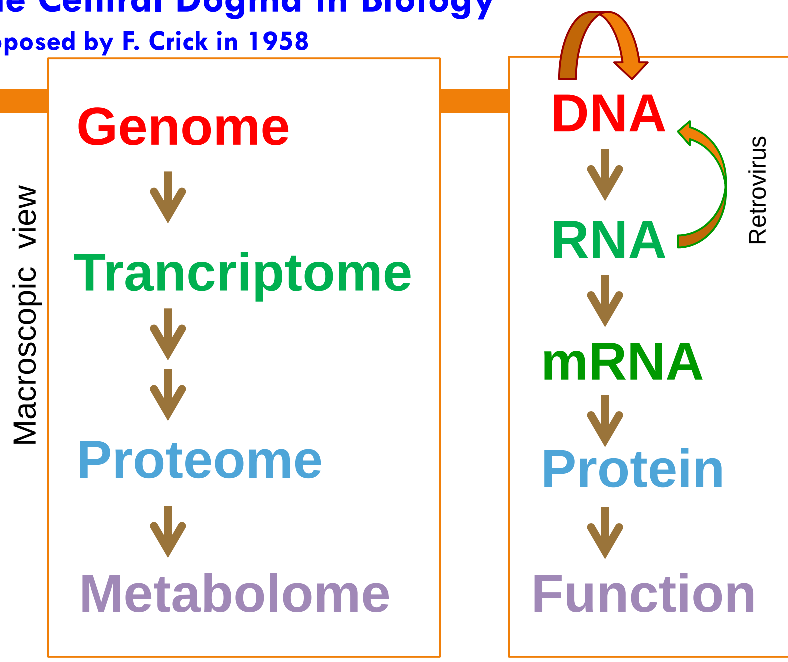
Replication
↓
Transcription
↓
Translation

DNA
↓
RNA
↓
mRNA
↓
Protein
↓
Function

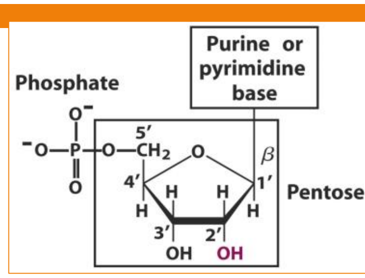
Retrovirus

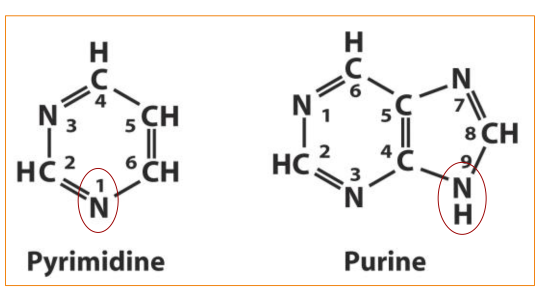
The Central Dogma in Biology

Proposed by F. Crick in 1958



Nucleotide structure





Purines vs. Pyrimidines

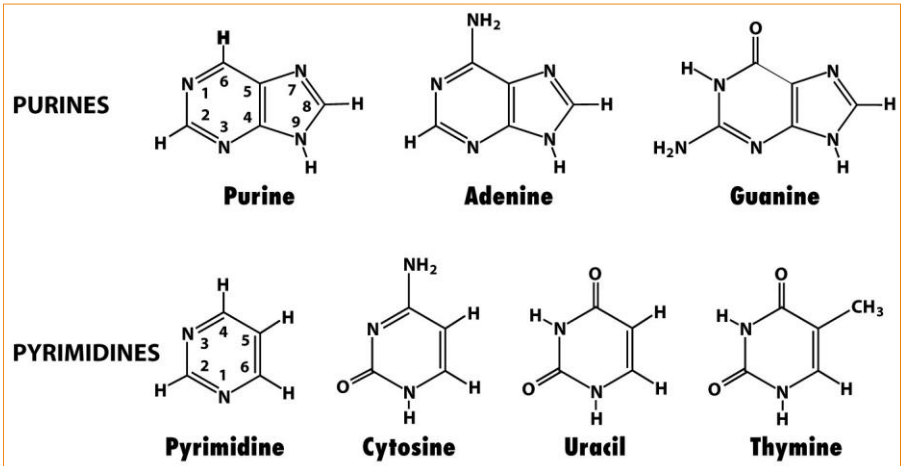


Figure 4-4
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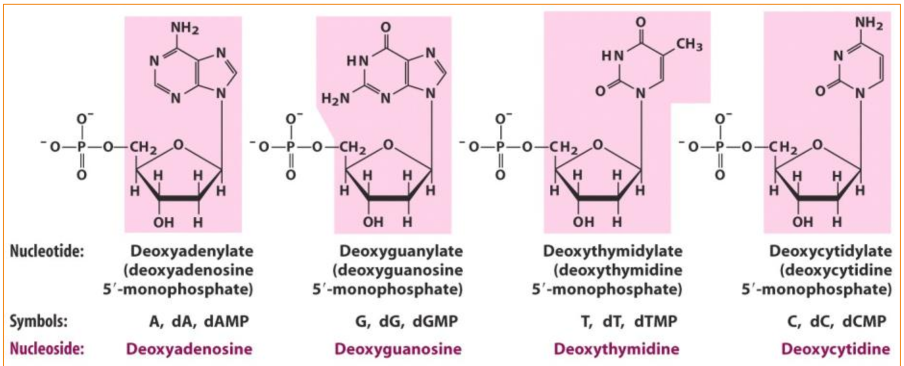
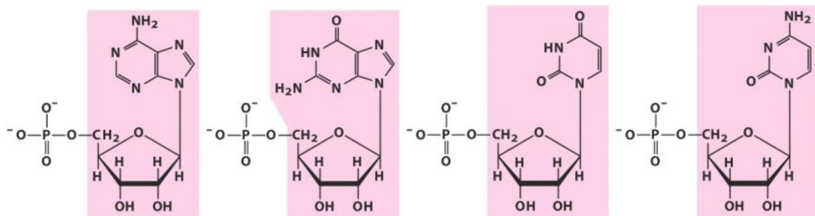
Deoxynucleotides



(a) Deoxyribonucleotides

Ribinucleotides



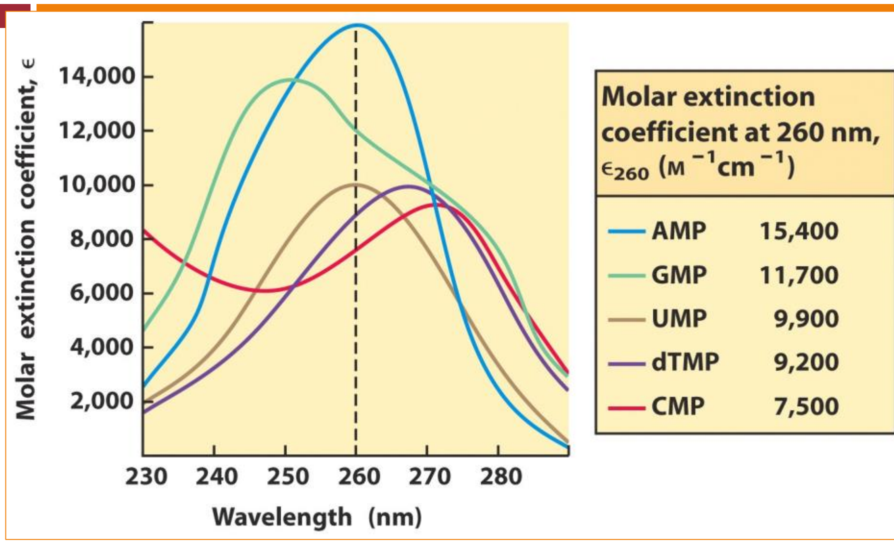
Nucleotide:	Adenylate (adenosine 5′-monophosphate)	Guanylate (guanosine 5′-monophosphate)	Uridylate (uridine 5′-monophosphate)	Cytidylate (cytidine 5′-monophosphate)
Symbols:	A, AMP	G, GMP	U, UMP	C, CMP
Nucleoside:	Adenosine	Guanosine	Uridine	Cytidine

(b) Ribonucleotides

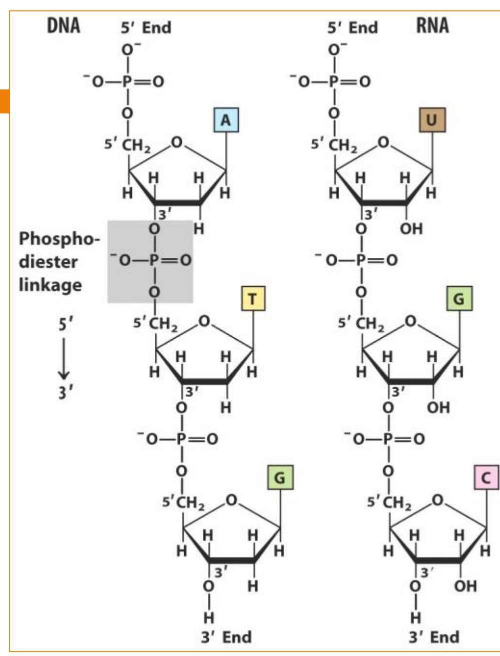
TABLE 8–1 Nucleotide and Nucleic Acid Nomenclature

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

UV absorption of nucleotides



Nucleic acids: strand orientation



Why did DNA evolve to be the carrier of genetic information in the cell as opposed to RNA?

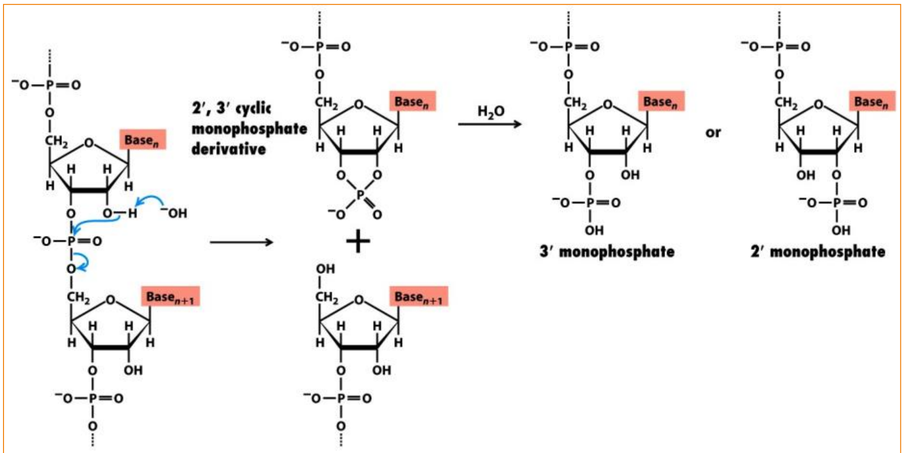


Figure 4-6
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A slow (OH-) catalyzed hydrolysis of RNA at neutral pH

Chemical directionality of a nucleic acid strand

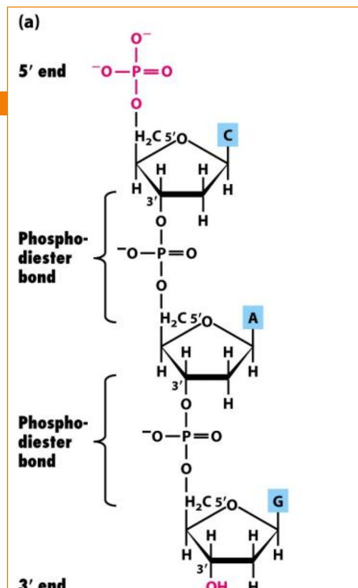
(5'⟶3')

Backbone: S-P-S…

Phosphate is ionized at pH~7.0

Oligonucleotides <50 nts

Polynucleotides >50 nuts



pCAG

pCpApG

p-C-A-G-OH

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Watson –Crick model of DNA: hydrogen bonding

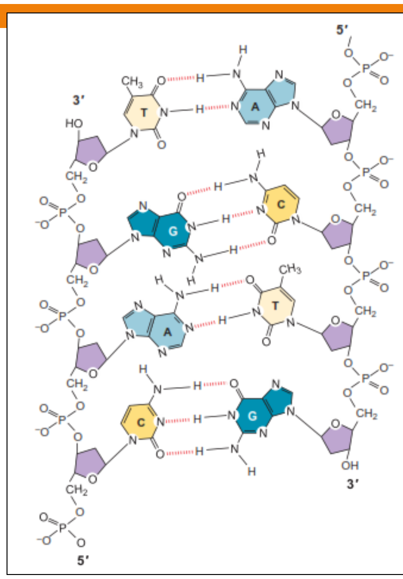
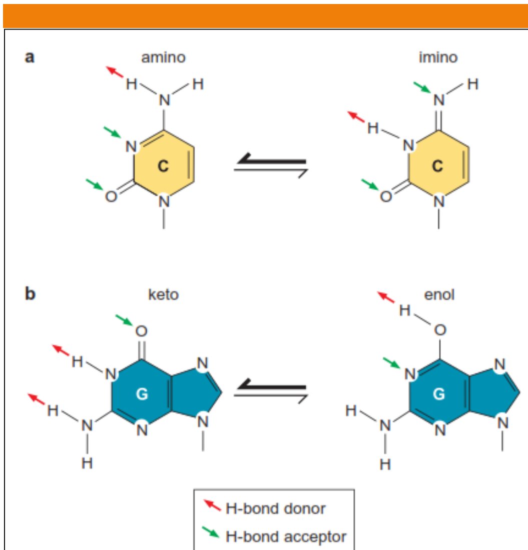


Fig 6-3

Base tautomeres



Cytosine is usually in the AMINO form & rarely forms the IMINO configuration

Guanine is usually in KETO form & is rarely found in the ENOL configuration

Ability to form tautomeres is a frequent source of errors during DNA synthesis

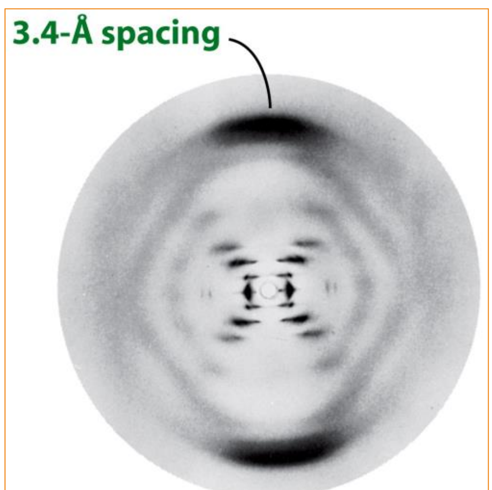
Discovery of DNA double helix

- In 1952, after the Hershey-Chase experiment demonstrated that the genetic material was most likely DNA, a race was on to:
  - Describe the structure of DNA and
  - Explain how the structure and properties of DNA can account for its role in heredity

X-ray diffraction pattern of DNA

by Rosalind Franklin & Maurice Wilkins

X-ray diffraction pattern of DNA: reveals a helical structure with two periodicities of 0.34 & 34 nm



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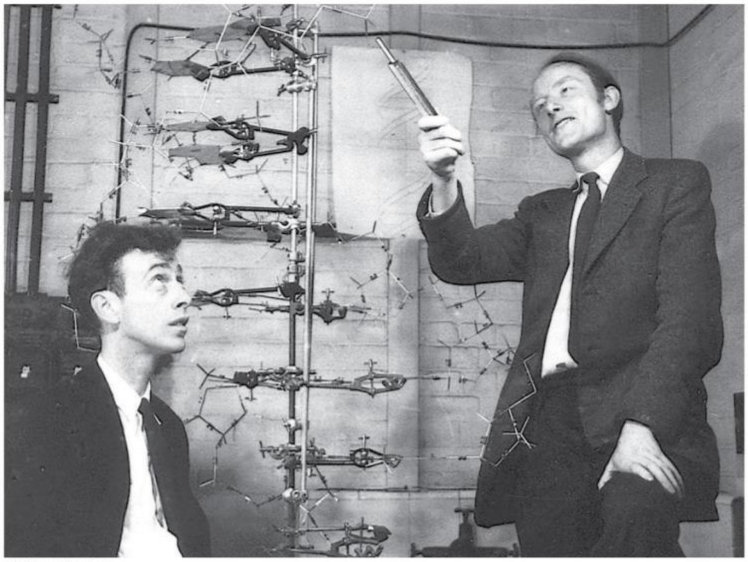
Watson & Crick & DNA double helix



Watson & Crick & structure of DNA

- In 1953, James D. Watson and Francis Crick deduced the secondary structure of DNA, using

1. X-ray crystallography data of DNA from the work of Rosalind Franklin & Maurice Wilkins, early 1950s
2. Chargaff's rules/observations: A=T & G=C, A+G=T+C,

DNA is a double Helix: Watson-Crick model

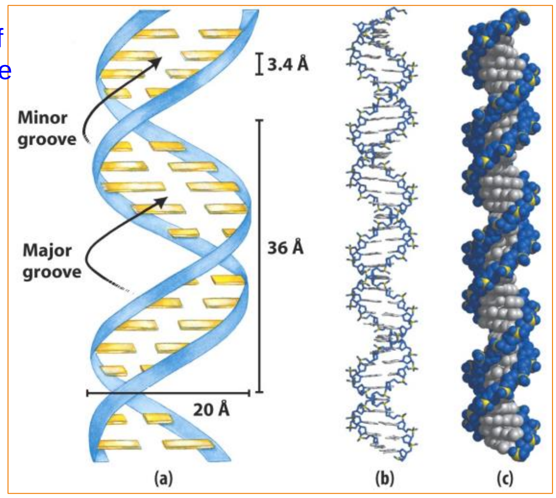
- Watson and Crick reported that DNA consisted of two polynucleotide strands wrapped into a double helix:
- The sugar-phosphate backbone is on the outside.
- The nitrogenous bases are perpendicular to the backbone in the interior.
- Specific pairs of bases give the helix a uniform shape.
  - A pairs with T, forming two hydrogen bonds, and
  - G pairs with C, forming three hydrogen bonds

Watson-Crick model *(continued)*

- Right-handed double helix,
- Antiparallel & complementary strands,
- Nts are 0.34 nm apart and 10nt/turn (3.4nm)

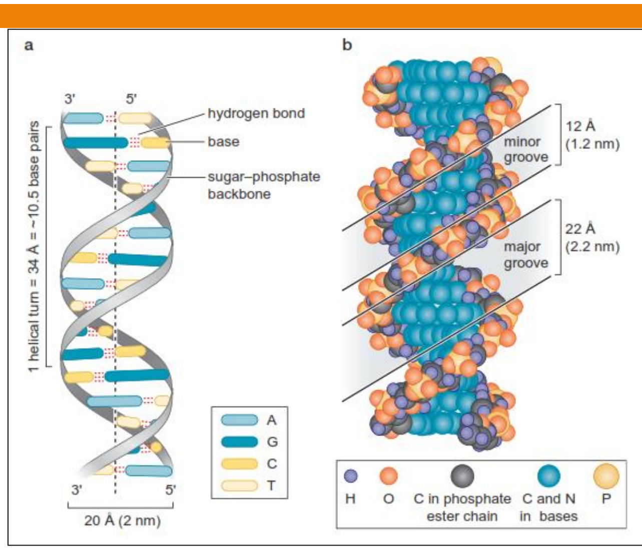
W-C model of DNA: a double helix of two complementary antiparallel strands

Chemical structure of DNA double helix



Space-filling model of B DNA

The Double helix has Minor & major grooves



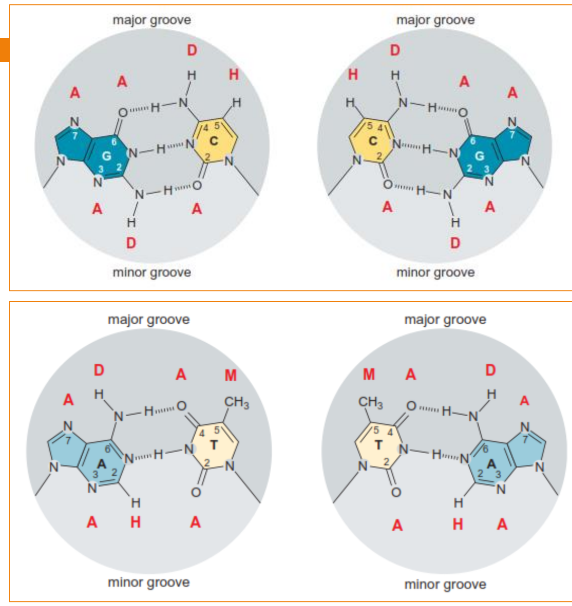
The Major groove is rich in chemical information

A: hydrogen bond acceptor

D: hydrogen bond donor

H: non-polar hydrogens

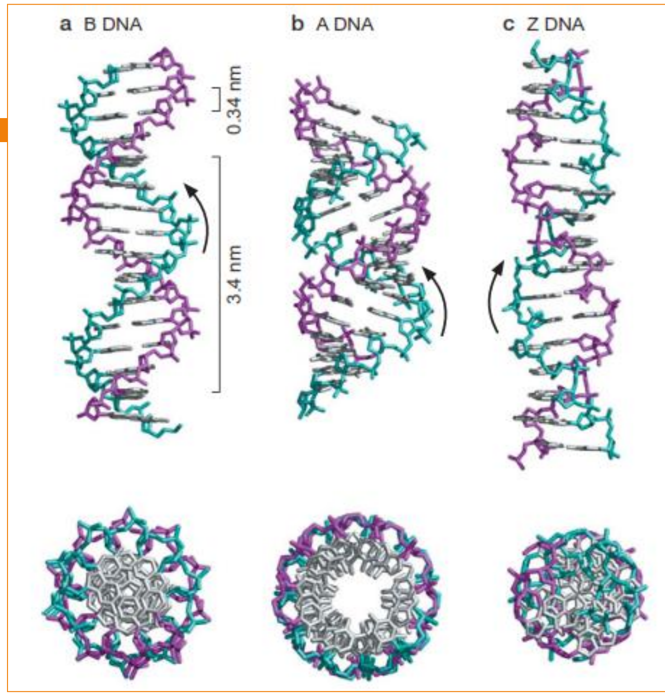
M: methyl groups



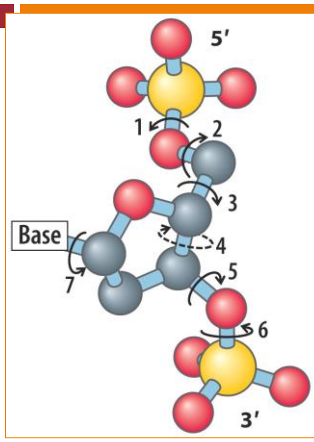
The double helix exist in multiple conformations

- DNA is flexible
- Considerable rotation is possible around a number of bonds in the S-P backbone
- Thermal fluctuations can produce bending, stretching and unpairing (denaturation or melting) of the strands
- Significant deviation in conformation from W-C model exist

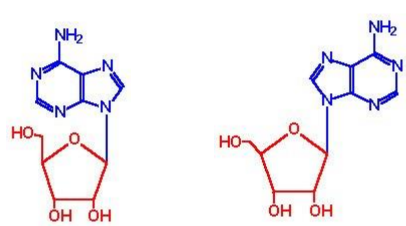
3 forms of DNA



Structural variation in DNA



Rotation around different bonds in DNA

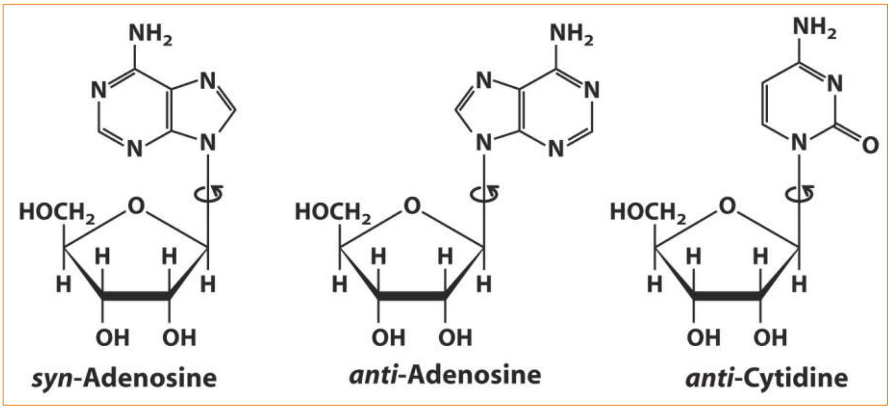


Syn-Adenosine *anti*-Adenosine

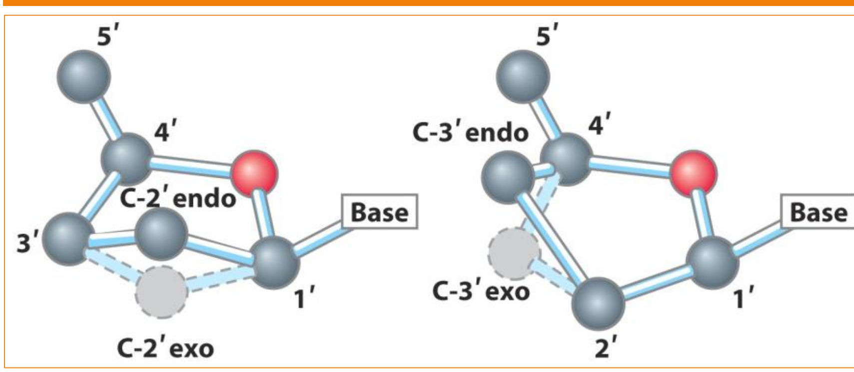
Purines occur in *anti or syn* conformation.

Pyrimidines occur only in *anti* conformation.

Structural variation in DNA



Different puckered Conformations of Ribose



Exo: opposite; Endo: same plane.

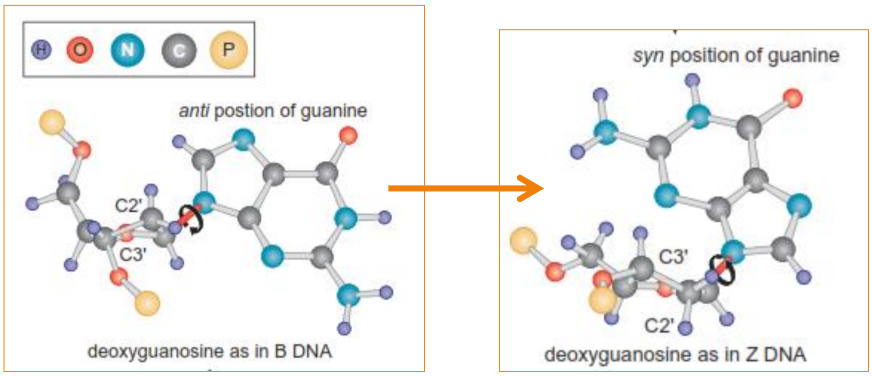
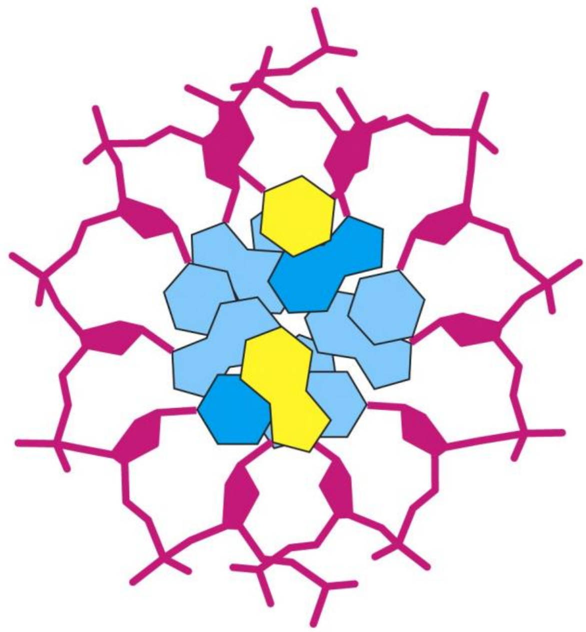


Fig 6-13

TABLE 4-2 A Comparison of the Structural Properties of A, B, and Z DNAs as Derived from Single-Crystal X-Ray Analysis

	Helix Type		
	A	B	Z
Overall proportions	Short and broad	Longer and thinner	Elongated and slim
Rise per base pair	2.3 Å	3.32 Å	3.8 Å
Helix-packing diameter	25.5 Å	23.7 Å	18.4 Å
Helix rotation sense	Right-handed	Right-handed	Left-handed
Base pairs per helix repeat	1	1	2
Base pairs per turn of helix	~11	~10	12
Rotation per base pair	33.6°	35.9°	−60° per 2 bp
Pitch per turn of helix	24.6 Å	33.2 Å	45.6 Å
Tilt of base normals to helix axis	+19°	−1.2°	−9°
Base-pair mean propeller twist	+18°	+16°	~0°
Helix axis location	Major groove	Through base pairs	Minor groove
Major-groove proportions	Extremely narrow but very deep	Wide and of intermediate depth	Flattened out on helix surface
Minor-groove proportions	Very broad but shallow	Narrow and of intermediate depth	Extremely narrow but very deep
Glycosyl-bond conformation	*anti*	*anti*	*anti* at C, *syn* at G

Adapted, with permission, from Dickerson R.E. et al. 1982. *Cold Spring Harbor Symp. Quant. Biol.* **47:** 14. © Cold Spring Harbor Laboratory Press.



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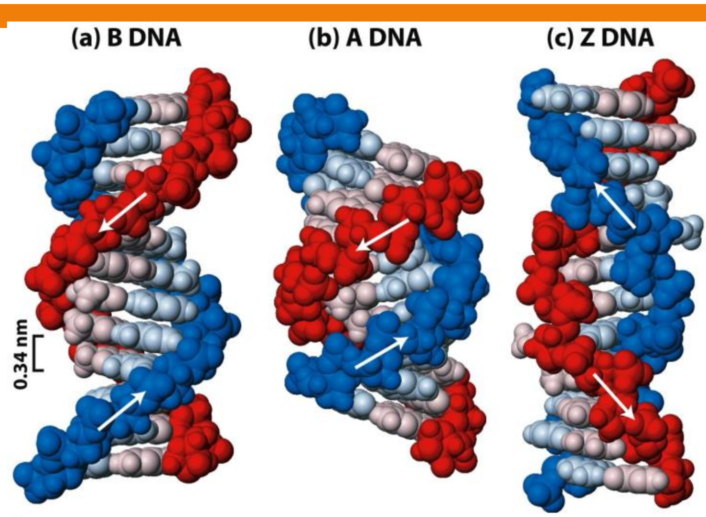
DNA can occur in different 3D forms



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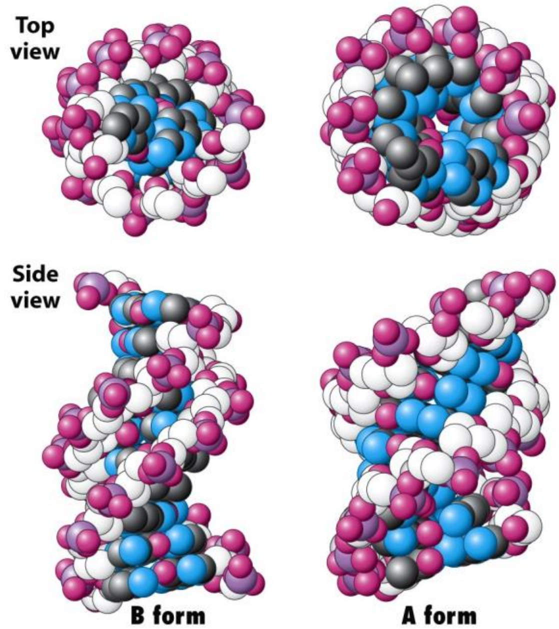

Figure 28-3
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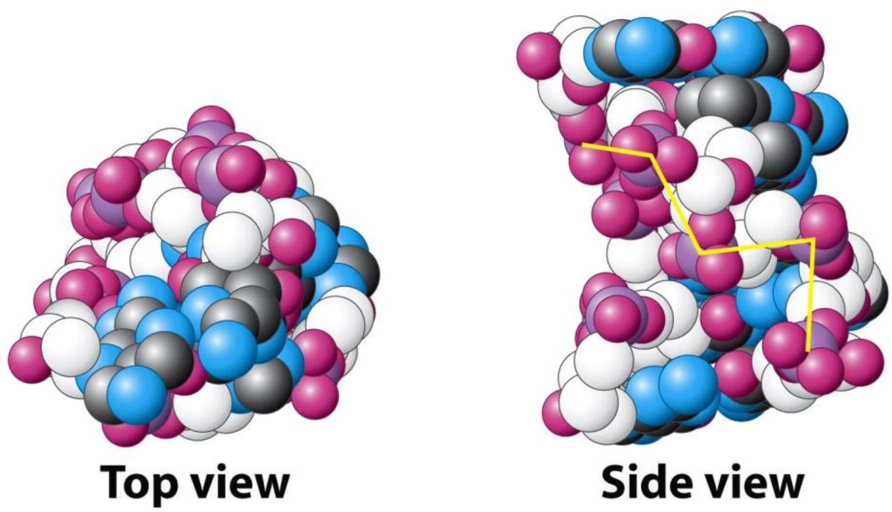

Figure 28-8
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DNA can undergo reversible strand separation: the hyperchromic effect

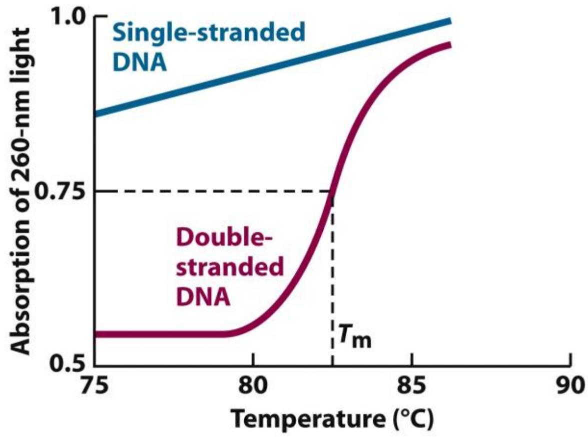

Figure 4-7a
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DNA can undergo reversible strand separation: Tm is affected by GC content

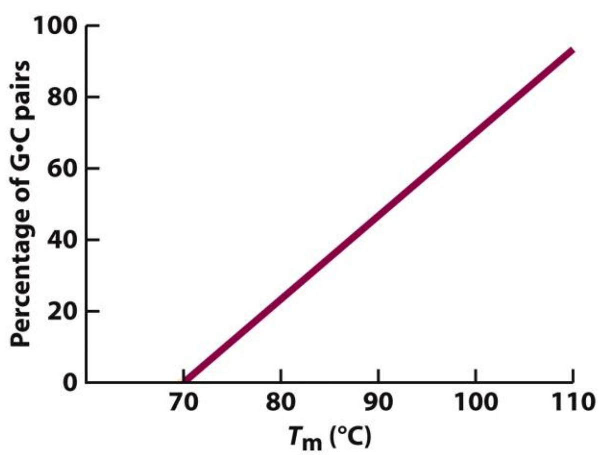

Figure 4-7b
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