OVERVIEW OF NUCLEIC ACIDS STRUCTURE

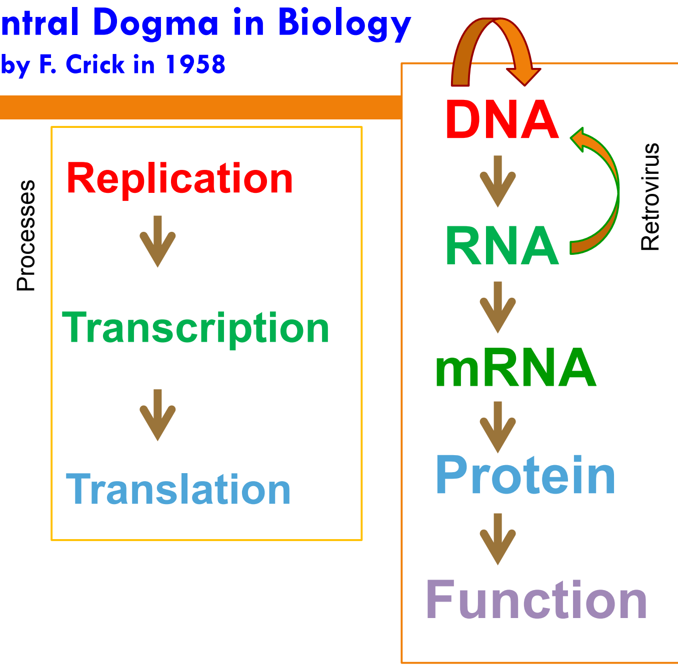
Course: Molecular Biology (BIOL 333)

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



The Central Dogma in Biology

Proposed by F. Crick in 1958

Macroscopic view

Additional levels :-

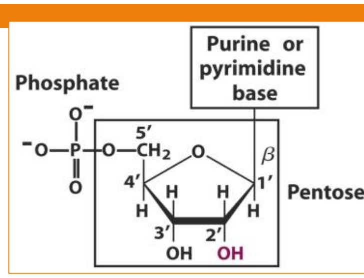
Genome
↓
Trancriptome
↓
↓
Proteome
↓
Metabolome

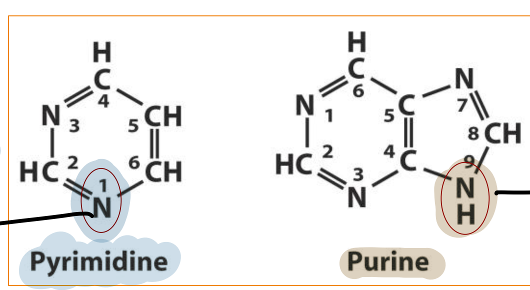
DNA
↓
RNA
↓
mRNA
↓
Protein
↓
Function

Retrovirus

Nucleotide structure

consist of :- sugar , phosphate group , nitrogenous base





N-1 نيتروجين إلي مرتبط بالسكر الخماسي

N-9 نيتروجين إلي مرتبط بالسكر

للتوضيح : السكر في "purine" و "pyrimidine" مابختلفه في النوع ولكن بختلف في القواعد المرتبطة فيه

(C, T و U) ← ترتبط القاعدة نيتروجين بالسكر عن طريق "N-1"

(A, G) ← "N-9"

Purines vs. Pyrimidines

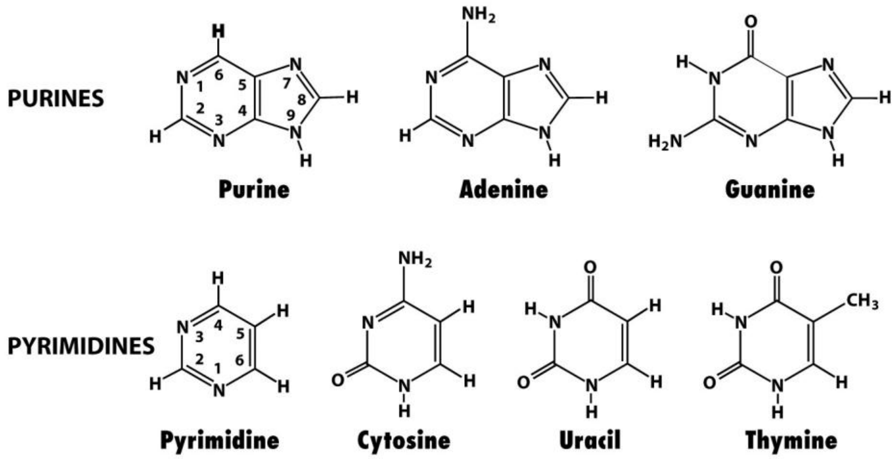


Figure 4-4
Biochemistry, Sixth Edition

نوع السكر

deoxyribose ←

Deoxynucleotides

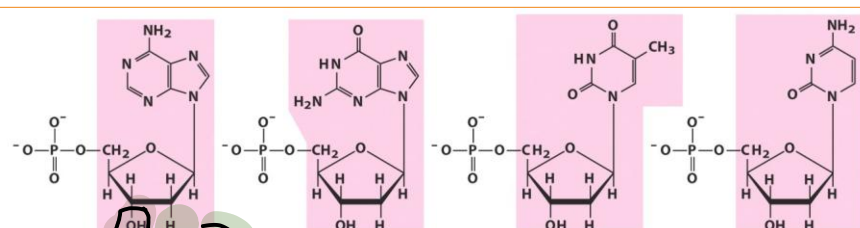
OH → وحدة في Deoxy

consist of:-

1. Nitrogenous base
   - ↙ purine
   - ↘ pyrimiden

لمكوناتهم

2. deoxy ribose
   تكون من ريبوزي



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

(a) Deoxyribonucleotides

يفتقد لمجموعة هيدروكسيل (OH) على C رقم '2 مما يعطيه أكثر استقرار من RNA

3 - phosphate group
ترتبط بالفوسفات الآخر في سلسلة DNA
عنصر الهيكل للحمض النووي

U ← RNA ← T ← DNA *

يوراسيل

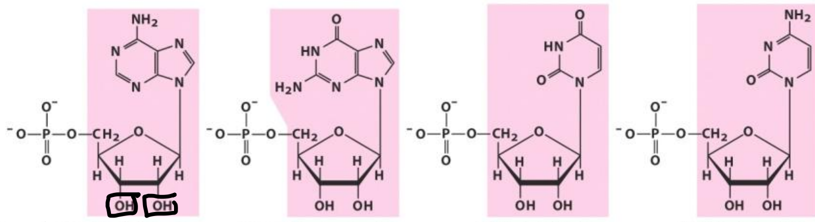
يمين O

←Ribinucleotides→

Smilar to deoxy nucleotides but have an OH group at 2'position

نيوكليوتايد في RNA وتحتوي على سكر الرايبوز

- consist of :-
  1) Nitrogenbase → purine, pyrimidine → C, U → بدل T
  2) Ribose → سكر خماسي يحتوي على (OH) على 2' كربون → وعشان هيك بيكون أقل استقرار وأكثر عرضة للتحلل
  3) phoshate group → ترتبط النيوكليوتيدات معًا لتكون سلسلة RNA



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

ATP ← تخزين مسارات الطاقة ←

أهمية ← تشكل ← mRNA, rRNA, tRNA

- Some of "RNA" molecules تعمل as enzyme → "Ribozymes"

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

Adenine, Guanine → double ring structure

Cytosine, Thymine, Uracil → single ring structure

Nitrogen base → absorbent on UV

Nucleic acid → directionaly (5' → 3')

A 260/280 ←

1.8 – 2.0 pure dNA

↓

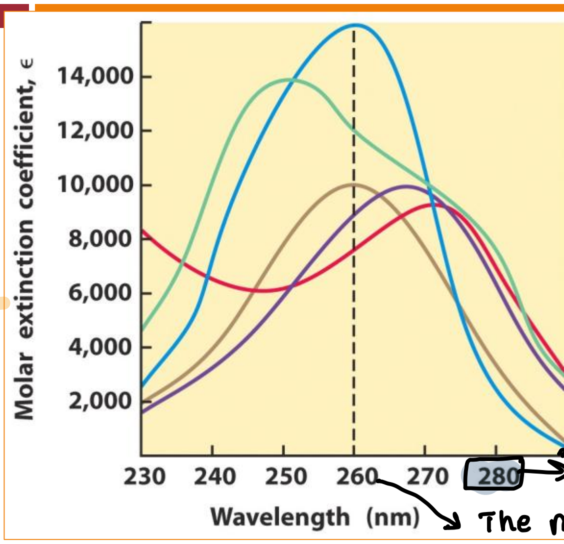
1.4 dNA have contamination due to the protein

↳ 280 it not good to use in lab

↓

Lipid بالعادة ما تقدل مشاكل لأنها ما بتذوبي الـ proteins

UV absorption of nucleotides



280 → protein

260 → The most uv absorbent

Molar extinction coefficient at 260 nm, ϵ_{260} ($M^{-1}cm^{-1}$)	
AMP	15,400
GMP	11,700
UMP	9,900
dTMP	9,200
CMP	7,500

→ 1mol molecule absorbed نقيس under condition

5' end → consist of (-PO₃²⁻) phoshate group حرة

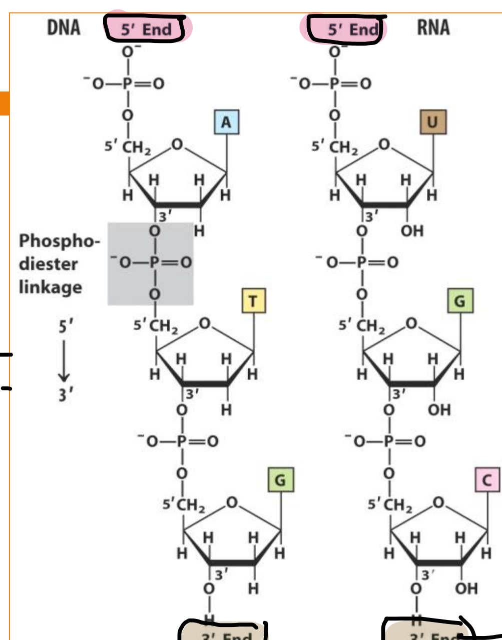
Nucleic acids: strand orientation

Nucli tied linked together → phosphodiester bond between the 3' carbon of one nucle tied sugar and the 5' car bon of the next nucletied

Nucleic acid strand:- Directionality

replication و transcription

- as enzyme like dNA polymerase read 3'→5' but Synthesize the new strand 5'→3'



لما بدي أبني سلسلة جديدة أثناء نفك أو ننسخ بضيفه نيوكليوتات جديدة عطرف 3'

3' end → consist of hydroxylgroup (OH) حرة على كل الطرفين .

* RNA → more prone to degradation due to the 2'OH group
مثلا لو حطيت عينة دم وارجعتلها بعد أقل من ساعة بكون RNA قل لا عكس DNA

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

قدر أربط بين RNA ssRNA إذا حكي ب فتح مصدر أرجله

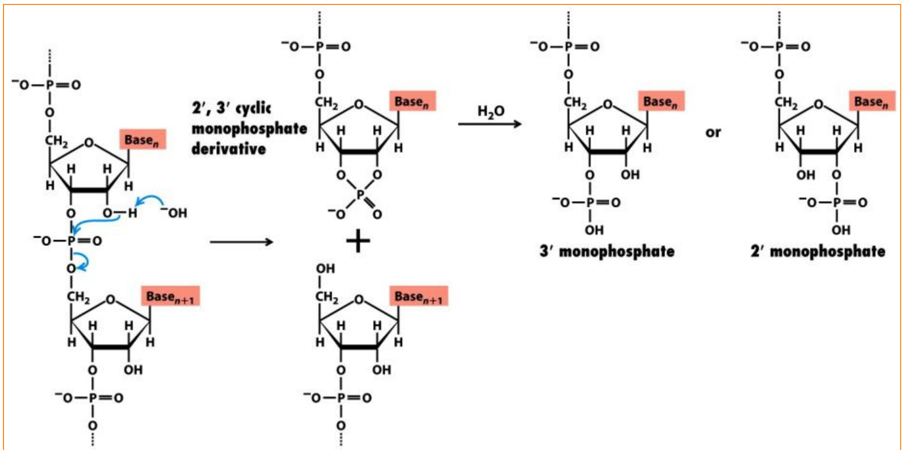


Figure 4-6
Molecular Cell Biology, Sixth Edition

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

Chemical directionality of a nucleic acid strand

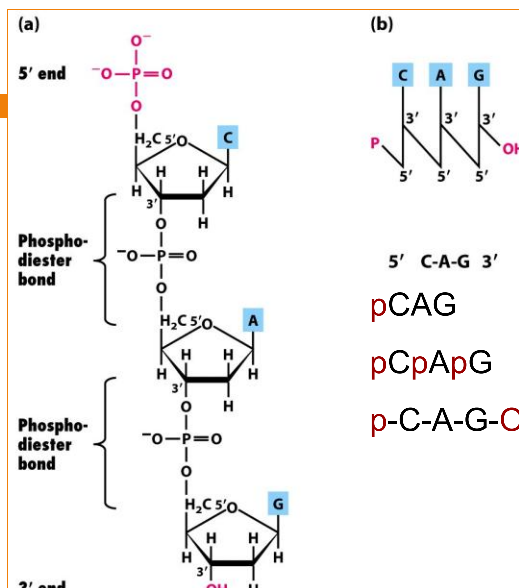
(5'⟶3')

Backbone: S-P-S…

Phosphate is ionized at pH~7.0

Oligonucleotides <50 nts

Polynucleotides >50 nuts



pCAG

pCpApG

p-C-A-G-OH

Figure 4-2
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Watson –Crick model of DNA: hydrogen bonding

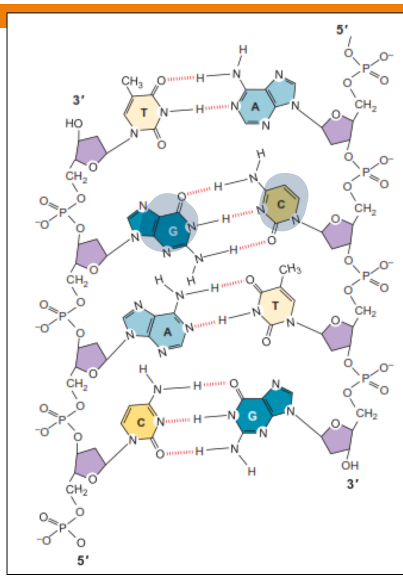
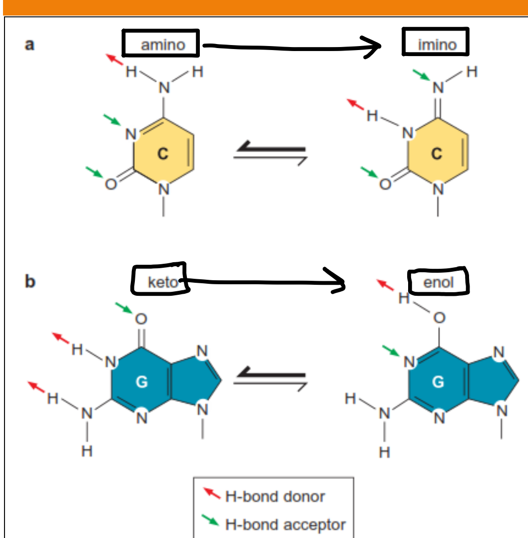


Fig 6-3

→ antipararil 3→5'
→ complemantary
G→C
→ "A–T" ⇒ 2 hydrogen bond
→ "G–C" → 3 hydrogen bond

Base tautomeres → accour "susbontoncly"

"donor → acceptor"



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

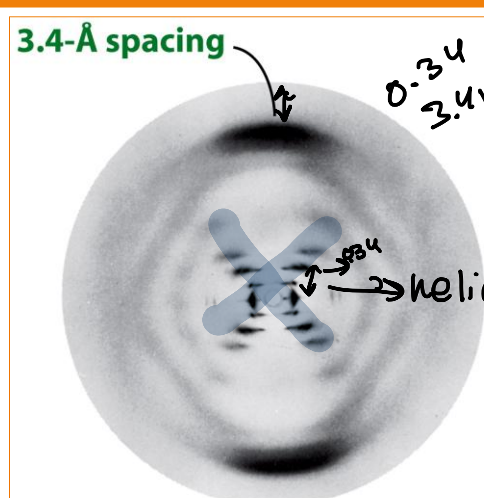


Figure 4-10
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Watson & Crick & DNA double helix

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

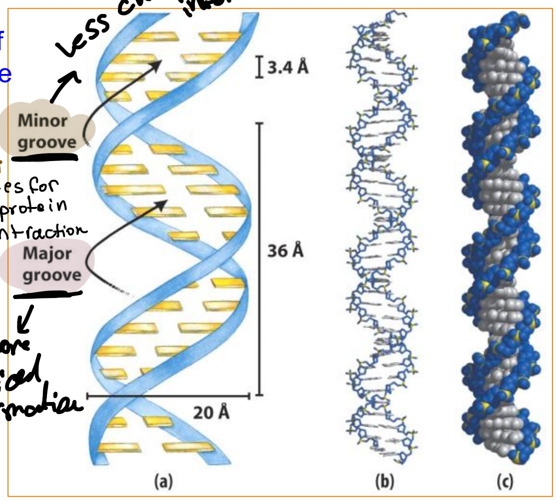
- Watson and Crick reported that DNA consisted of two polynucleotide strands wrapped into a double helix:
- The sugar-phosphate backbone is on the outside.
- The nitrogenous bases are perpendicular to the backbone in the interior.
- Specific pairs of bases give the helix a uniform shape.
  - A pairs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

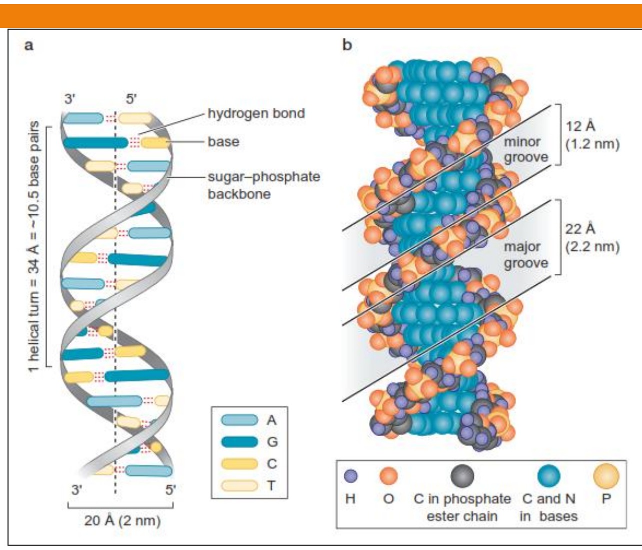
Chemical structure of DNA double helix



Space-filling model of B DNA

The Double helix has Minor & major grooves

Å 10^{-10} m
nm 10^{-9} m



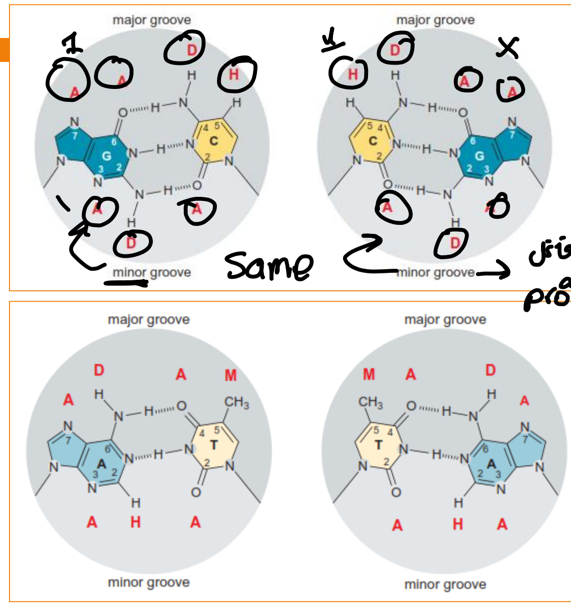
The Major groove is rich in chemical information

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 → can make diffrent conformation
- 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

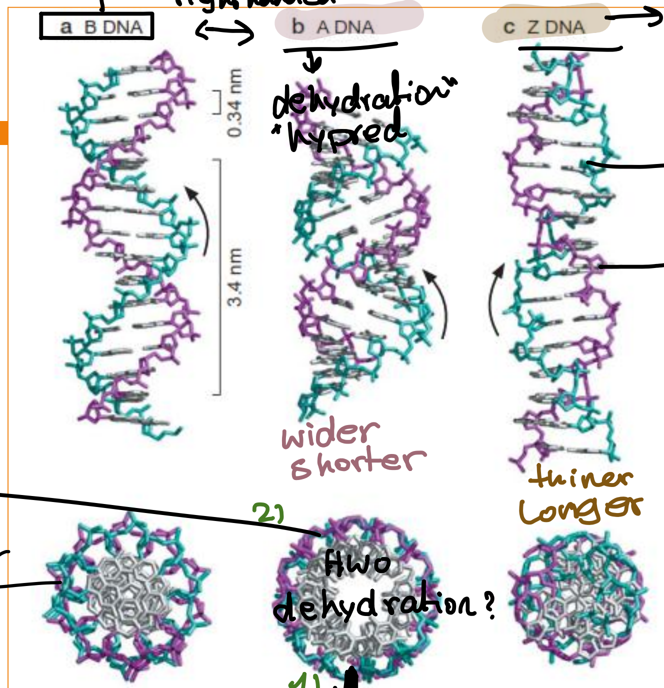
موجود في أغلب DNA

different conformation

double helix الأكوفي

dNA , dNA

3 forms of DNA



right handed

left handed

dehydration "hypred"

الماء خفيفة

compact

wider shorter

thiner Longer

"hypred"

"RNA, ANA"

"DNA, RNA"

A form

?? 2 prime OH

ما تدخل بتوخذ حيز بتدفش بيوا ← wider

pripr endicular Nitrogen base

حلقات حوالبعض

2) two dehydration?

1) add alcohol → بسحب الماء

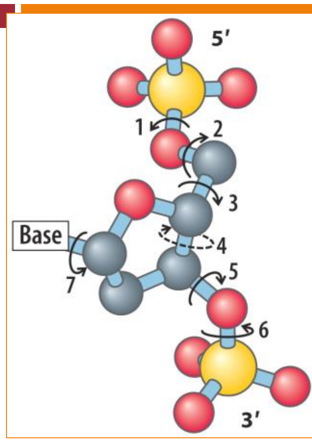
+ added salt after that

"Salt" هو مرتبط في Salt ويمل بنزبه مع الماء "DNA" عشان تضعف ارتباط

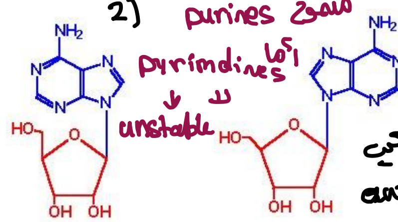
"Salt" ← بخوفي جزيئات الماء قلت وحلها Salt "wider

Ribose → "rotation 2 ..."

Structural variation in DNA



Rotation around different bonds in DNA



Syn-Adenosine *anti*-Adenosine

syn ← إذا لفت

2) purines 2 ...

pyrimidines لأ ↓ unstable

1) حيث يكون Nitrogen base و Ribose مابكونوا فوق بعض

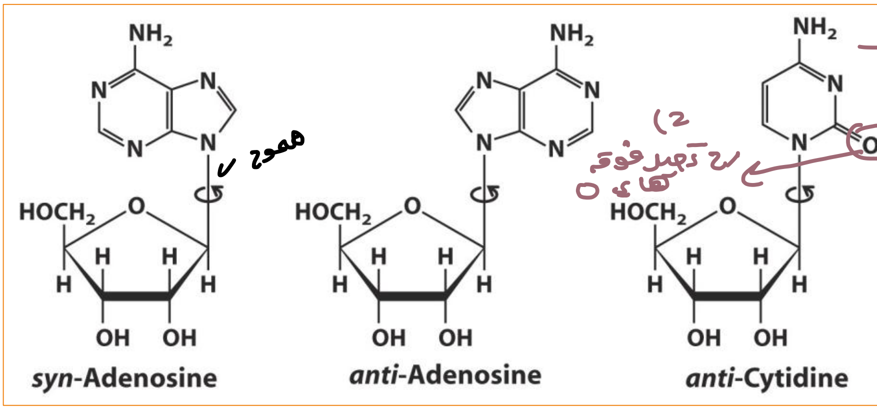
في الوضع الطبيعي بوخذ شكل anti

Purines occur in *anti or syn* conformation.

Pyrimidines occur only in *anti* conformation.

Strech of purins → syn ← معوجة ورا بعض
في جزء hilex بتغير

Structural variation in DNA



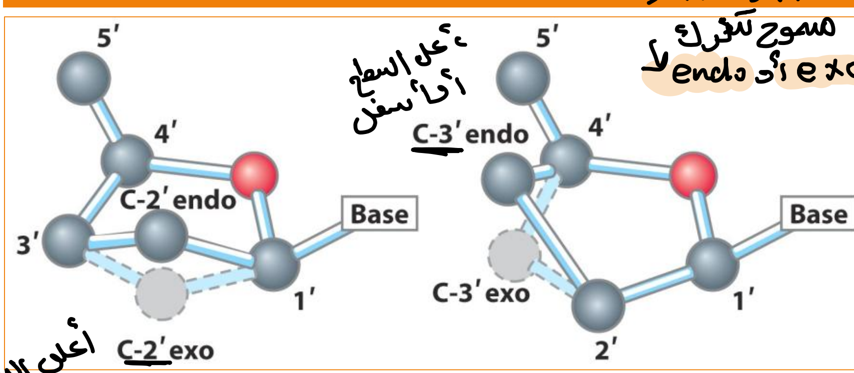
1) مش مسموح تصير syn لأنه
3) فبتالي بخلق تنافر pyrimidines مابتوخذ syn و بتظهر تتوزع anti

في حين purine A و G مسافة بين N و O كبيرة ← فلا يحدث تنافر

Different puckered Conformations of Ribose

مسموح روتيشن ومن يصير different conformation

في DNA و RNA مسموح تتحرك endo أو exo



أعلى السطح أو أسفل

Exo: opposite; Endo: same plane.

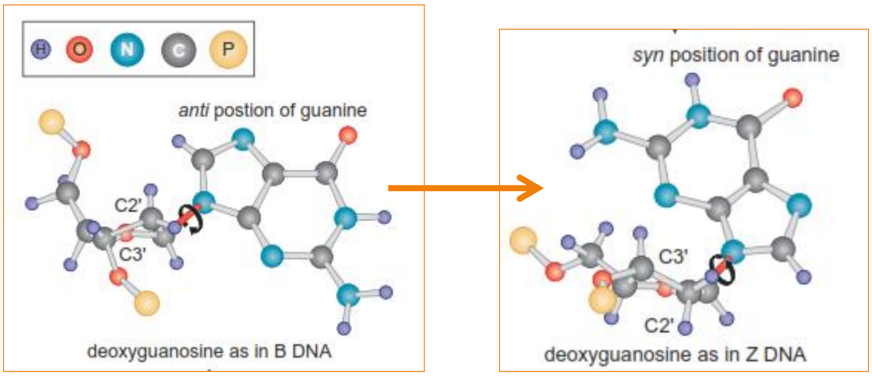


Fig 6-13

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.

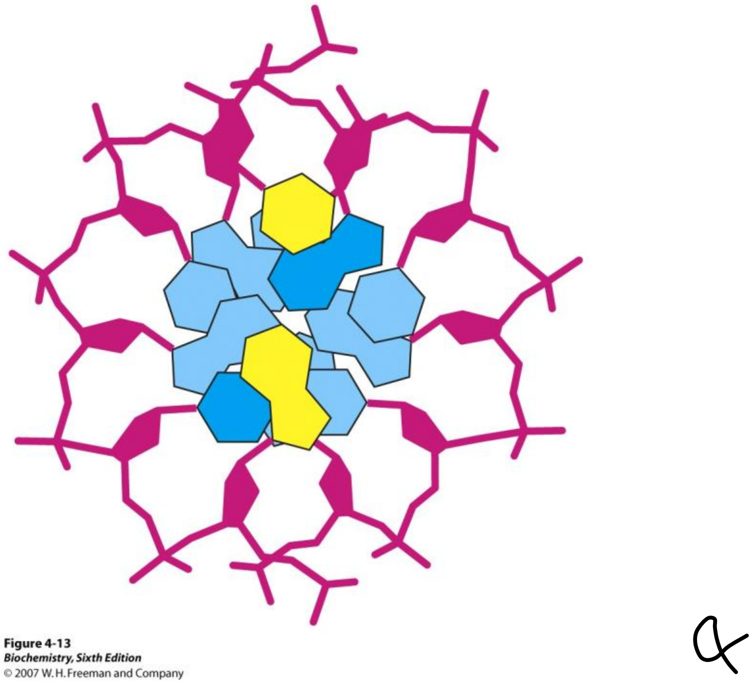


Figure 4-13
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DNA can occur in different 3D forms

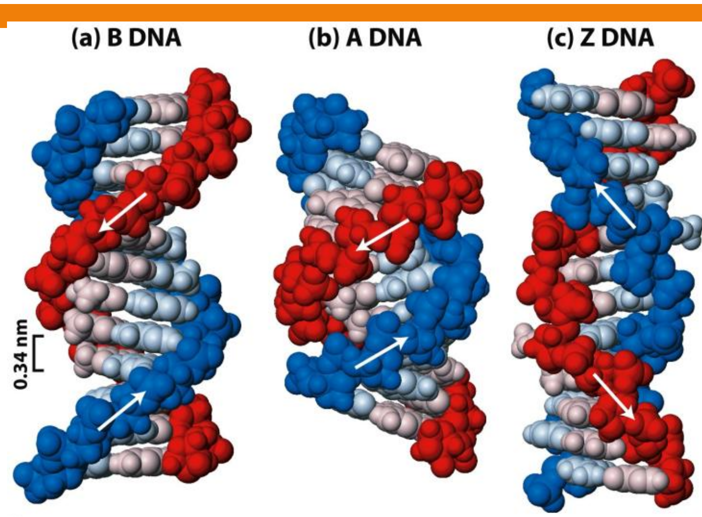

Figure 4-4
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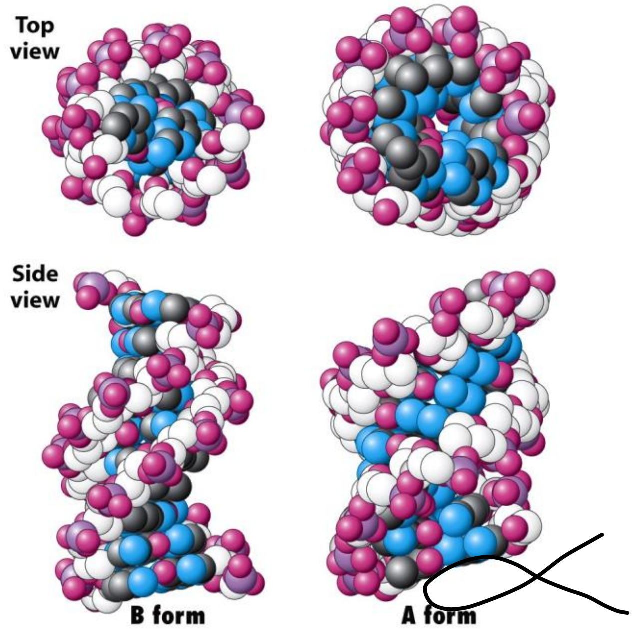

Figure 28-3
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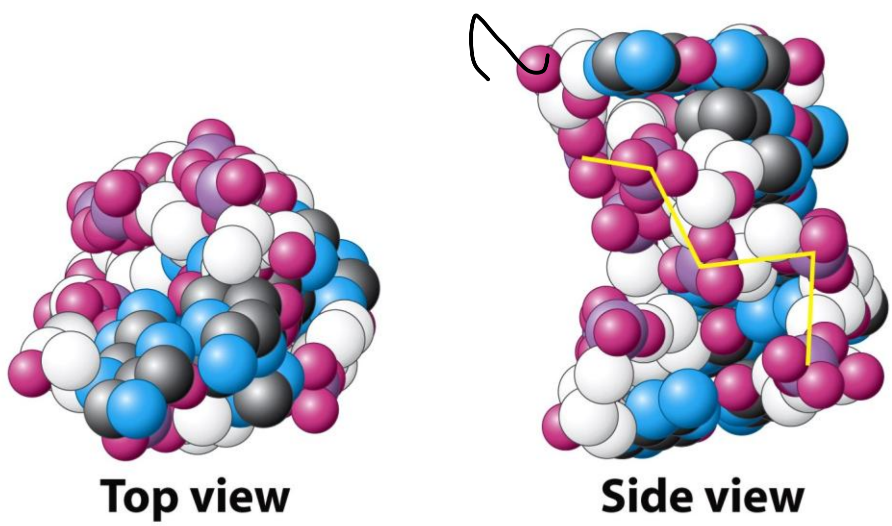

Figure 28-8
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DNA can undergo reversible strand separation: the hyperchromic effect

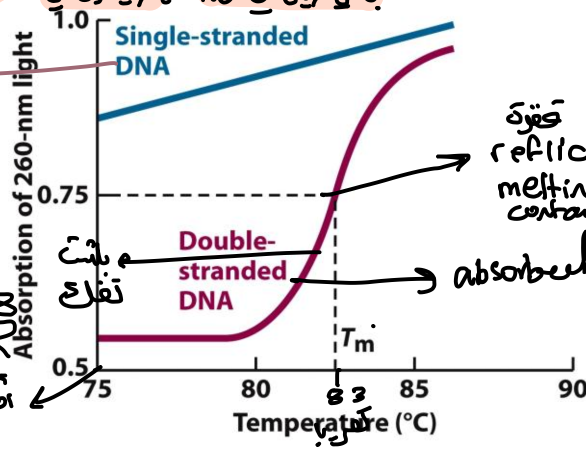

Figure 4-7a
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DNA can undergo reversible strand separation: Tm is affected by GC content

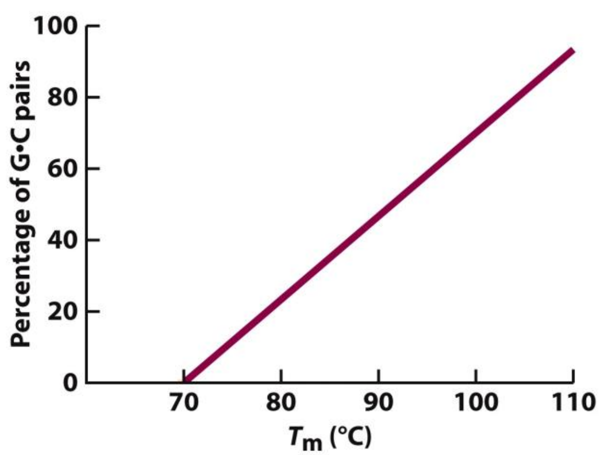

Figure 4-7b
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absorbent الأساسي → DNA نتج عن → Nitrogen base →

Double strand
Nitrogen bases
كانت محصورة
في الوسط

وهي محصورة بتحل absorbent بس لما تتحول لـ "single" صارت exposed

يعني قدرة على تحل absorbent أعلى صار ت

"يتطبق على DNA و RNA"

Single → تغير minimal
لأنه كان لا يقع عليه أو عامل secondary structure
فأنا مدتيه فبالتالي تغير قليل
لأنه مش عامل double strand
وعملية coiling قلت
→ تغير قليل

* مش ممكن "bacterial DNA" ← يفك
على حرارة أقل من "75 - 70"