Molecular Biology (1)

Structure of nucleic acids

Prof. Mamoun Ahram
Second semester, 2020-2021

Course resources

- Lectures
- The Cell: A Molecular Approach, Geoffrey M. Cooper and Robert E. Hausmann, 7th edition, Sinauer Associates, 2018

Outline

- Nucleic acid structure
- Basic techniques
- The human genome
- DNA replication
- DNA mutations
- DNA repair
- Transcription
- Regulation of transcription in prokaryotes
- Regulation of transcription in eukaryotes
- Analysis of gene expression
- Translation and its regulation

Resources

- This lecture
- Cooper, Ch. 2, pp. 54-56, Ch. 4, 116-118, Ch. 6, pp.203-208

What is molecular biology?

Biochemistry but in DNA and RNA

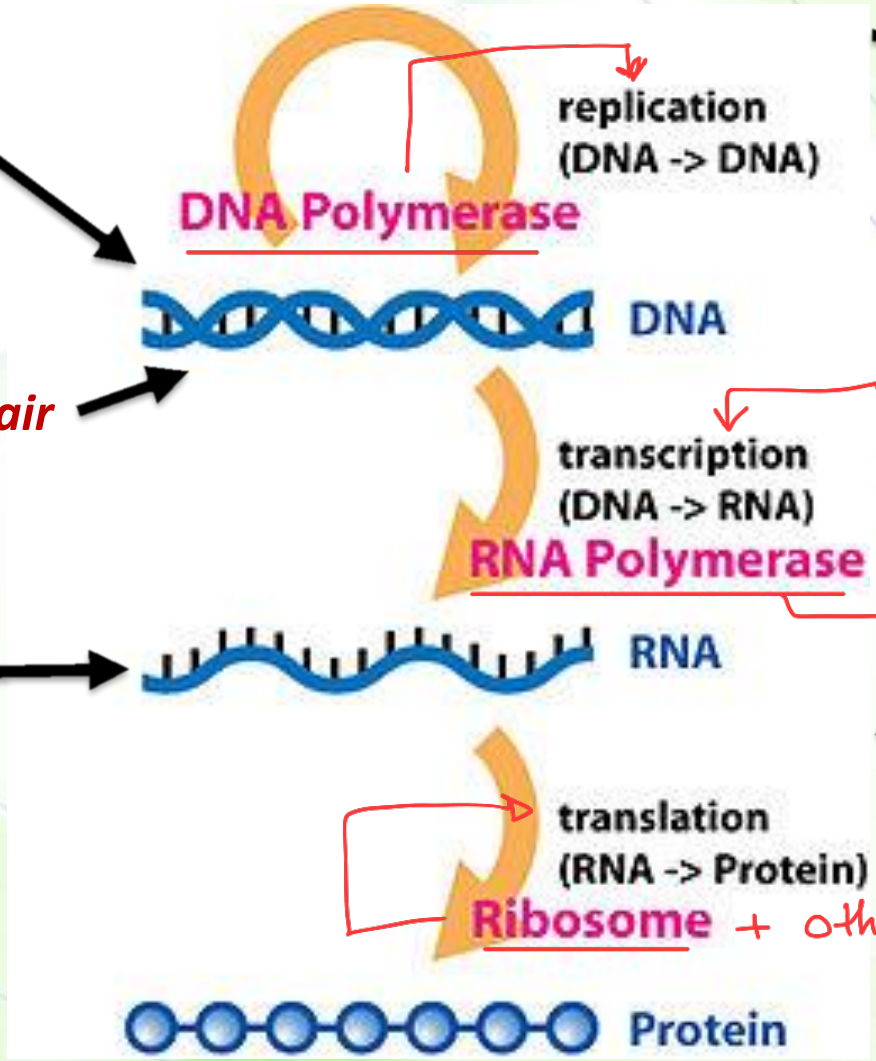
Central dogma of molecular biology

main idea

Organization

Mutations and repair

Types

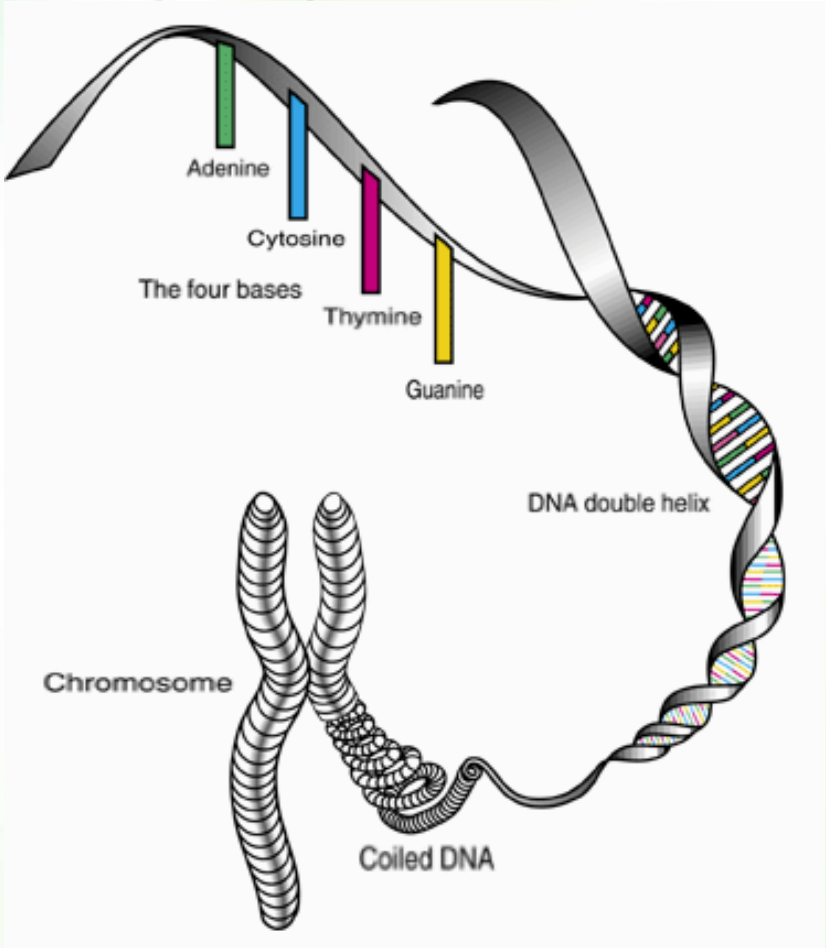


Techniques

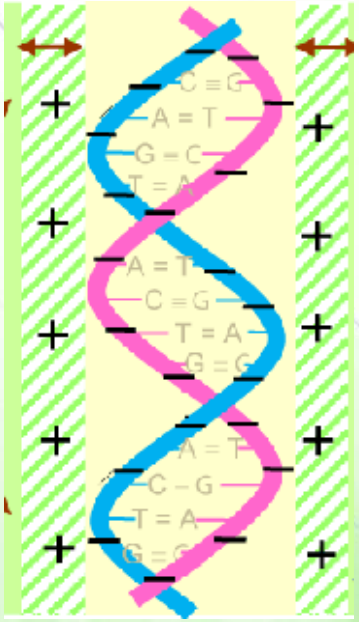
Nucleic acids

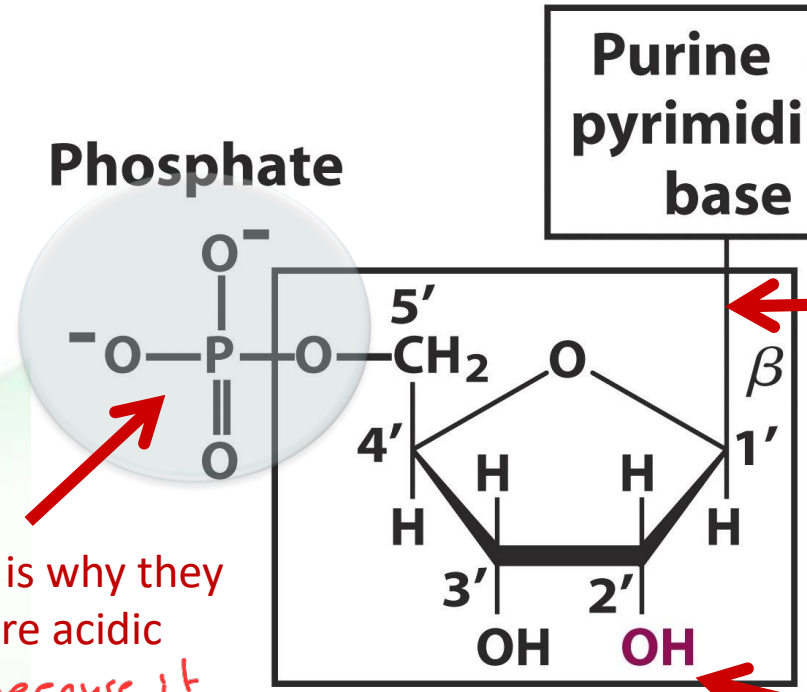
these are polymers

- There are types
  - Deoxyribonucleic acid (DNA)
  - Ribonucleic acid (RNA)
- The primary structure of nucleic acids is linear polymers of nucleotides (monomers) bound to each other via phosphodiester bonds.
- DNA is coiled and can be associated with proteins forming chromosomes.



Chemical composition and bonds





→ N base
Connect with 1'

because it is negative

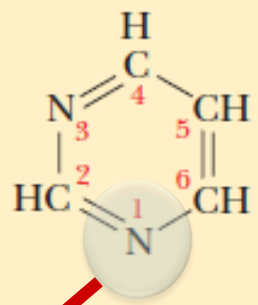
in RNA

↳ in DNA
↳ without O on 2'

five carbons

- Positively charged ions (Na^+ or Mg^{2+}) associate with the phosphate groups.
  - Example: histones

Nitrogenous bases

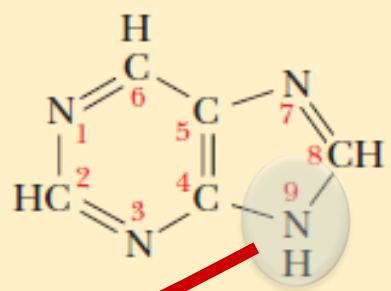


Pyrimidine

الكلمة الصغيرة للمركب الكبير

Glycosidic bond

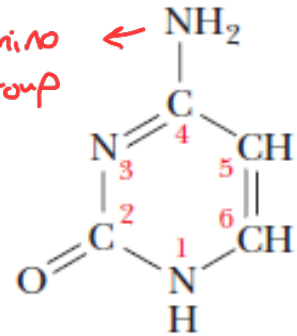
1 and 9



Purine

the carbon numbers without ' is for N bases Carbon

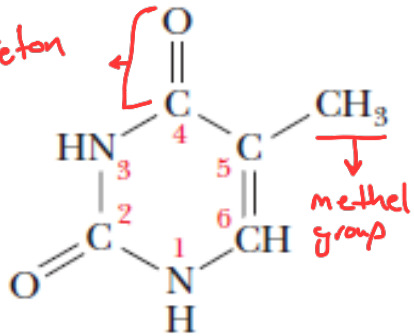
Amino group



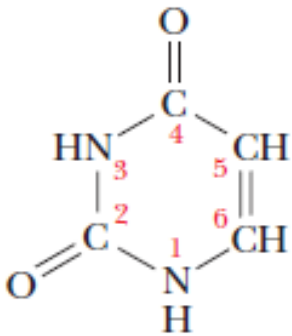
Cytosine
(in DNA & RNA)

keton

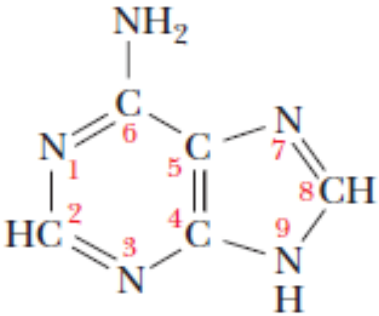
methel group



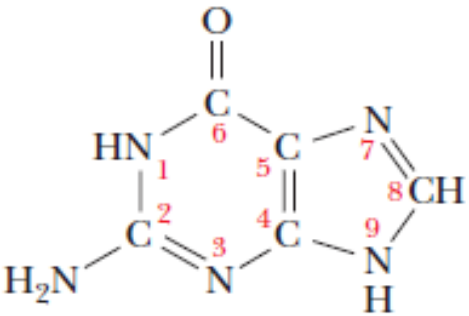
Thymine
(in DNA & some RNA)



Uracil
(in RNA)



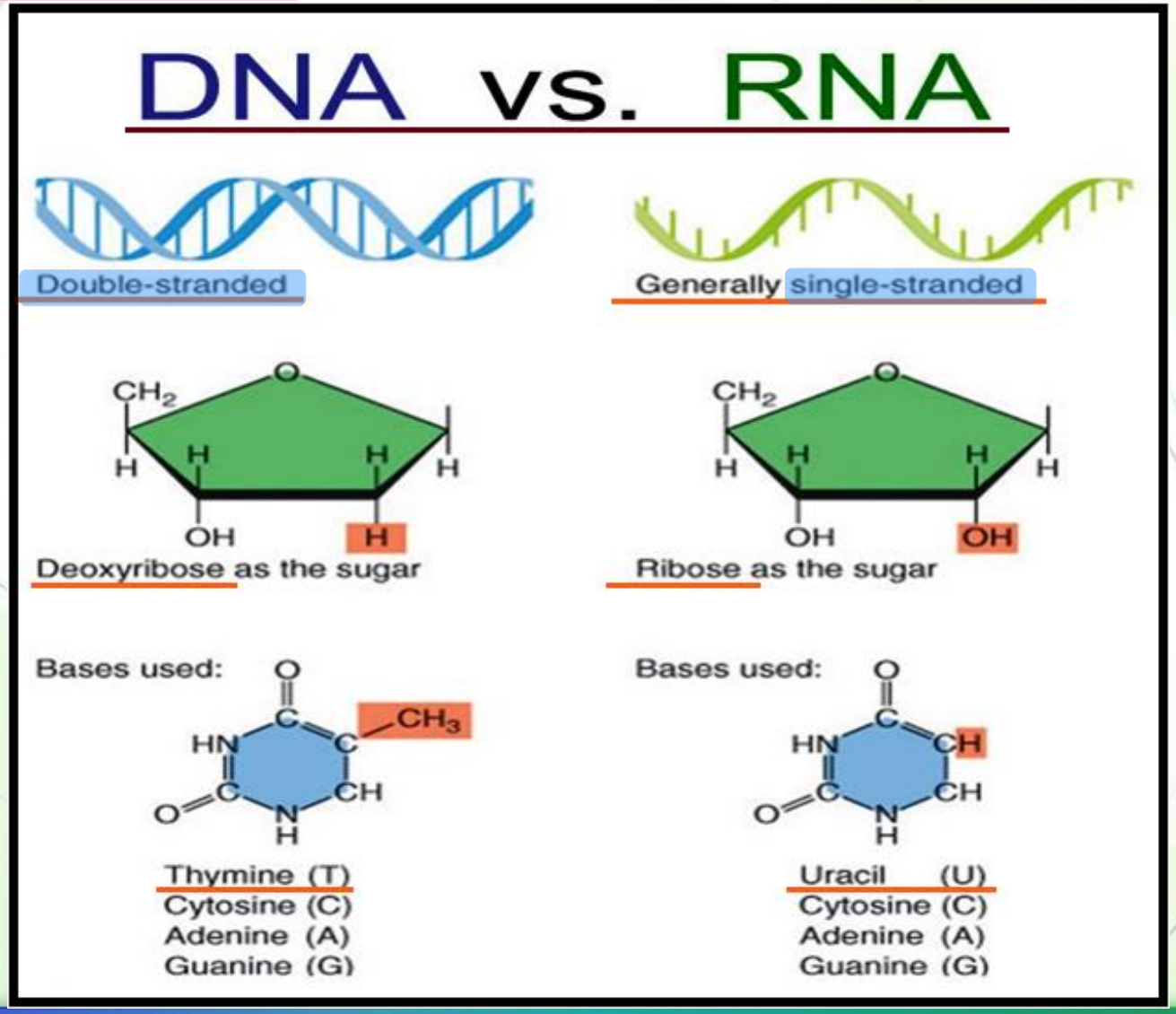
Adenine
(in DNA & RNA)



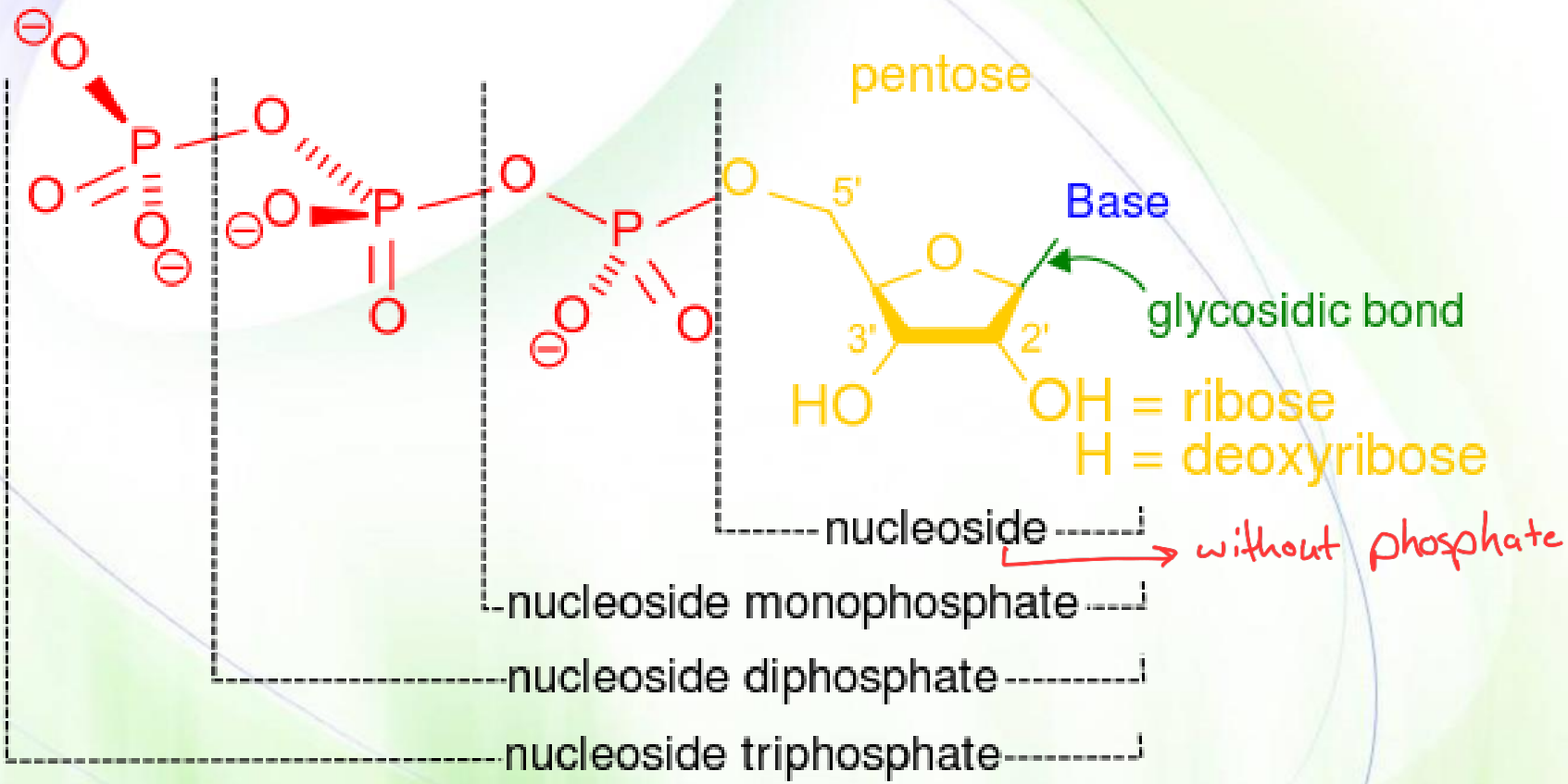
Guanine
(in DNA & RNA)

In prokaryotes and eukaryotes

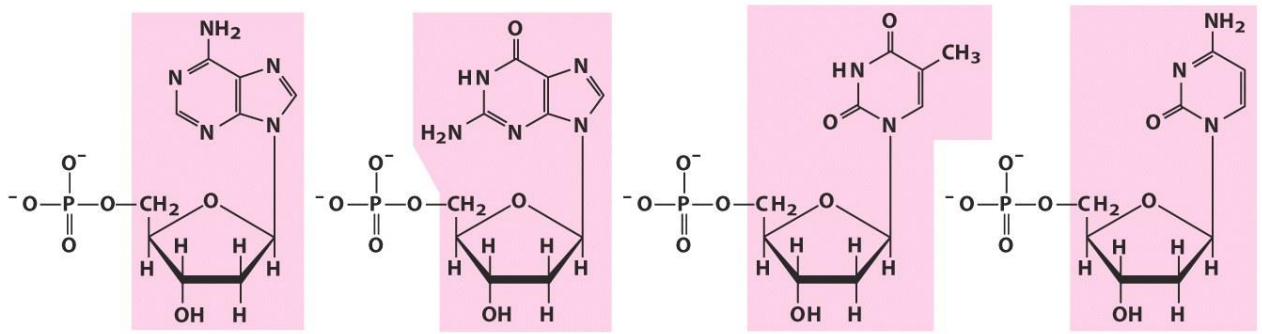
not viruses



Nucleotides vs. Nucleosides



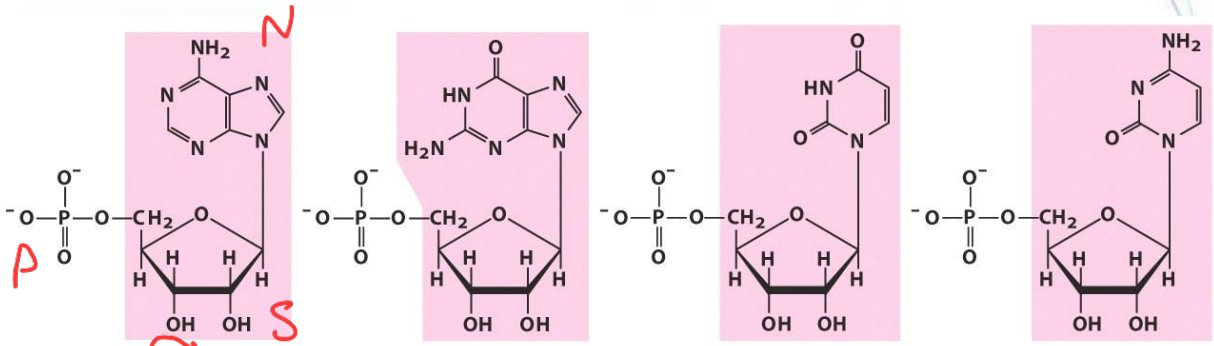
Nucleotides vs. Nucleosides



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

So its Nucleotide and in spesific Nucleotide monophosphate and on 2' hydroxyl group So ribose sugar and N is Purine and has Amino group So Adenin

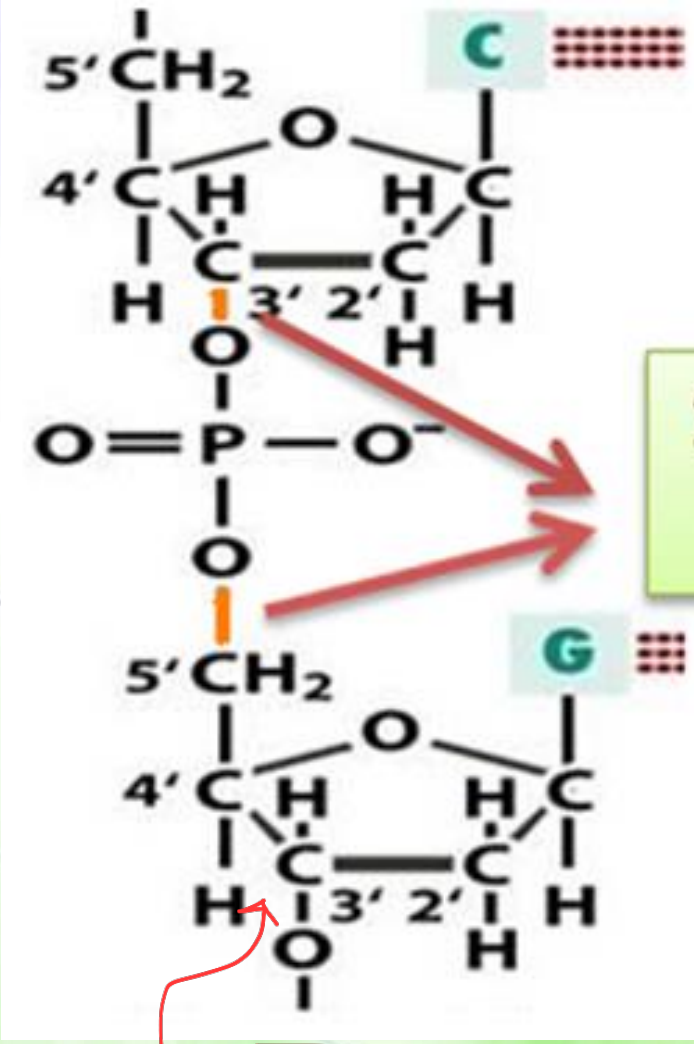


Nucleotide:	Adenylate (adenosine 5′-monophosphate)	Guanylate (guanosine 5′-monophosphate)	Uridylate (uridine 5′-monophosphate)	Cytidylate (cytidine 5′-monophosphate)
Symbols:	A, AMP	G, GMP	U, UMP	C, CMP
Nucleoside:	Adenosine	Guanosine	Uridine	Cytidine

Adenin + sugar

(b) Ribonucleotides

Formation of a nucleic acid polymer



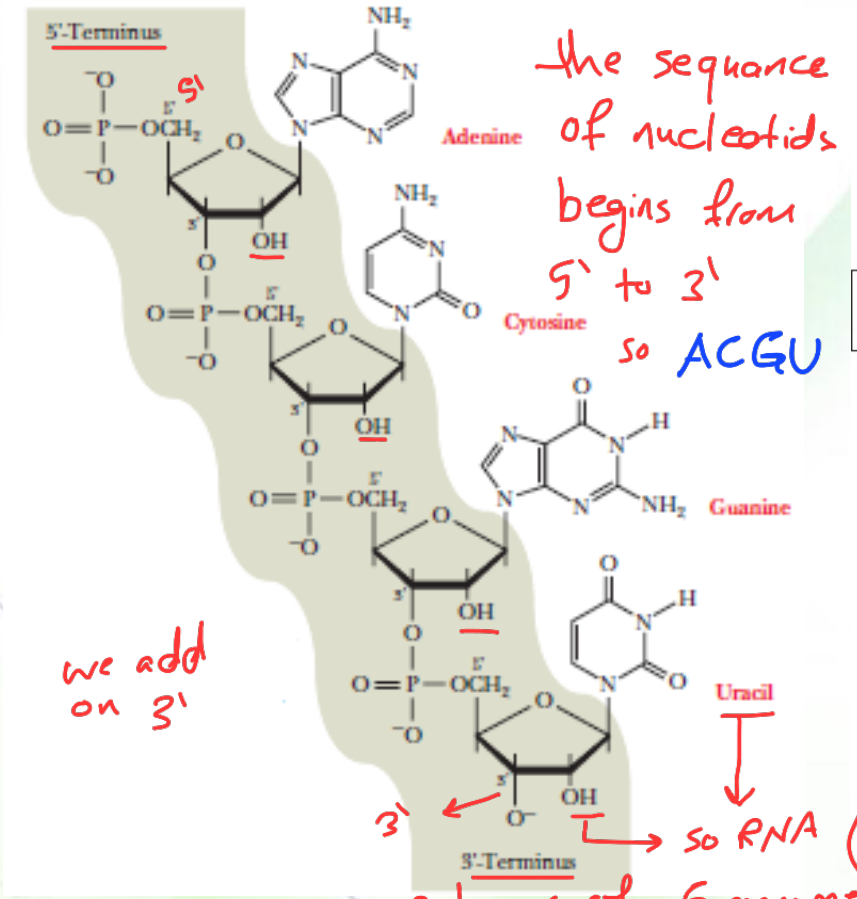
1st and 2nd ester linkage (phosphodiester bond)

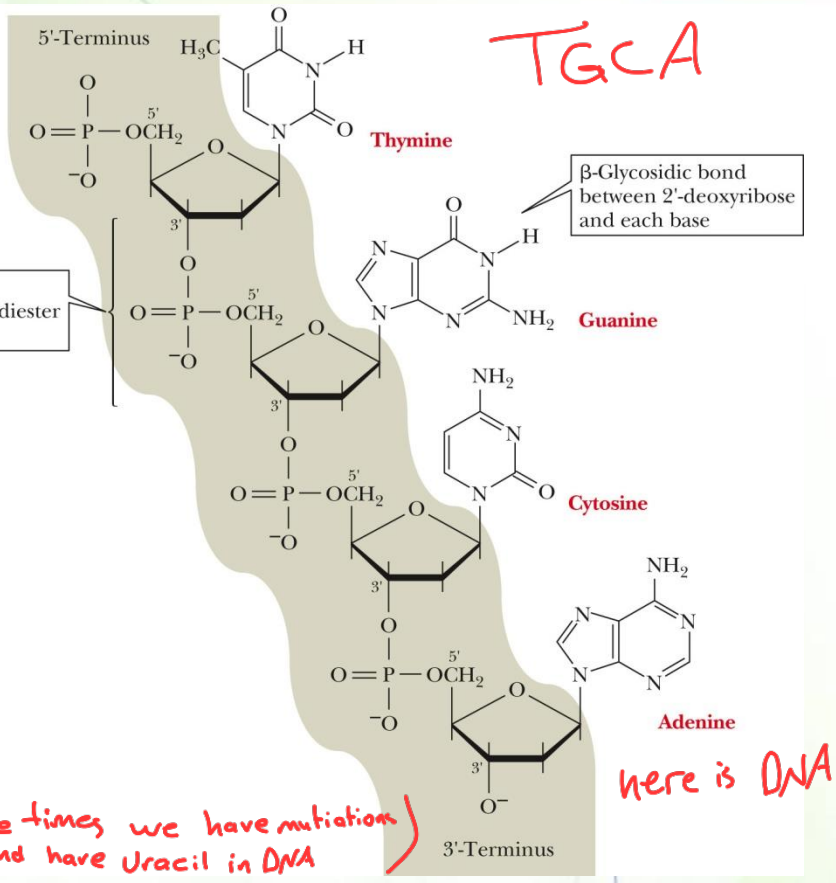
between 3′ and 5′

so addition will be on 3′end

3′ end

Nucleic acid polymers



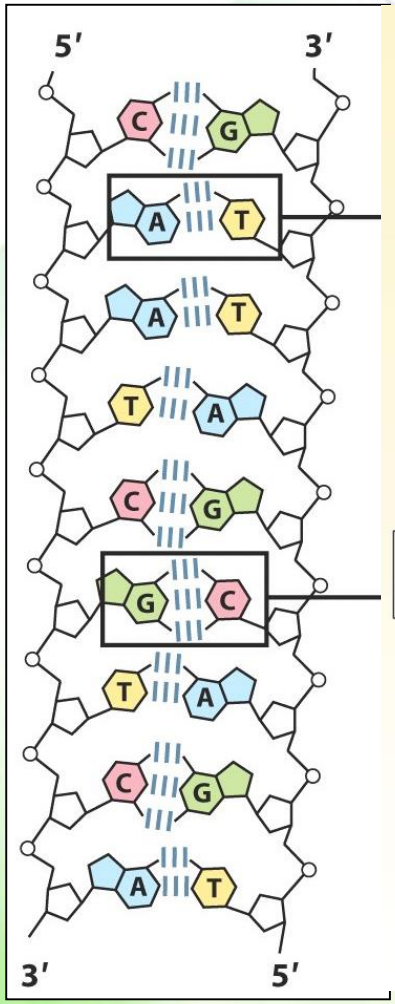


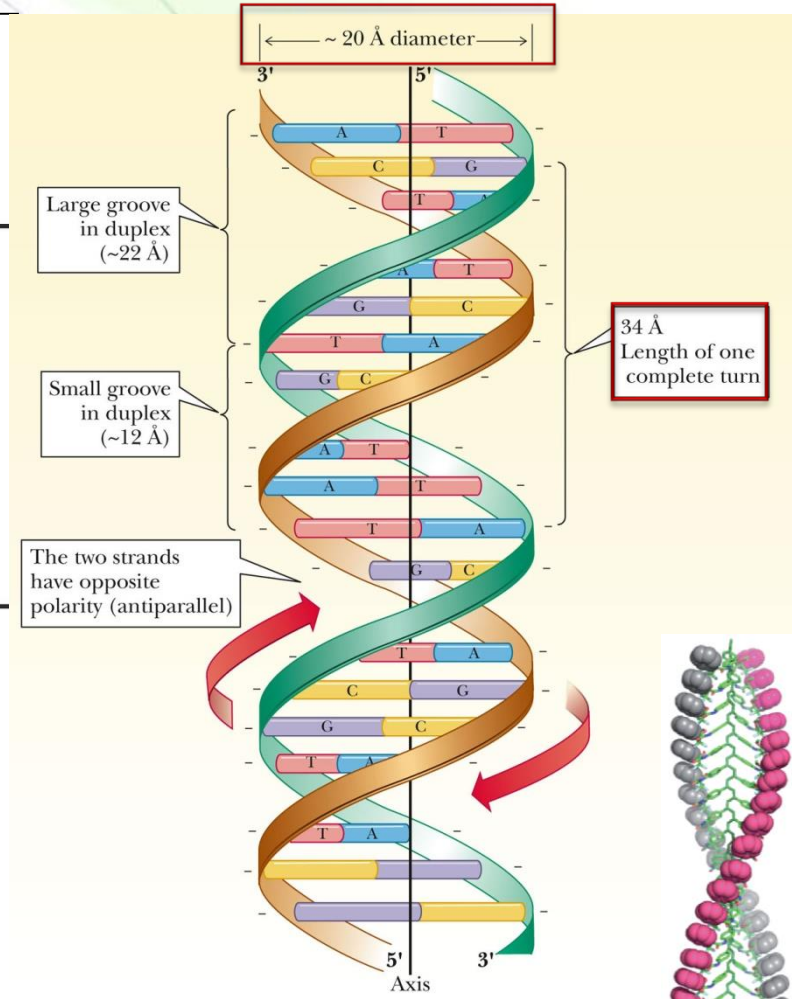
- A letter d can be added to indicate a deoxyribonucleotide residue.
  - for example, dG is substituted for G.
  - The deoxy analogue of a ribooligonucleotide would be d(GACAT).

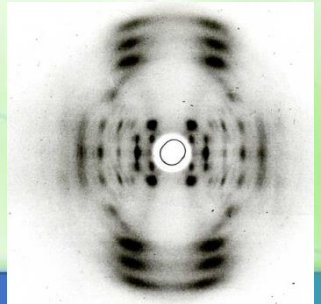
DNA structure

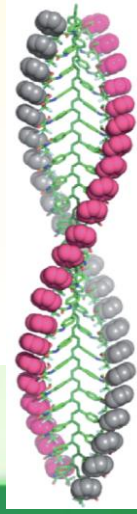
two strands in helical struture

- A double helix
- Specific base-pairing
  - A = T; G = C; Pur = pyr
- Complementary
- Backbone vs. side chains
- Antiparallel
- Stability vs. flexibility
- Groovings

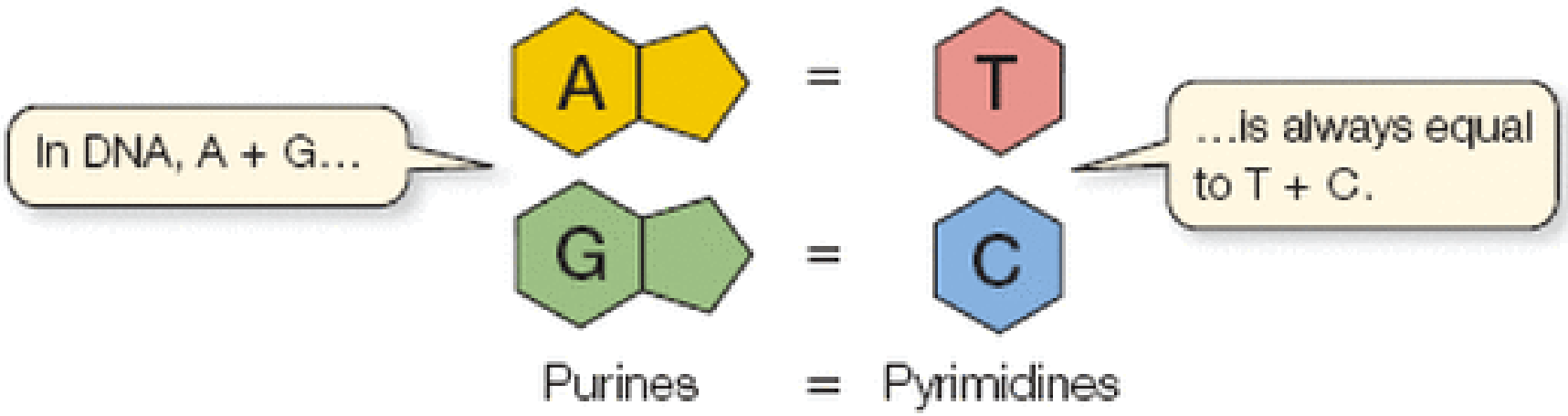








Chargaff's rules

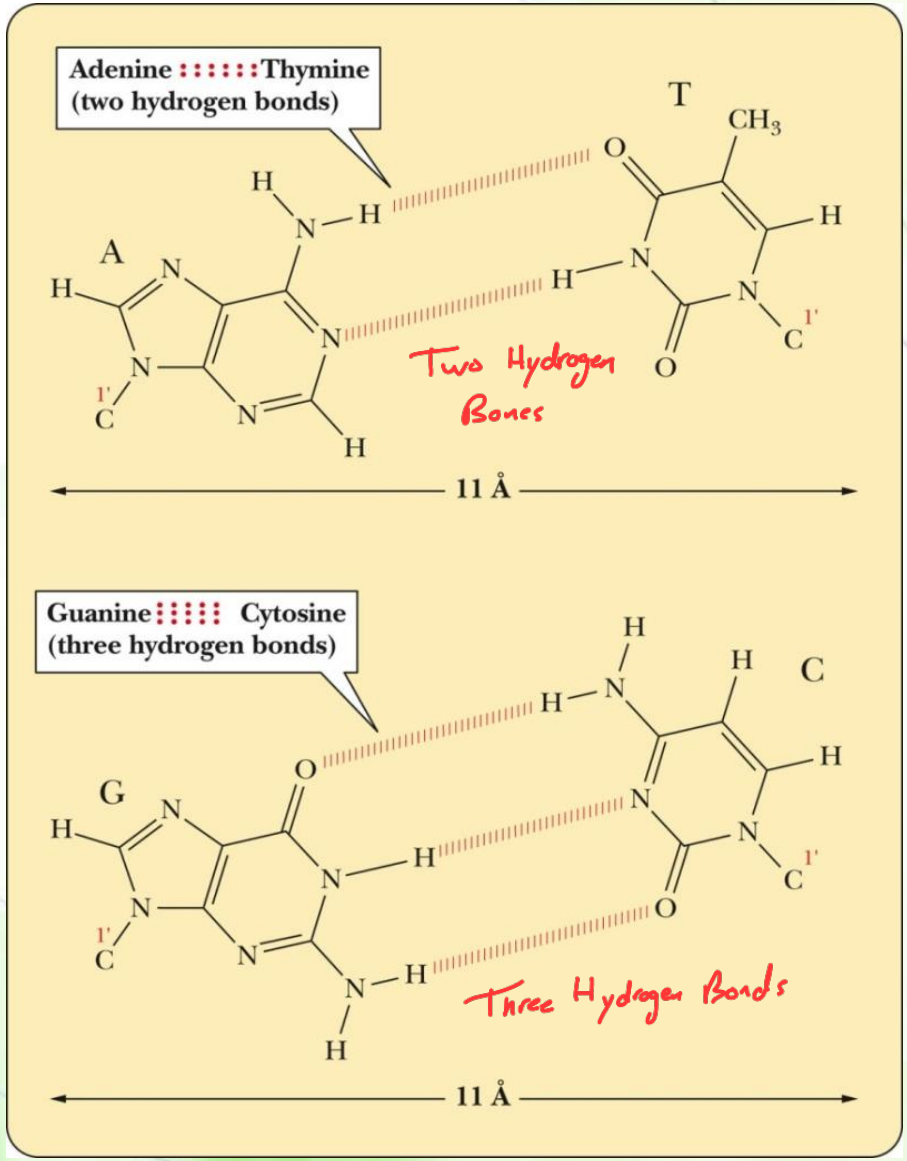


Base pairing

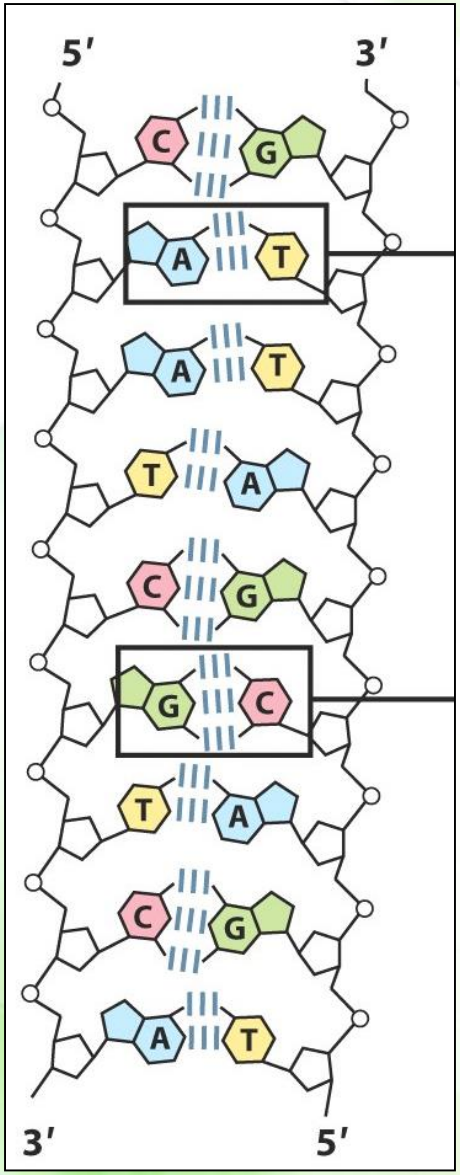
A = T

C ≡ G

So the number of Bonds is matter

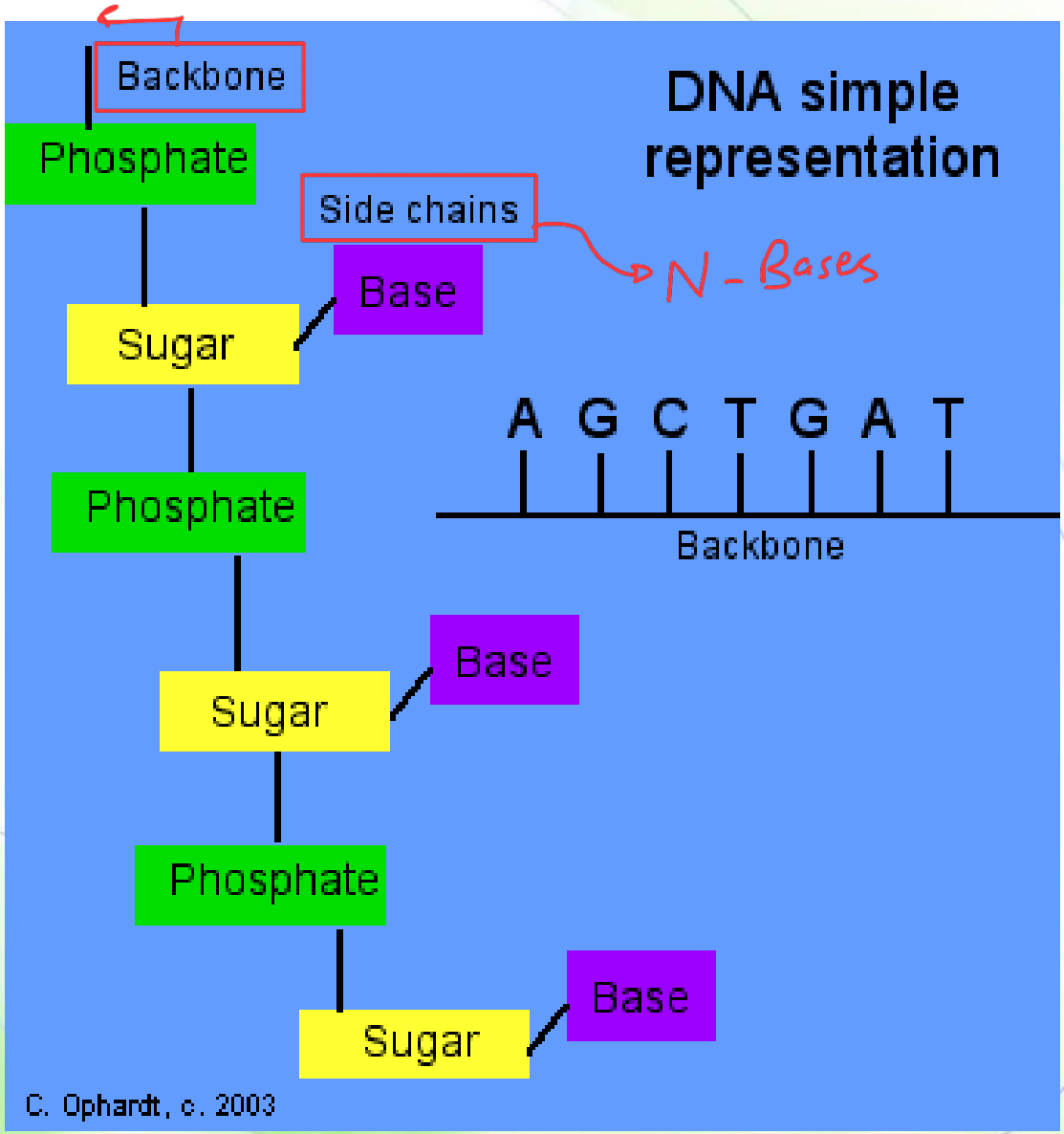


DNA is complementary

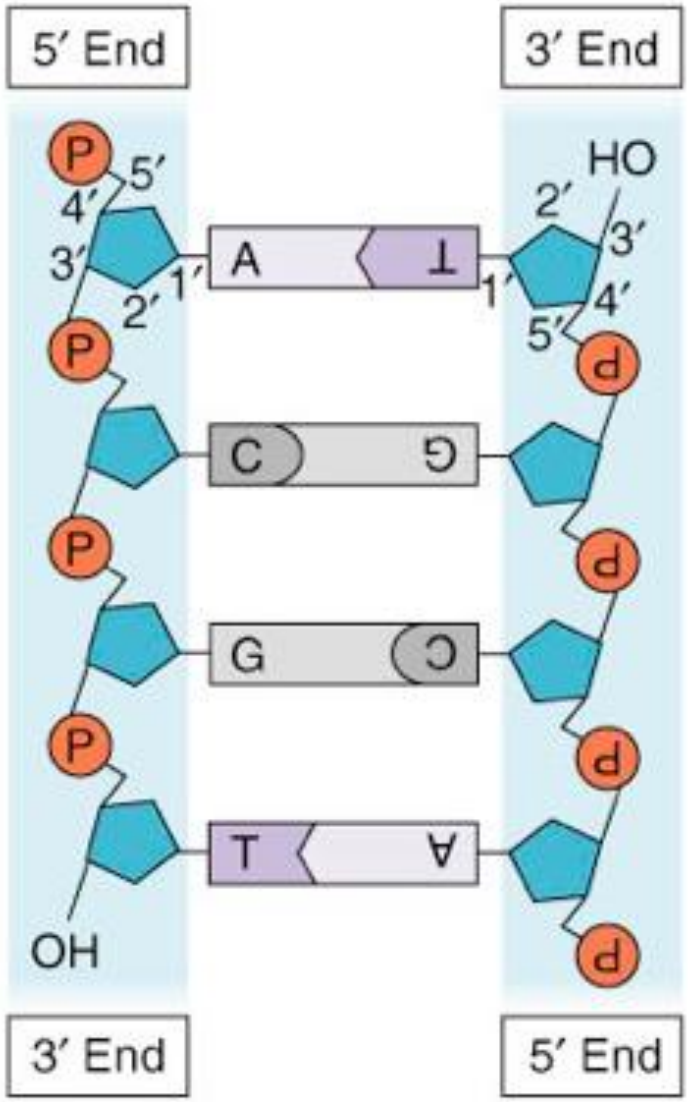


Backbone vs. side chains

P+ Sugar



DNA is anti-parallel



Writing the sequence of nucleic acids

DNA

5' ...A T G G C C T G G A C T T C A... 3'
3' ...T A C C G G A C C T G A A G T... 5'

always we begin with 5'

always 3'

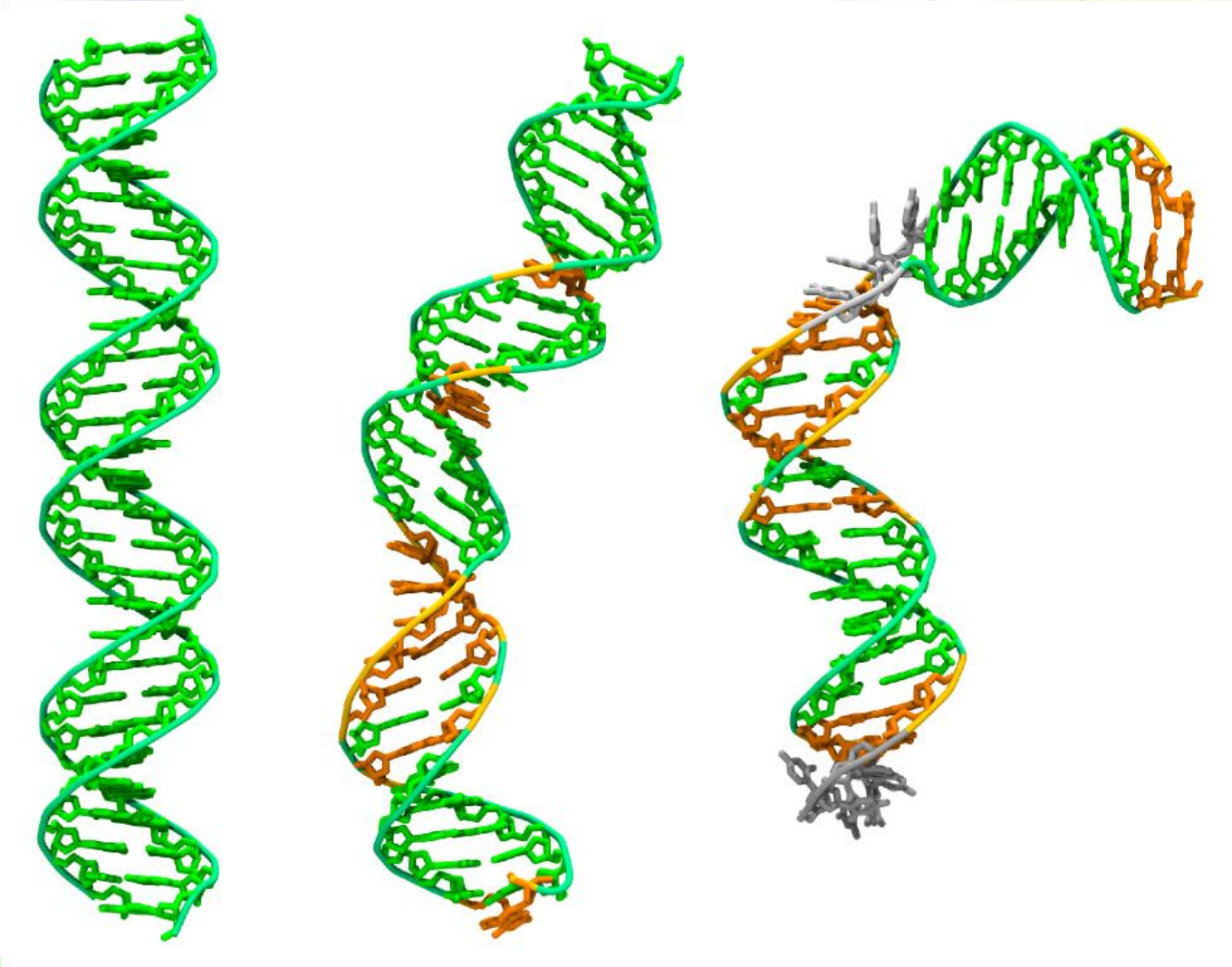
OR A T G G C C T G G A C T T C A. only the Top

RNA

5' ...A U G G C C U G G A C U U C A... 3'

DNA is flexible, yet stable

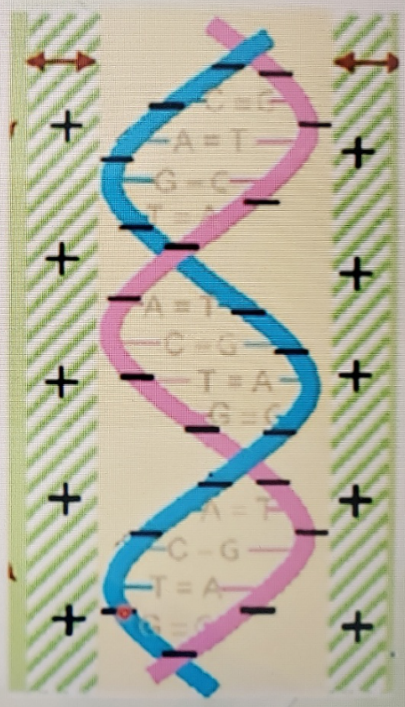
strong

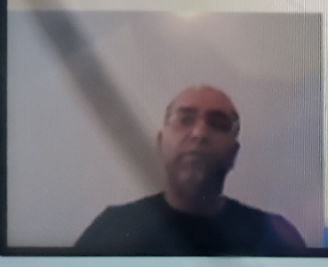


Ions stabilize DNA

- There is so much repulsion among the negative charges of the phosphates.
- Positively charged ions (Na^+ or Mg^{2+}) associate with the phosphate groups.
  - Example: histones

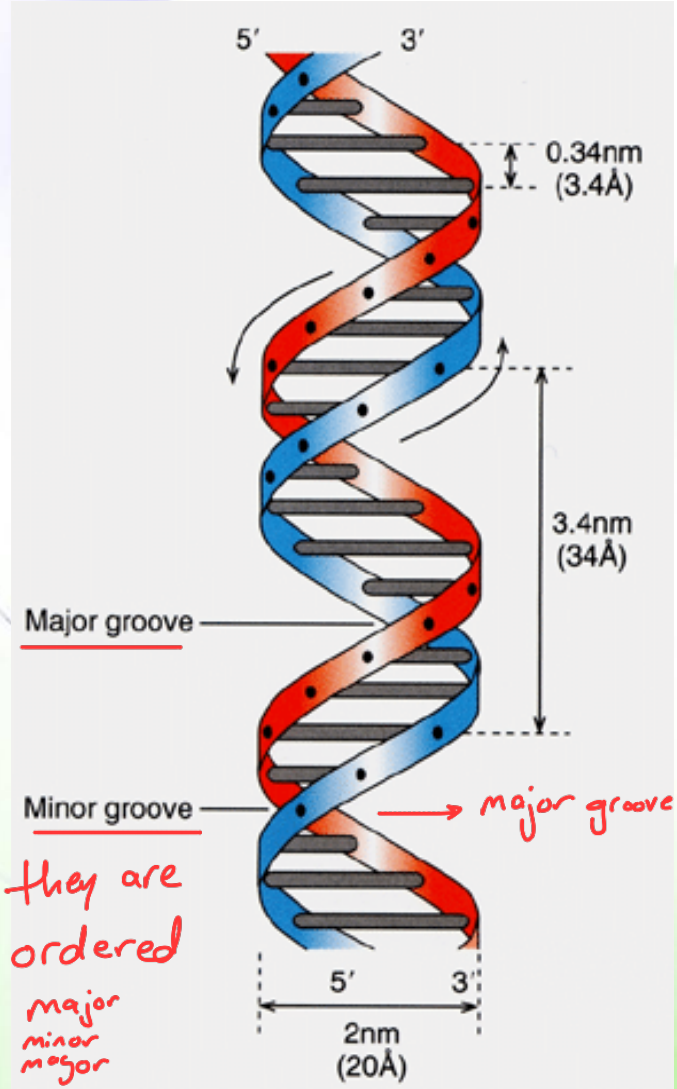
So if we add positive charge we will increase the stability





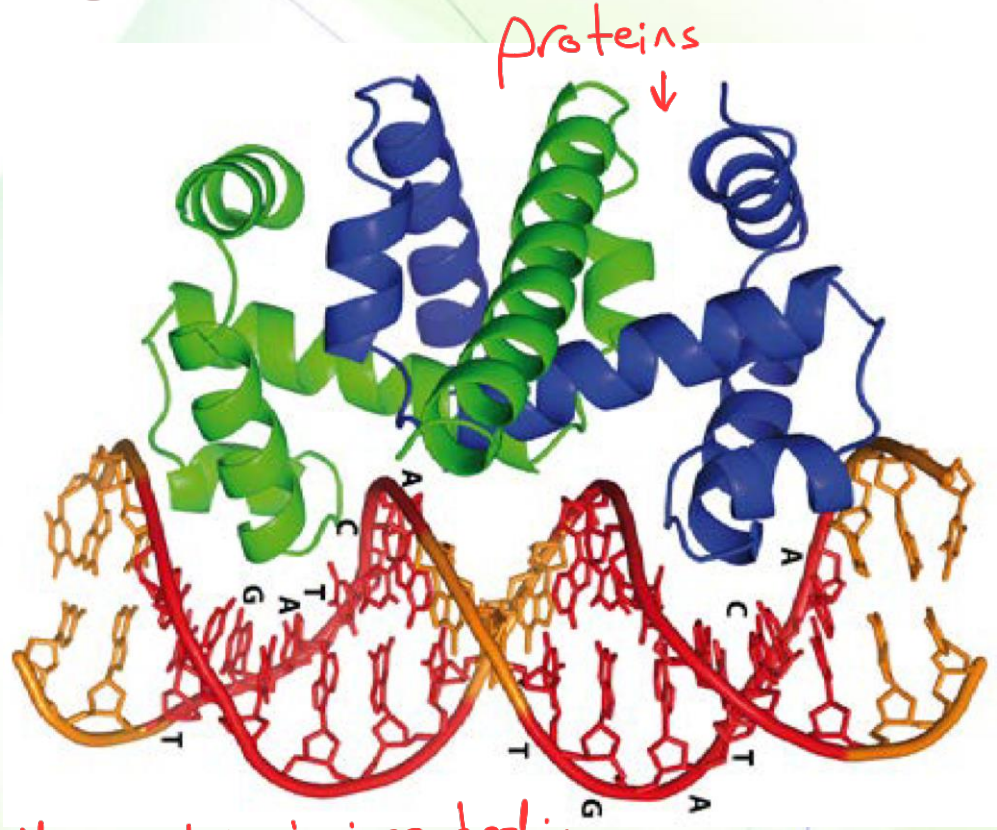
DNA grooves

non-covelant interactions
① electrostatic
② Hydrogen
③ Hydrophobic
④ Van der wals



→ major groove

they are ordered
major
minor
major
minor
⋮

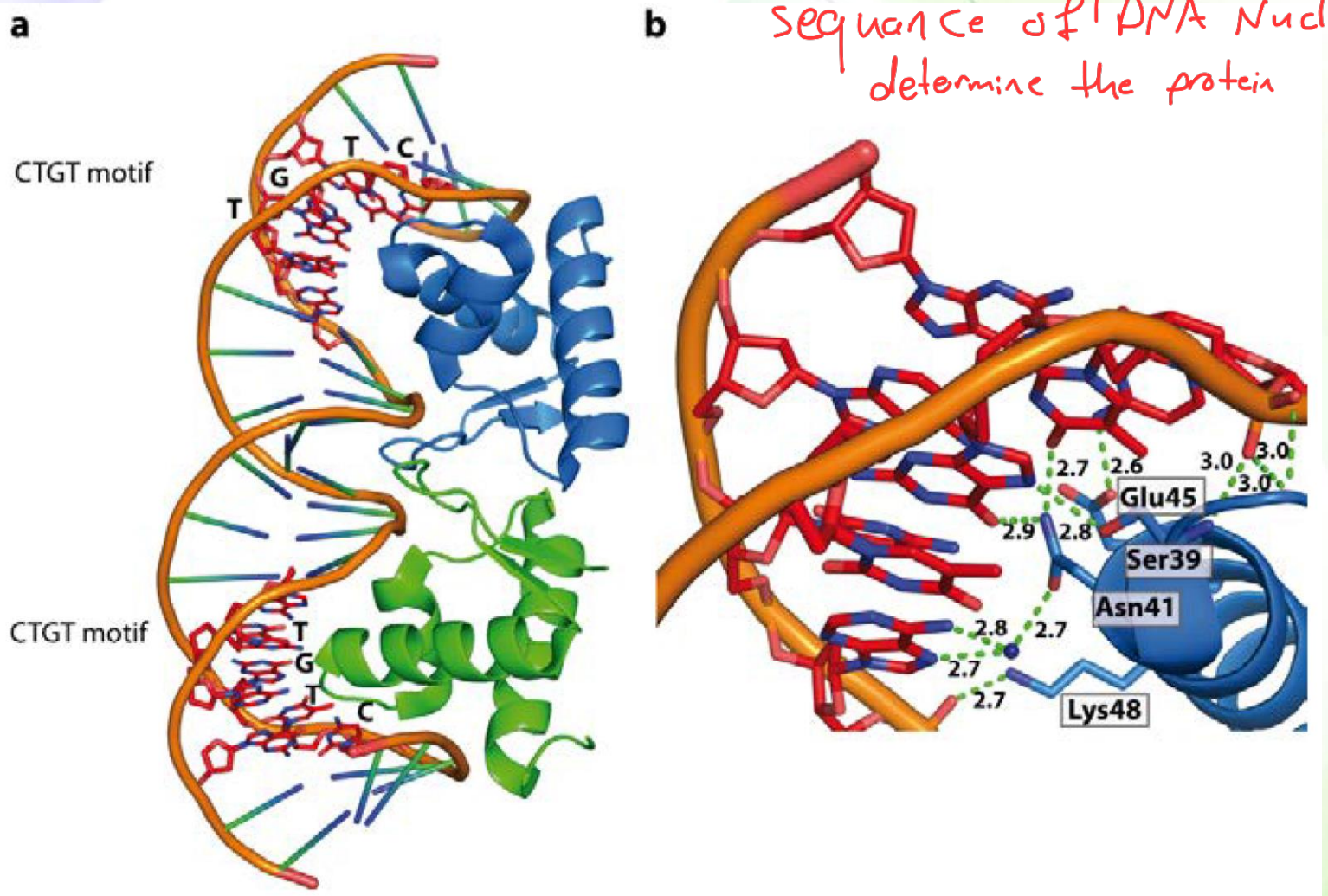


the protein is inserted in major groove because its larger and do interactions between amino acids and nucleotids ↳ non-covelant

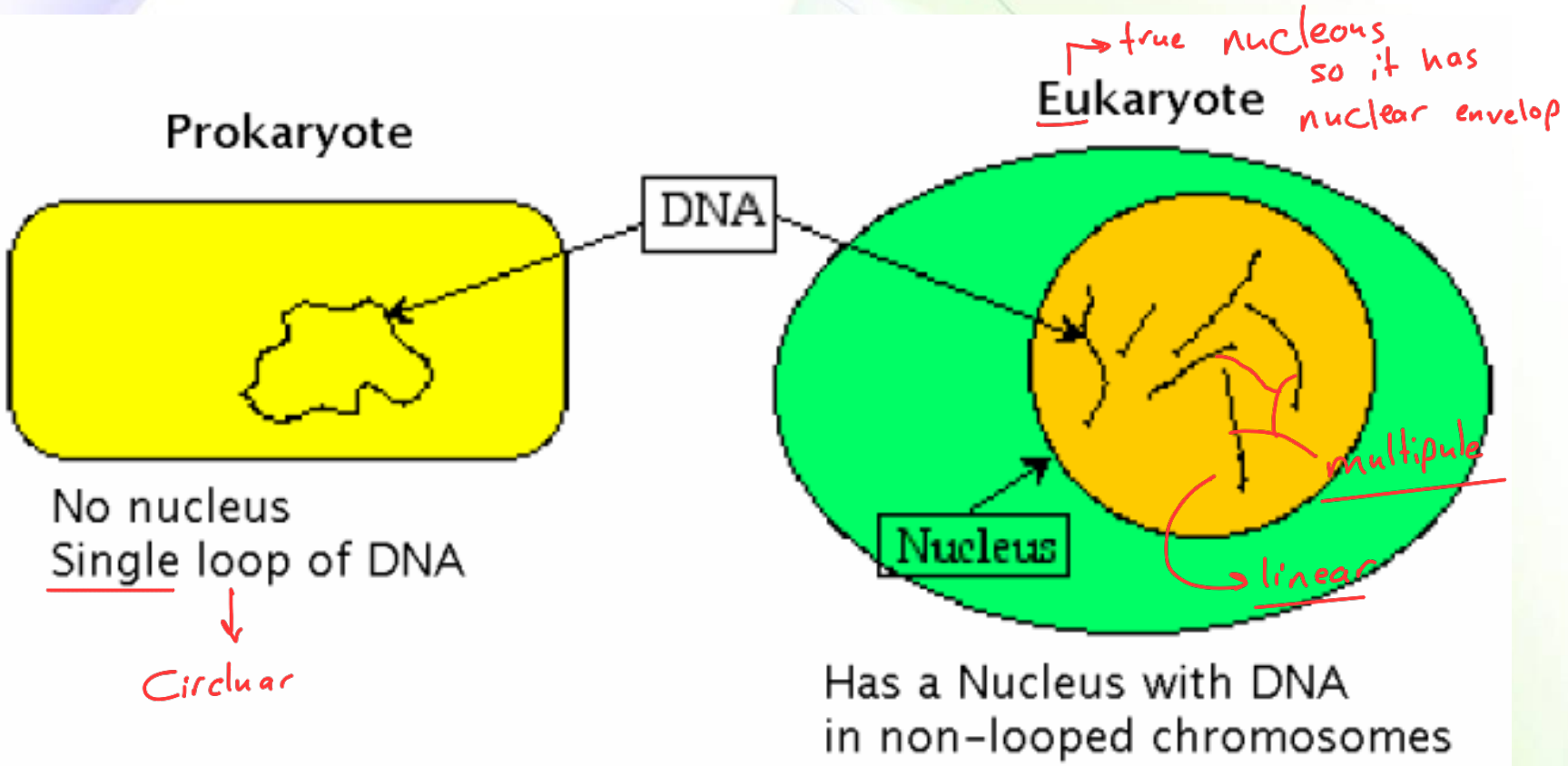
DNA-protein interaction

exposed

sequance of DNA Nucleotids determine the protein



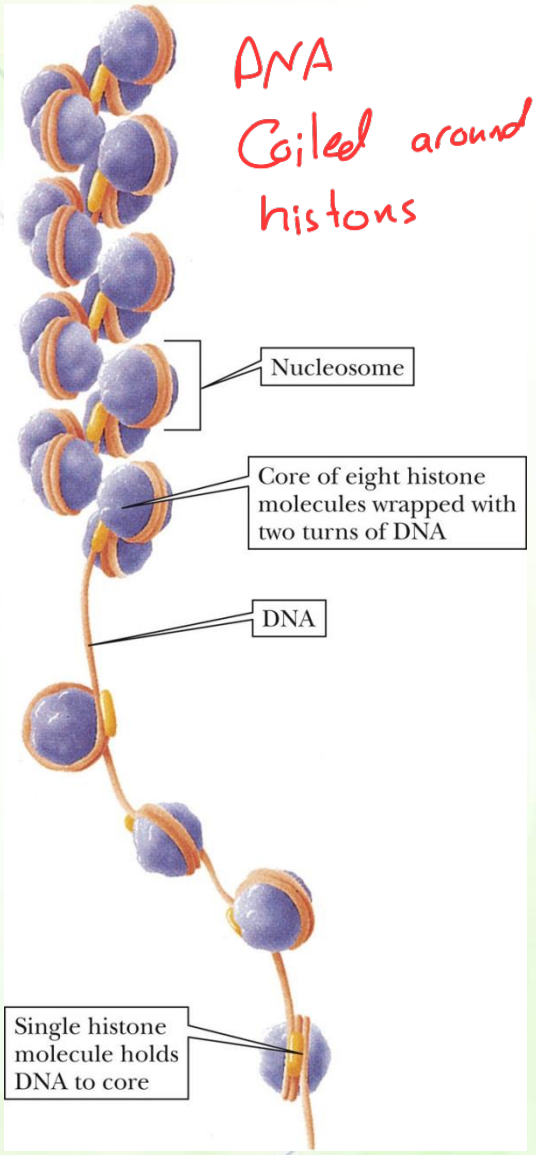
Prokaryotes versus eukaryotes



In eukaryotes…

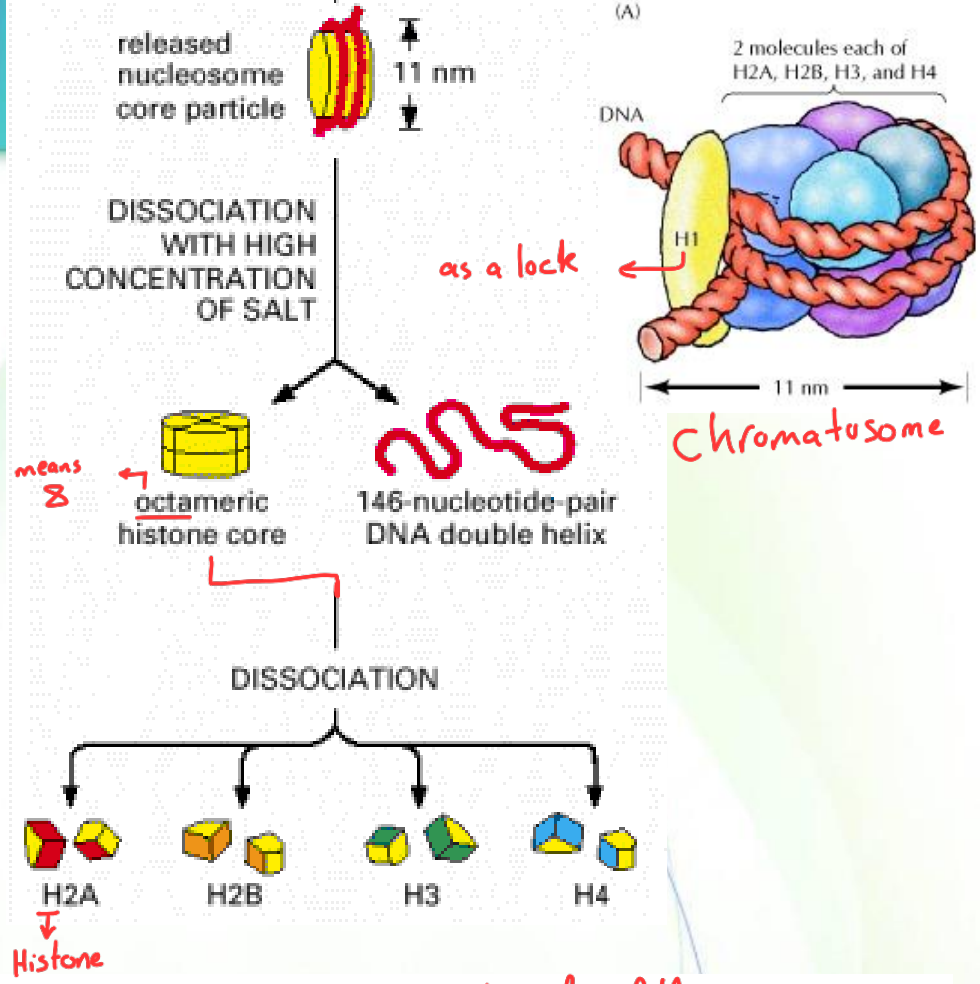
- In eukaryotes, DNA is coiled to package the large DNA.
- Eukaryotic DNA is complexed with a number of proteins, principally histones, which package DNA.
- Chromatin = DNA molecule + proteins.
- The basic structural unit of chromatin is known as a nucleosome.

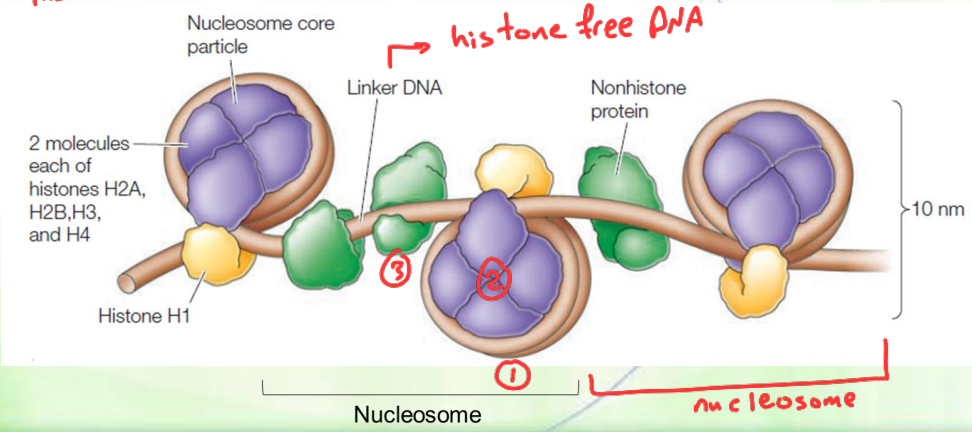
histones with DNA Coiled around it

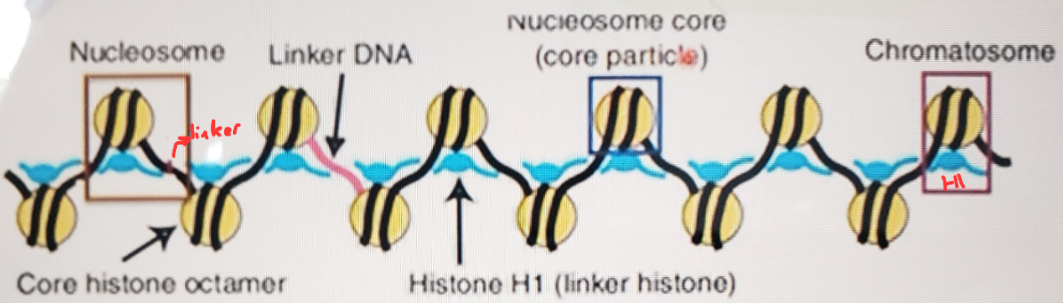


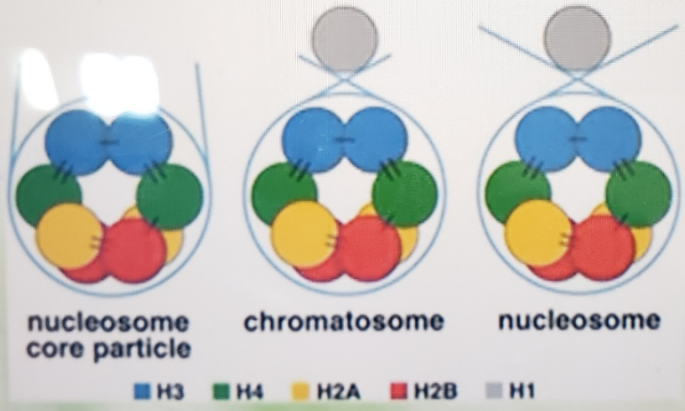
Nucleosomes

- A nucleosome consists of DNA wrapped around a nucleosome core particle, linker DNA, and histone H1.
- The histone core particle is an octamer (two molecules of histones H2A, H2B, H3, and H4) and the DNA wrapped around it.
- A linker DNA connects two nucleosome core particles.
- Histone H1 is bound to the octamer and wrapped DNA (a chromatosome).
- Histones are positively charged facilitating DNA interaction and charge neutralization.

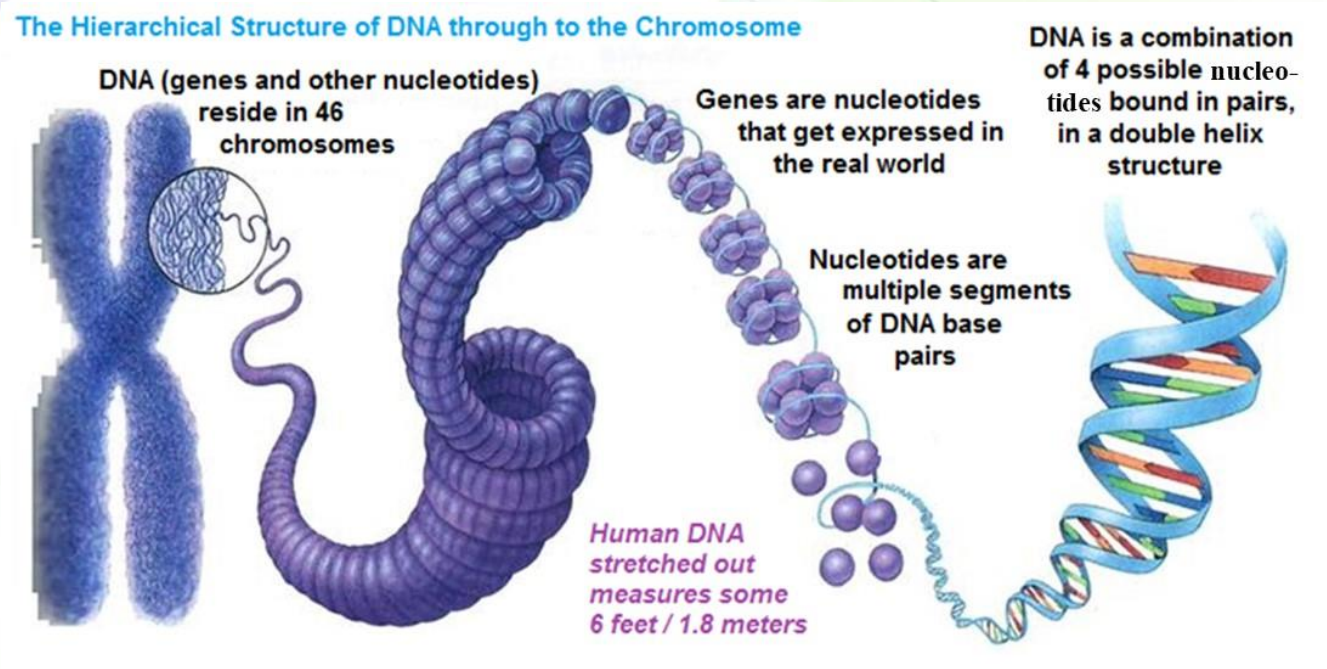


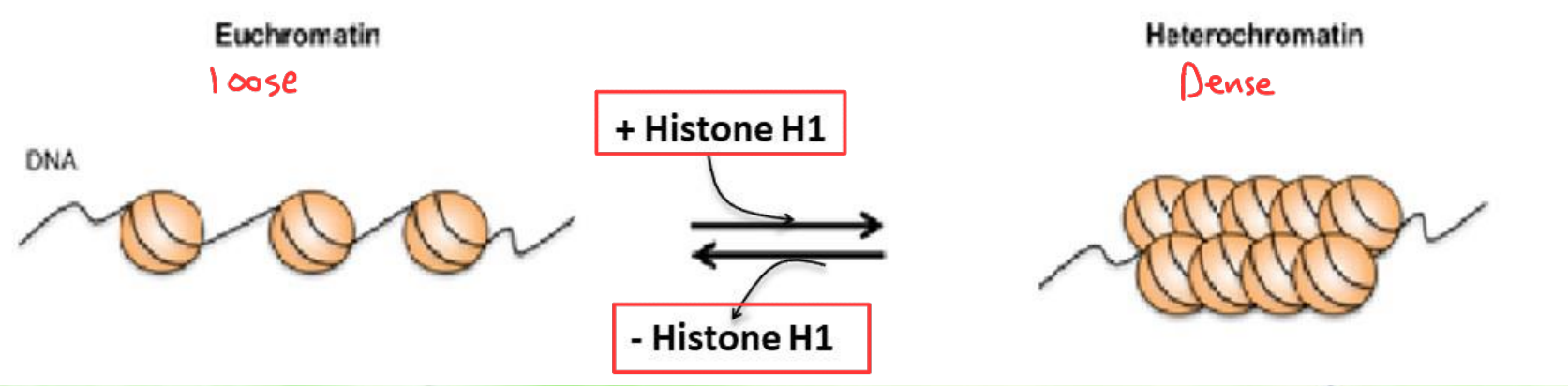



Nucleosome
Linker DNA
Nucleosome core
(core particle)
Chromatosome
linker
H1
Core histone octamer
Histone H1 (linker histone)

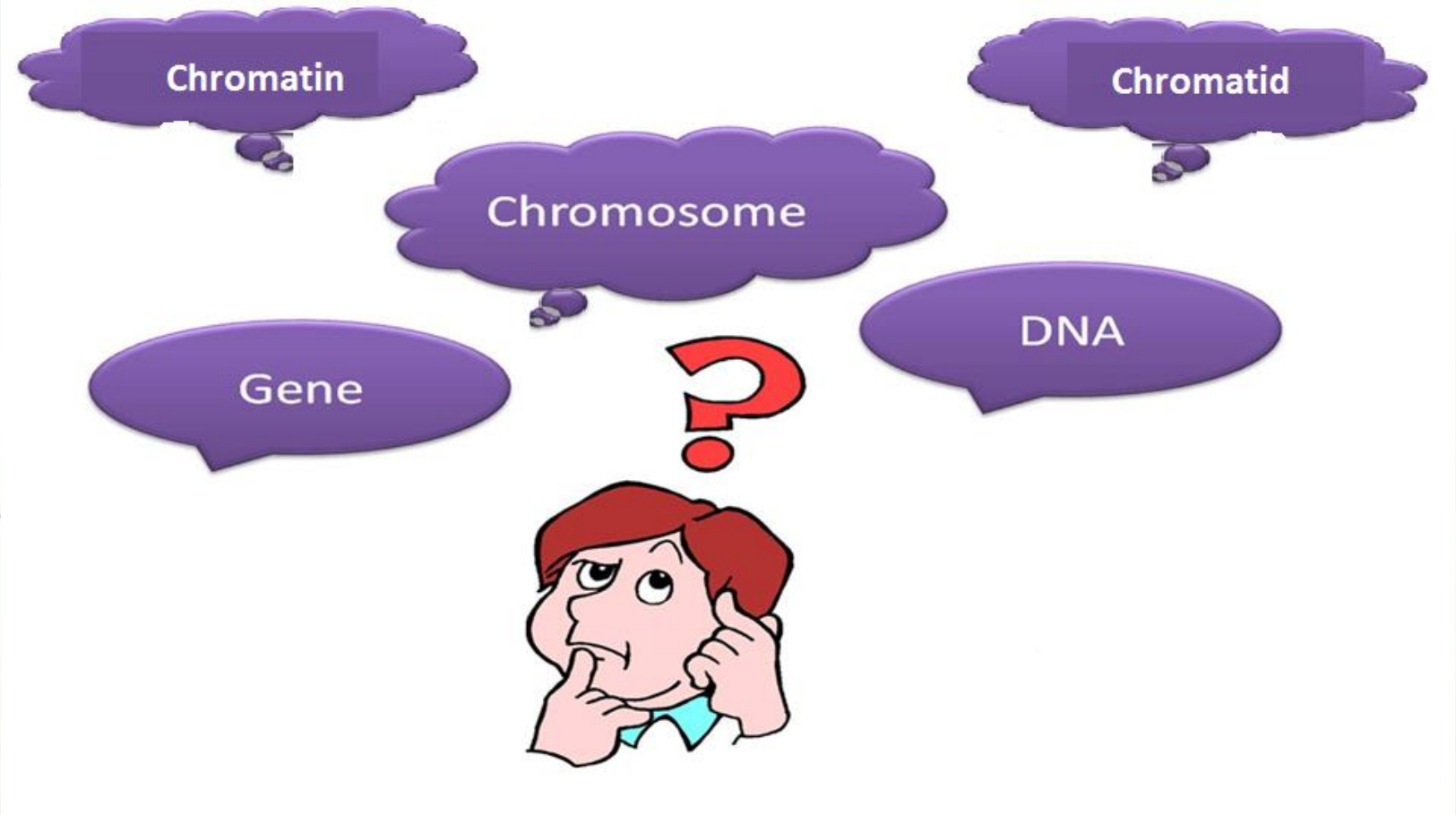

nucleosome
core particle
chromatosome
nucleosome
H3
H4
H2A
H2B
H1

Histones package chromosomes

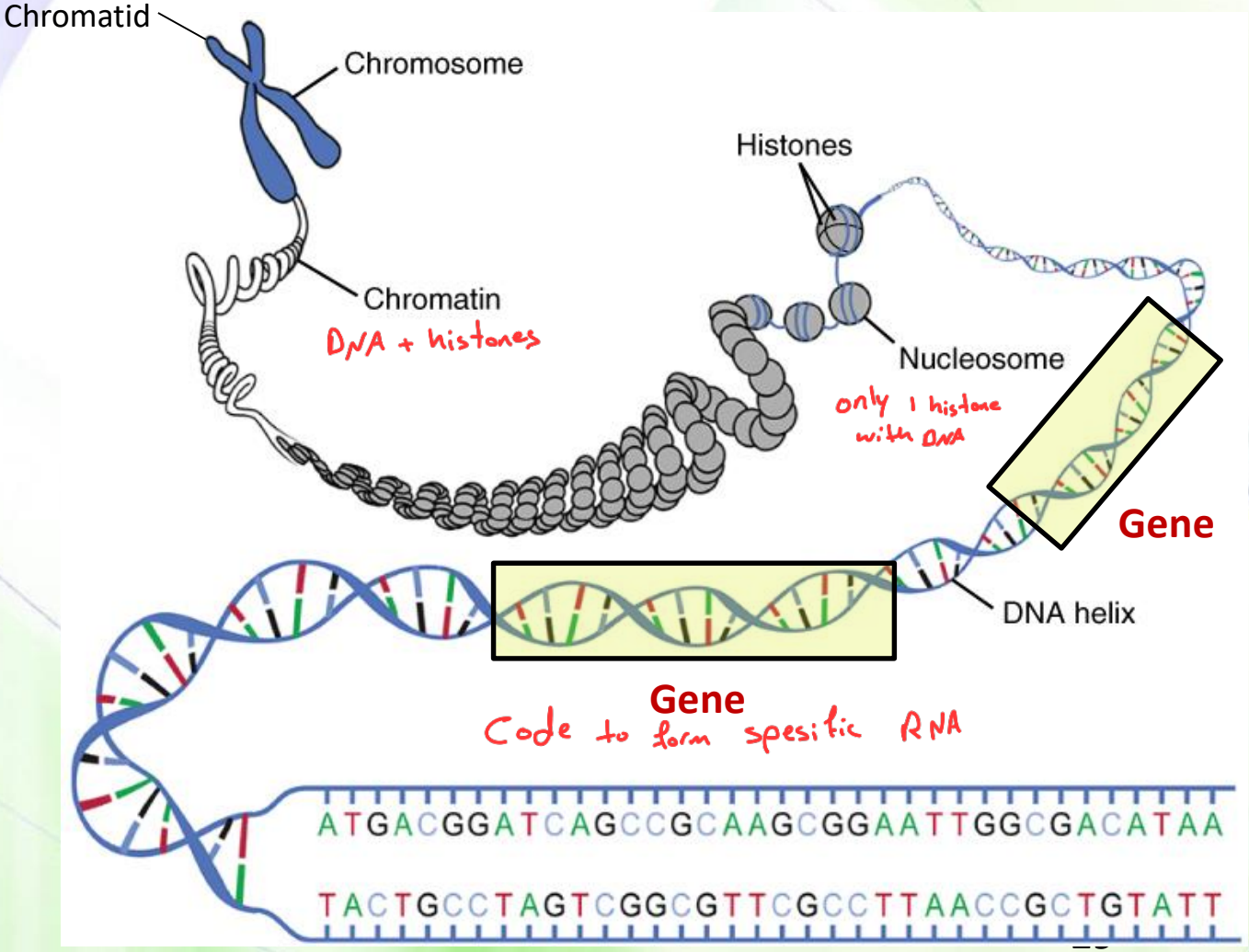




Terms to know



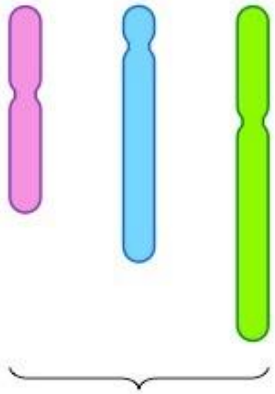
and if it was one chromatin
it is called chromosome too.



Remember…we are diploid

Haploid (n)

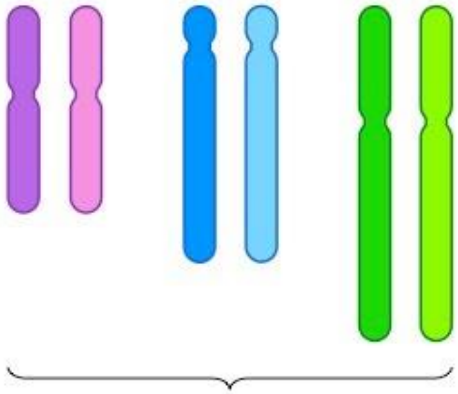
One copy of each chromosome



Three non-homologous chromosomes

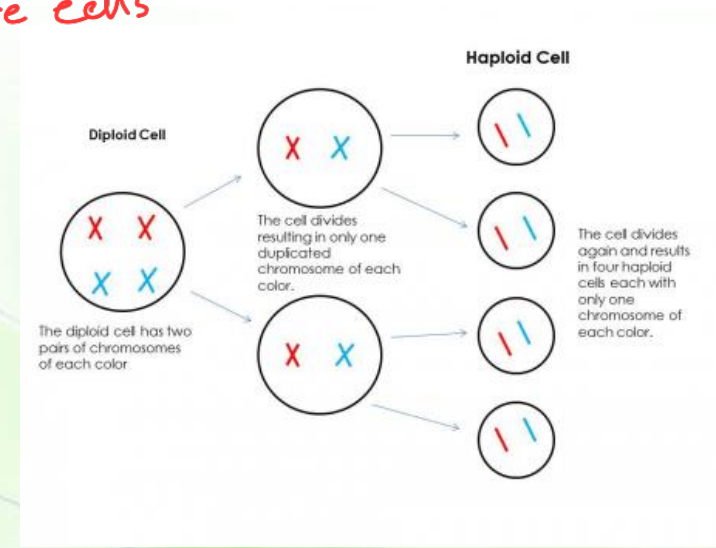
Diploid (2n)

Two copies of each chromosome



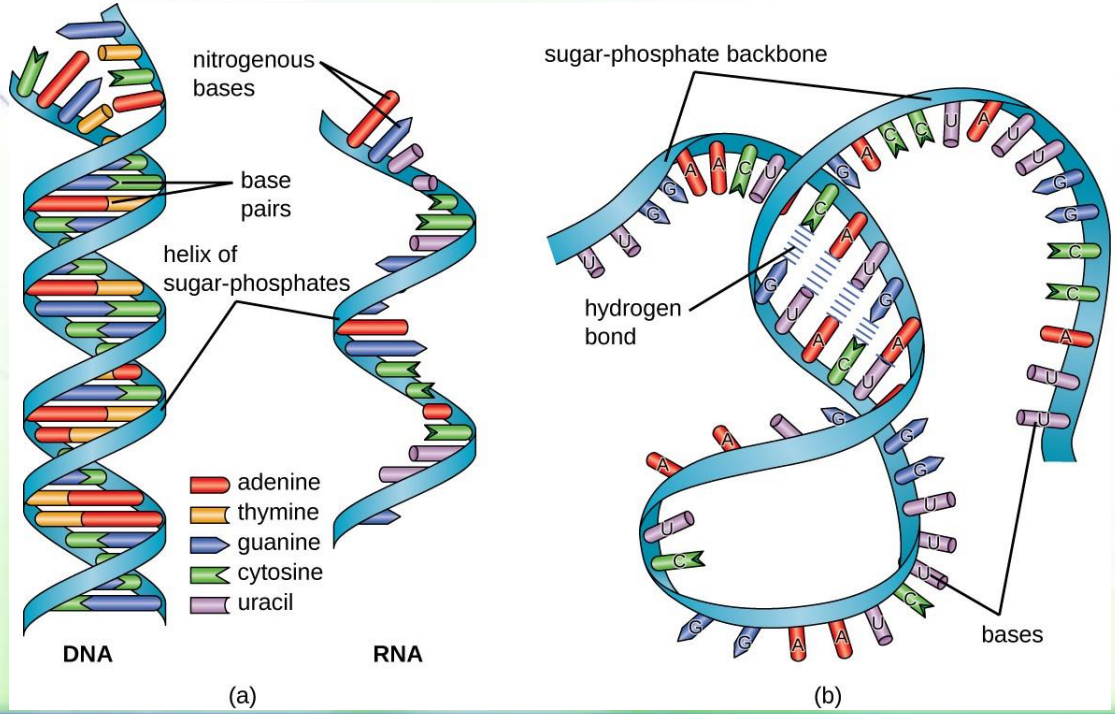
Three pairs of homologous chromosomes (of maternal and paternal origin)

reproductive cells



RNA

- It consists of long, unbranched chains of nucleotides joined by phosphodiester bonds between the 3'-OH of one pentose and the 5'-PO_4^- of the next.
- The pentose unit is a ribose (it is 2-deoxyribose in DNA).
- The pyrimidine bases include uracil and cytosine (thymine and cytosine in DNA).
- In general, RNA is single stranded (DNA is double stranded).



RNA does not have a precise structure, but it can fold on itself forming hydrogen bonds within the same molecule.

when complementry Bases meet each other

Types of RNA

Symbol	Non-Coding RNAs	Functions
* tRNA	Transfer RNA	mRNA translation (structural)
* rRNA	Ribosomal RNA	mRNA translation (structural)
* miRNA	micro RNAs	Post-transcriptional transposon repression
piRNA	Piwi-interacting RNA	DNA methylation, transposon repression
* siRNA	Short interfering RNA	RNA interference
snoRNA	Small nucleolar RNAs	RNA modification, rRNA processing
PROMPT's	Promoter upstream transcripts	Associated with chromatin changes
tiRNAs	Transcripton initation RNAs	Epigenetic regulation
lincRNAs	Long intergenic ncRNA	Epigenetic regulators of transcription
rasiRNA	Repeat associated small interfering RNA	Involved in the RNA interference (RNAi) pathway
eRNA	Enhancer-like ncRNA	Transcriptional gene activation
T-UCRs	Transcribed ultraconserved regions	Regulation of miRNA and mRNA levels
NATs	Natural antisense transcripts	mRNA stability
PALRs	Promoter-associated long RNAs	Chromatin changes
tasiRNA	Trans-acting siRNA	Represses gene expression
* lncRNA	Long noncoding RNA	Regulation of gene transcription