



Structure of nucleic acids

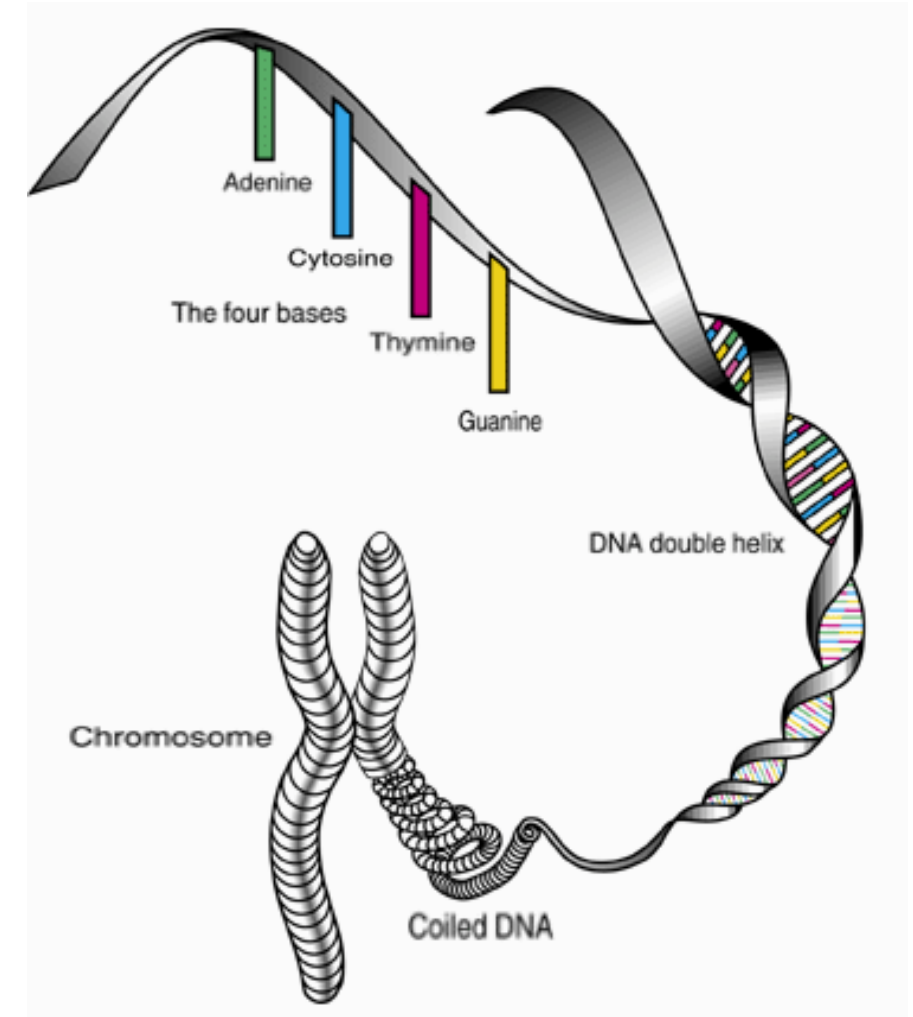
Prof. Mamoun Ahram

https://cdn.wou.edu/chemistry/files/2020/06/best-DNA-animation-ever.mp4?_=1

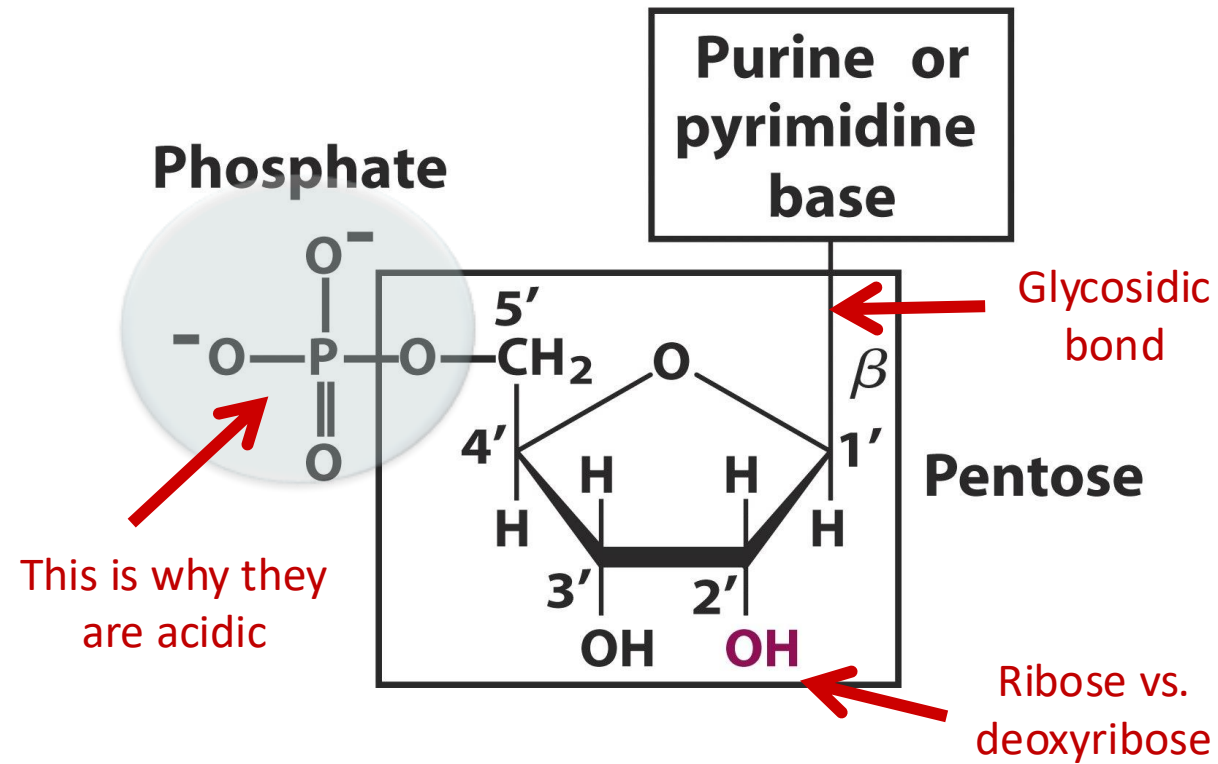
Nucleic acids



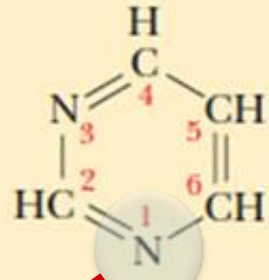
- There are 2 types of nucleic acids:
 - Deoxyribonucleic acid (DNA)
 - Ribonucleic acid (RNA)
- The primary structure of nucleic acids is linear polymers of nucleotides (monomers) bound to each other via phosphodiester bonds.
- DNA is coiled and can be associated with proteins forming chromosomes.



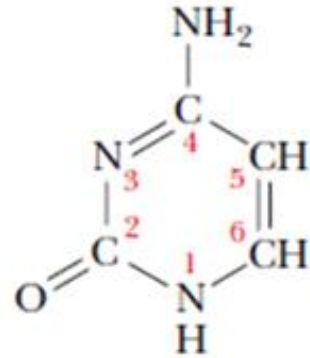
Chemical composition and bonds of nucleotides



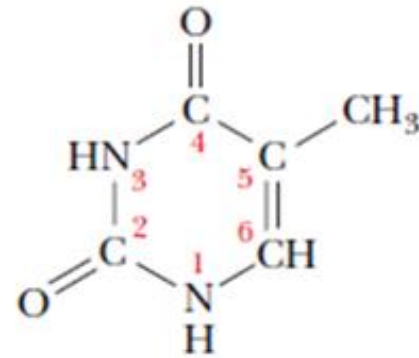
Nitrogenous bases



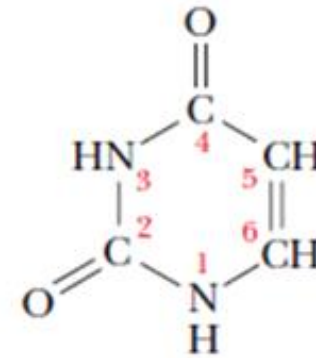
Pyrimidine



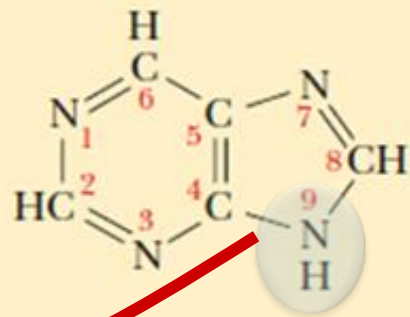
Cytosine
(in DNA & RNA)



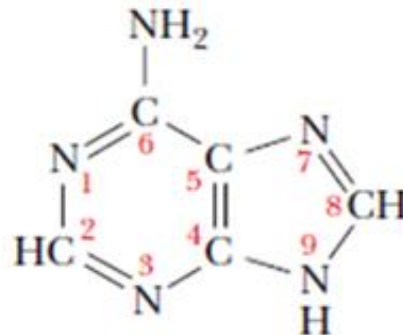
Thymine
(in DNA)



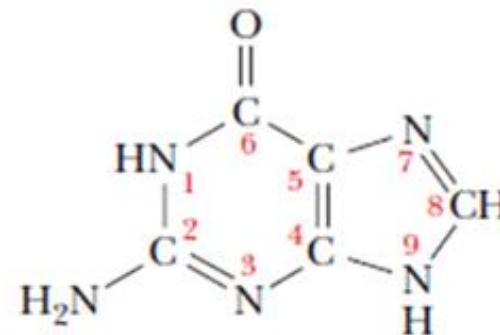
Uracil
(in RNA)



Purine

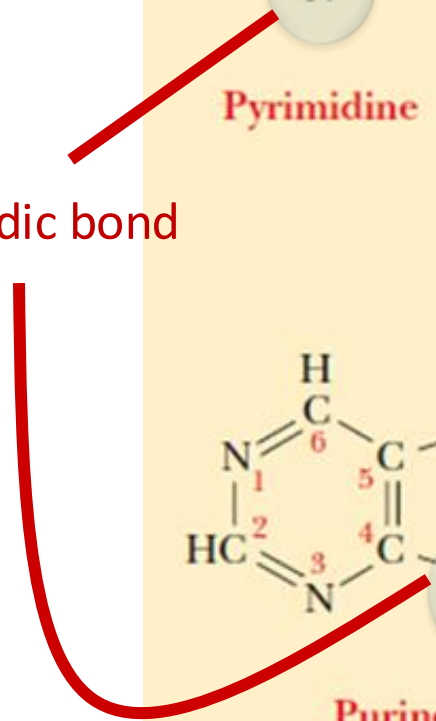


Adenine
(in DNA & RNA)



Guanine
(in DNA & RNA)

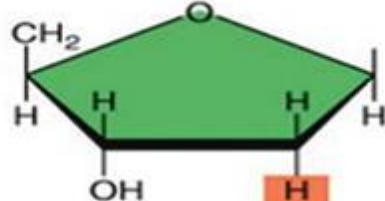
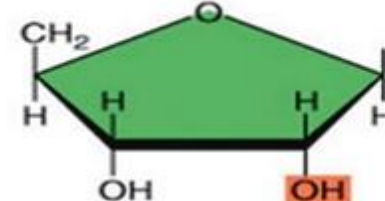
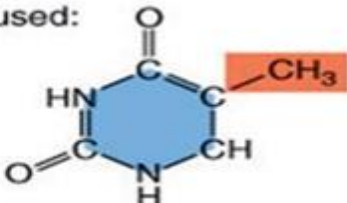
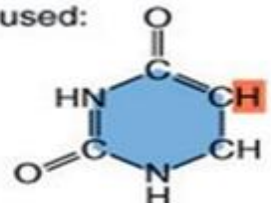
Glycosidic bond



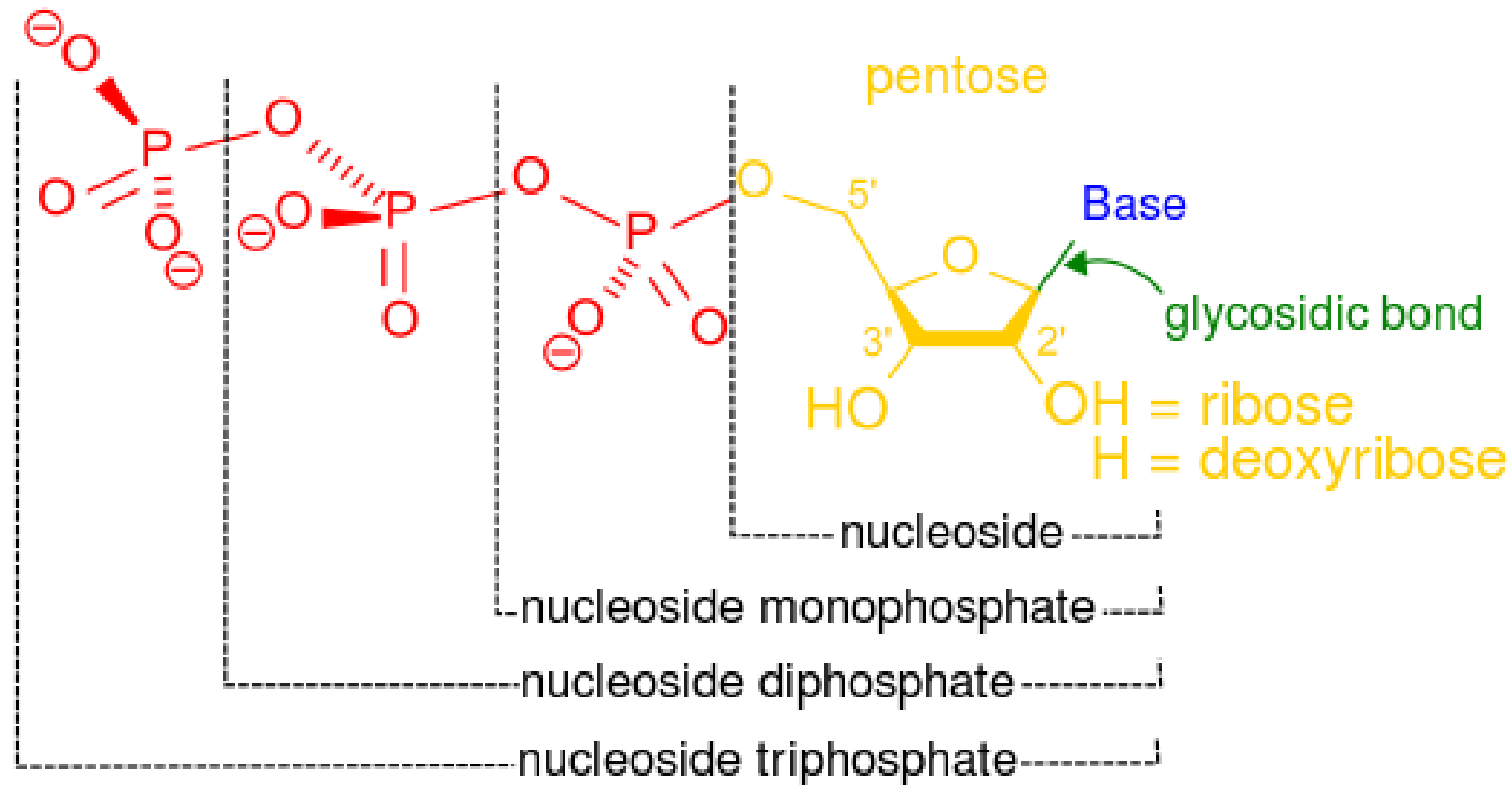
In prokaryotes and eukaryotes (not viruses)



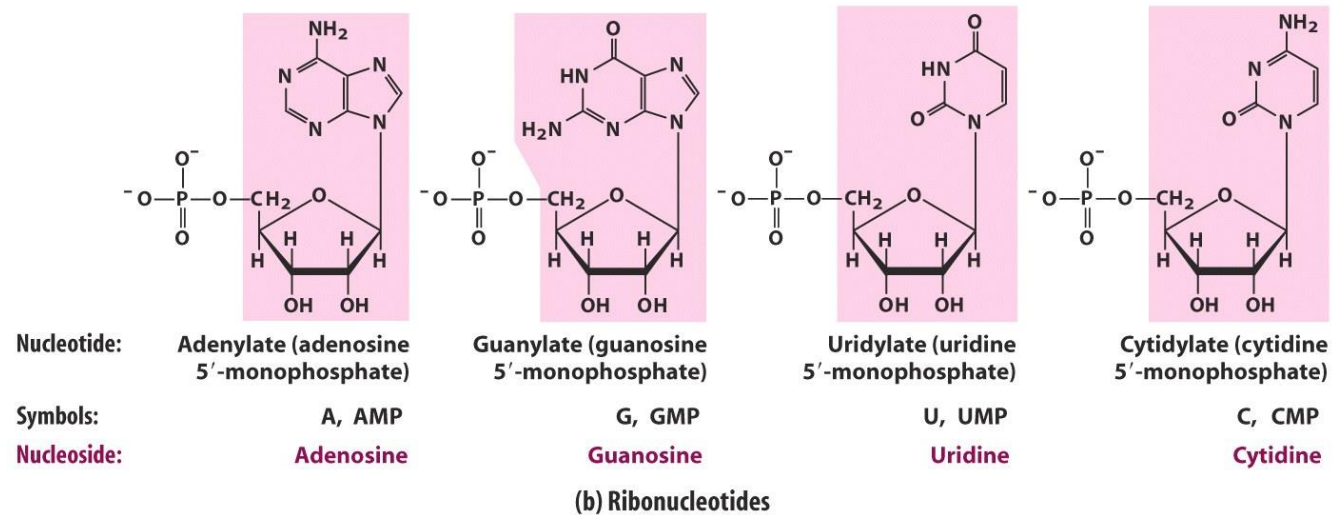
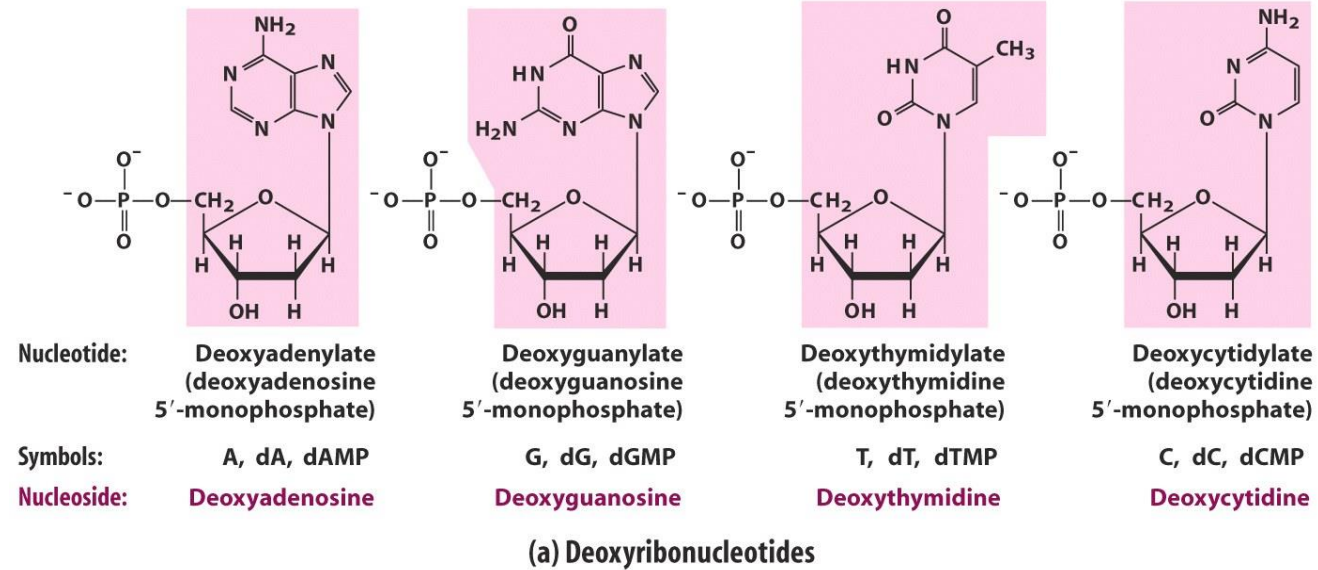
DNA vs. RNA

 <u>Double-stranded</u>	 <u>Generally single-stranded</u>
 <u>Deoxyribose as the sugar</u>	 <u>Ribose as the sugar</u>
Bases used:  <u>Thymine (T)</u> Cytosine (C) Adenine (A) Guanine (G)	Bases used:  <u>Uracil (U)</u> Cytosine (C) Adenine (A) Guanine (G)

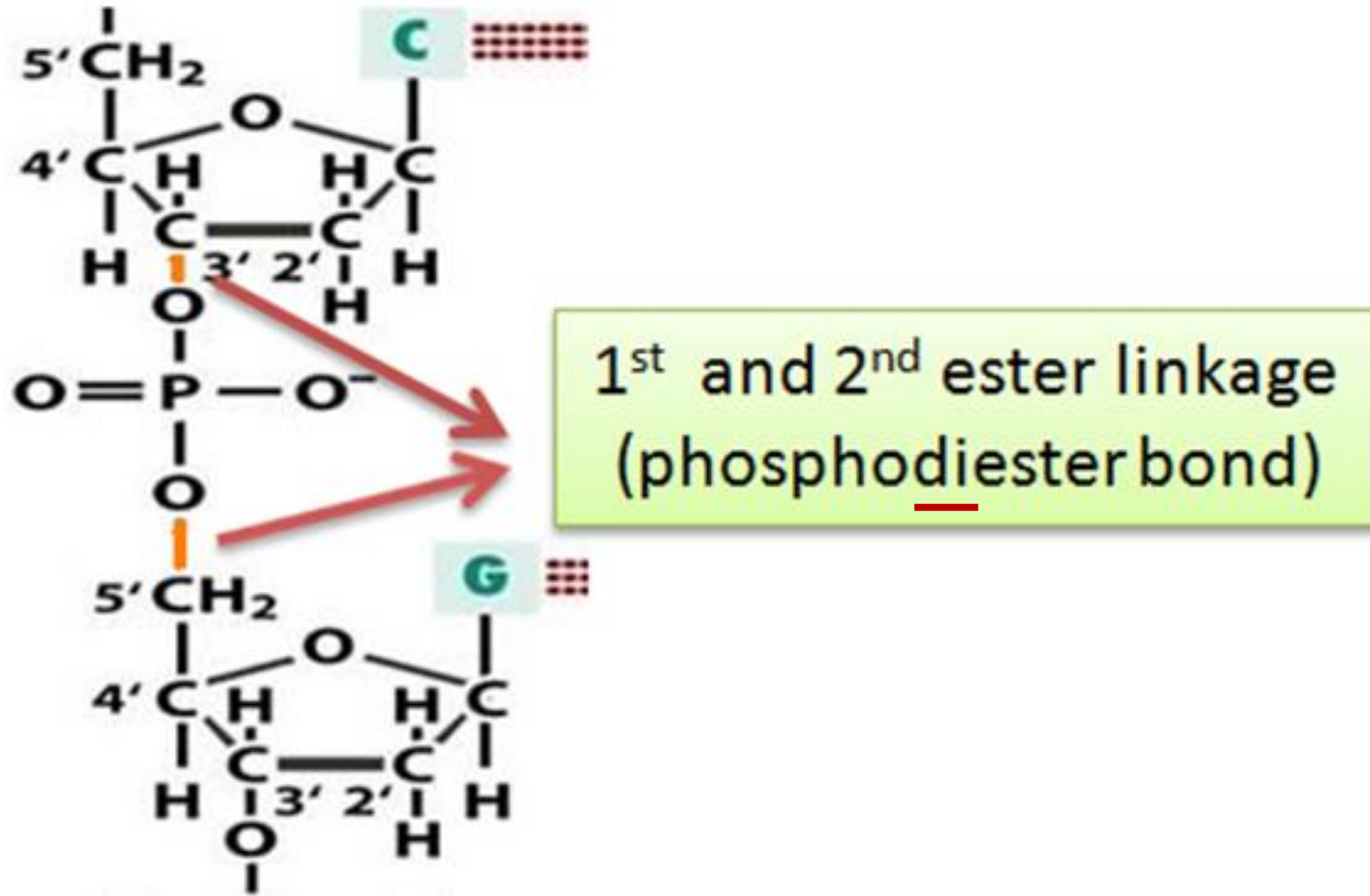
Nucleotides vs. Nucleosides



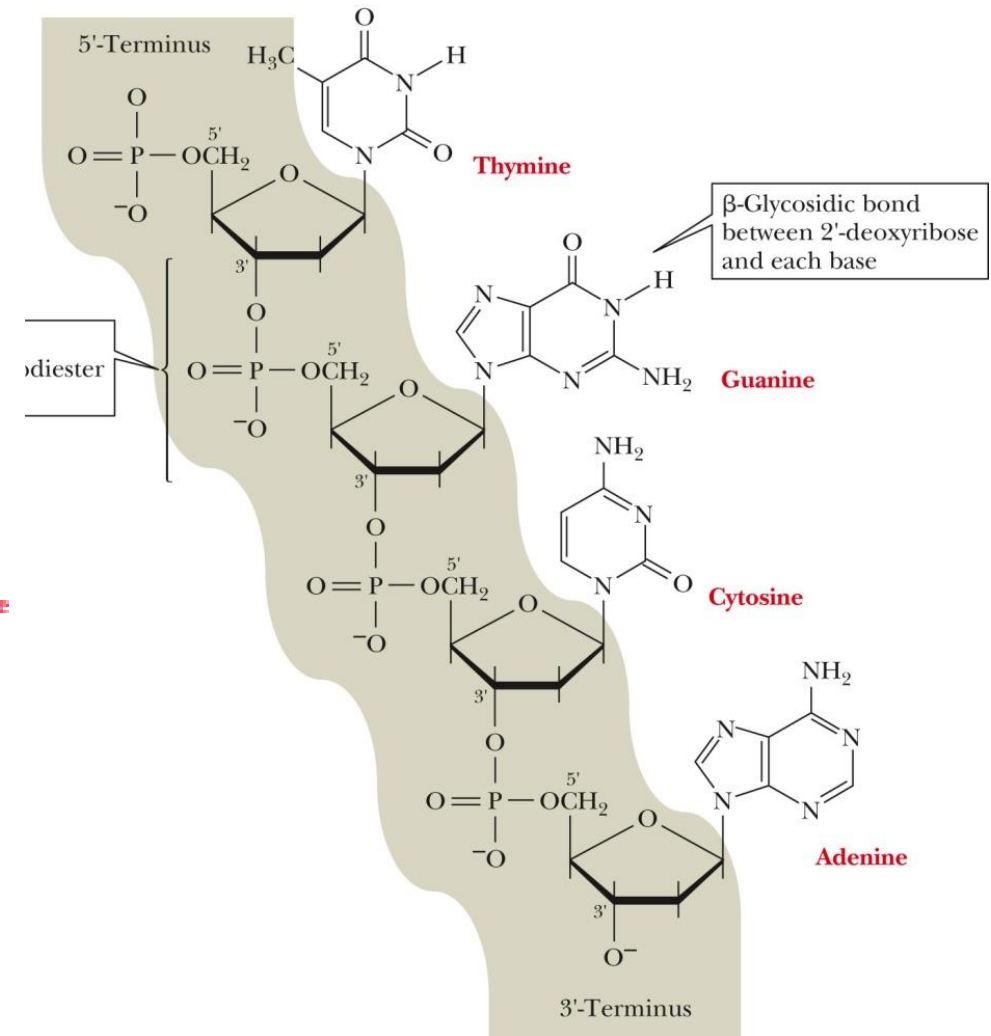
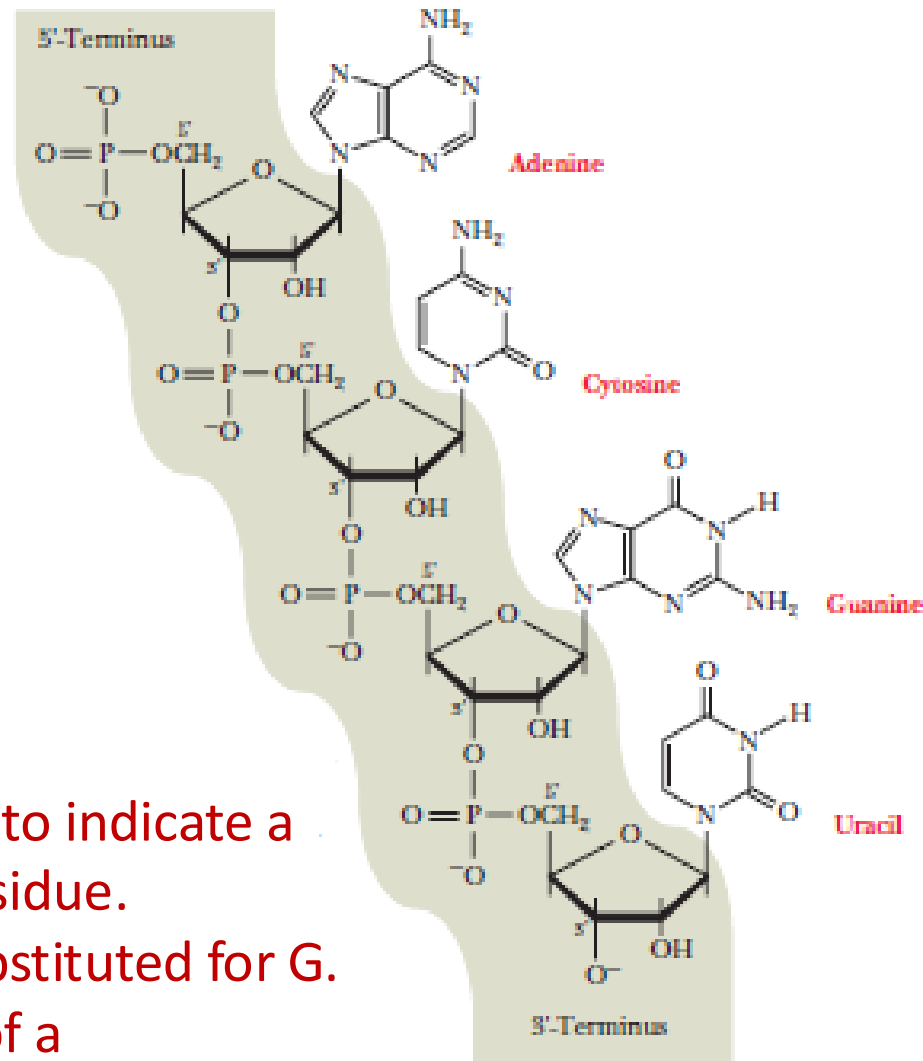
Nucleotides vs. Nucleosides



Formation of a nucleic acid polymer



Nucleic acid polymers

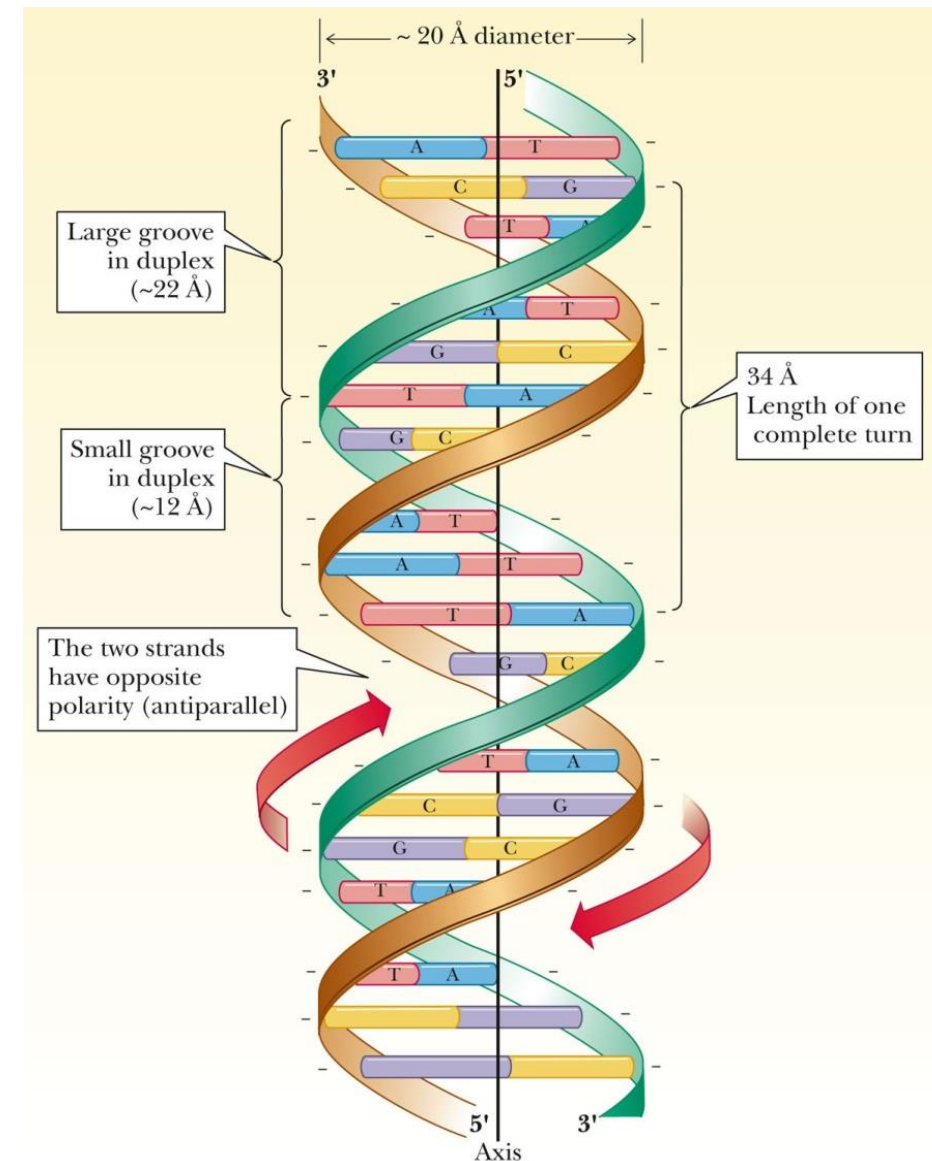
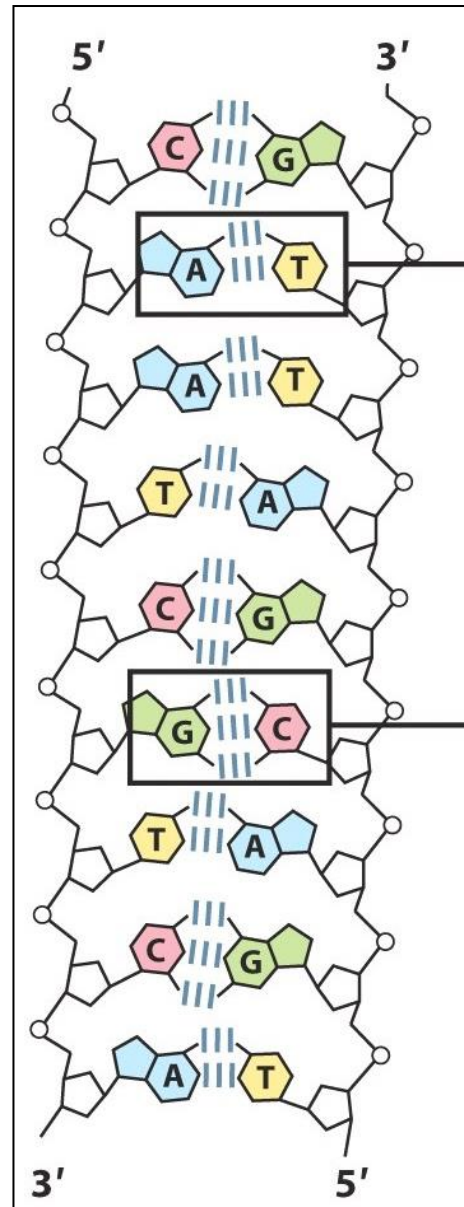
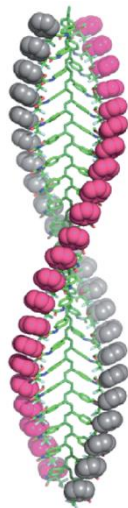
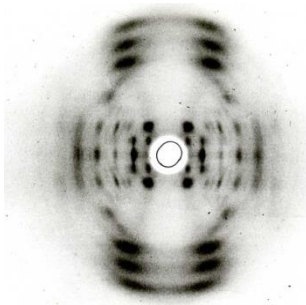


- A letter d can be added to indicate a deoxyribonucleotide residue.
- for example, dG is substituted for G.
- The deoxy analogue of a ribooligonucleotide would be d(GACAT).

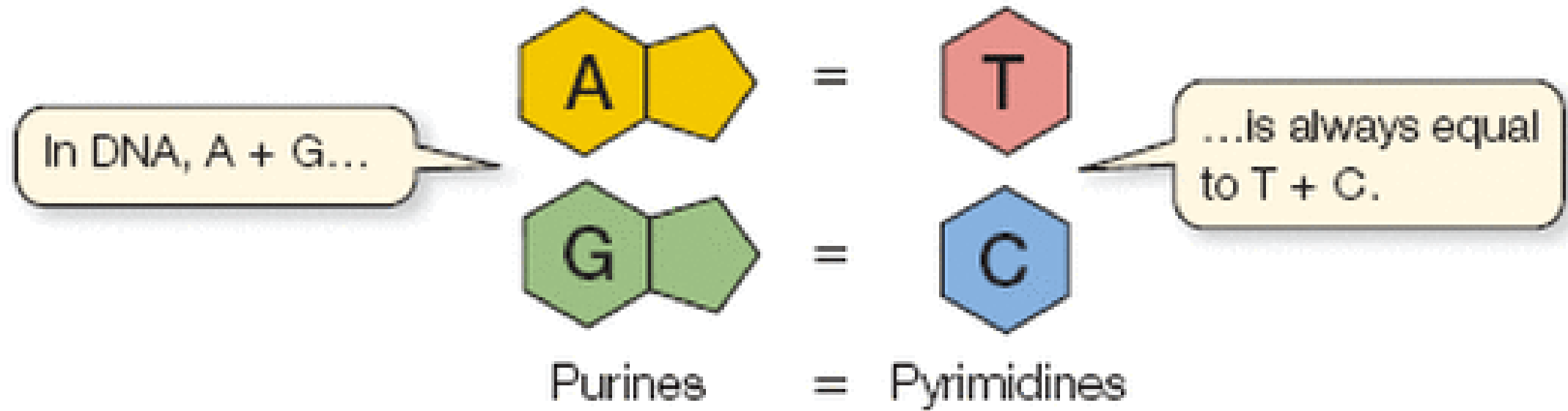
DNA structure



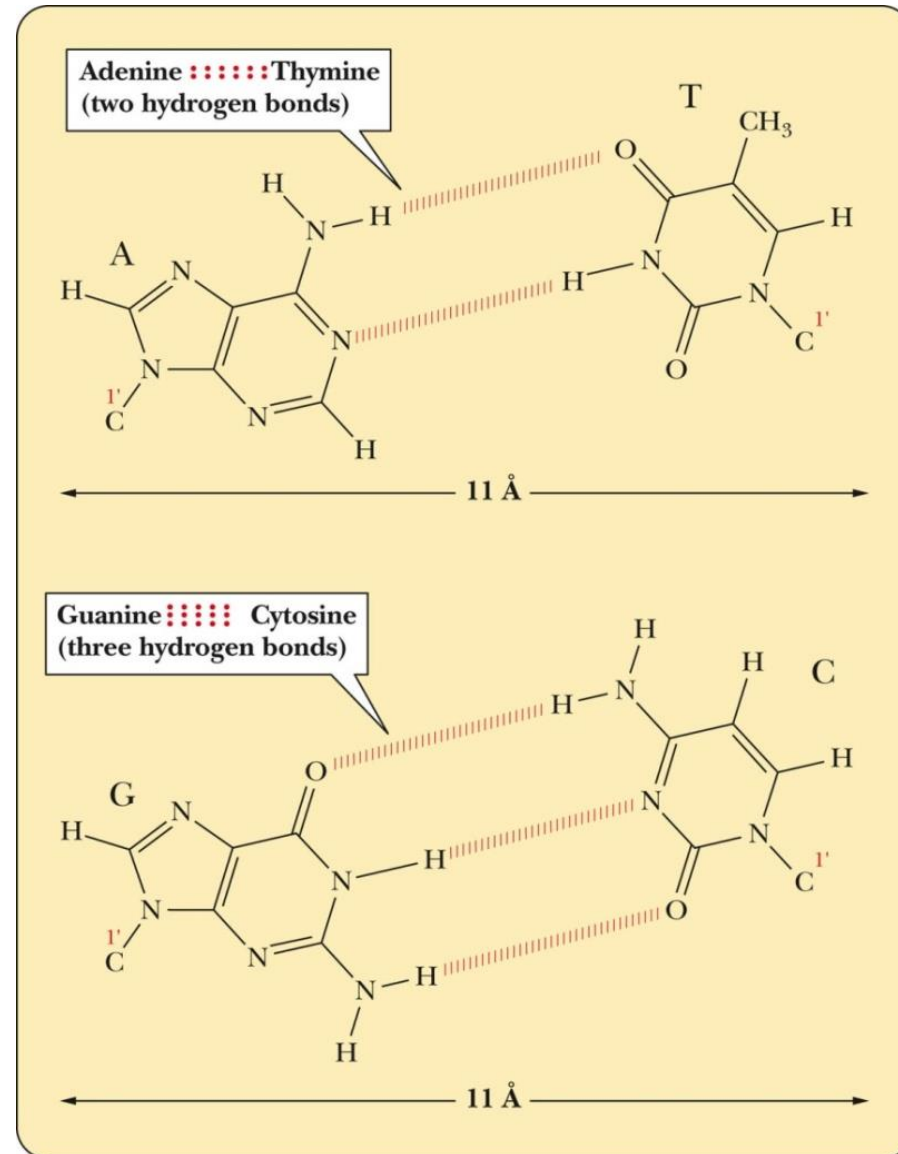
- A double helix
- Specific base-pairing
 - $A = T$; $G = C$; Pur = pyr
- Complementary
- Backbone vs. side chains
- Antiparallel
- Stability vs. flexibility
- Groovings



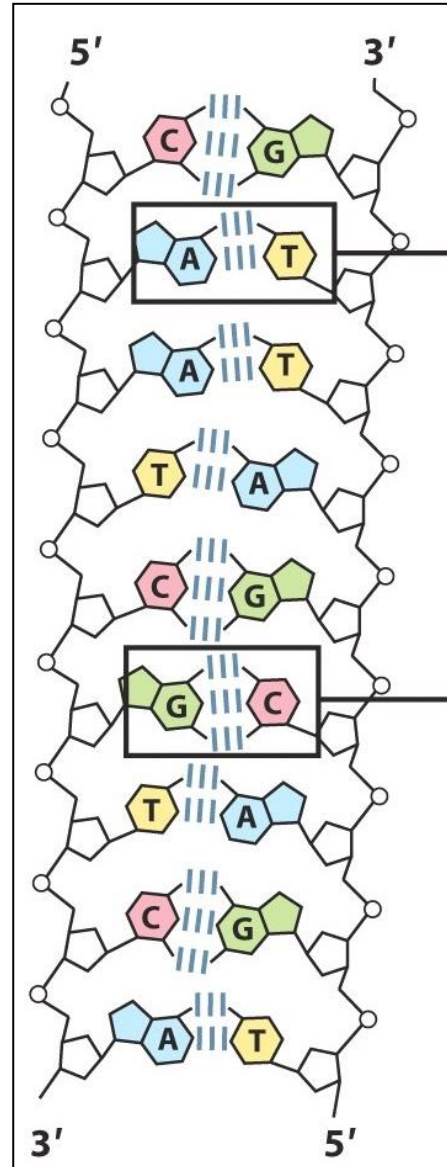
Chargaff's rules



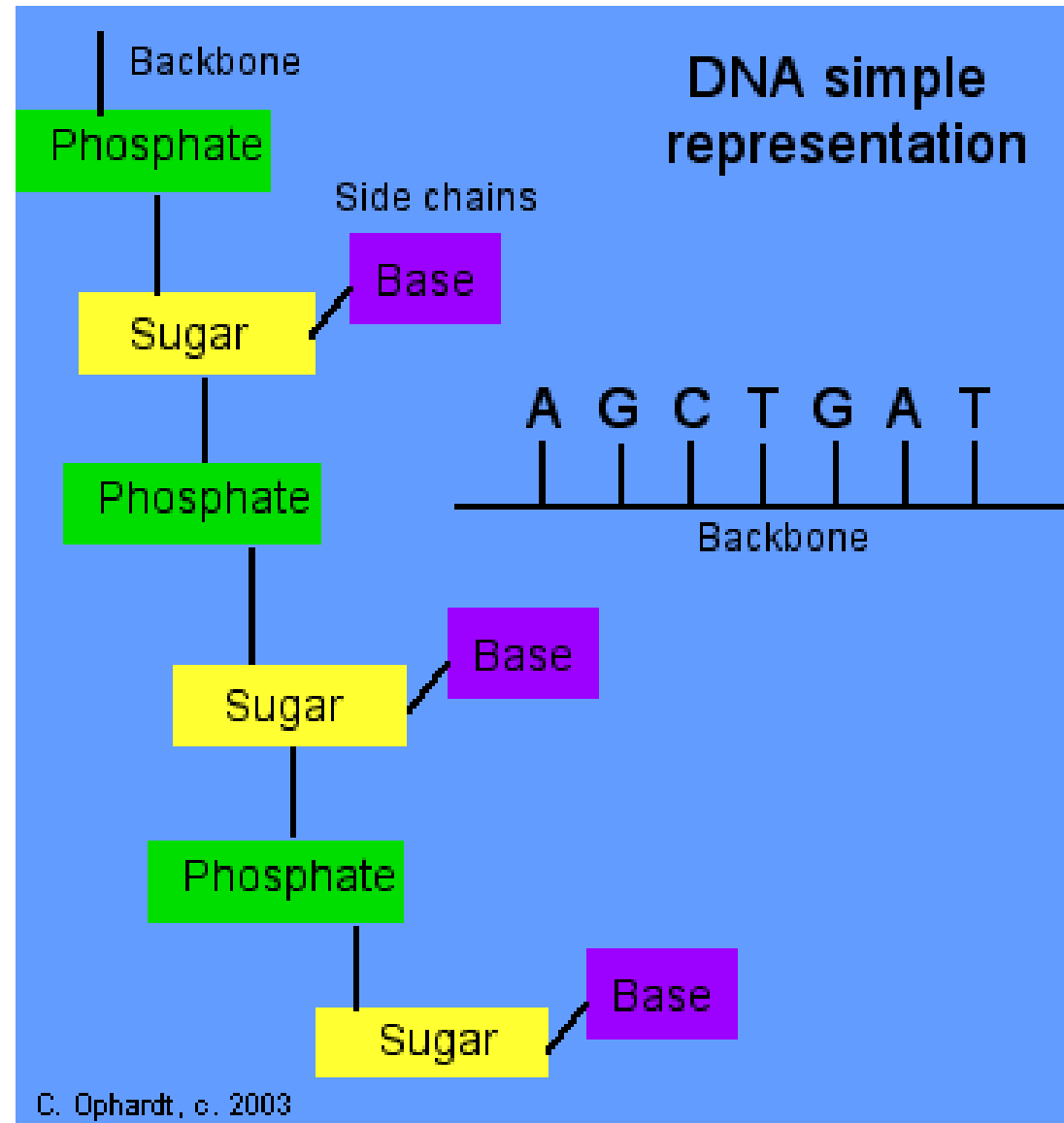
Base pairing



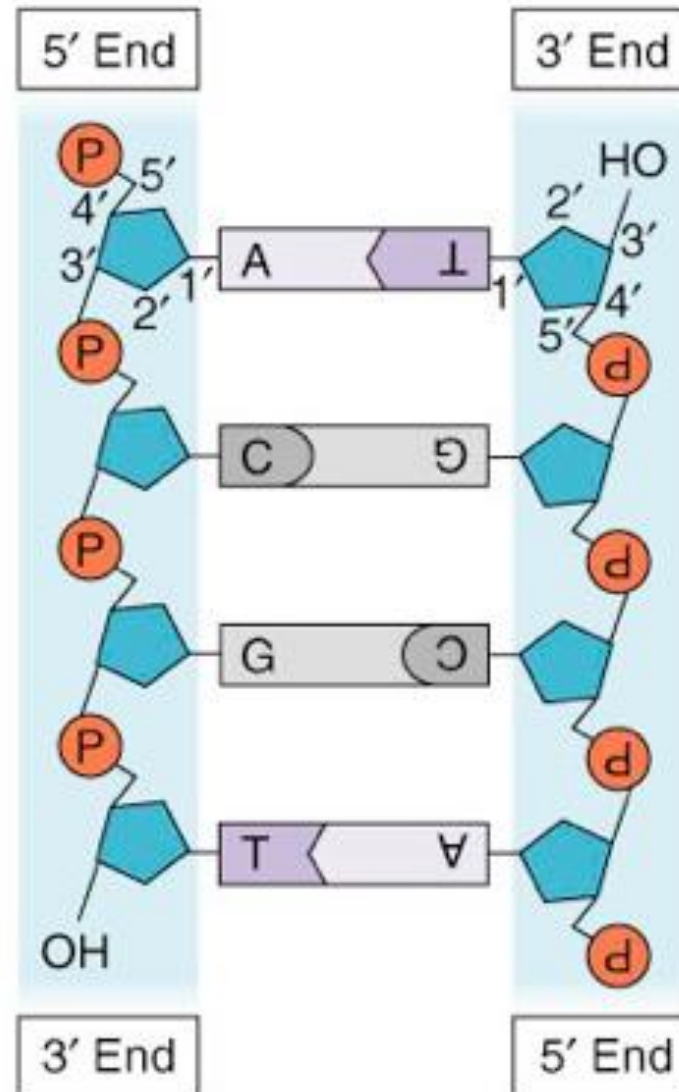
DNA is complementary



Backbone vs. side chains



DNA is anti-parallel



Writing the sequence of nucleic acids

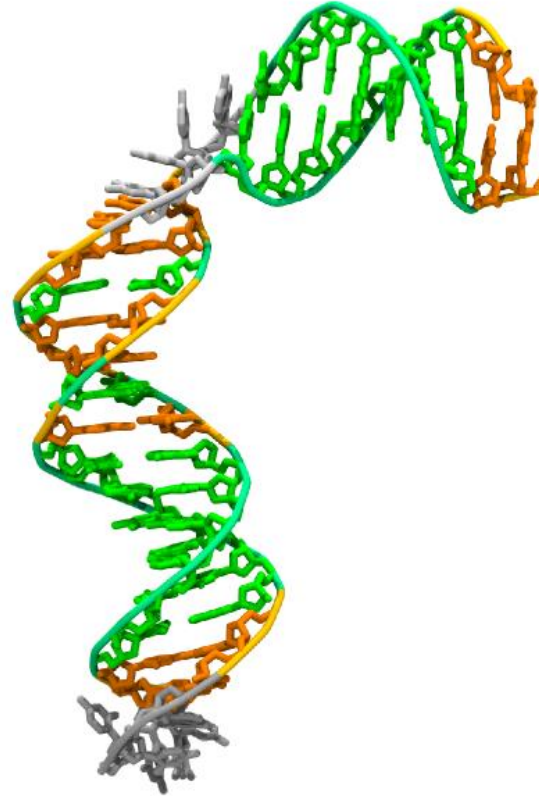
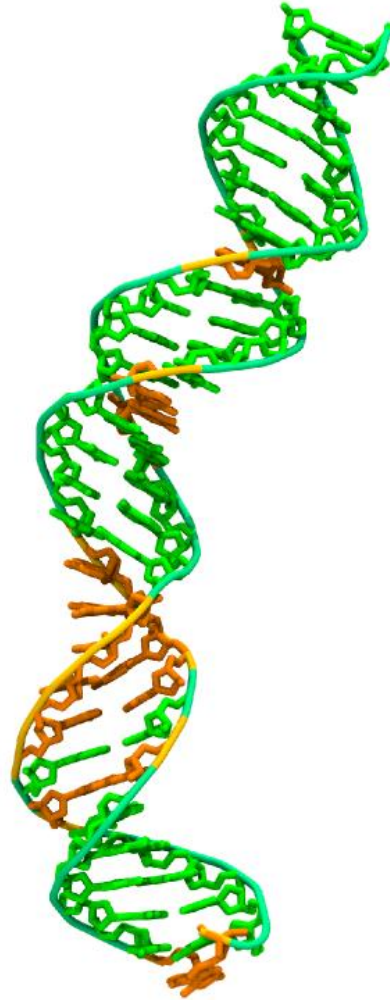
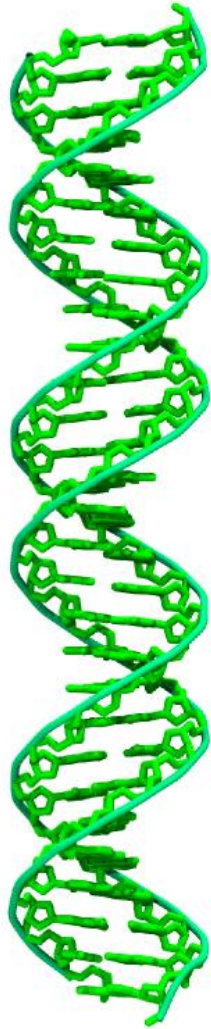


DNA 5' ...A T G G C C T G G A C T T C A... 3'
 3' ...T A C C G G A C C T G A A G T... 5'

OR A T G G C C T G G A C T T C A.

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

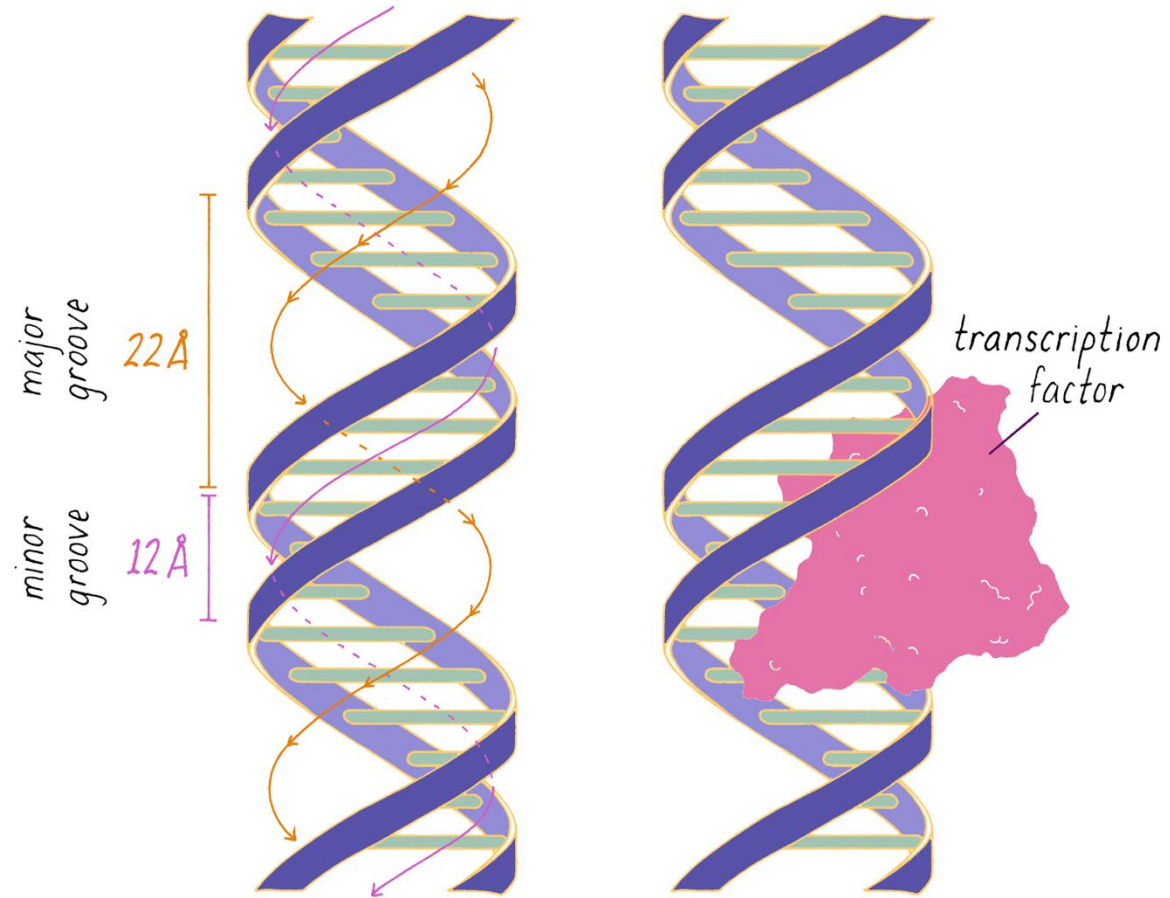
DNA is flexible, yet stable



DNA grooves

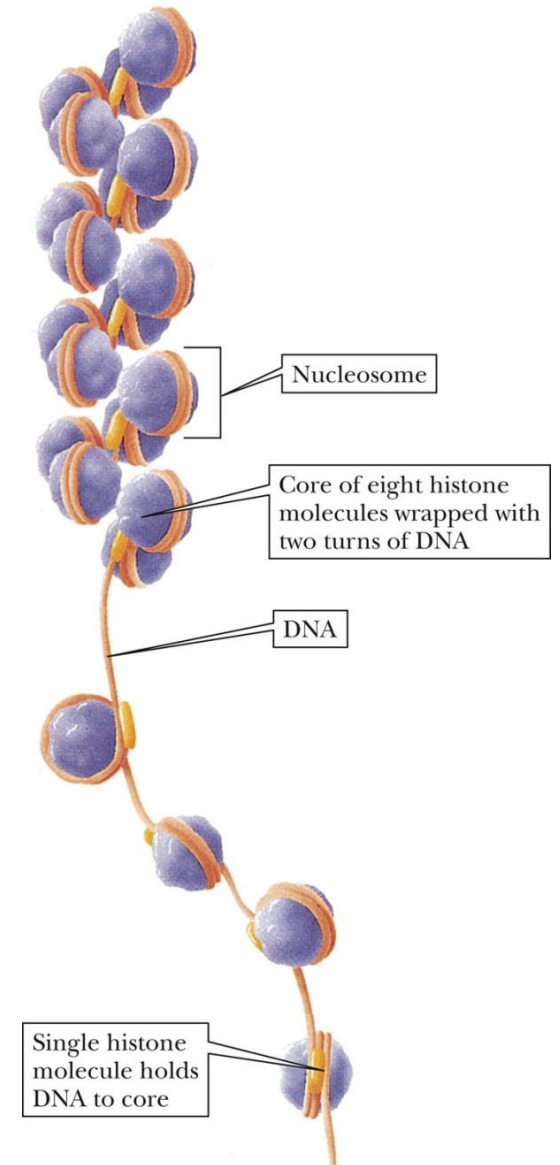


MAJOR & MINOR GROOVES



In eukaryotes...

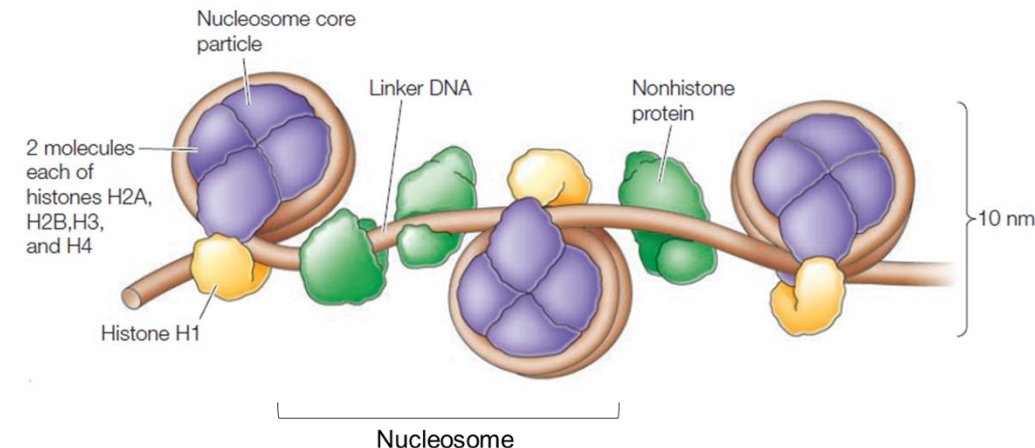
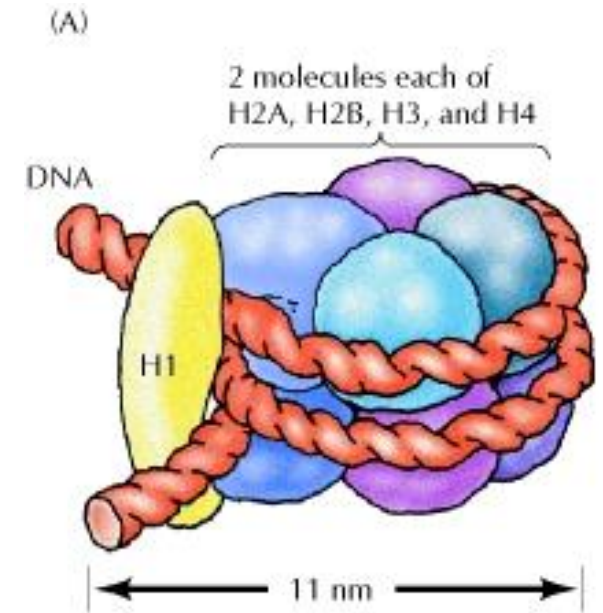
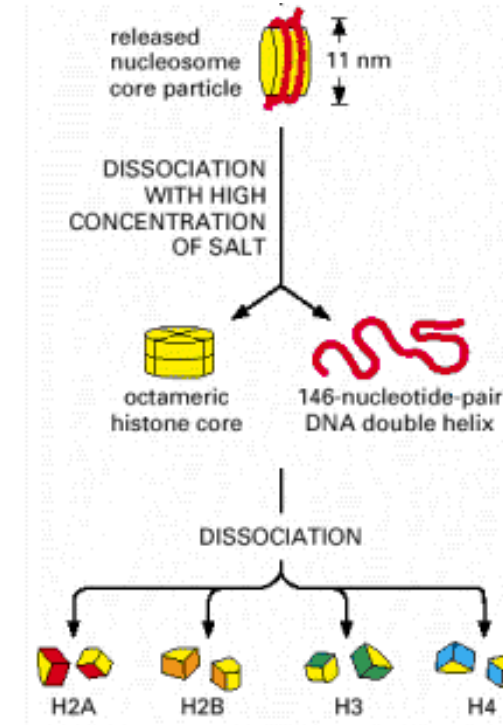
- In eukaryotes, DNA is coiled to package the large DNA.
- Eukaryotic DNA is complexed with a number of proteins, principally histones, which package DNA.
- Chromatin = DNA molecule + proteins.
- The basic structural unit of chromatin is known as a nucleosome.

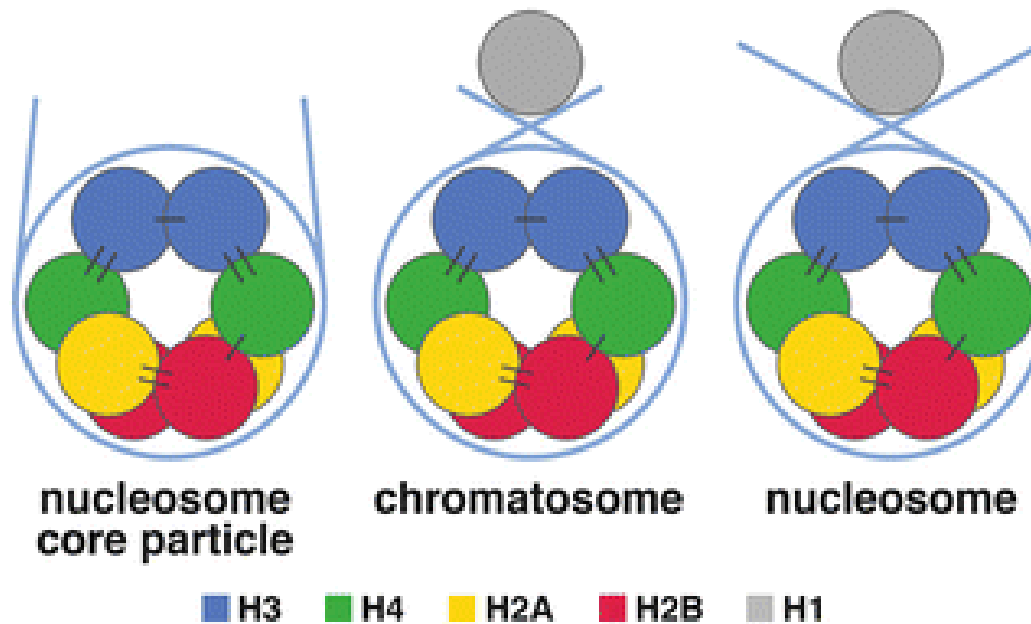
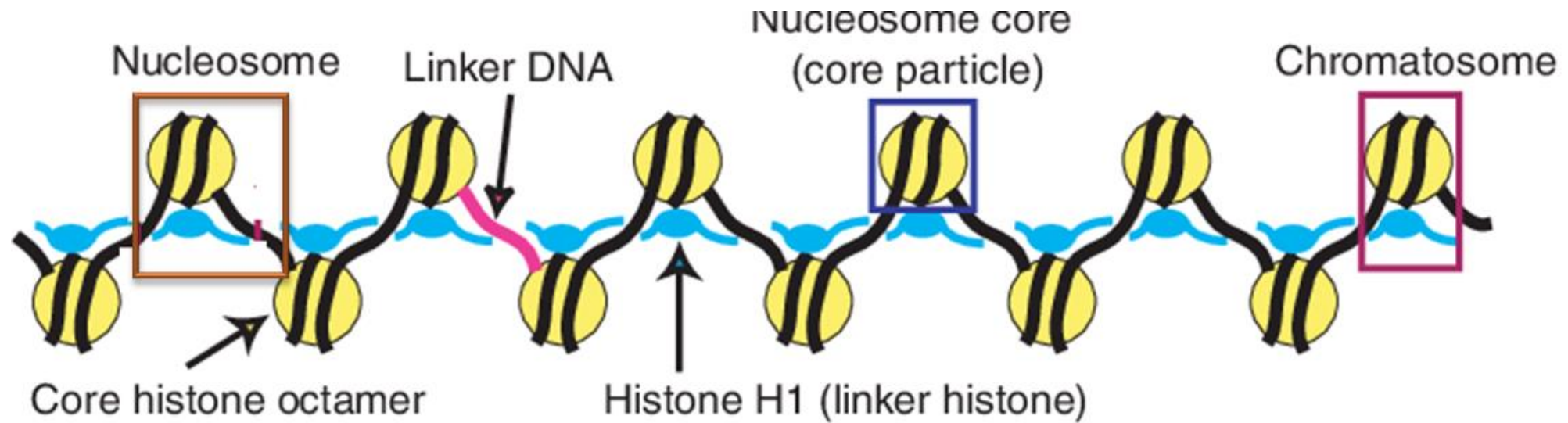


Nucleosomes



- The histone core particle is an octamer (two molecules of histones H2A, H2B, H3, and H4) and the DNA wrapped around it.
- Addition of histone H1 to the octamer and the wrapped DNA creates a chromatosome).
- Free DNA, called linker DNA, links two nucleosomal core particles to each other, forming a nucleosome.
- Histones are positively charged facilitating DNA interaction and charge neutralization.

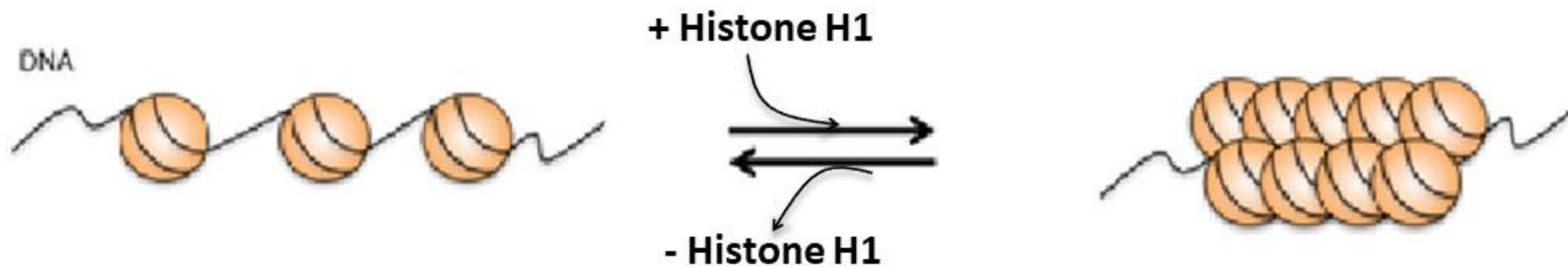
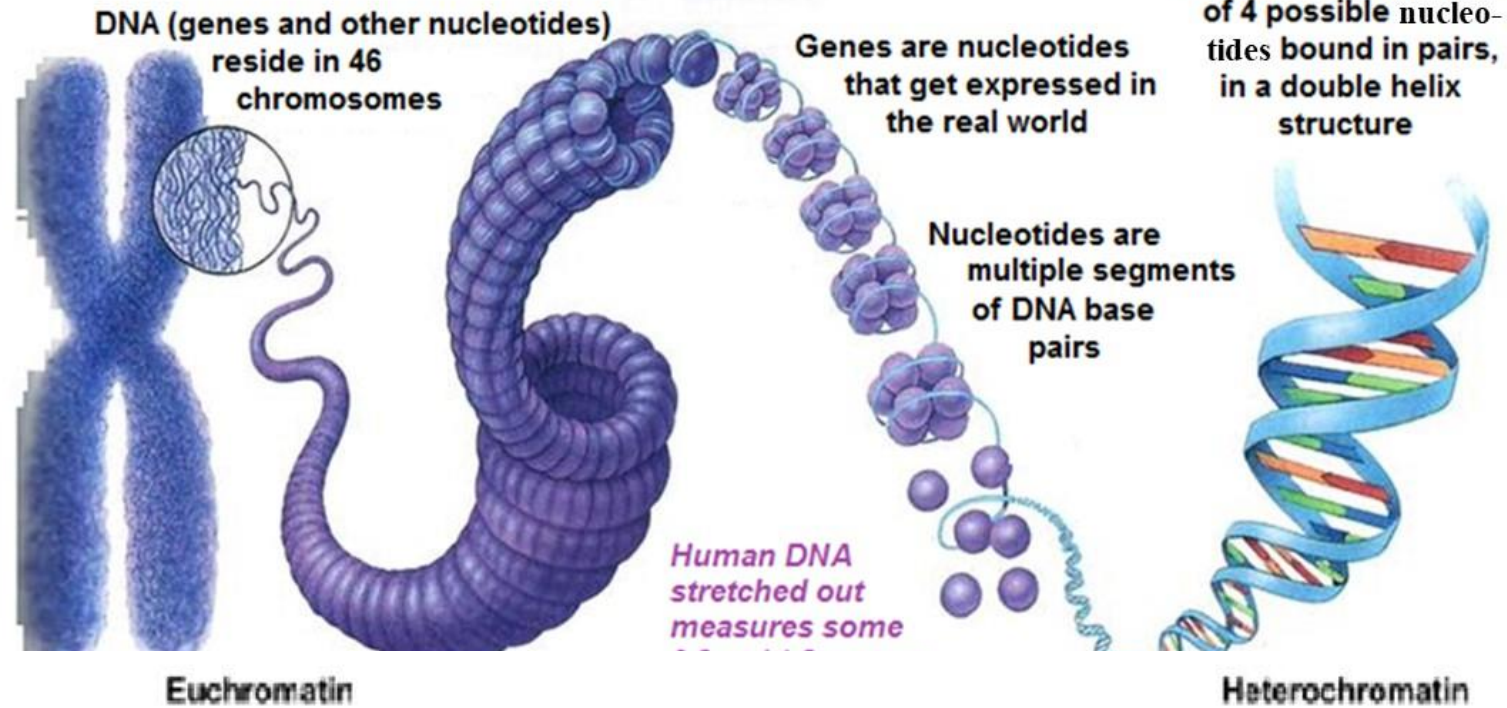




Higher organization of DNA and histone H1



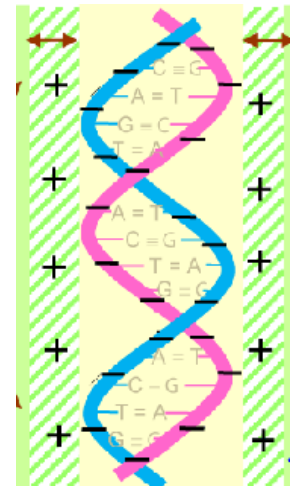
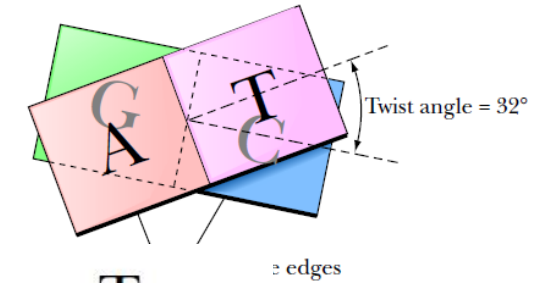
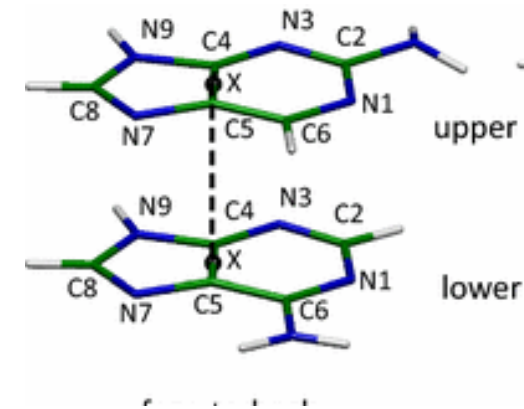
The Hierarchical Structure of DNA through to the Chromosome



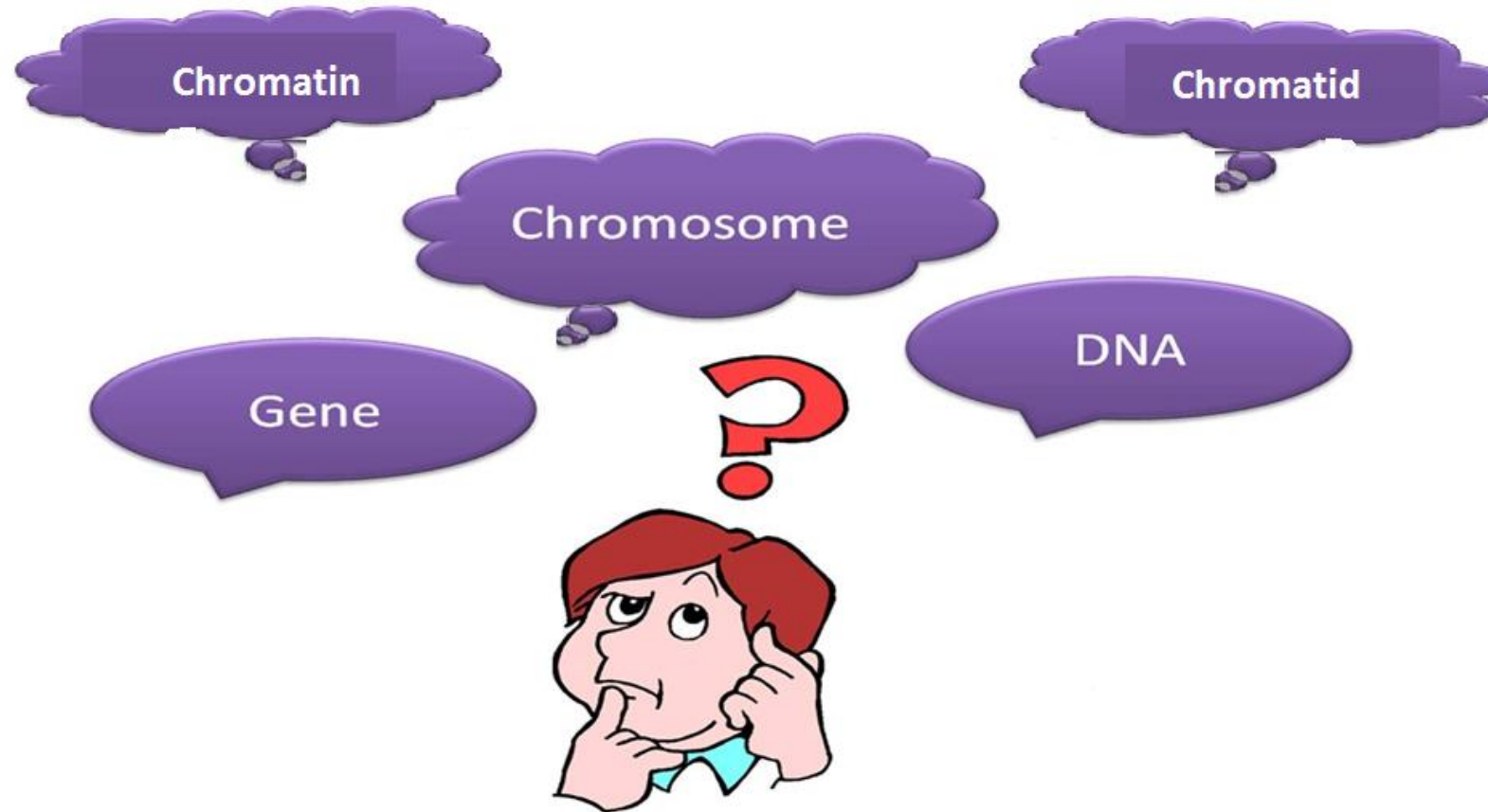
DNA-stabilizing forces



- Hydrogen bonds between complementary bases
- Hydrophobic stacking:** The hydrophobic rings of the bases that lie on top of each other interact with each other via hydrophobic interactions and van der Waals interactions.
- Helical twists:** Each base pair is rotated with respect to the preceding one for maximal base pairing.
- Propeller twists:** The bases twist for optimal base stacking.
- DNA-binding proteins (e.g., histones)
- Ions such as Na^+ or Mg^{2+} (and histones) reduce the repulsion created by the negatively-charged phosphates of the DNA.



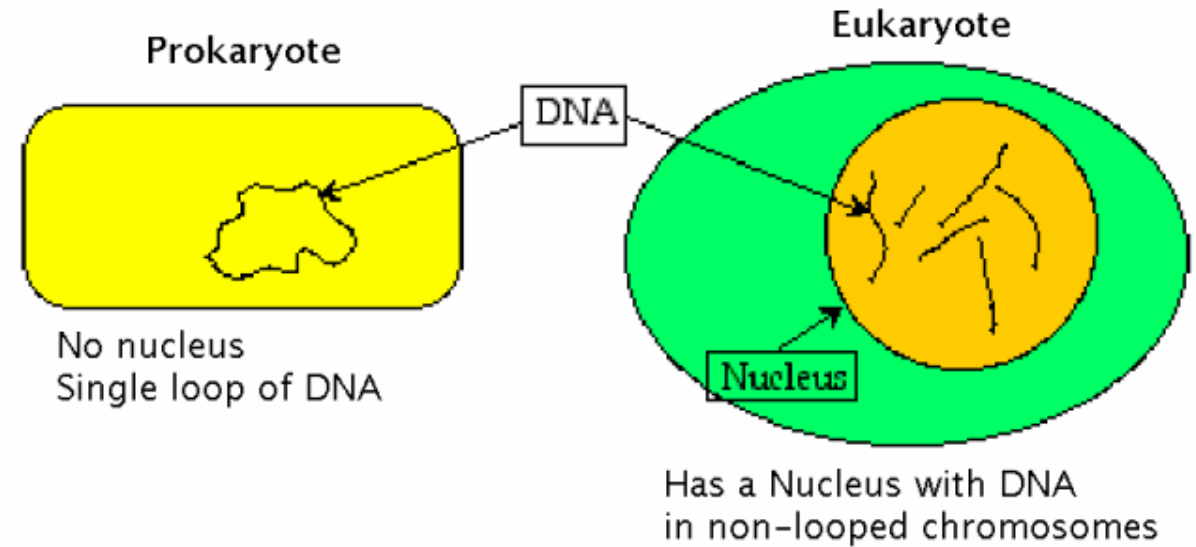
Terms to know



The genome of prokaryotes versus eukaryotes



- Genome: the total genetic material of a living being (bacteria vs. human), a species (monkey vs. human) , an individual (me vs. you), or a cell (brain vs. liver), etc.
- Prokaryote: an organism that lacks a nucleus or other organelles.
- Eukaryote: an organism that has a true (clearly defined) nucleus.



Bacterial chromosome and plasmids

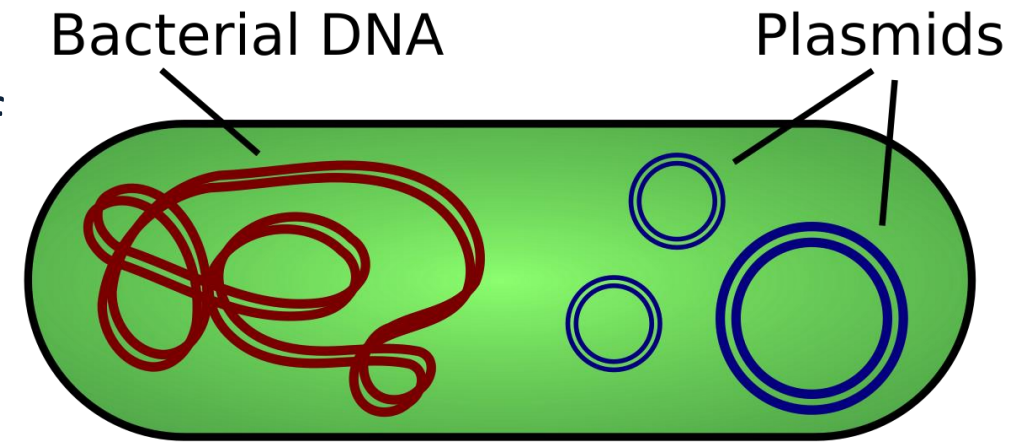


The genetic materials of bacteria are of 2 types:

1. The chromosome: One circular chromosome of double-stranded DNA.

- The entire chromosome of the bacterium *Escherichia coli* is composed of a single circular double-stranded DNA molecule, contains $>4 \times 10^6$ bp (length of 2 mm) carrying 4200 genes.

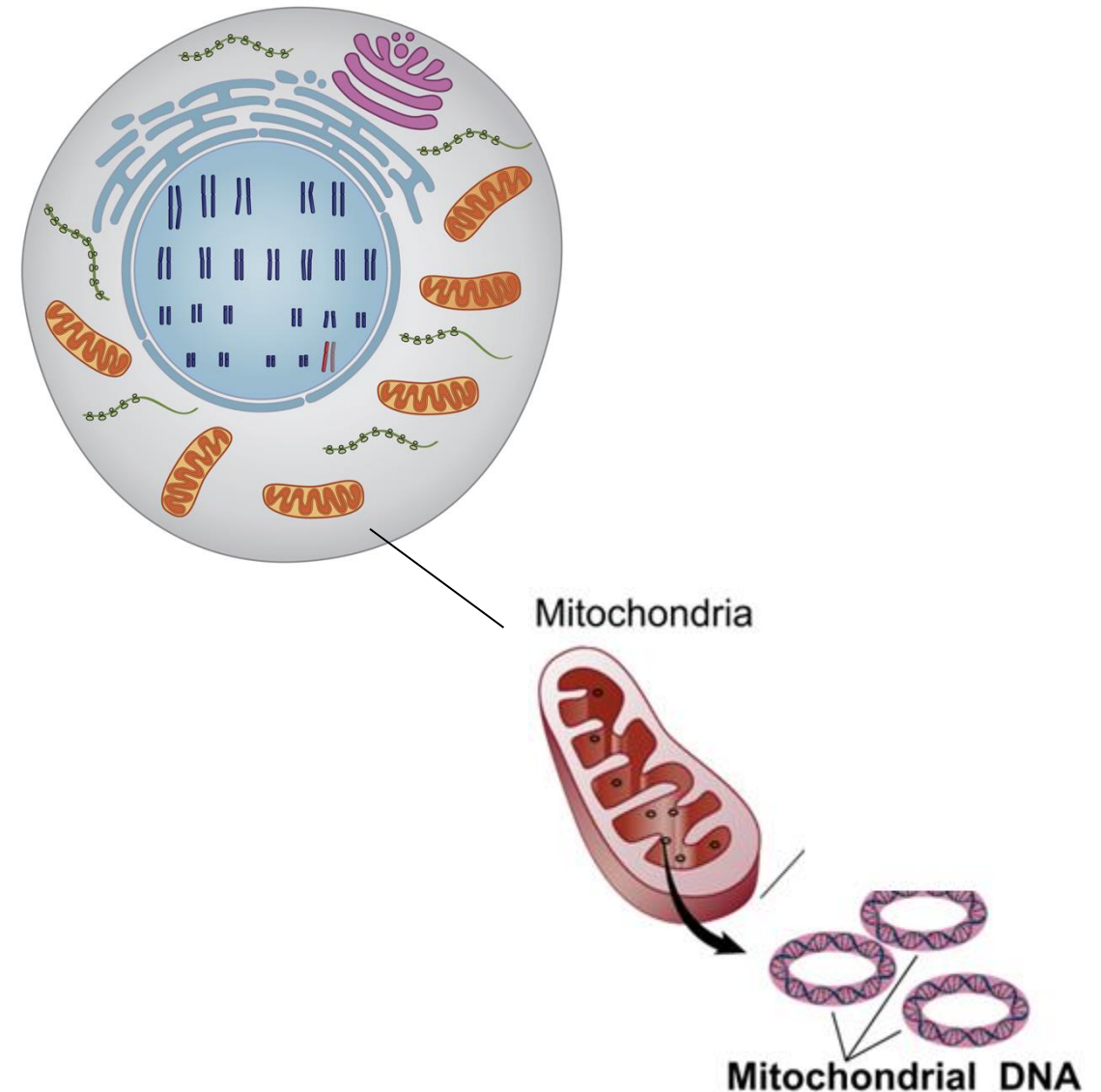
2. Plasmids: 1) Small, circular DNA molecules, 2) can replicate autonomously independent of the genomic chromosomes, 3) not infectious like viruses, 4) can carry genes, some of which confer resistance to antibiotics, and 5) exist as different types but one plasmid type per cell, 6) can exist as multiple copies, and 7) can transfer among bacterial cells.



The human genome



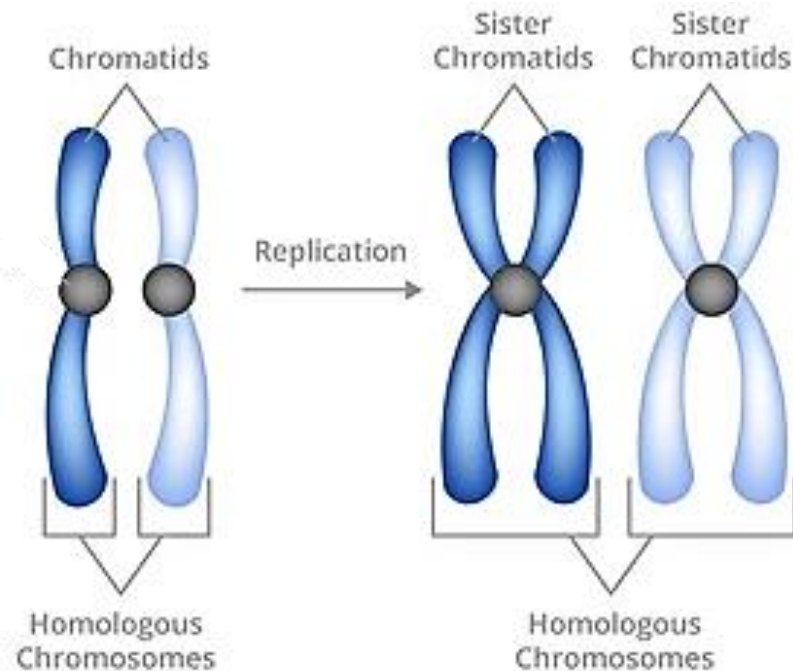
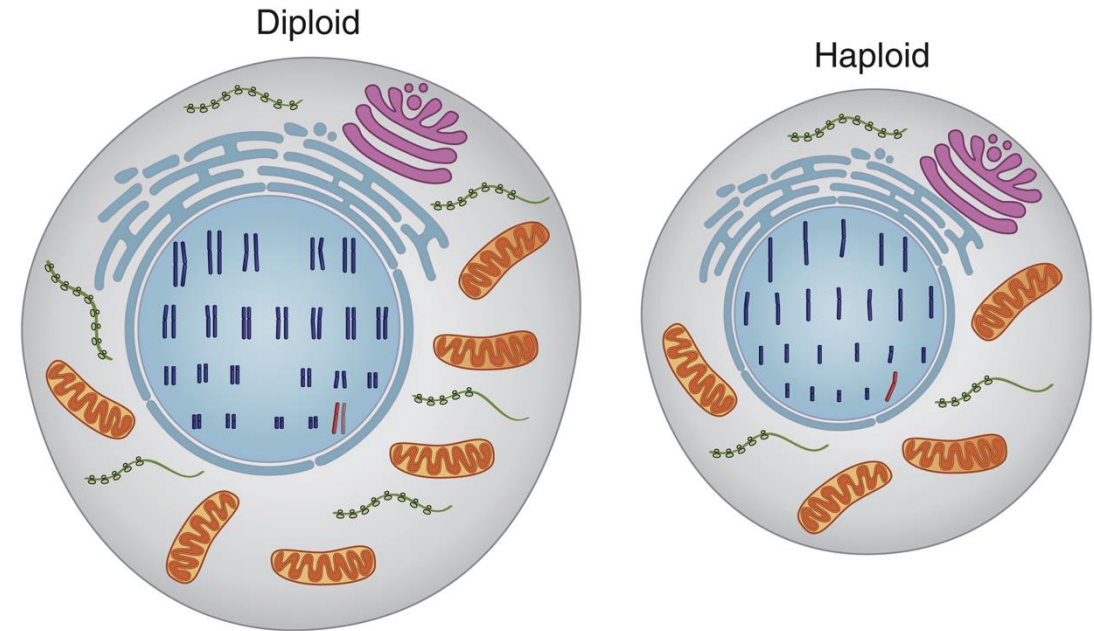
- The genetic material of humans is of 2 types:
 - The nuclear genome: organized as linear chromosomes that consist of $\sim 3 \times 10^9$ nucleotides in germline cells (sperm and egg), with a length of 1 meter per germline cell and that carry ~ 20000 genes.
 - The mitochondrial genome, which constitutes less than 0.1% of the total DNA in a cell (~ 16500 bp) and encodes 37 genes for proteins involved in the respiratory chain reaction.



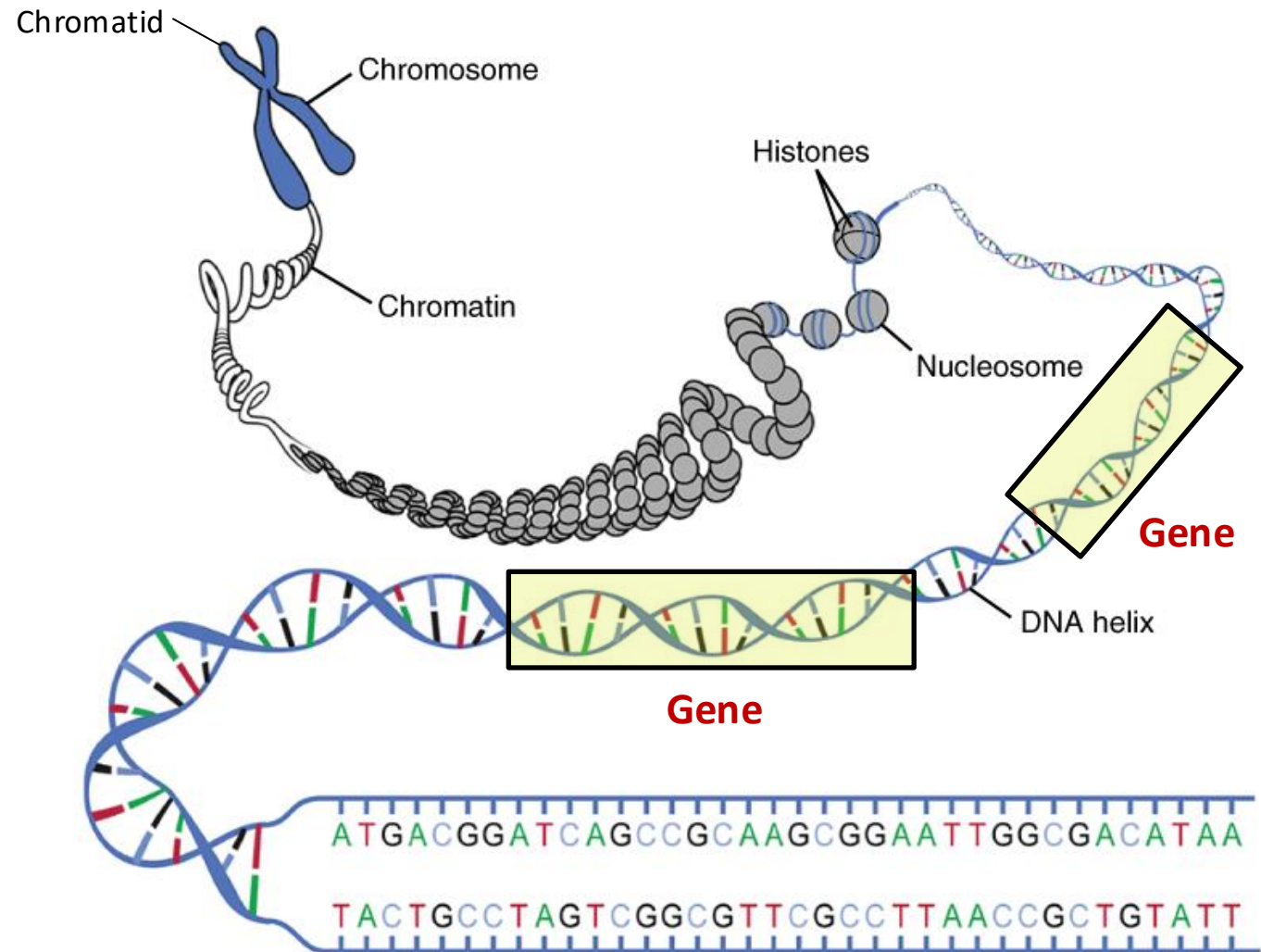
More eukaryotic terms



- Germline cells are haploid cells having one copy of every chromosome (either maternal or paternal).
- Somatic cells are diploid having two copies of every chromosome (maternal AND paternal) called homologous chromosomes.



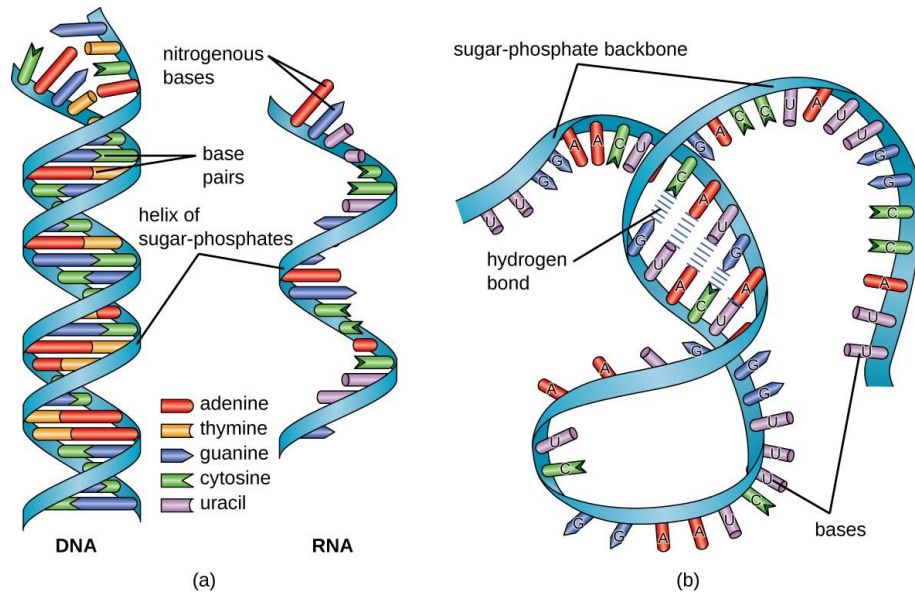
- Each chromosome can be made of one chromatid or sister chromatids.



RNA



- It consists of long, unbranched chains of nucleotides joined by phosphodiester bonds between the 3'-OH of one pentose and the 5'-PO₄⁻ 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), but can form double-stranded regions. If complementary.



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

Some RNAs can act as enzymes, known as ribozymes.

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 initiation 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