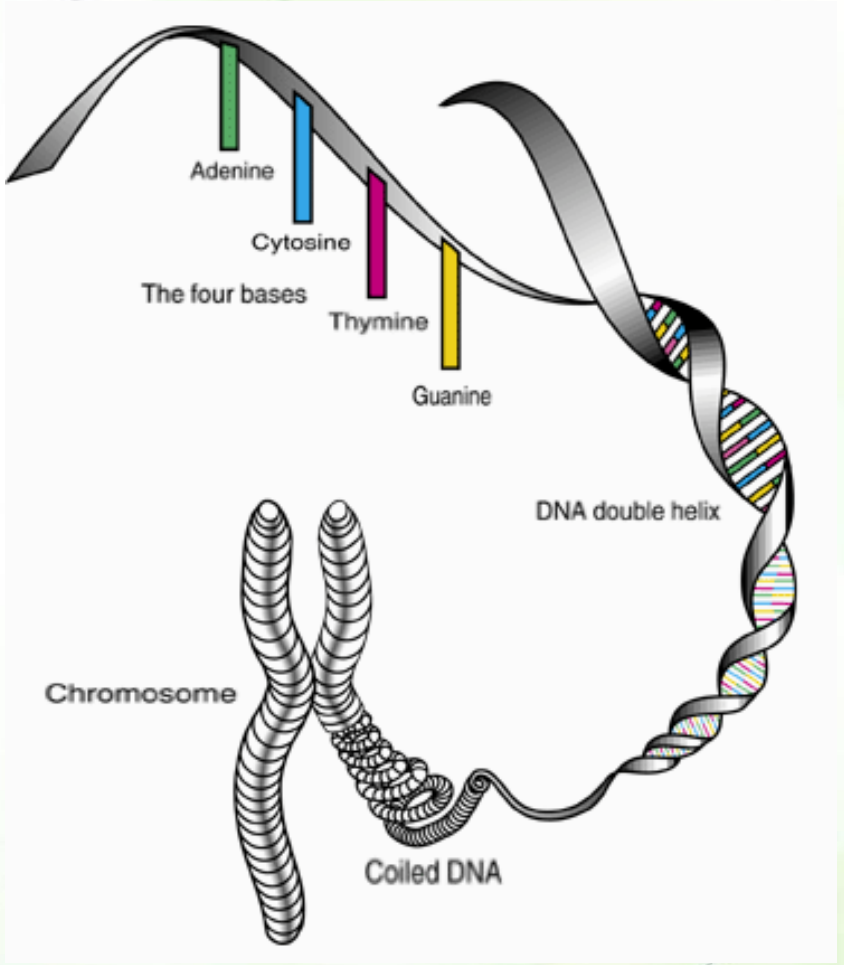
Structure of nucleic acids

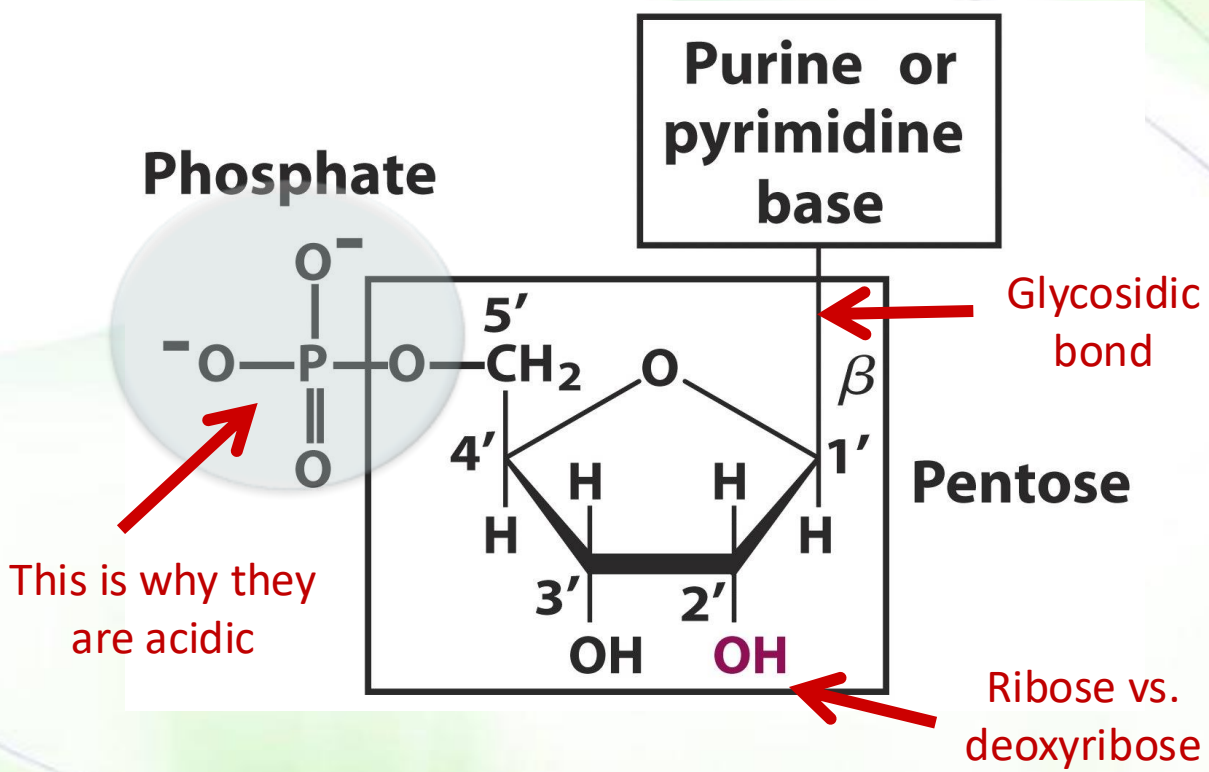
Summer 2024

Nucleic acids

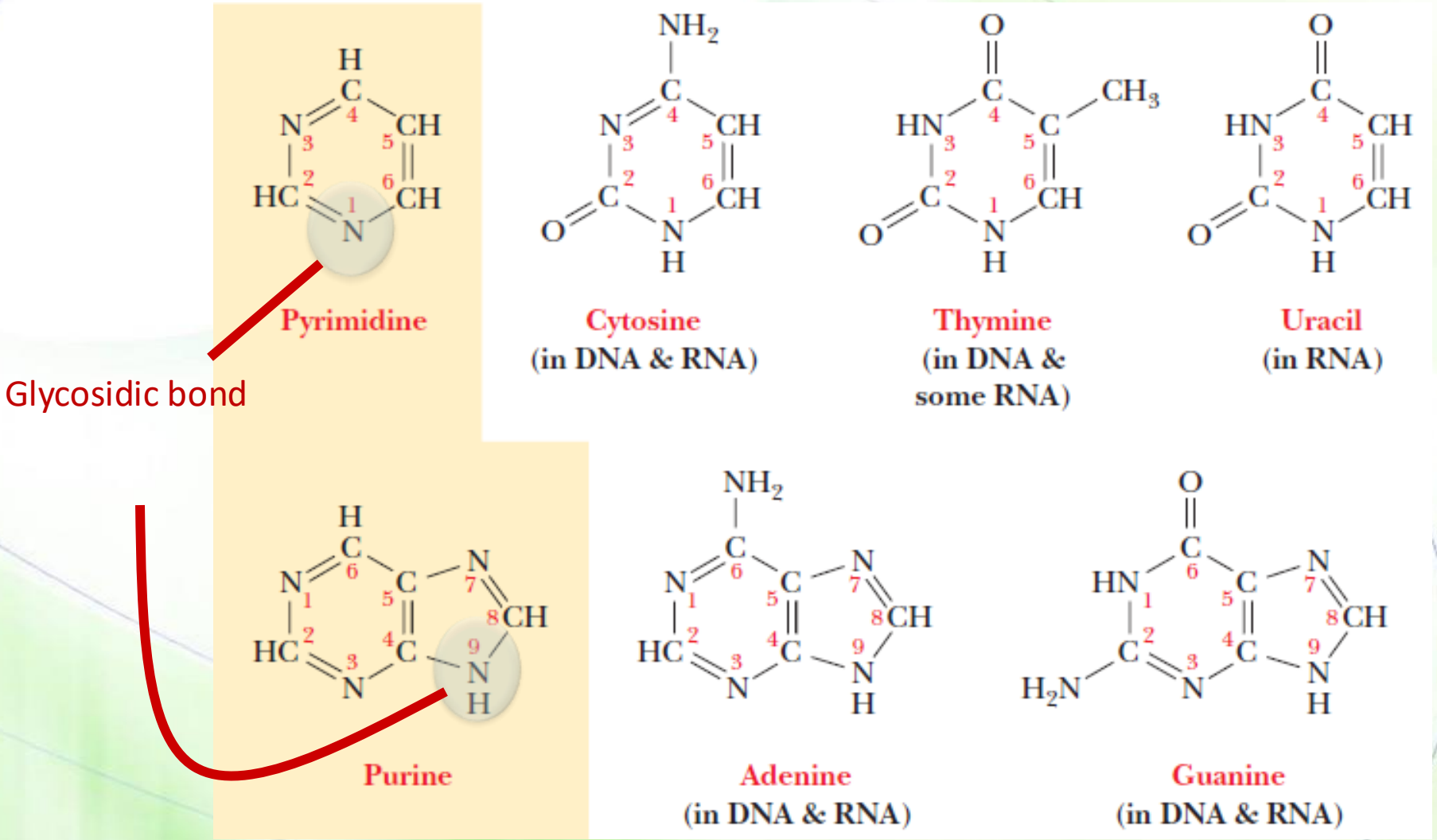
- There are 2 types
  - Deoxyribonucleic acid (DNA)
  - Ribonucleic acid (RNA)
- The primary structure of nucleic acids is linear polymers of nucleotides (monomers) bound to each other via phosphodiester bonds.
- DNA is coiled and can be associated with proteins forming chromosomes.



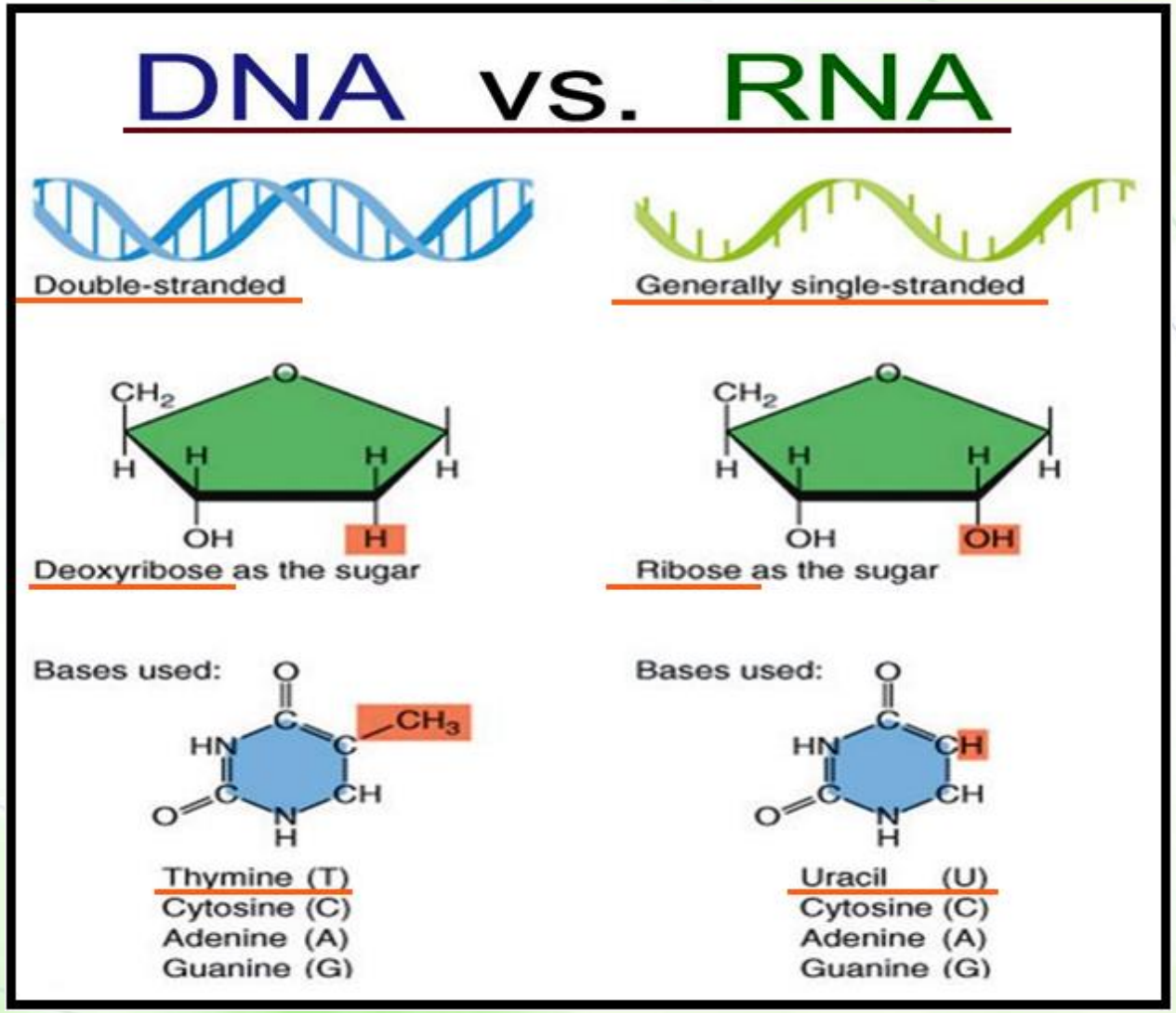
Chemical composition and bonds



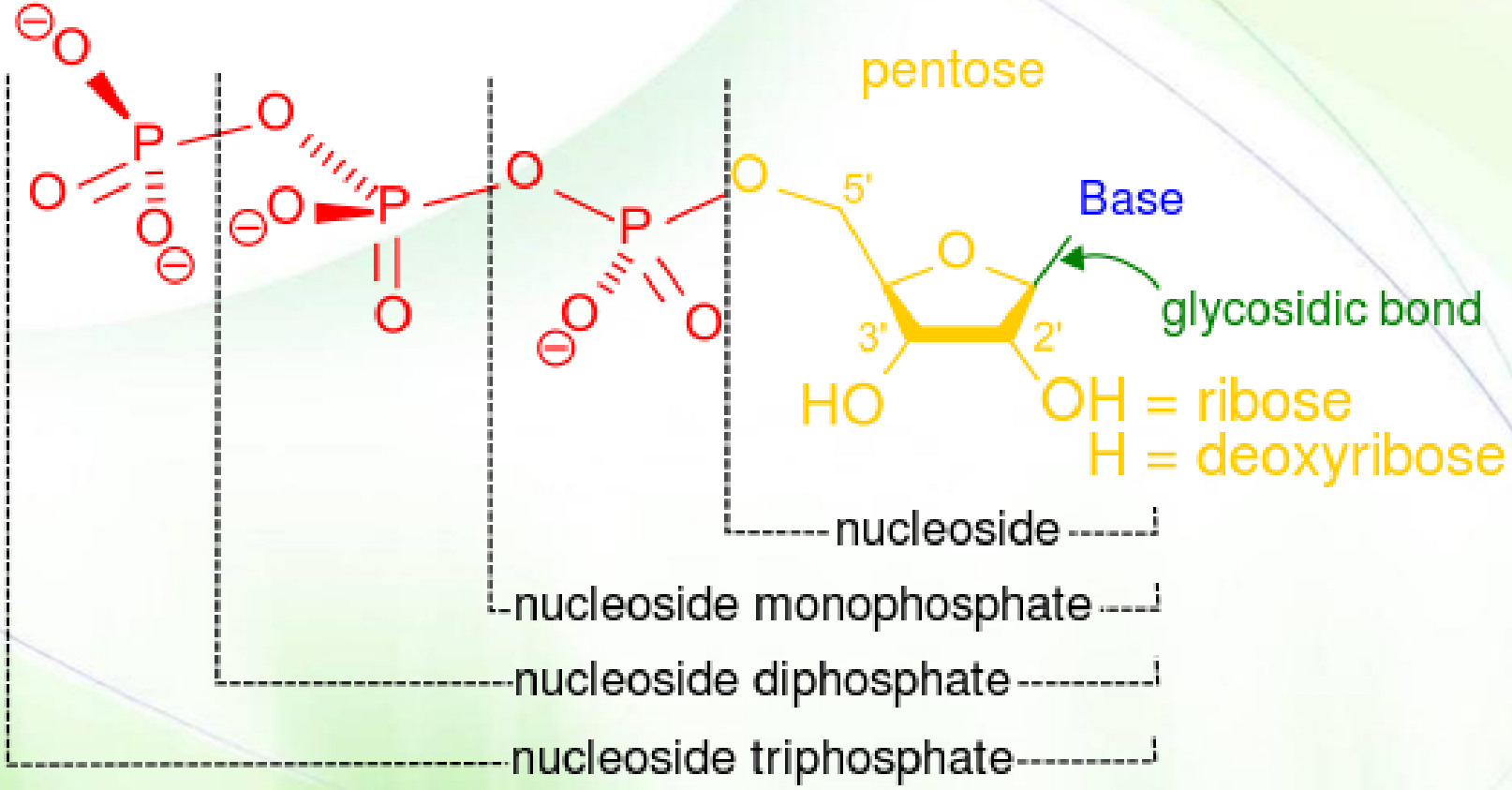
Nitrogenous bases



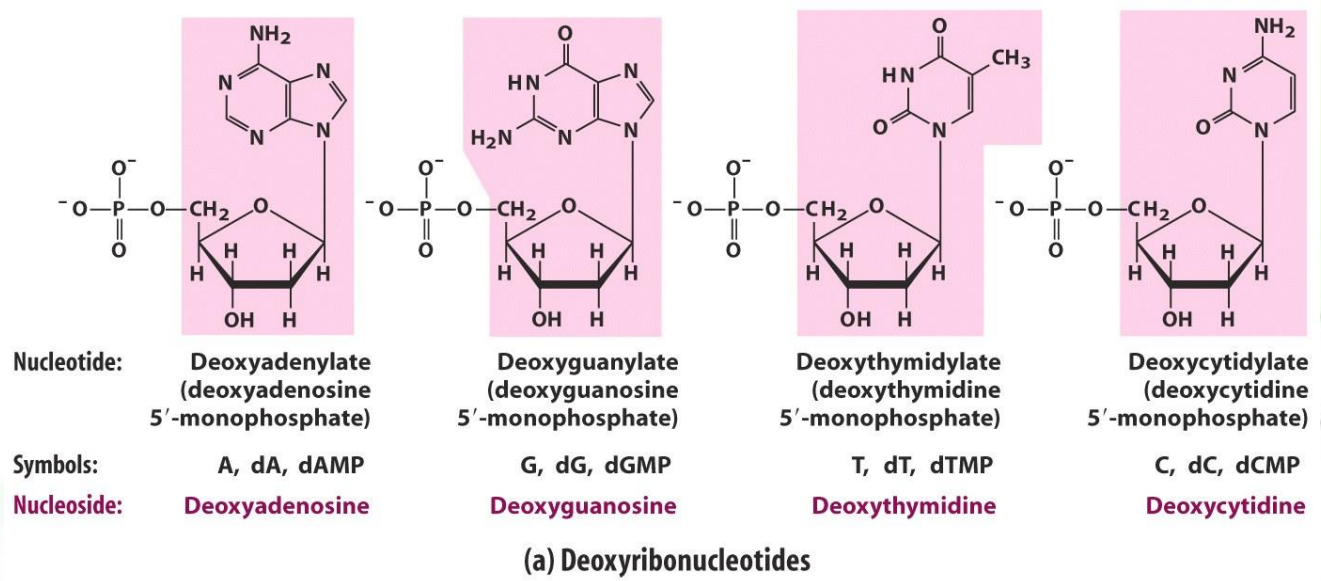
In prokaryotes and eukaryotes (not viruses)



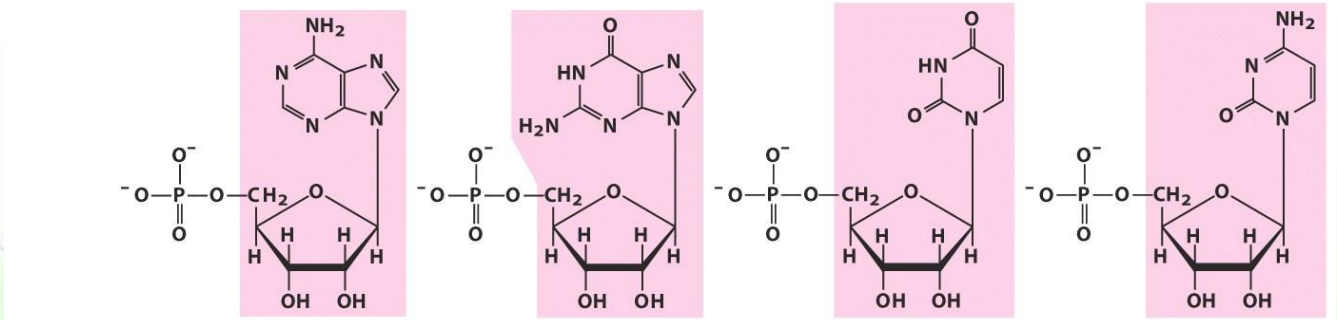
Nucleotides vs. Nucleosides



Nucleotides vs. Nucleosides

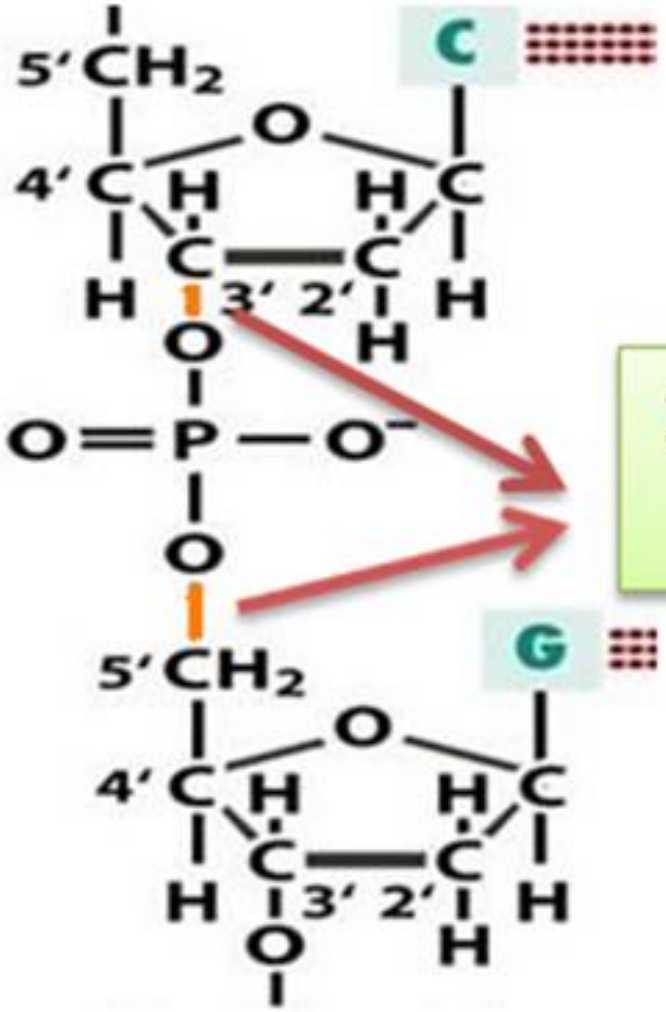


(a) Deoxyribonucleotides



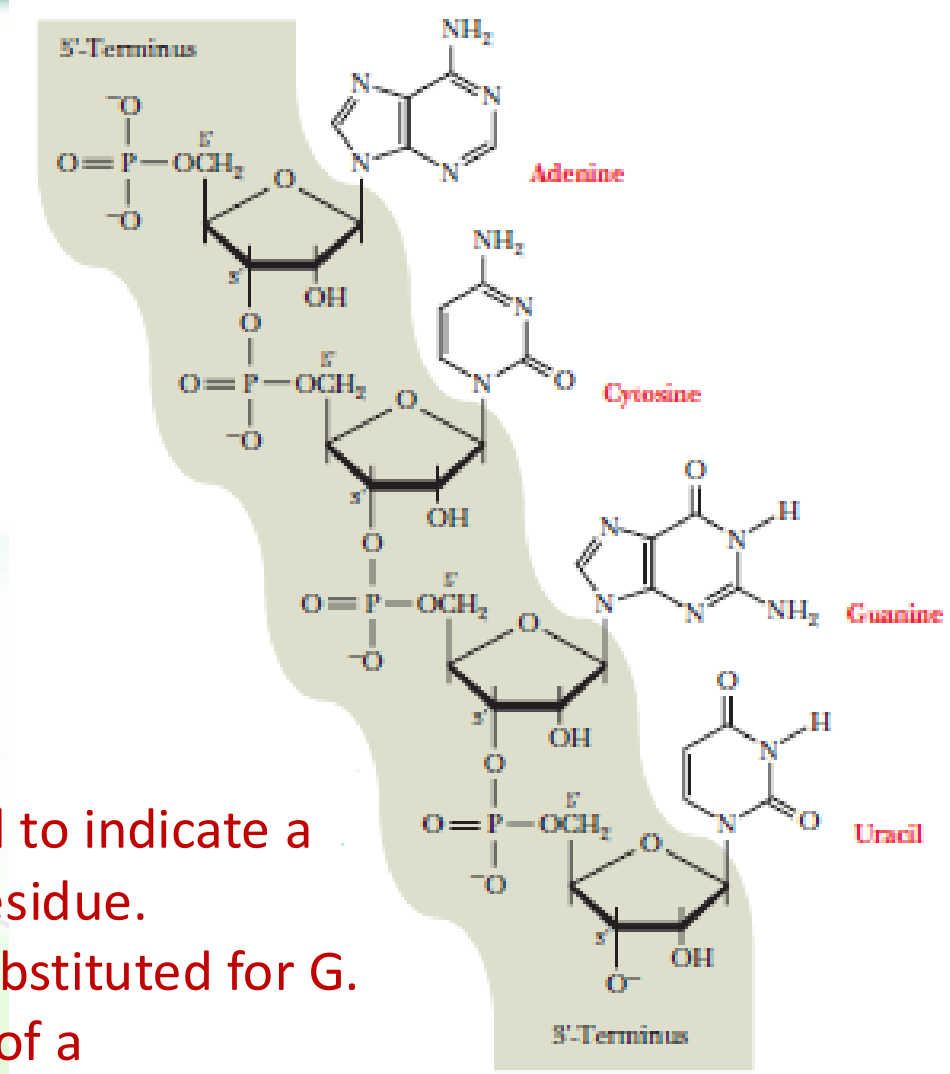
(b) Ribonucleotides

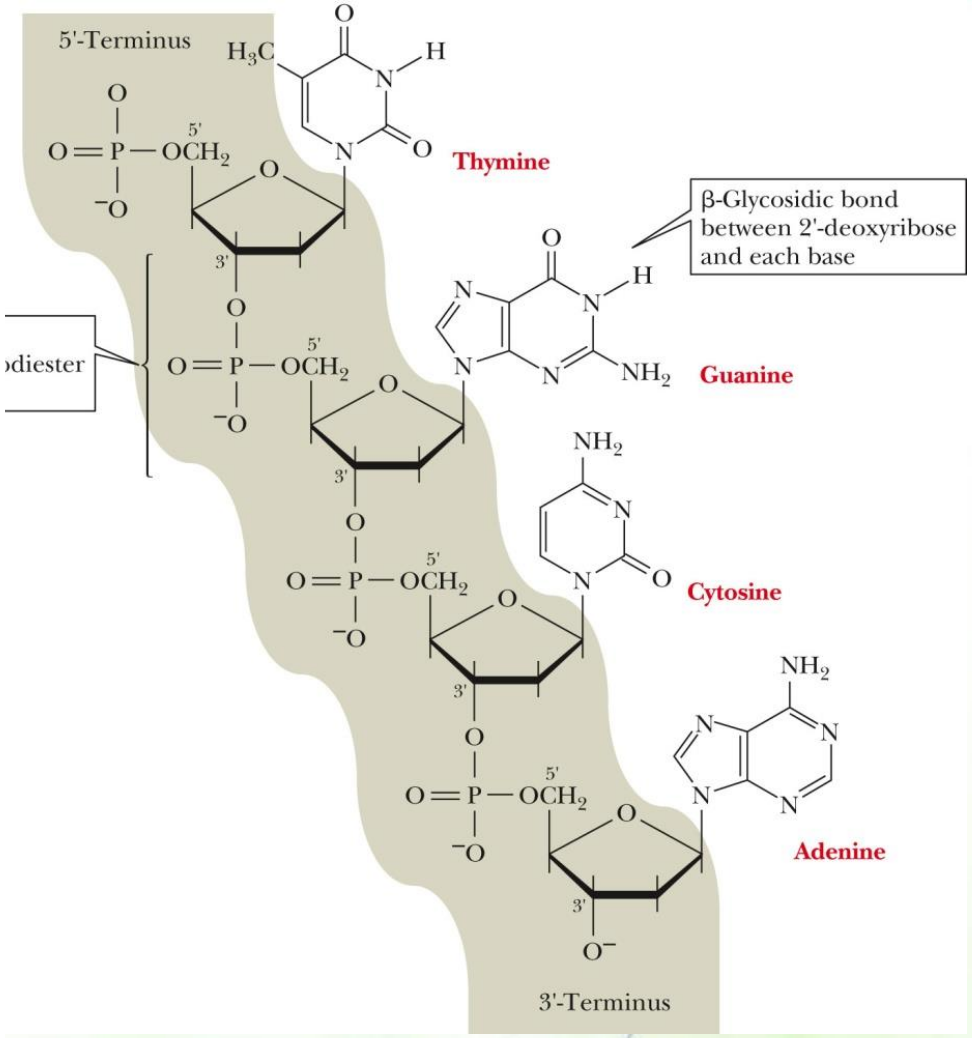
Formation of a nucleic acid polymer



1st and 2nd ester linkage
(phosphodiester bond)

Nucleic acid polymers

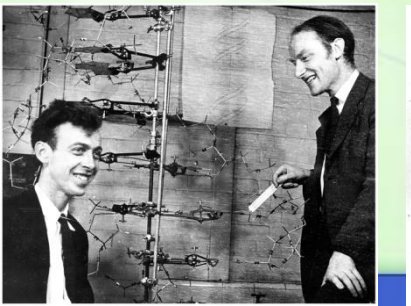


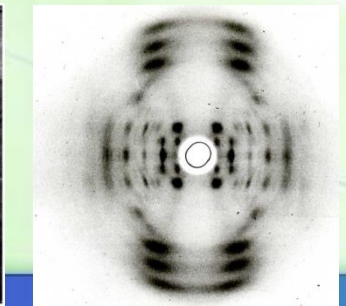


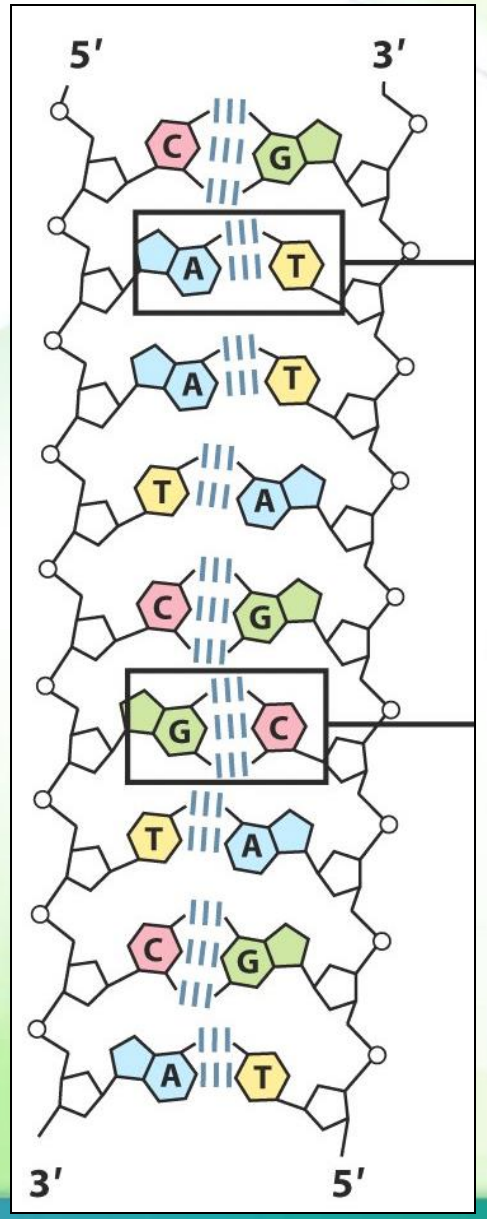
- A letter d can be added to indicate a deoxyribonucleotide residue.
  - for example, dG is substituted for G.
  - The deoxy analogue of a ribooligonucleotide would be d(GACAT).

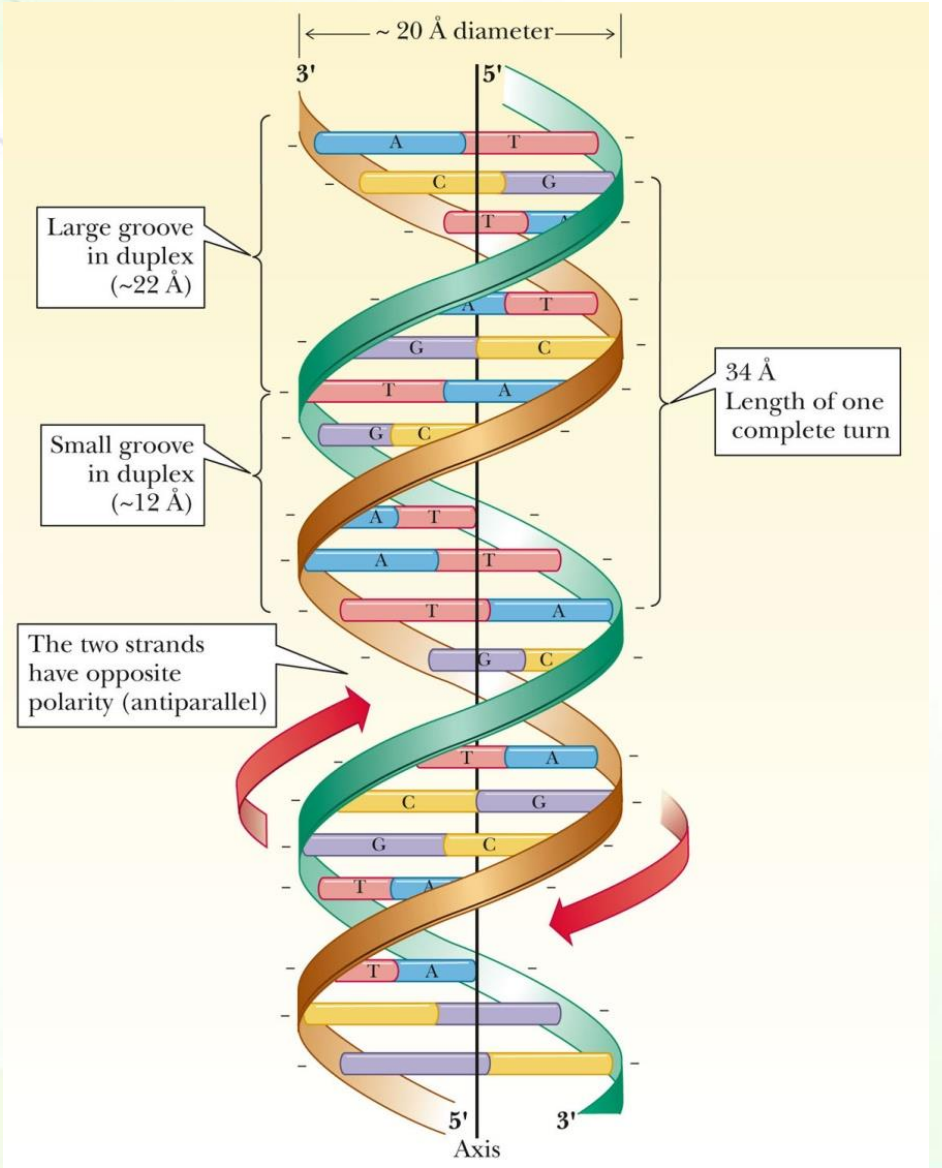
DNA structure

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

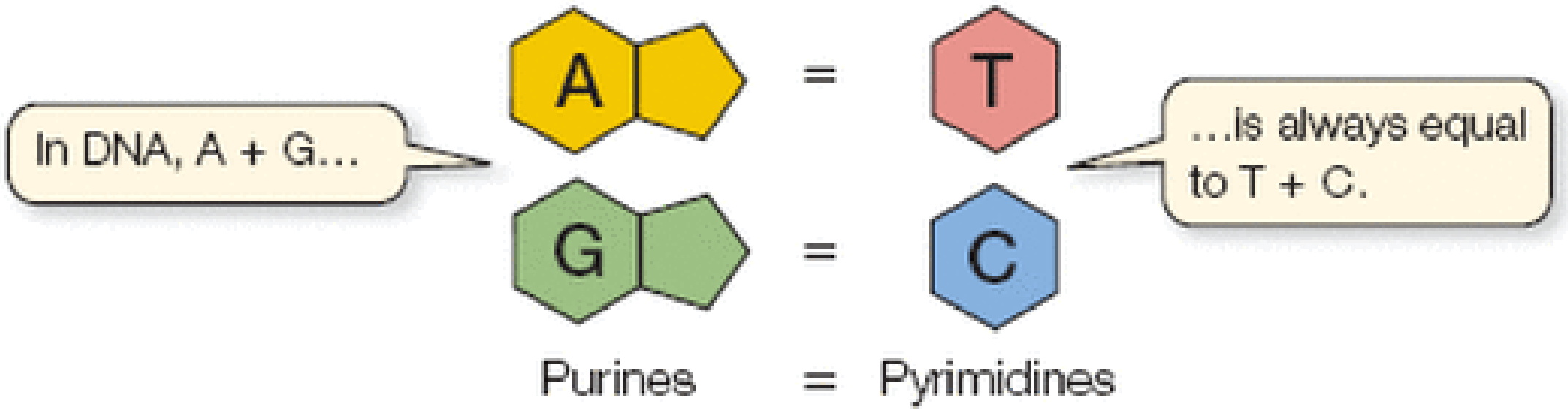




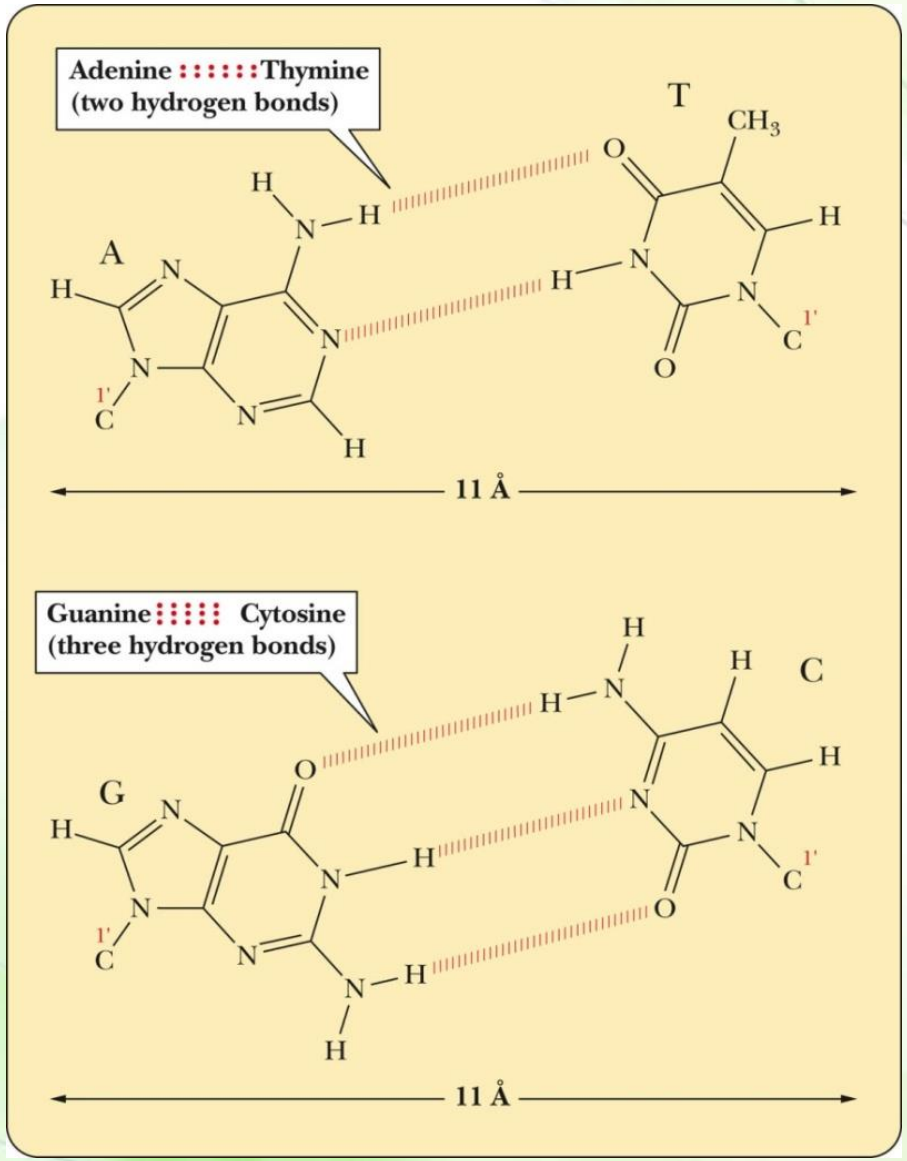




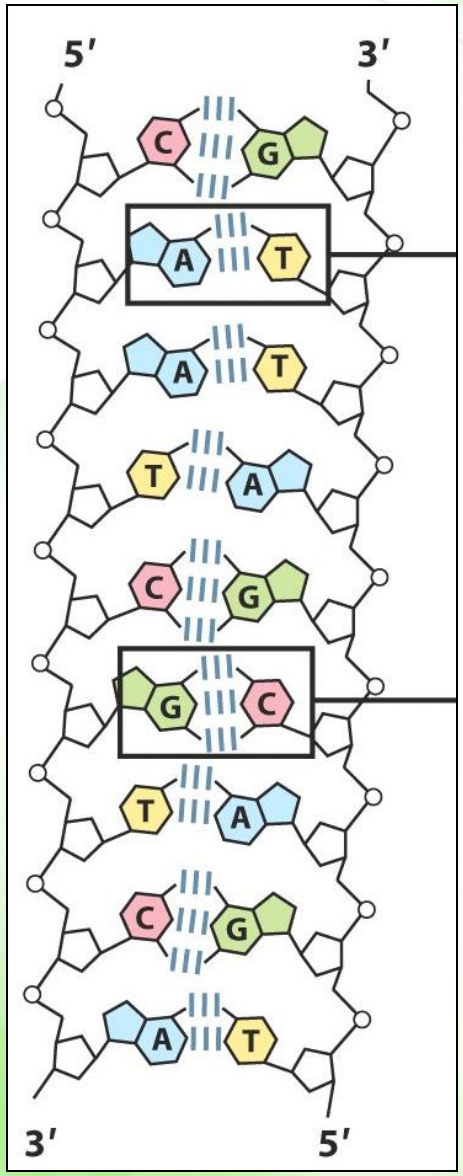
Chargaff's rules



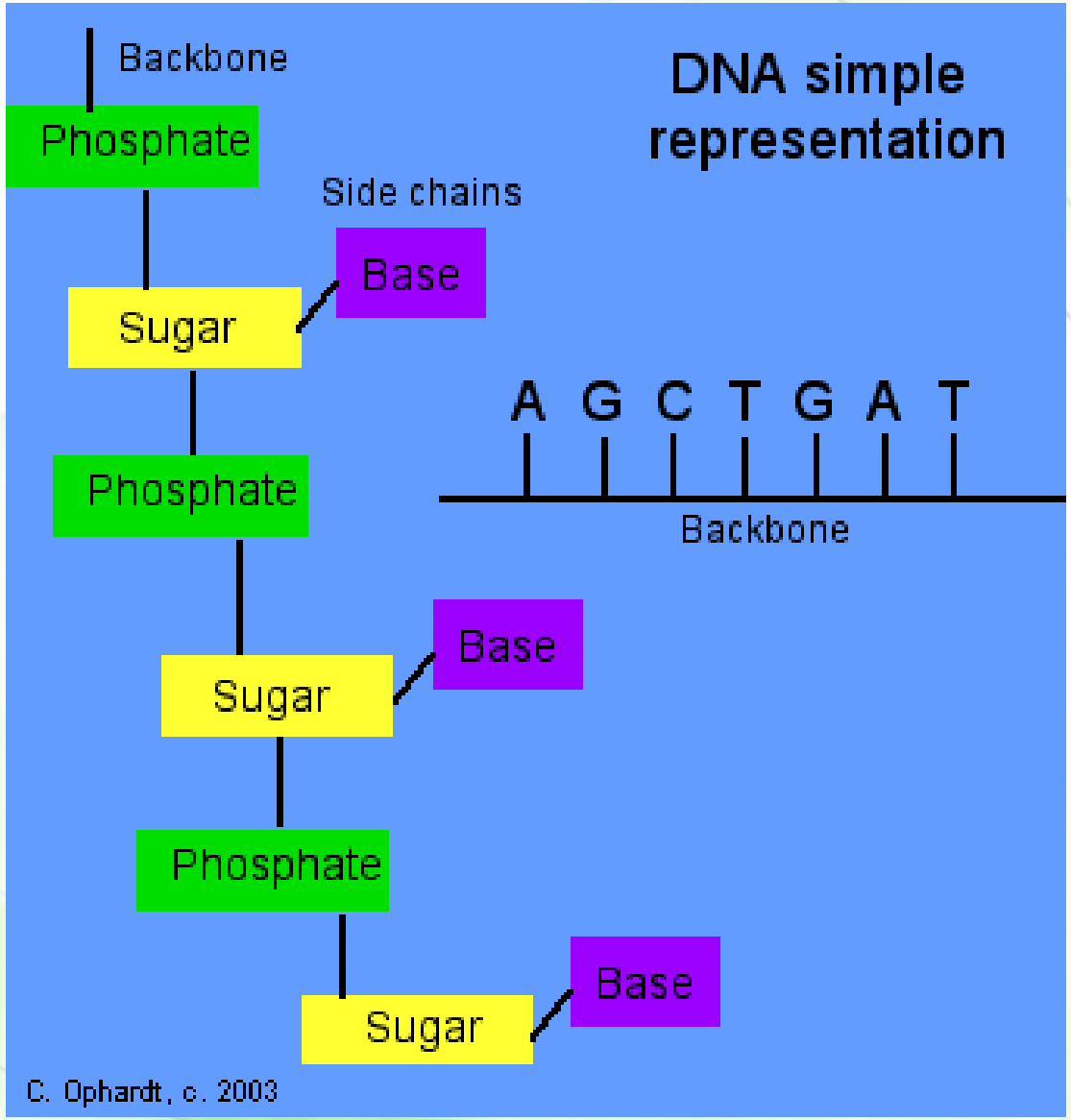
Base pairing



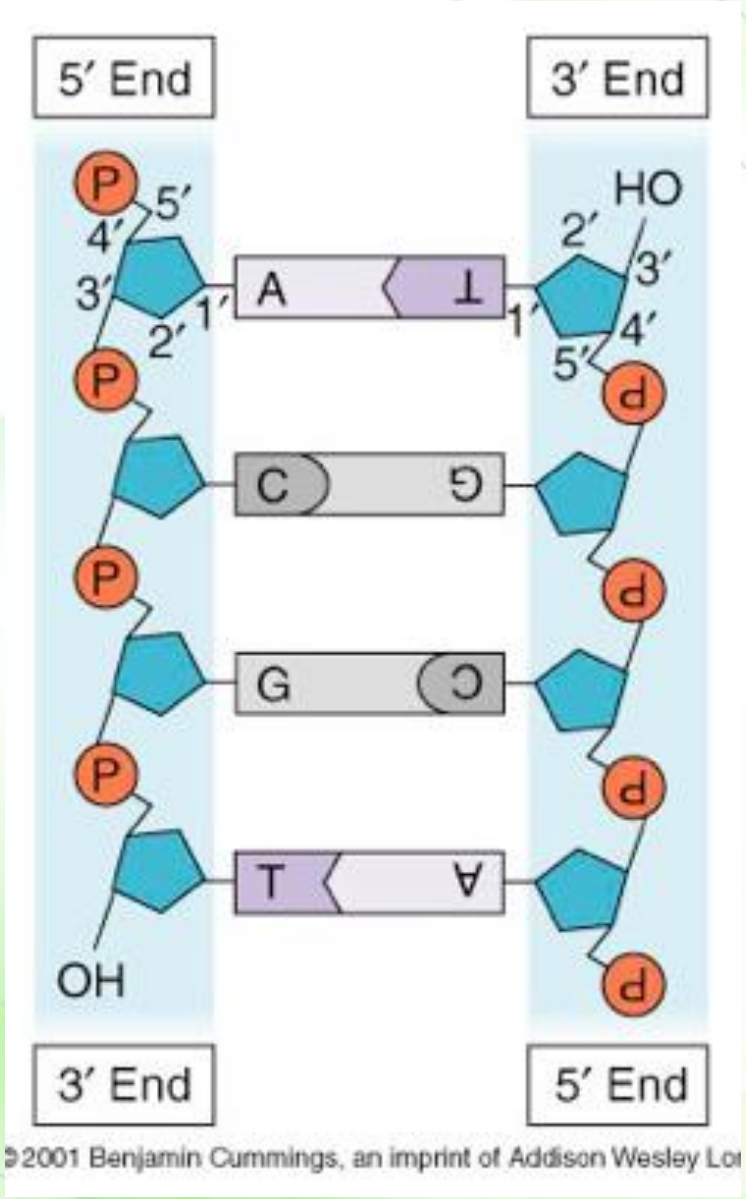
DNA is complementary



Backbone vs. side chains



DNA is anti-parallel



Writing the sequence of nucleic acids

DNA

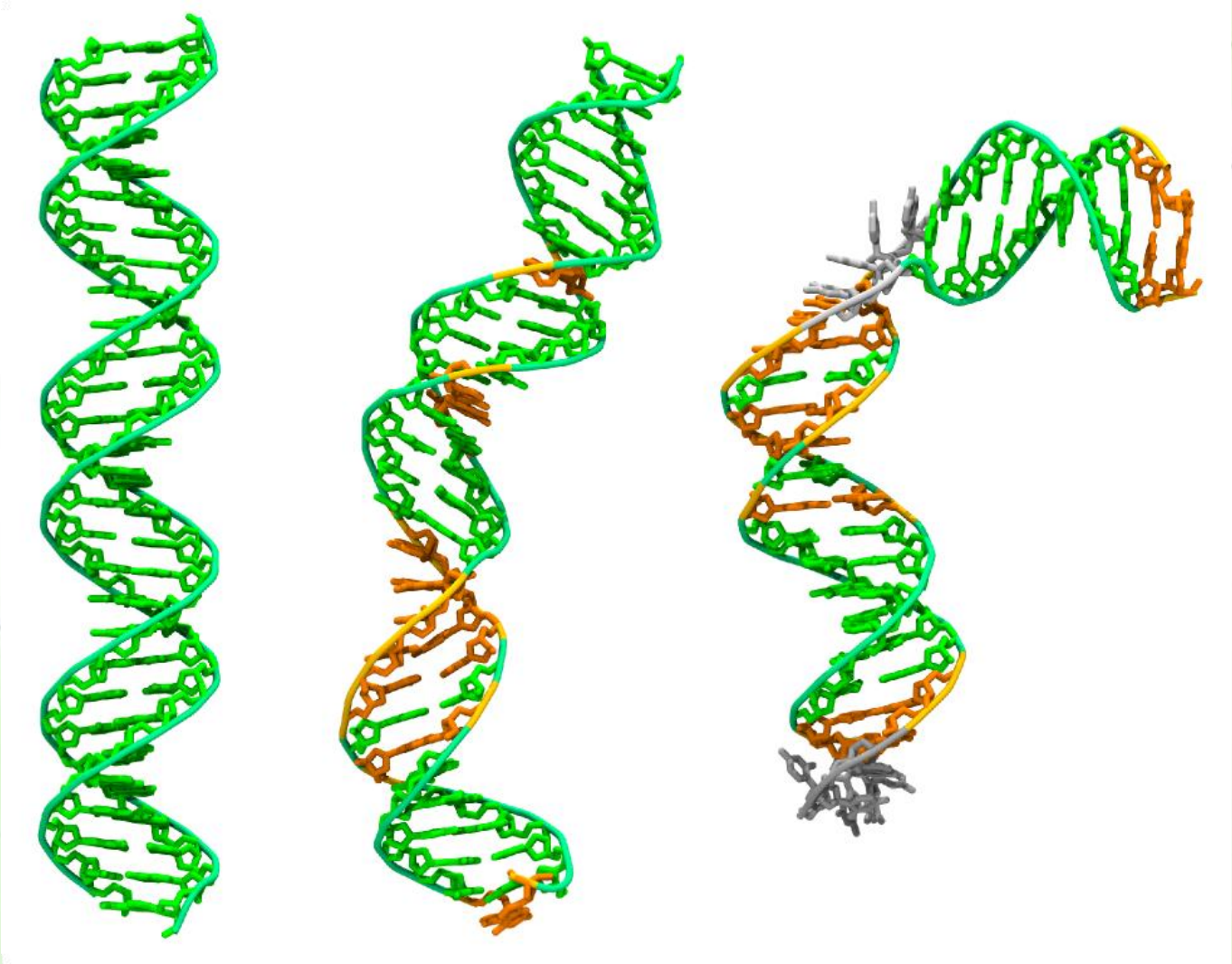
5’ ...A T G G C C T G G A C T T C A... 3’
3’ ...T A C C G G A C C T G A A G T... 5’

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

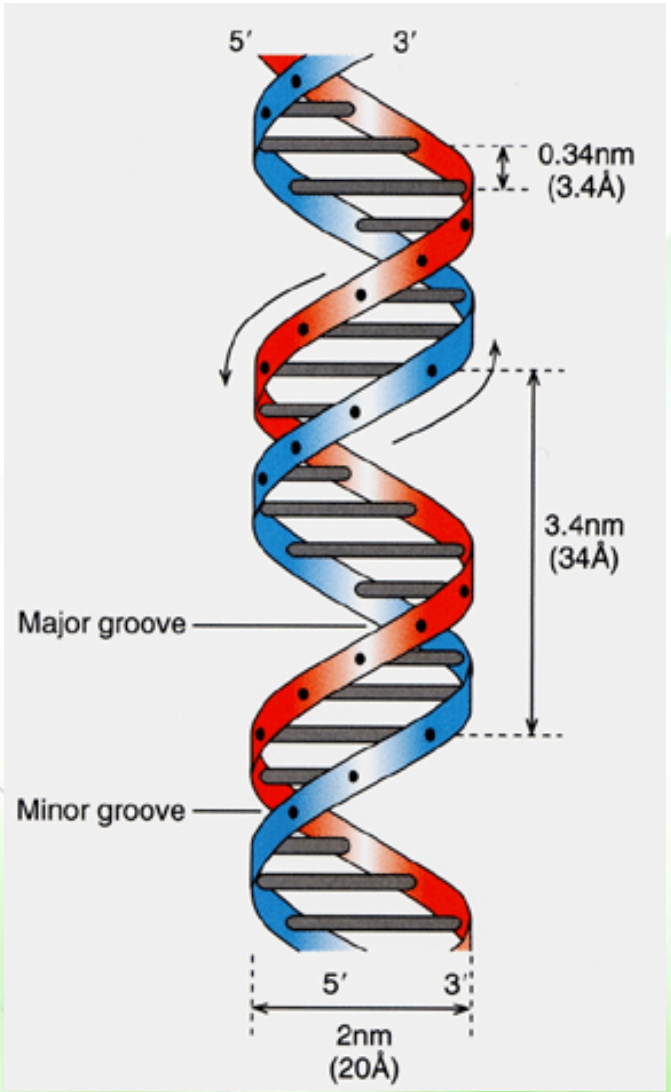
RNA

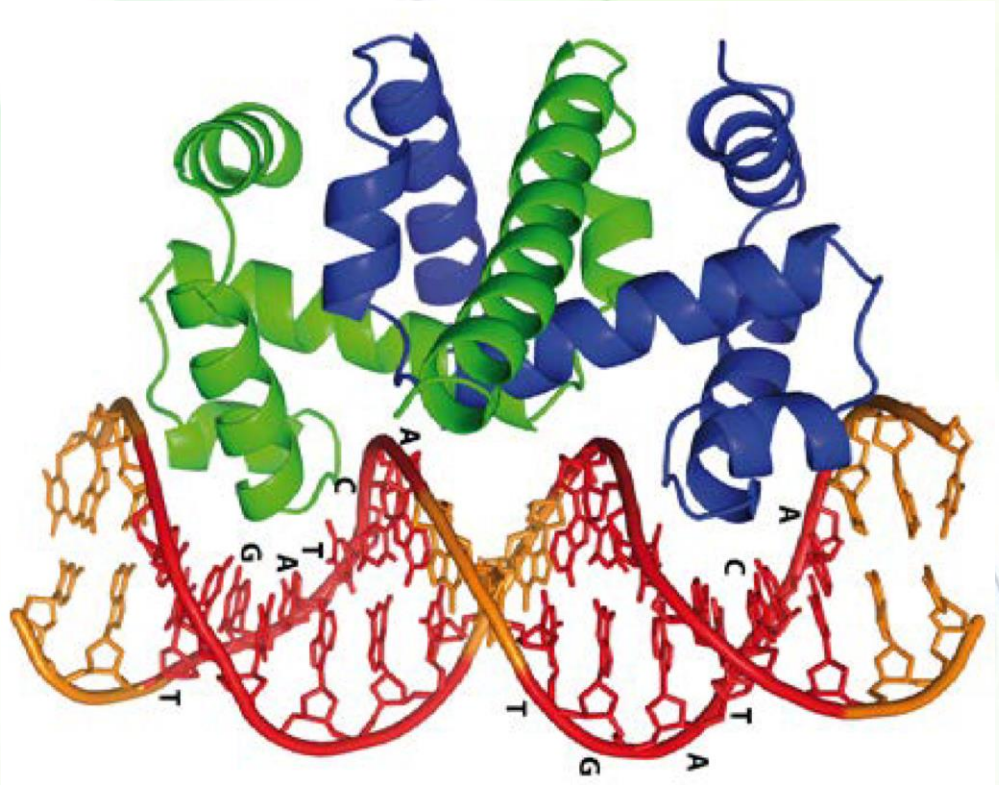
5’ ...A U G G C C U G G A C U U C A... 3’

DNA is flexible, yet stable

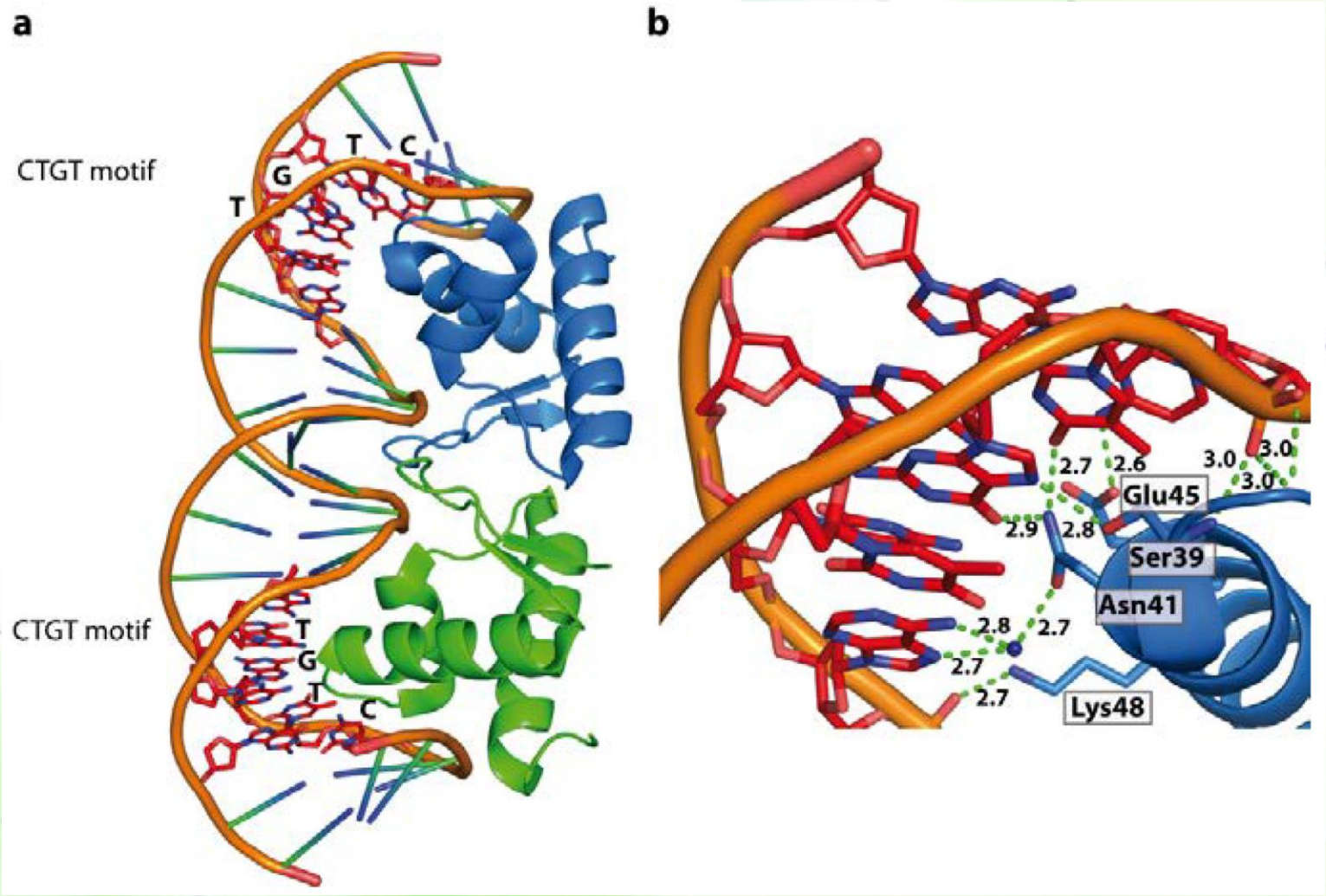


DNA grooves



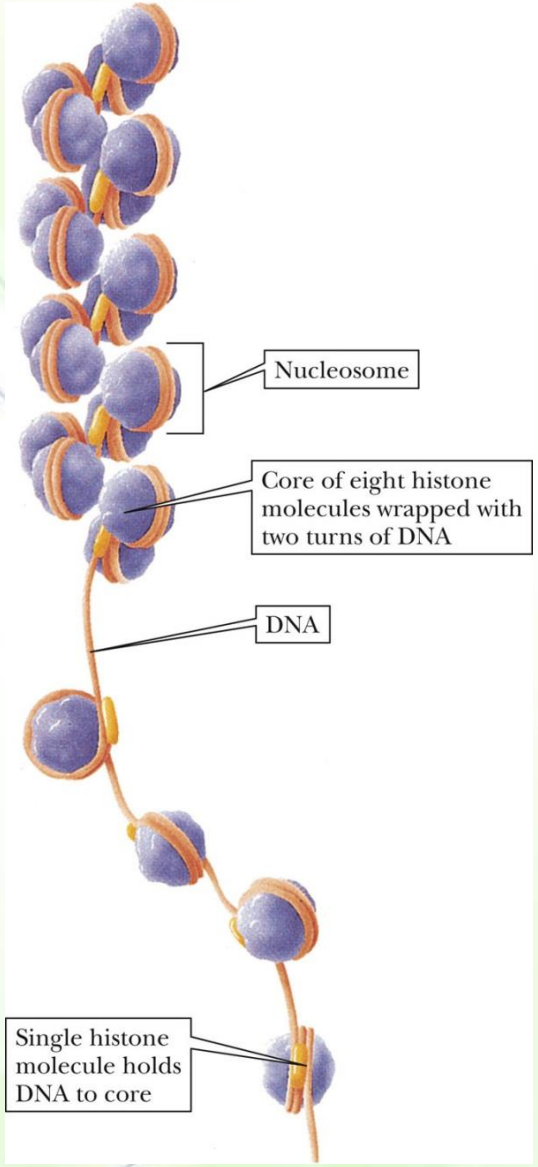


DNA-protein interaction



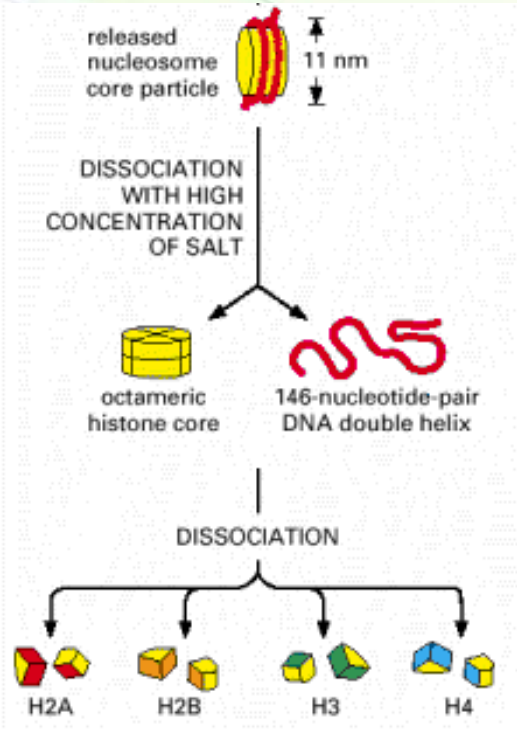
In eukaryotes...

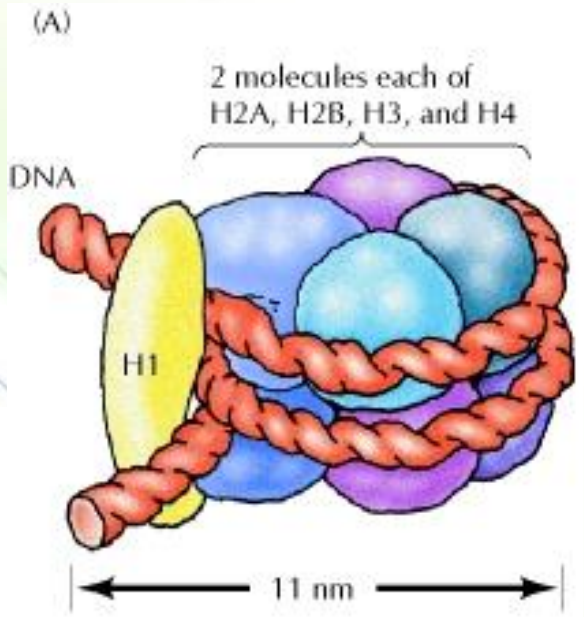
- In eukaryotes, DNA is coiled to package the large DNA.
- Eukaryotic DNA is complexed with a number of proteins, principally histones, which package DNA.
- Chromatin = DNA molecule + proteins.
- The basic structural unit of chromatin is known as a nucleosome.

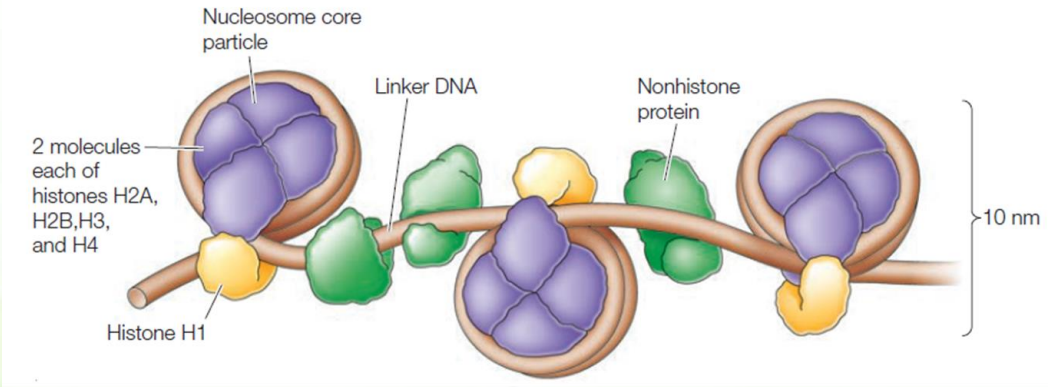


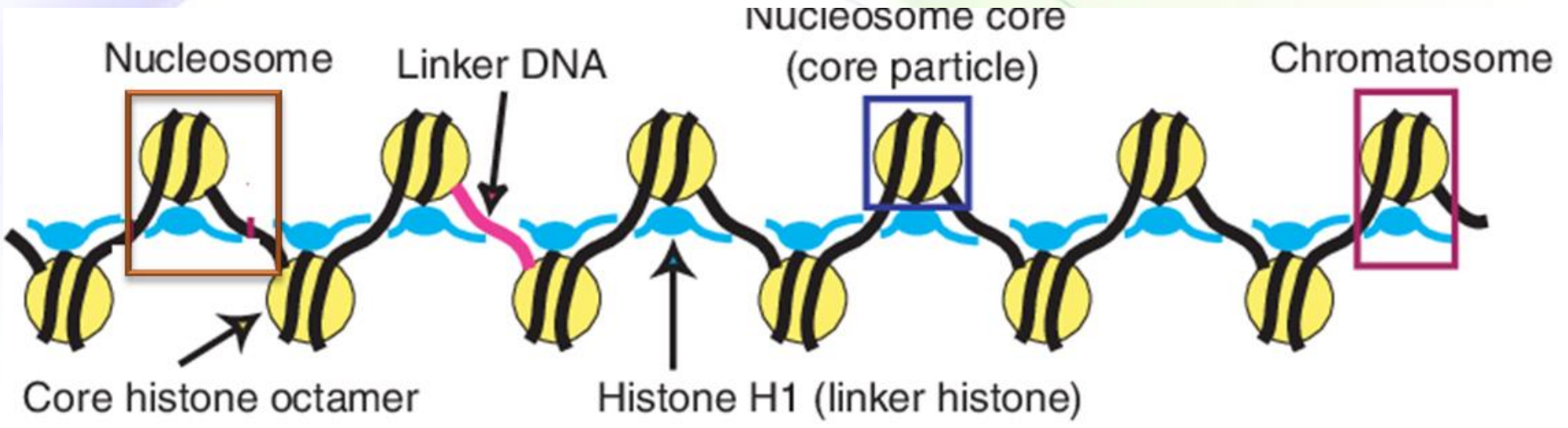
Nucleosomes

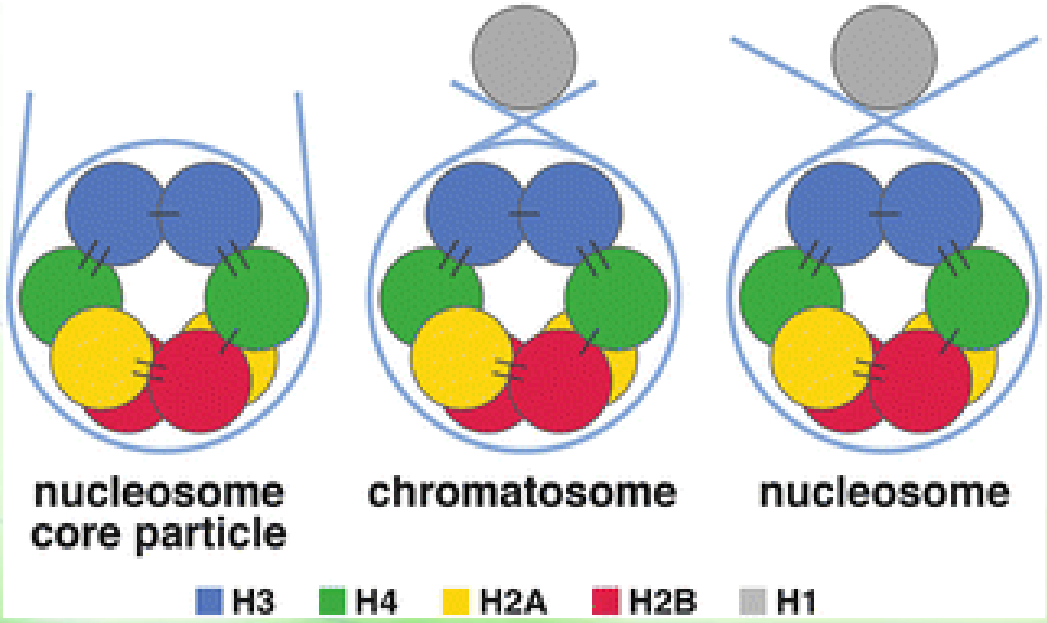
- A nucleosome consists of DNA wrapped around a nucleosome core particle, linker DNA, and histone H1.
- The histone core particle is an octamer (two molecules of histones H2A, H2B, H3, and H4) and the DNA wrapped around it.
- A linker DNA connects two nucleosome core particles.
- Histone H1 is bound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



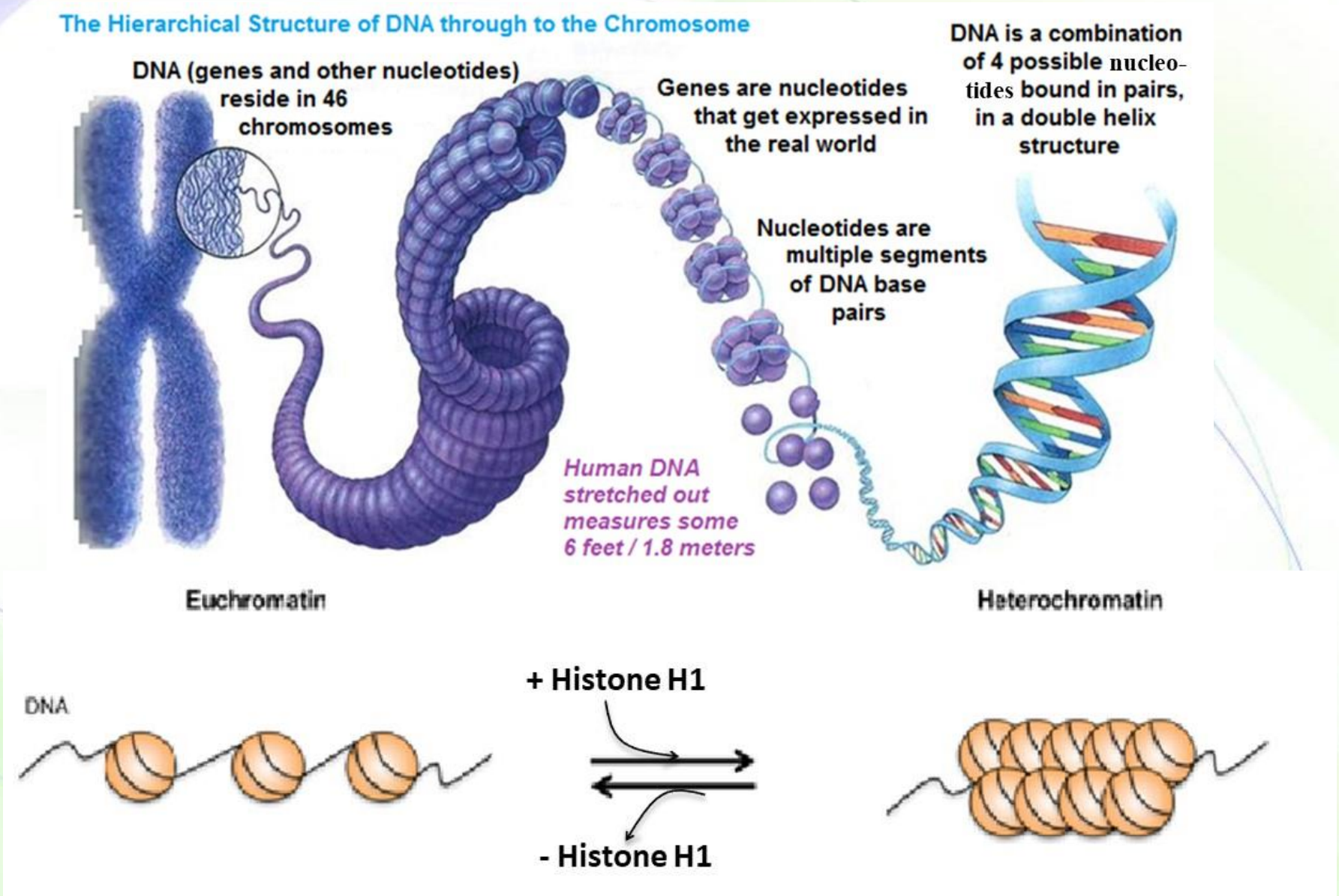





Nucleosome
Linker DNA
Nucleosome core
(core particle)
Chromatosome
Core histone octamer
Histone H1 (linker histone)

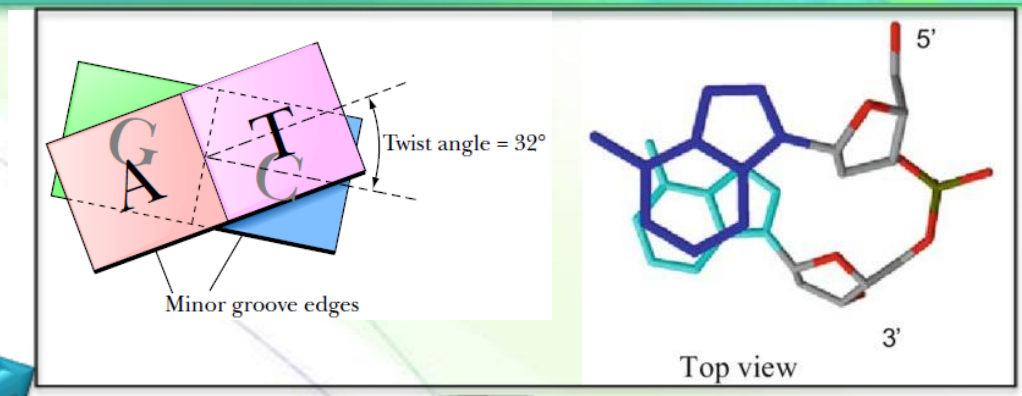

nucleosome
core particle
chromatosome
nucleosome
H3
H4
H2A
H2B
H1

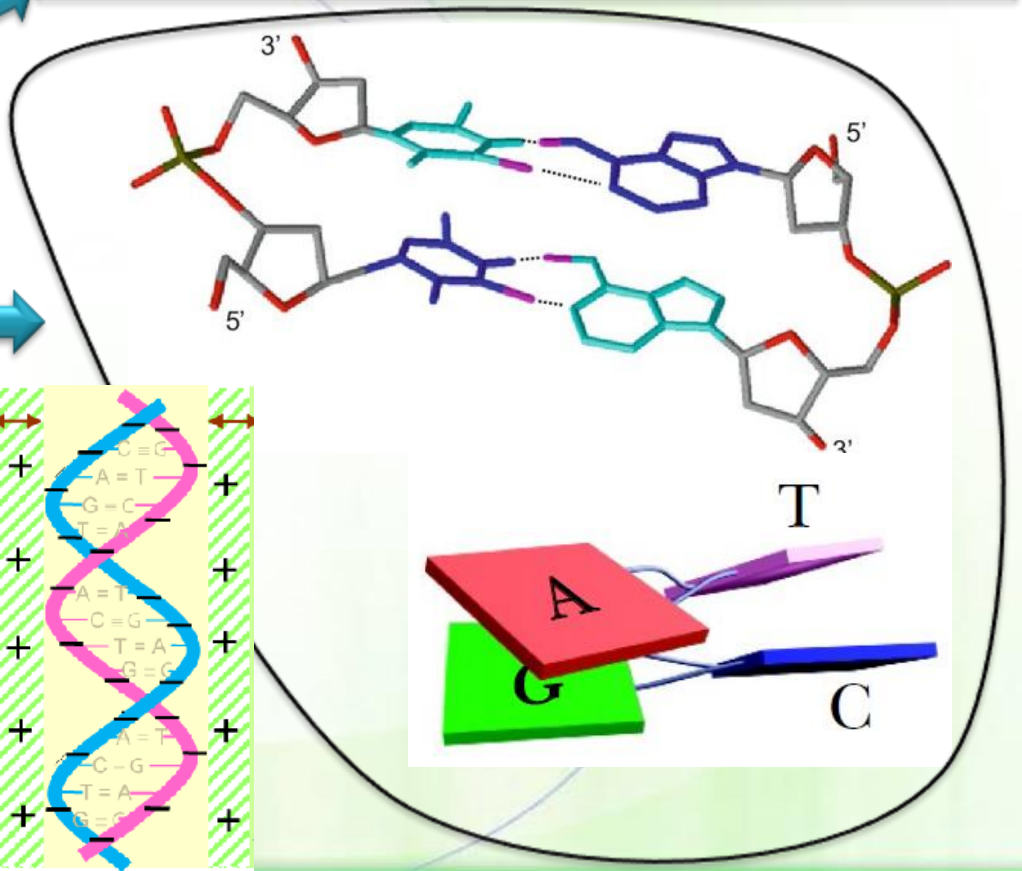
Histones package chromosomes



DNA-stabilizing forces

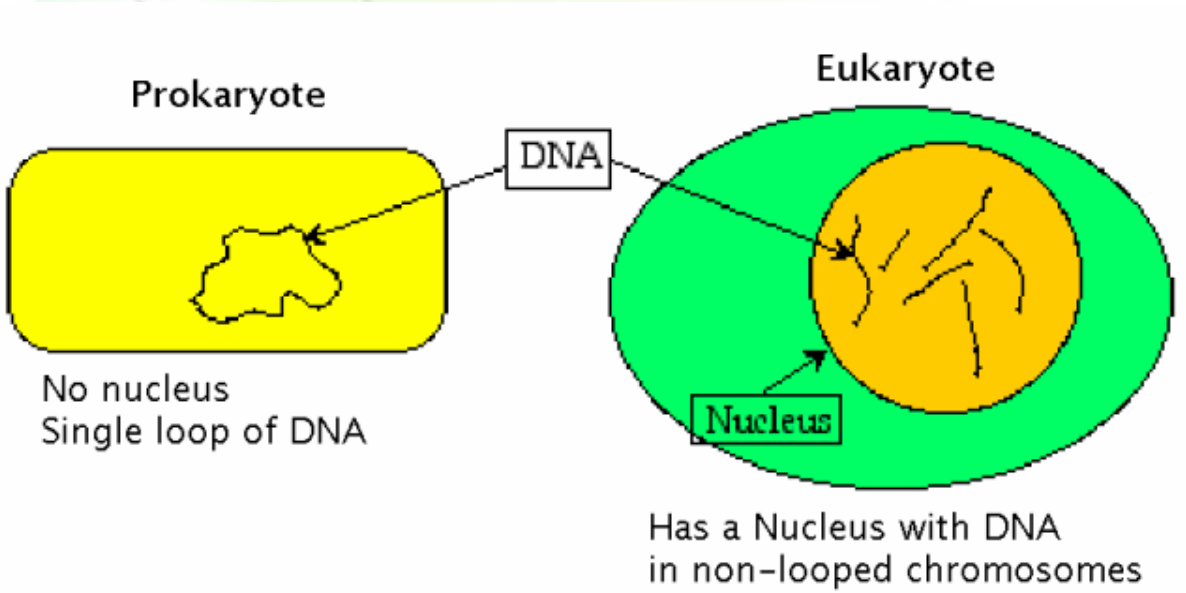
- Hydrogen bonds between complementary bases
- **Hydrophobic stacking: T**he hydrophobic rings of the bases interact with each other via hydrophobic interactions and van der Waals interactions.
- Helical twists: Each base pair is rotated with respect to the preceding one for maximal base pairing.
- Propeller 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.





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.

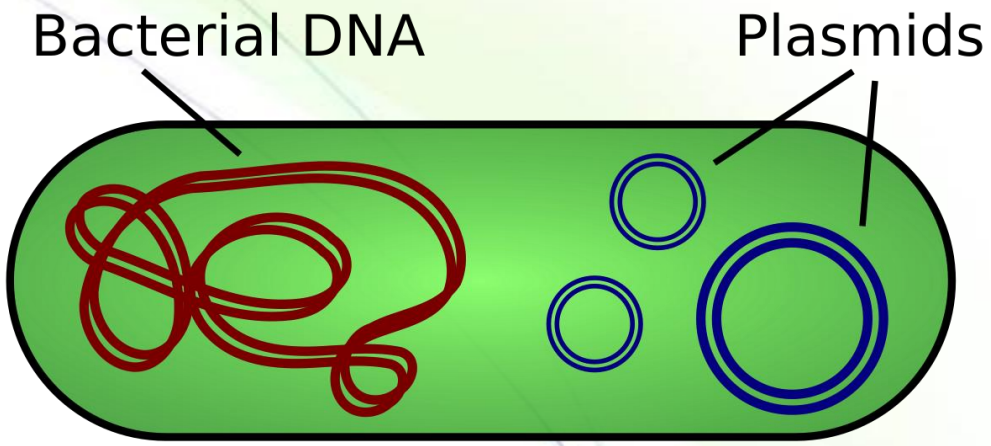


Bacterial chromosome and plasmids

The genetic materials of bacteria is of 2 types:

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

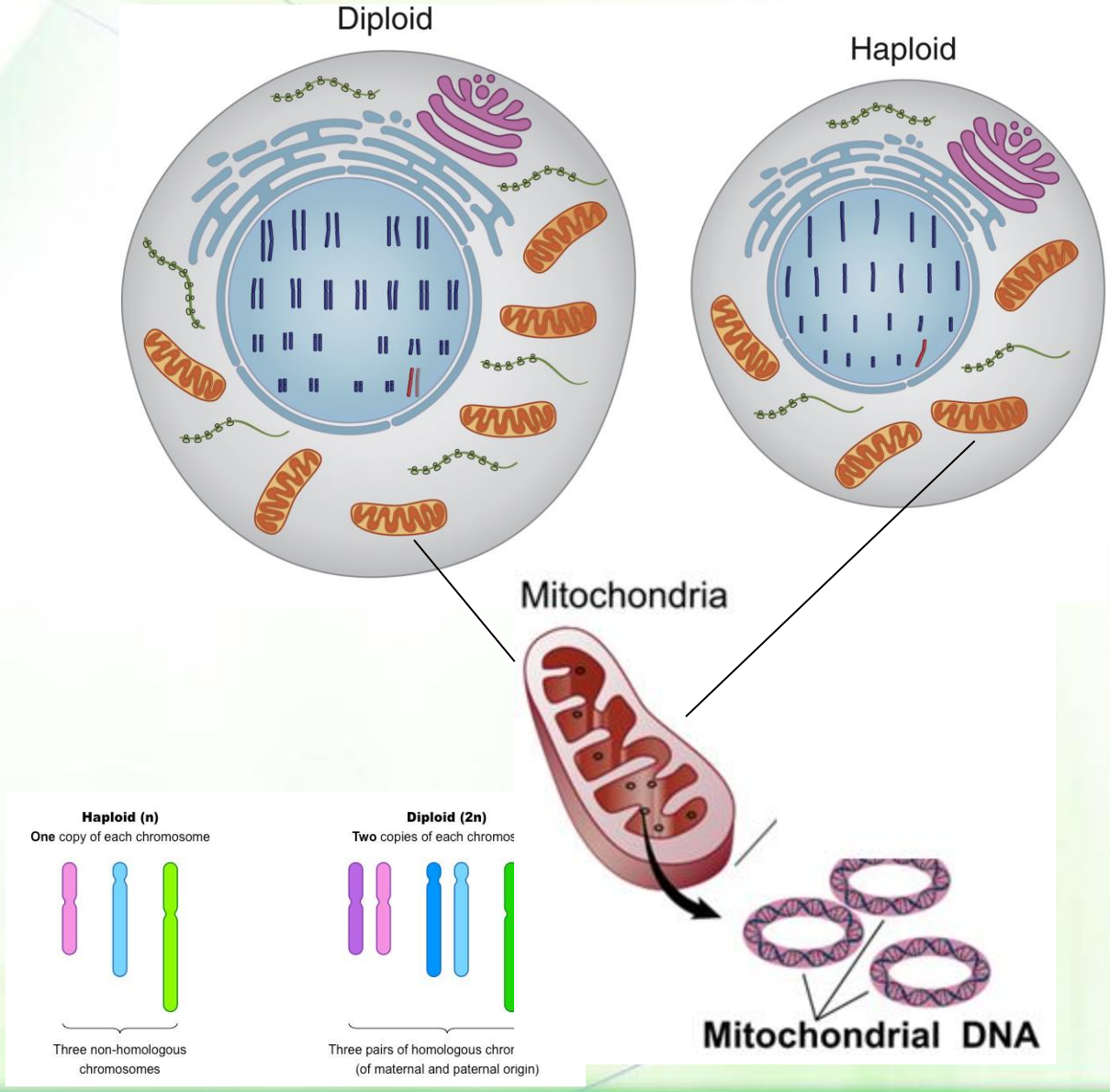
- The entire chromosome of the bacterium Escherichia coli is composed of a single circular double-stranded DNA molecule, contains >4 × 10^6 bp (length of 2 mm) carrying 4200 genes.



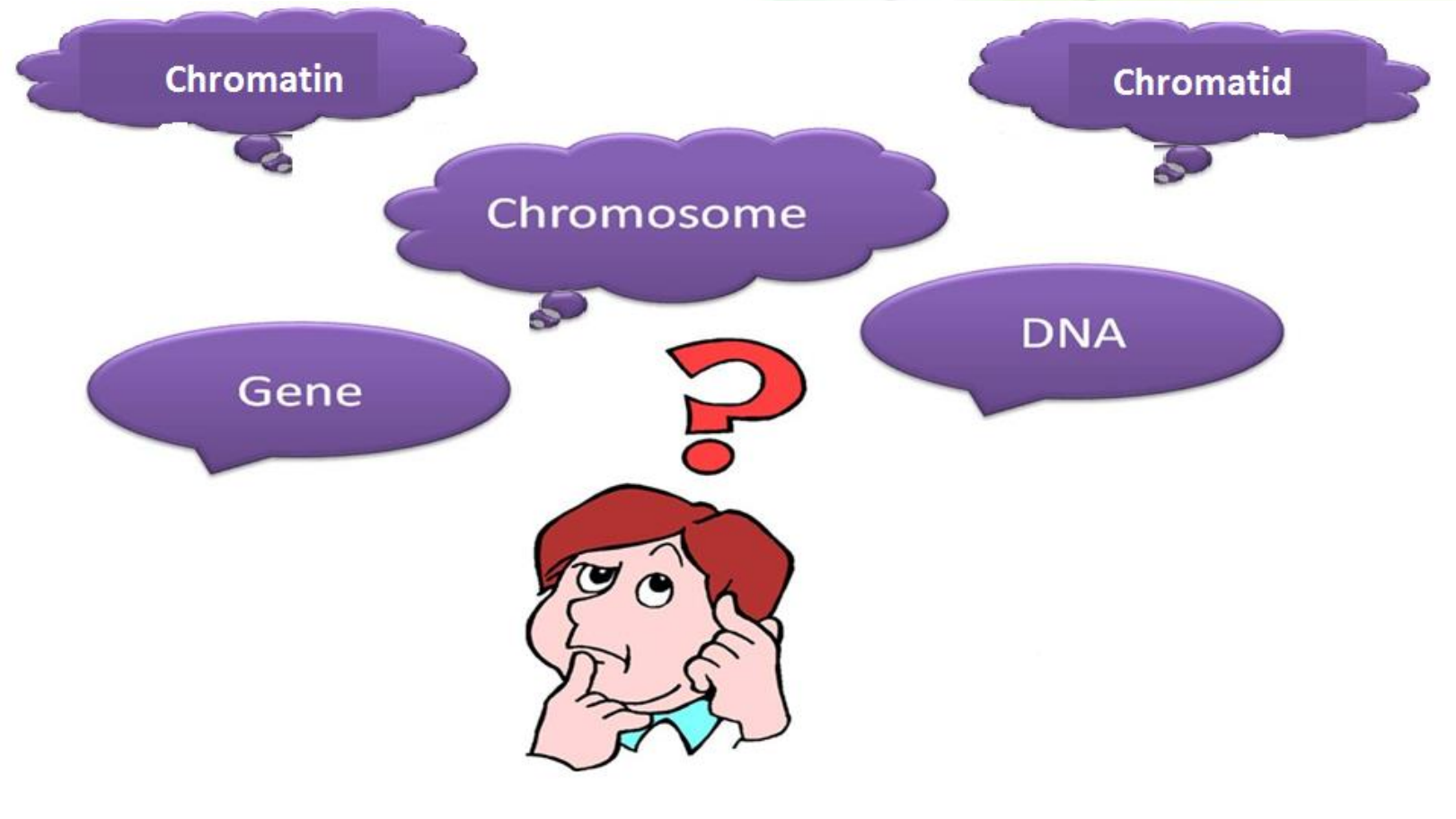
2. Plasmids: 1) Small, circular DNA molecules, 2) can replicate autonomously independent of the genomic chromosomes, 3) not infectious like viruses, 4) can carry genes, some of which confer resistance to antibiotics, and 5) exist as different types but one plasmid type per cell, 6) can exist as multiple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

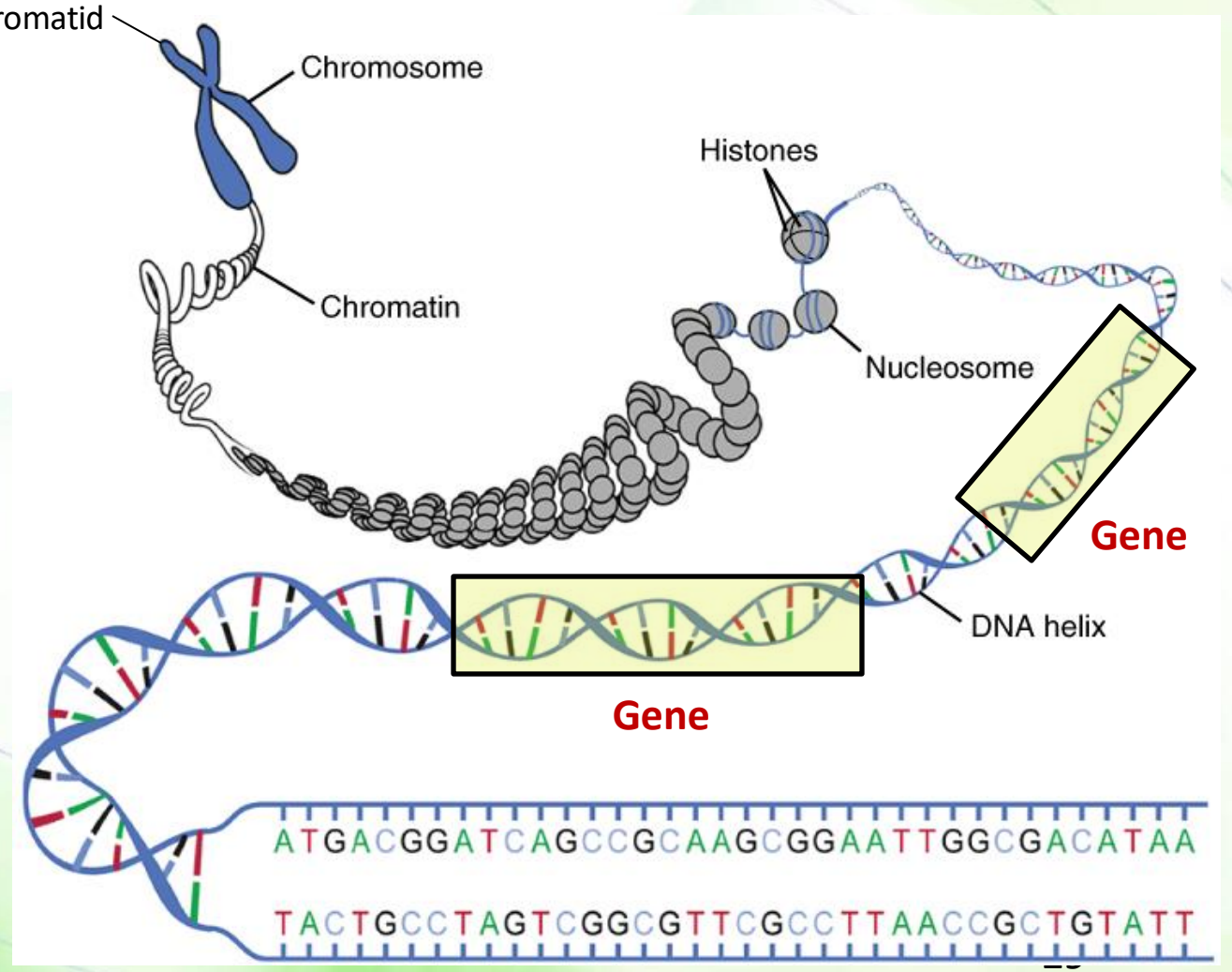
Human genomes

- The genetic material of humans is of 2 types:
  - The nuclear genome: organized as linear chromosomes that consists of ~$3x10^9$ nucleotides in haploid cells (sperm and egg) with a length of 1m per cell and that carry ~20000 genes.
    - Our somatic cells are diploid.
  - The mitochondrial genome, which constitutes less than 0.1% of the total DNA in a cell (~16500 bp) and encodes 37 genes.



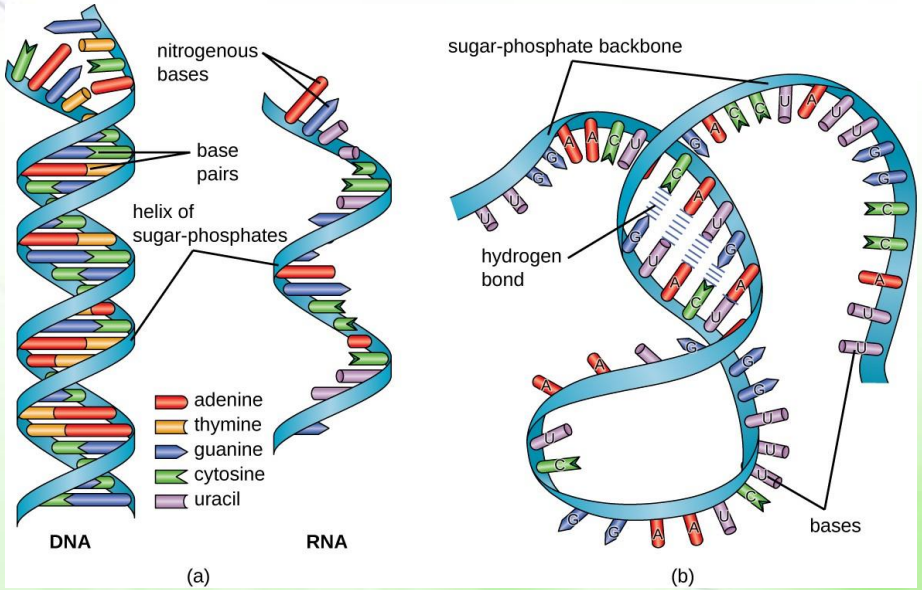
Terms to know




Chromatid
Chromosome
Histones
Chromatin
Nucleosome
Gene
DNA helix
Gene
ATGACGGATCAGCCGCAAGCGGAATTGGCGACATAA
TACTGCCTAGTCGGCGTTCGCCTTAACCGCTGTATT

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), 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 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