



Molecular Biology (1)

Structure of nucleic acids

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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

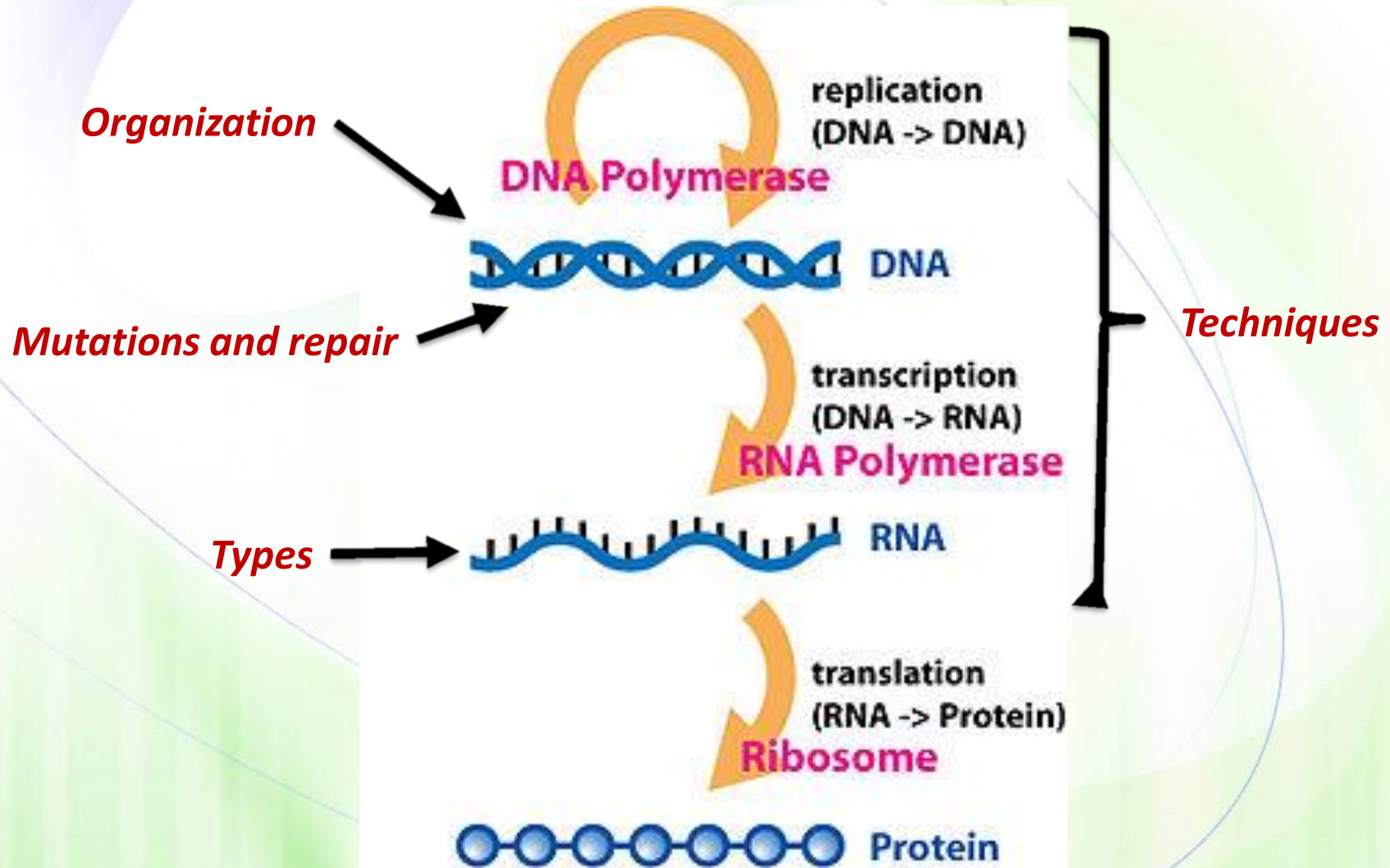


- This lecture
- Cooper, Ch. 2, pp. 54-56, Ch. 4, 116-118, Ch. 6, pp.203-208

What is molecular biology?



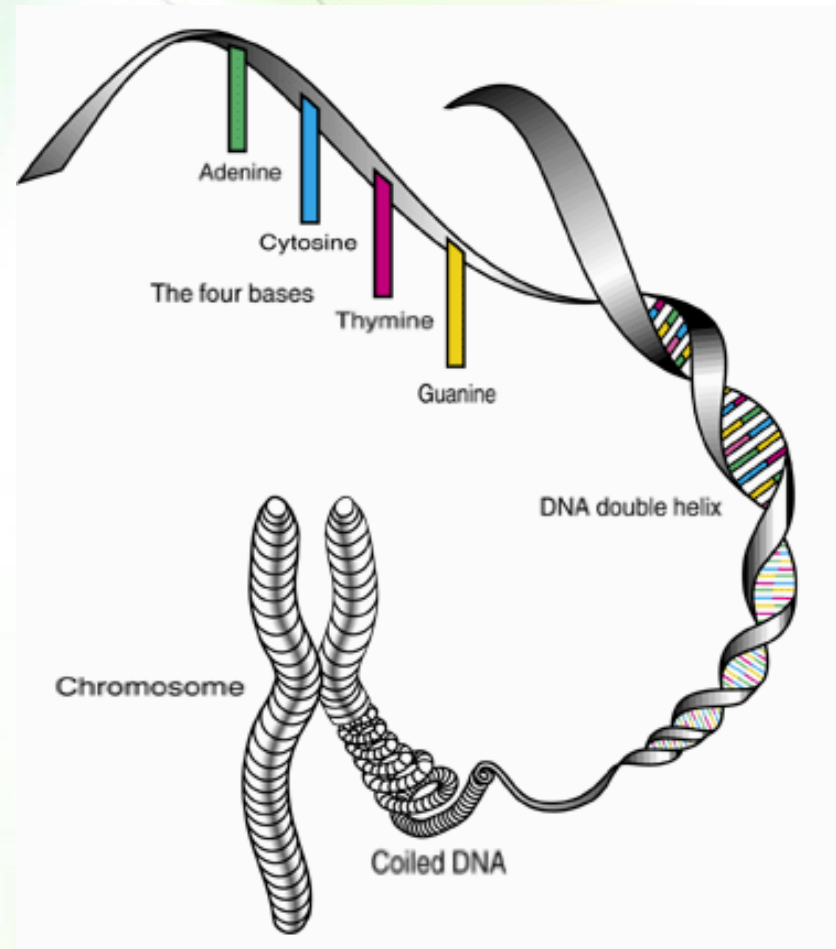
Central dogma of molecular biology



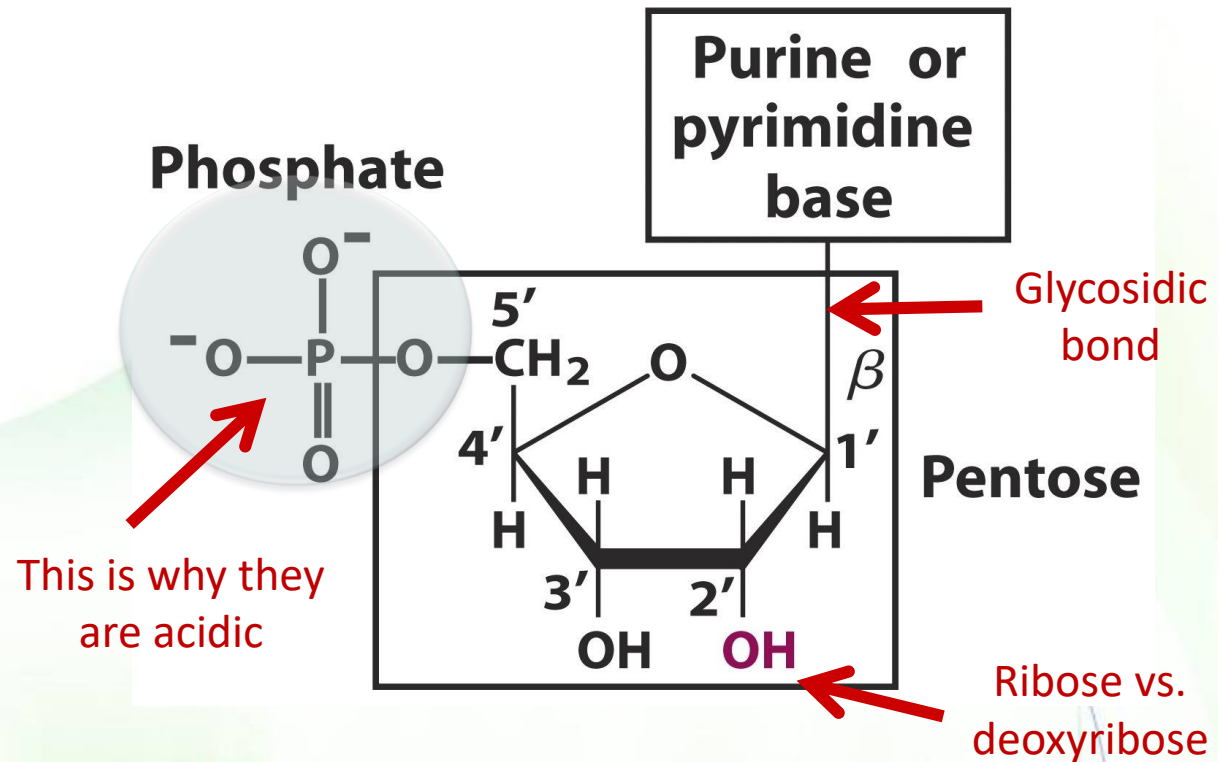
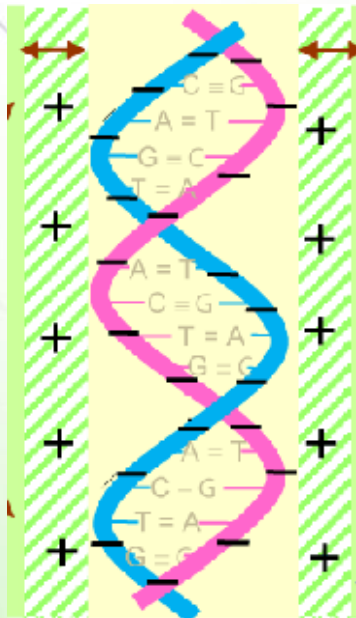
Nucleic acids



- 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.

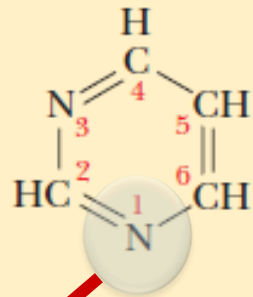


Chemical composition and bonds



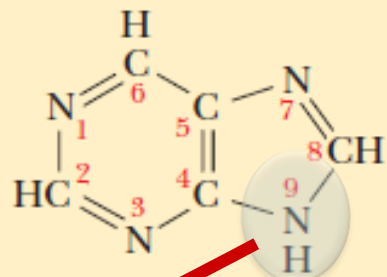
- Positively charged ions (Na^+ or Mg^{2+}) associate with the phosphate groups.
 - Example: histones

Nitrogenous bases

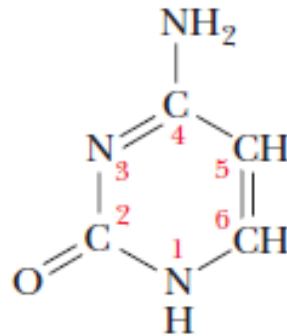


Pyrimidine

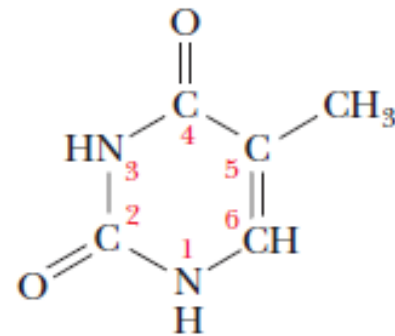
Glycosidic bond



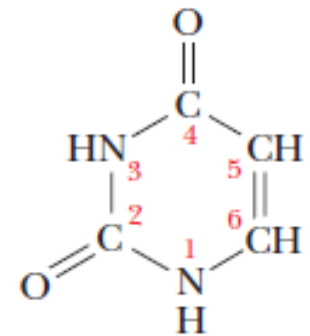
Purine



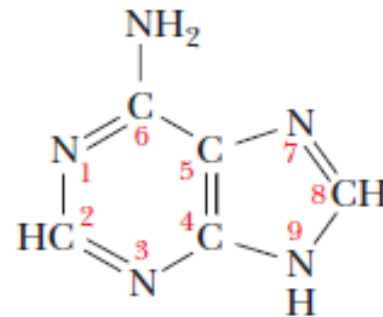
Cytosine
(in DNA & RNA)



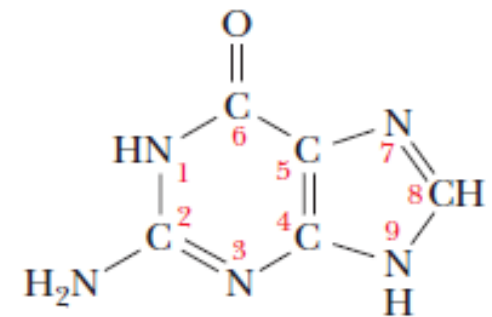
Thymine
(in DNA & some RNA)



Uracil
(in RNA)



Adenine
(in DNA & RNA)



Guanine
(in DNA & RNA)

In prokaryotes and eukaryotes



not viruses

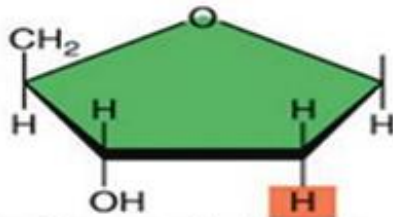
DNA vs. RNA



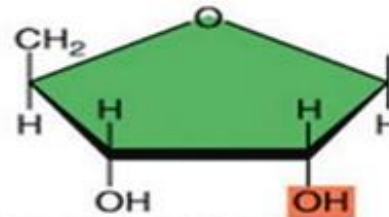
Double-stranded



Generally single-stranded

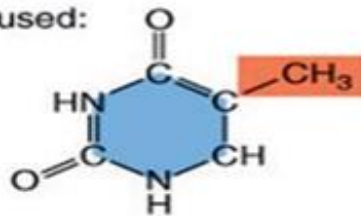


Deoxyribose as the sugar



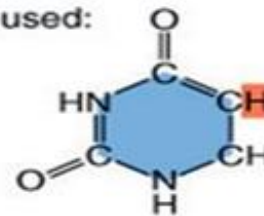
Ribose as the sugar

Bases used:



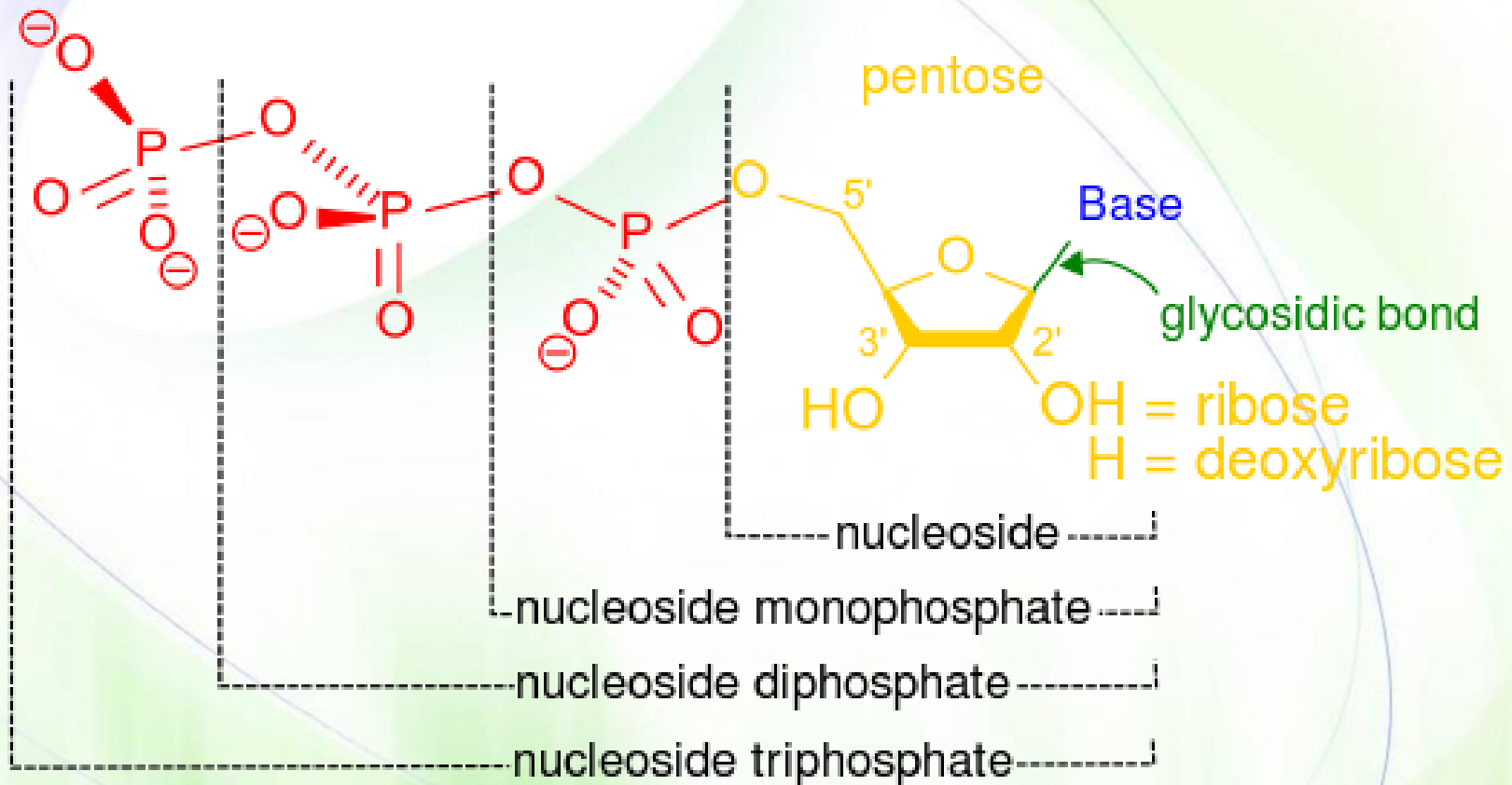
Thymine (T)
Cytosine (C)
Adenine (A)
Guanine (G)

Bases used:

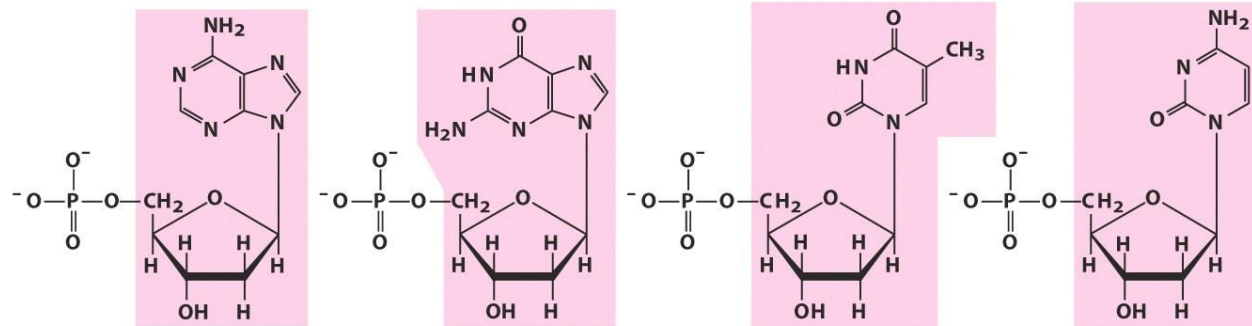


Uracil (U)
Cytosine (C)
Adenine (A)
Guanine (G)

Nucleotides vs. Nucleosides



Nucleotides vs. Nucleosides



Nucleotide: Deoxyadenylate
(deoxyadenosine 5'-monophosphate)

Symbols: A, dA, dAMP

Nucleoside: Deoxyadenosine

Nucleotide: Deoxyguanylate
(deoxyguanosine 5'-monophosphate)

Symbols: G, dG, dGMP

Nucleoside: Deoxyguanosine

Nucleotide: Deoxythymidylate
(deoxythymidine 5'-monophosphate)

Symbols: T, dT, dTMP

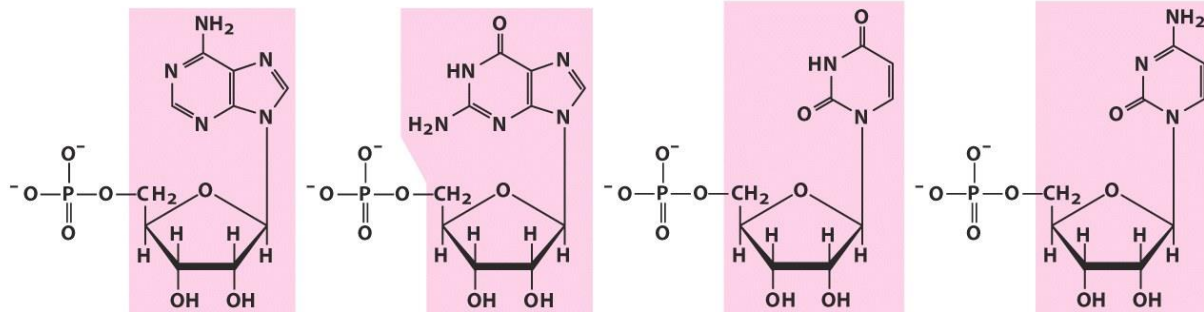
Nucleoside: Deoxythymidine

Nucleotide: Deoxycytidylate
(deoxycytidine 5'-monophosphate)

Symbols: C, dC, dCMP

Nucleoside: Deoxycytidine

(a) Deoxyribonucleotides



Nucleotide: Adenylate (adenosine 5'-monophosphate)

Symbols: A, AMP

Nucleoside: Adenosine

Nucleotide: Guanylate (guanosine 5'-monophosphate)

Symbols: G, GMP

Nucleoside: Guanosine

Nucleotide: Uridylate (uridine 5'-monophosphate)

Symbols: U, UMP

Nucleoside: Uridine

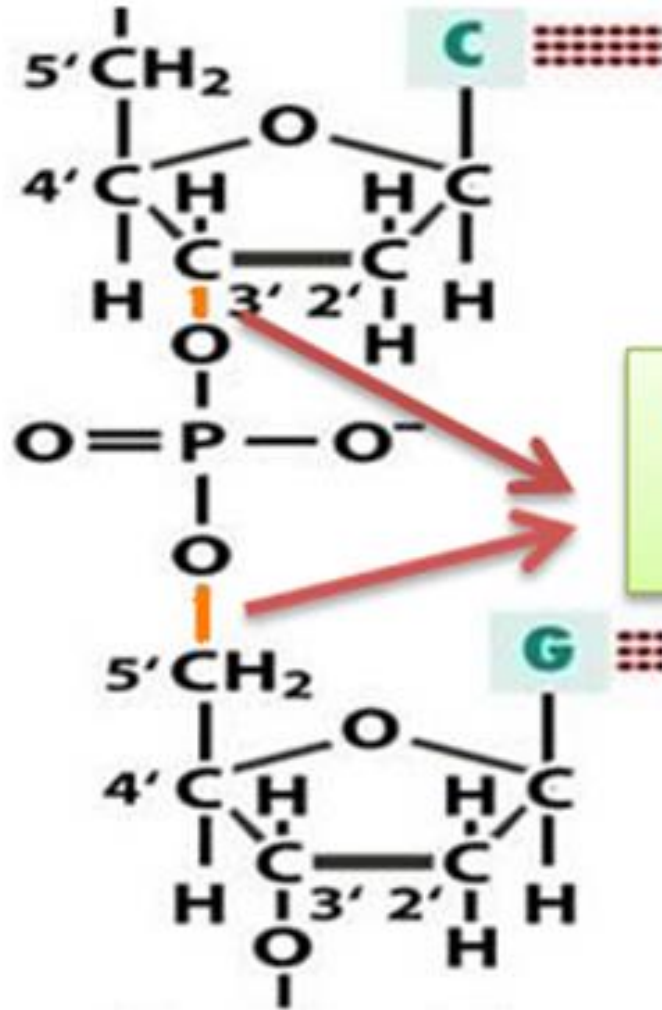
Nucleotide: Cytidylate (cytidine 5'-monophosphate)

Symbols: C, CMP

Nucleoside: Cytidine

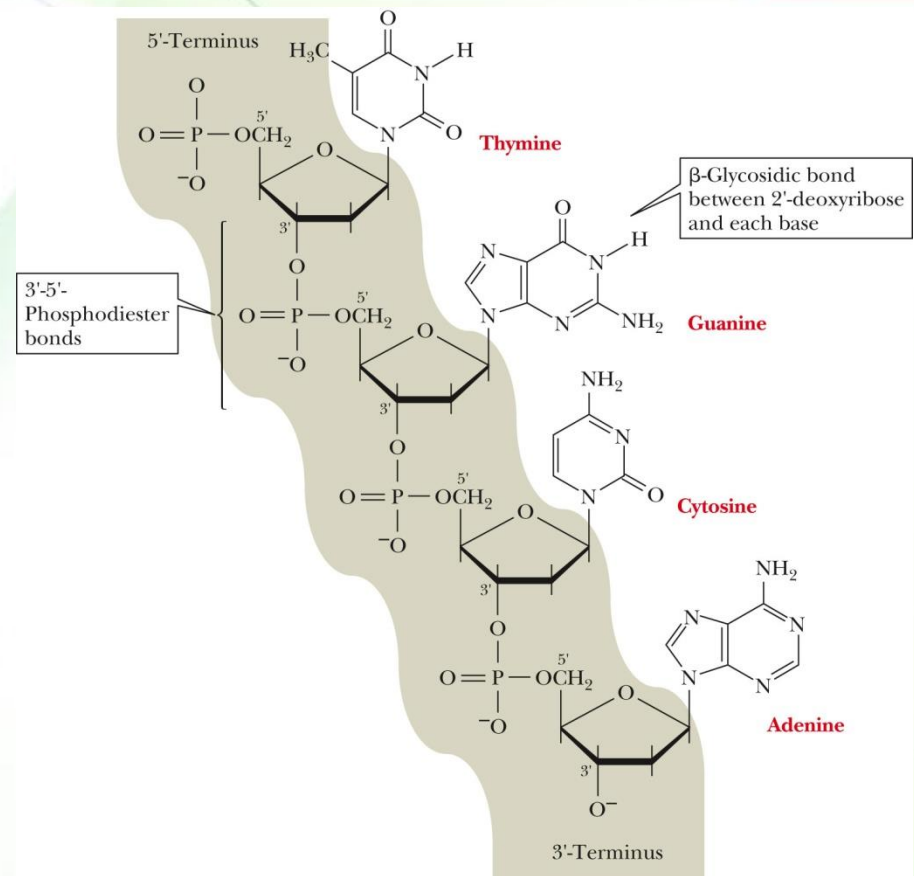
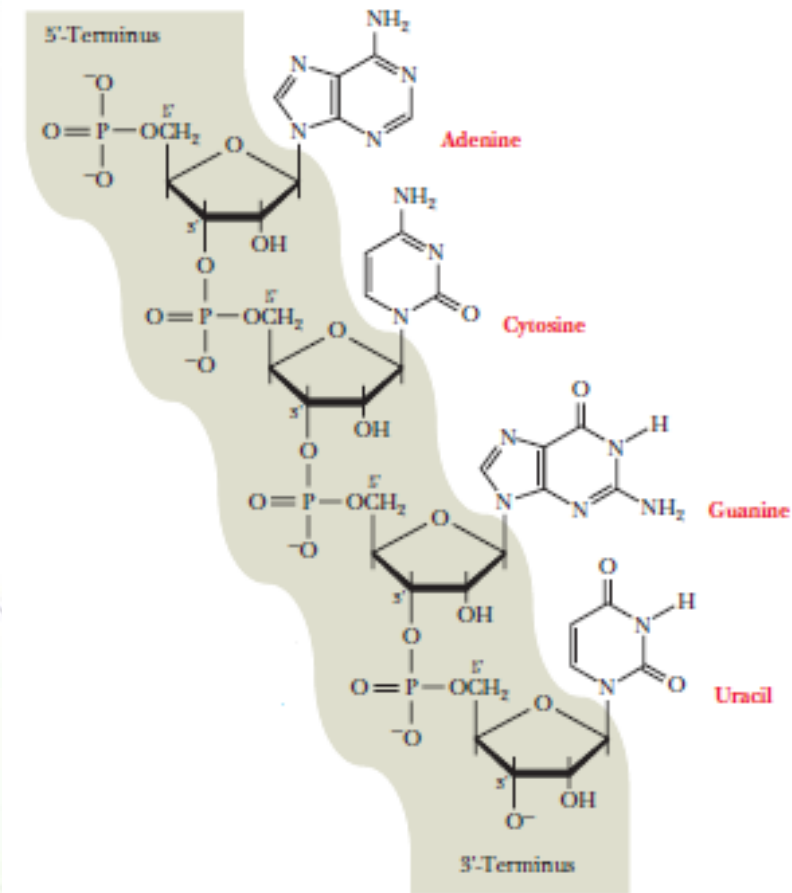
(b) Ribonucleotides

Formation of a nucleic acid polymer



1st and 2nd ester linkage
(phosphodiester bond)

Nucleic acid polymers

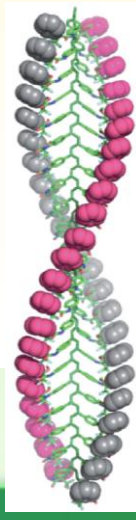
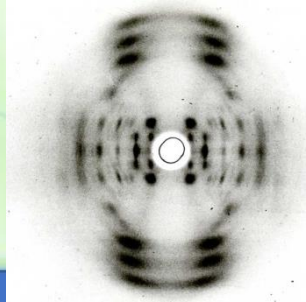
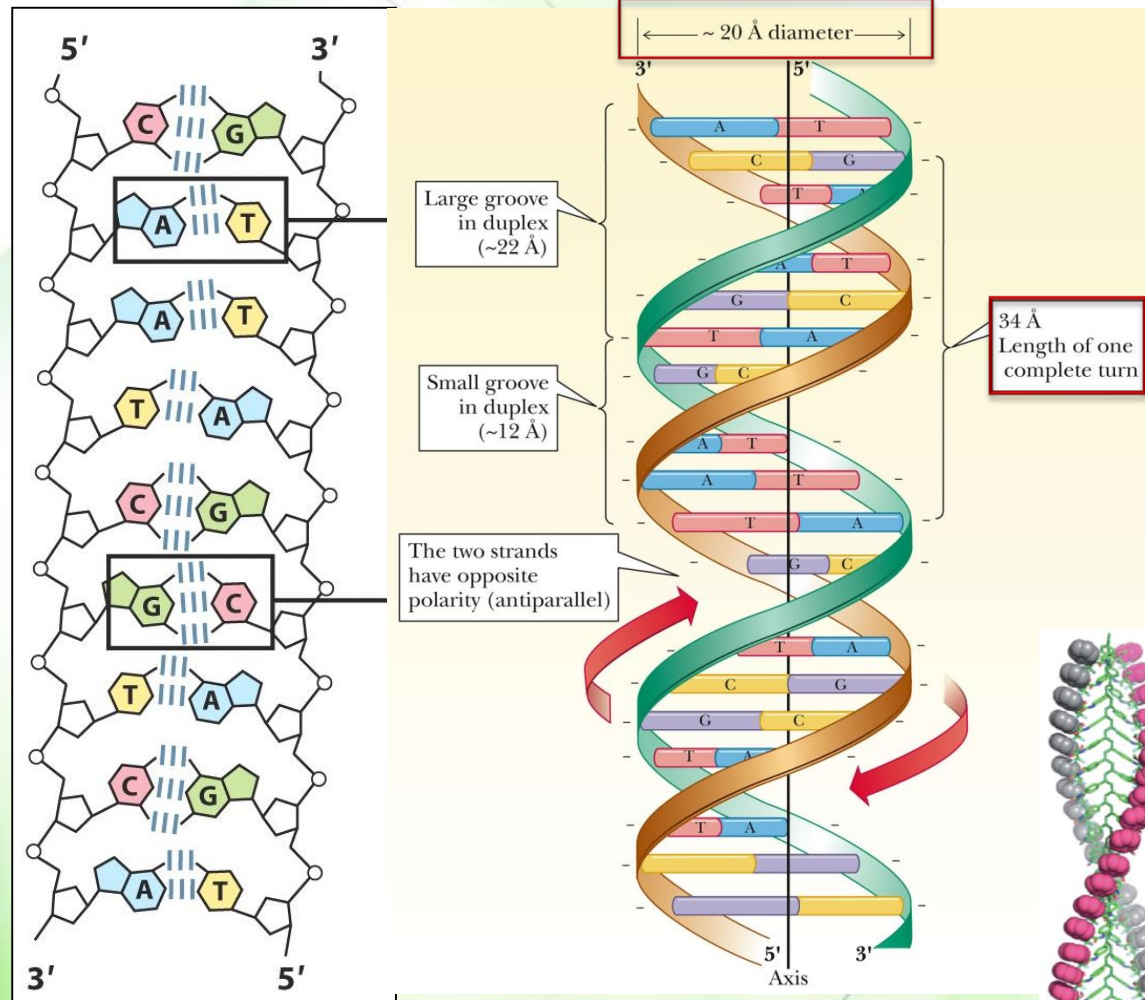


- A letter d can be added to indicate a deoxyribonucleotide residue.
- for example, dG is substituted for G.
- The deoxy analogue of a ribooligonucleotide would be d(GACAT).

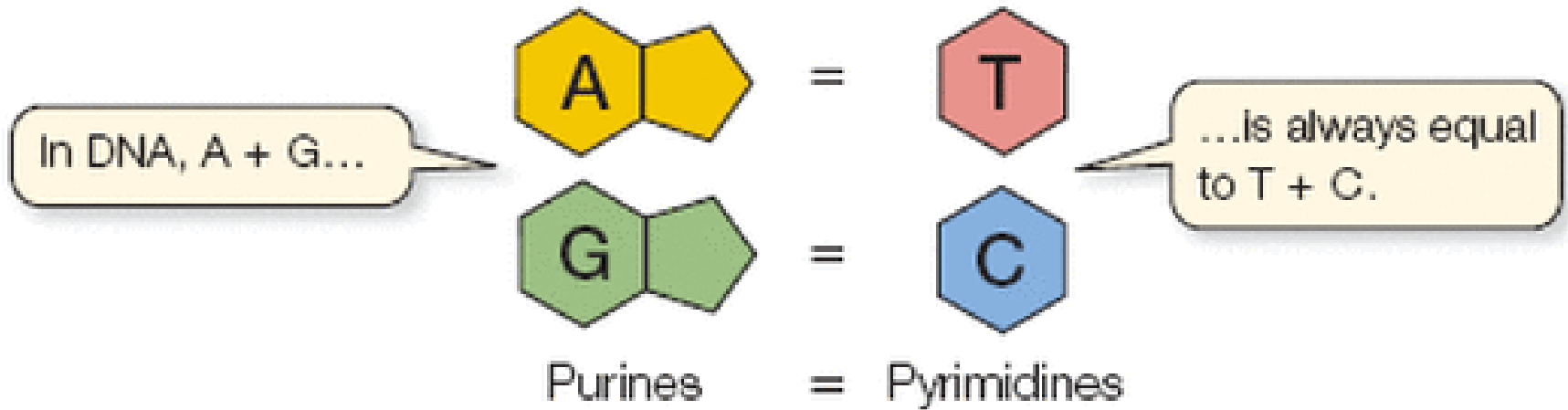
DNA structure



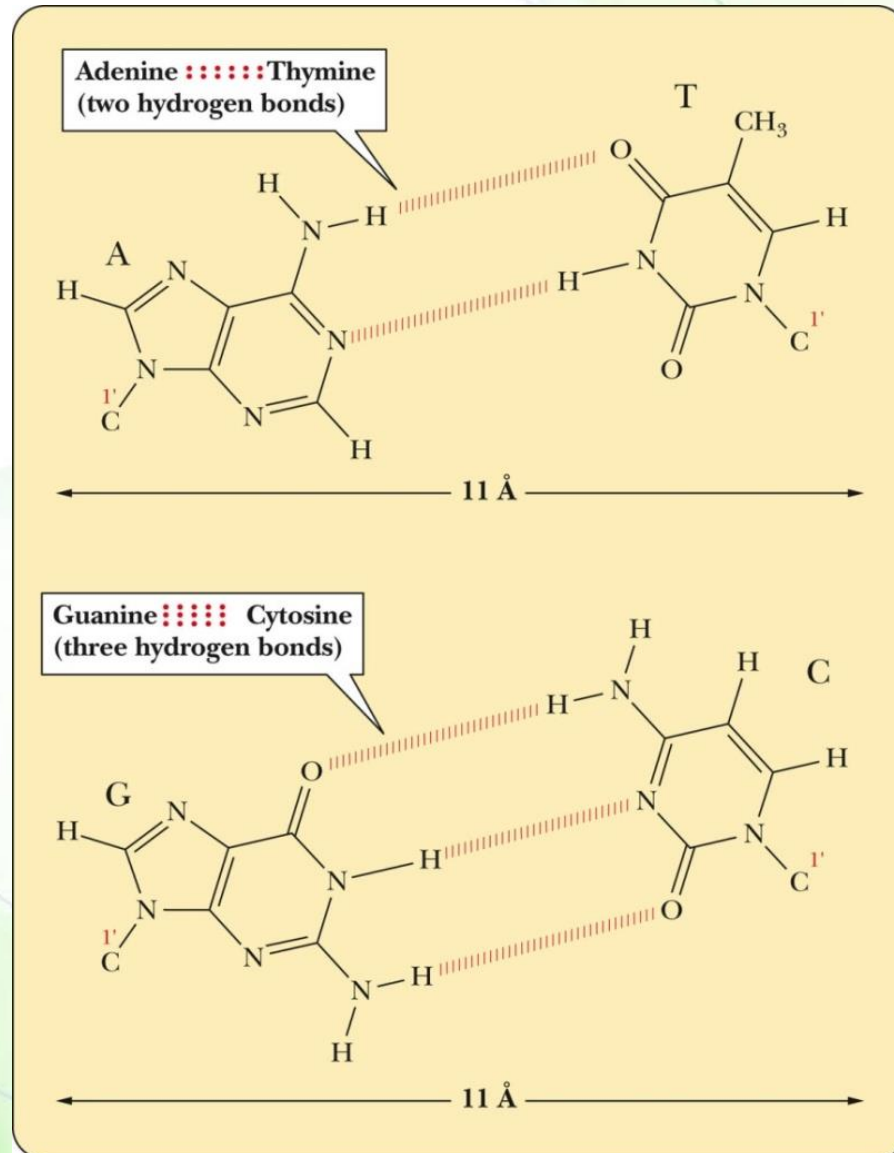
- A double helix
- Specific base-pairing
 - A = T; G = C; Pur = pyr
- Complementary
- Backbone vs. side chains
- Antiparallel
- Stability vs. flexibility
- Groovings



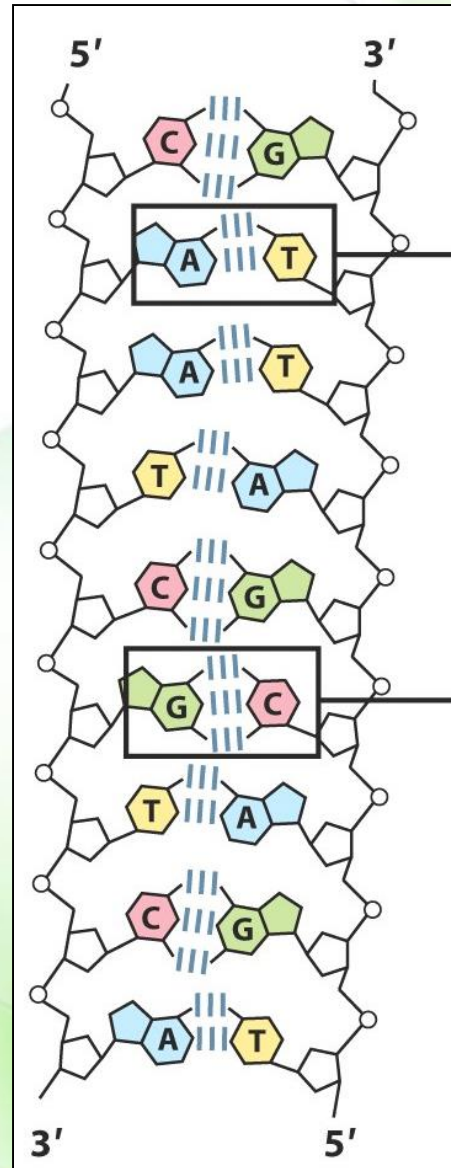
Chargaff's rules



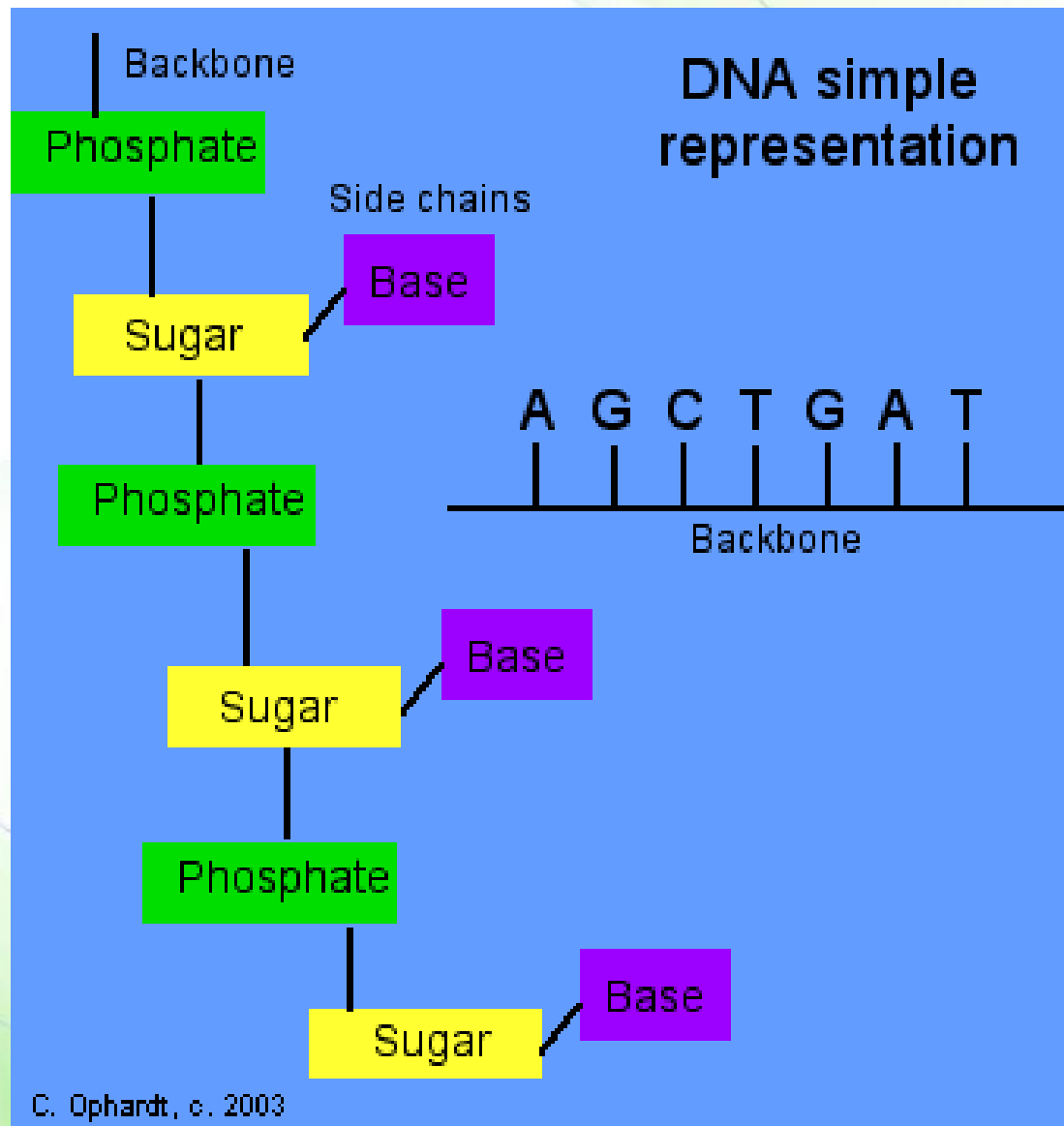
Base pairing



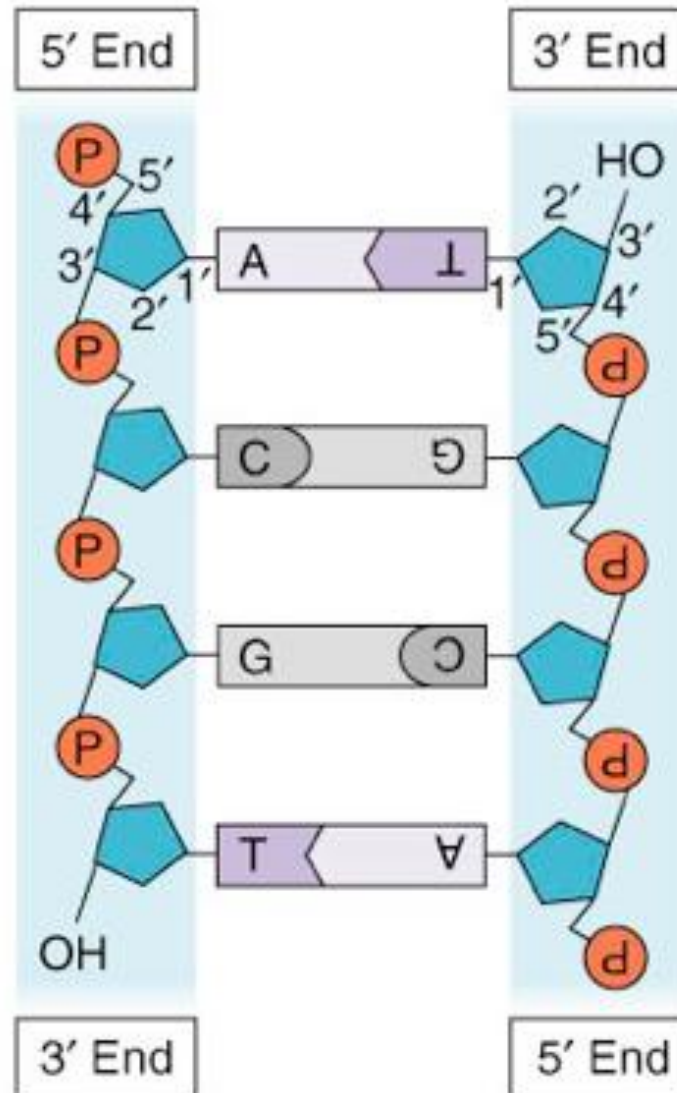
DNA is complementary



Backbone vs. side chains



DNA is anti-parallel



Writing the sequence of nucleic acids

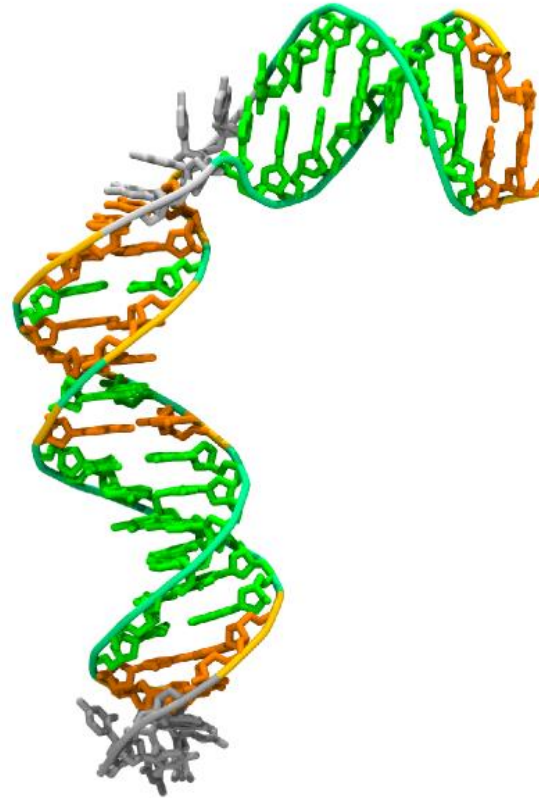
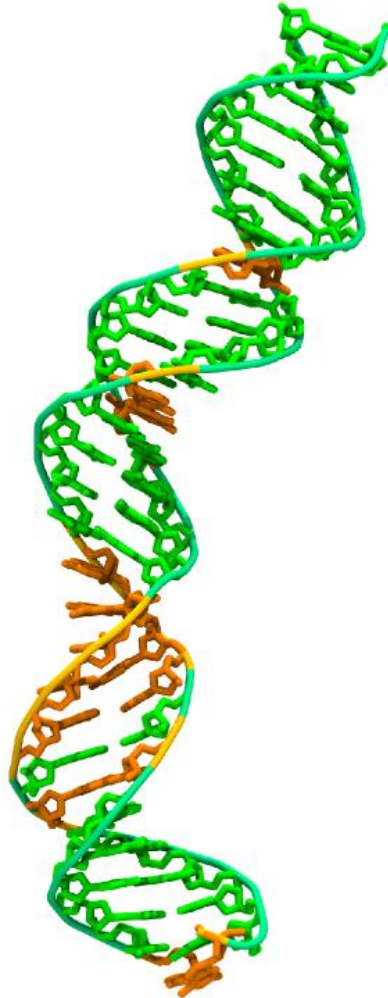
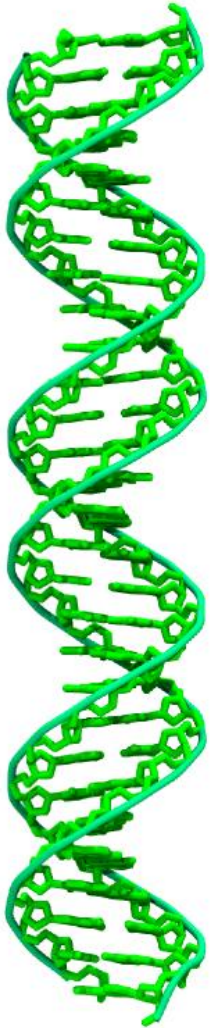


DNA 5' ...A T G G C C T G G A C T T C A... 3'
3' ...T A C C G G A C C T G A A G T... 5'

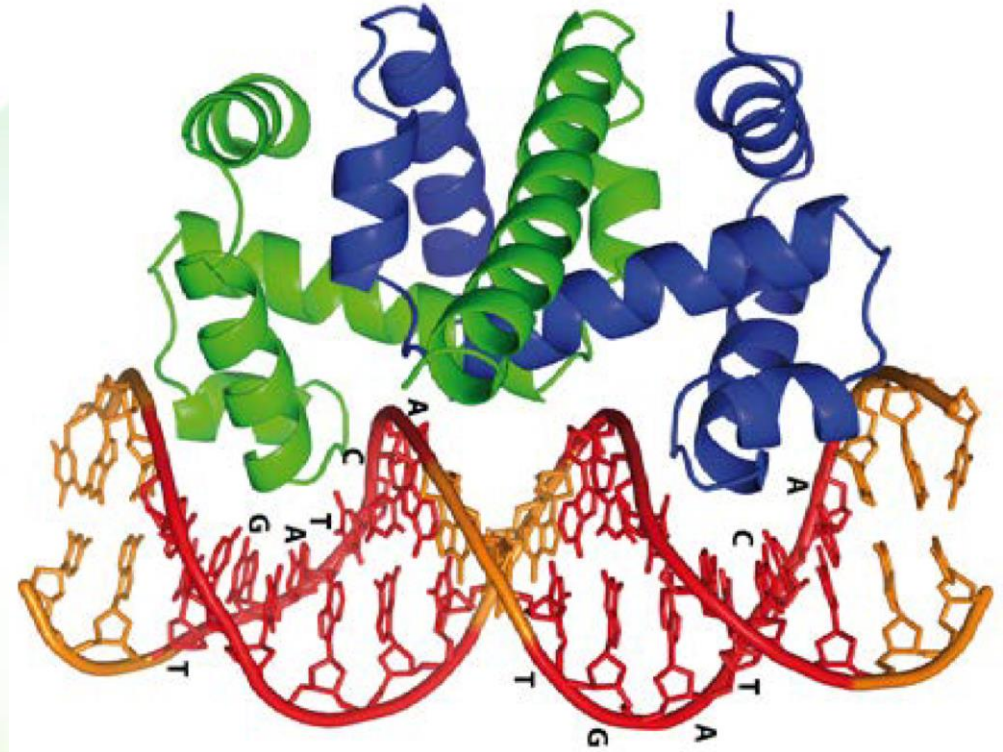
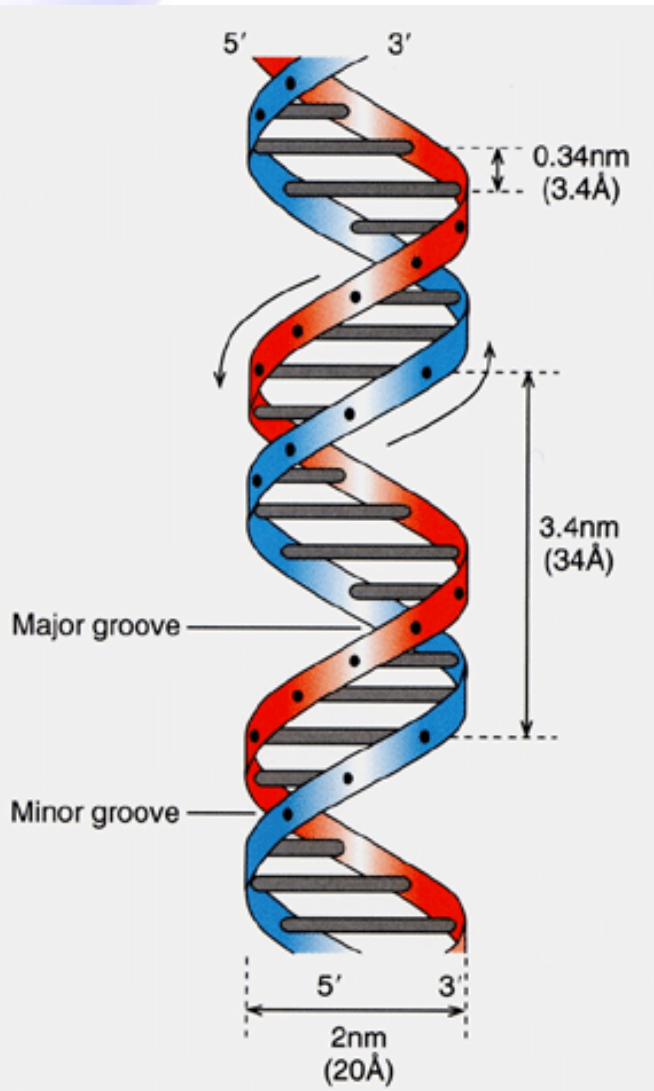
OR A T G G C C T G G A C T T C A.

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

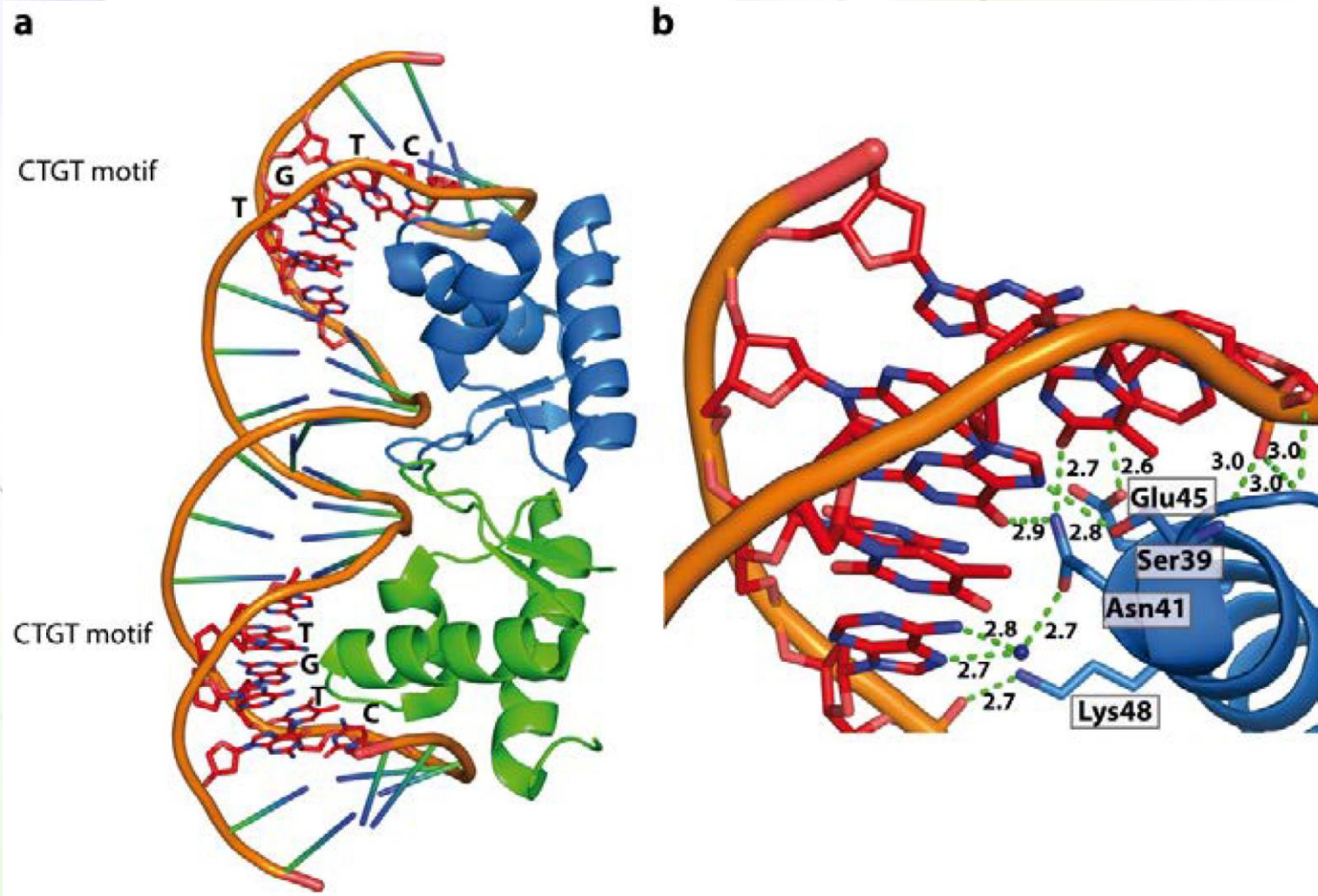
DNA is flexible, yet stable



DNA grooves



DNA-protein interaction



Prokaryotes versus eukaryotes



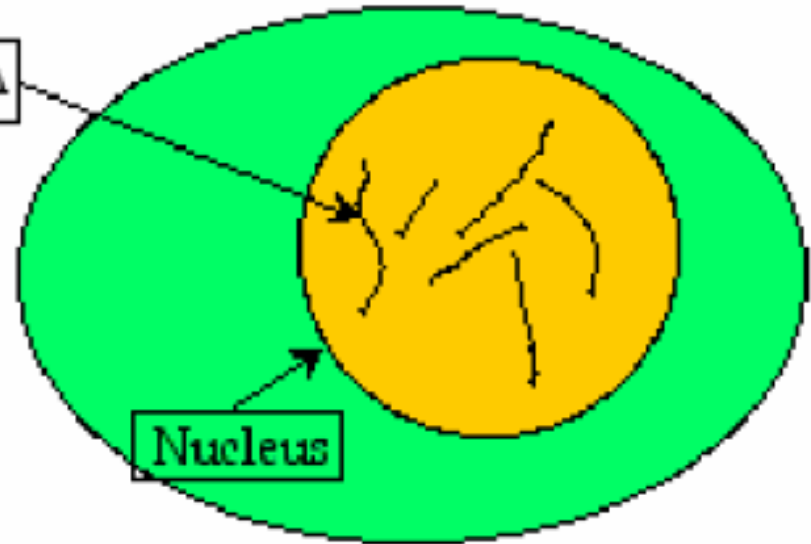
Prokaryote



No nucleus
Single loop of DNA

DNA

Eukaryote

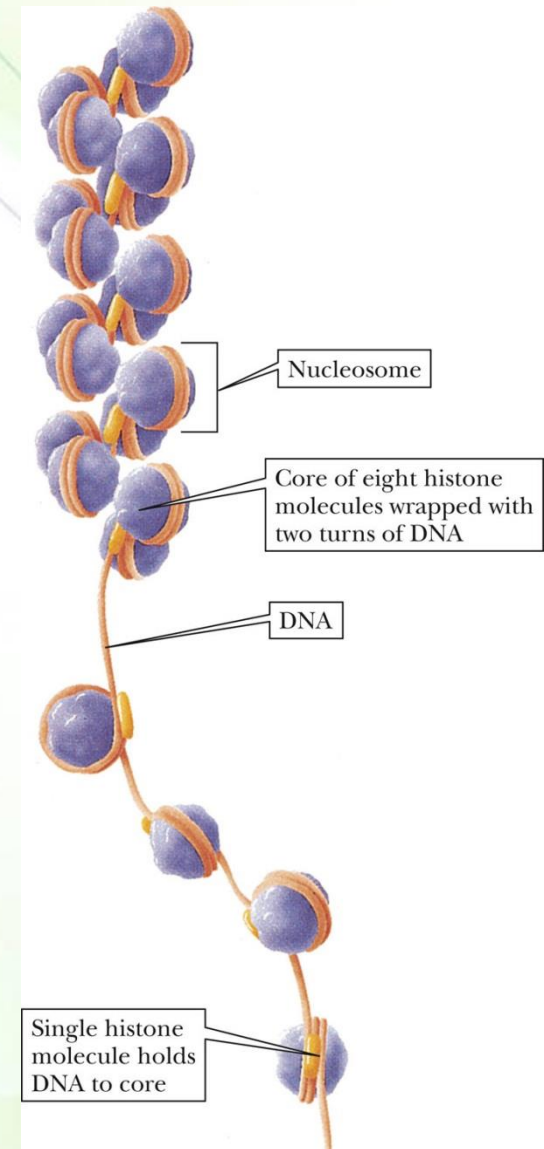


Has a Nucleus with DNA
in non-looped chromosomes

In eukaryotes...

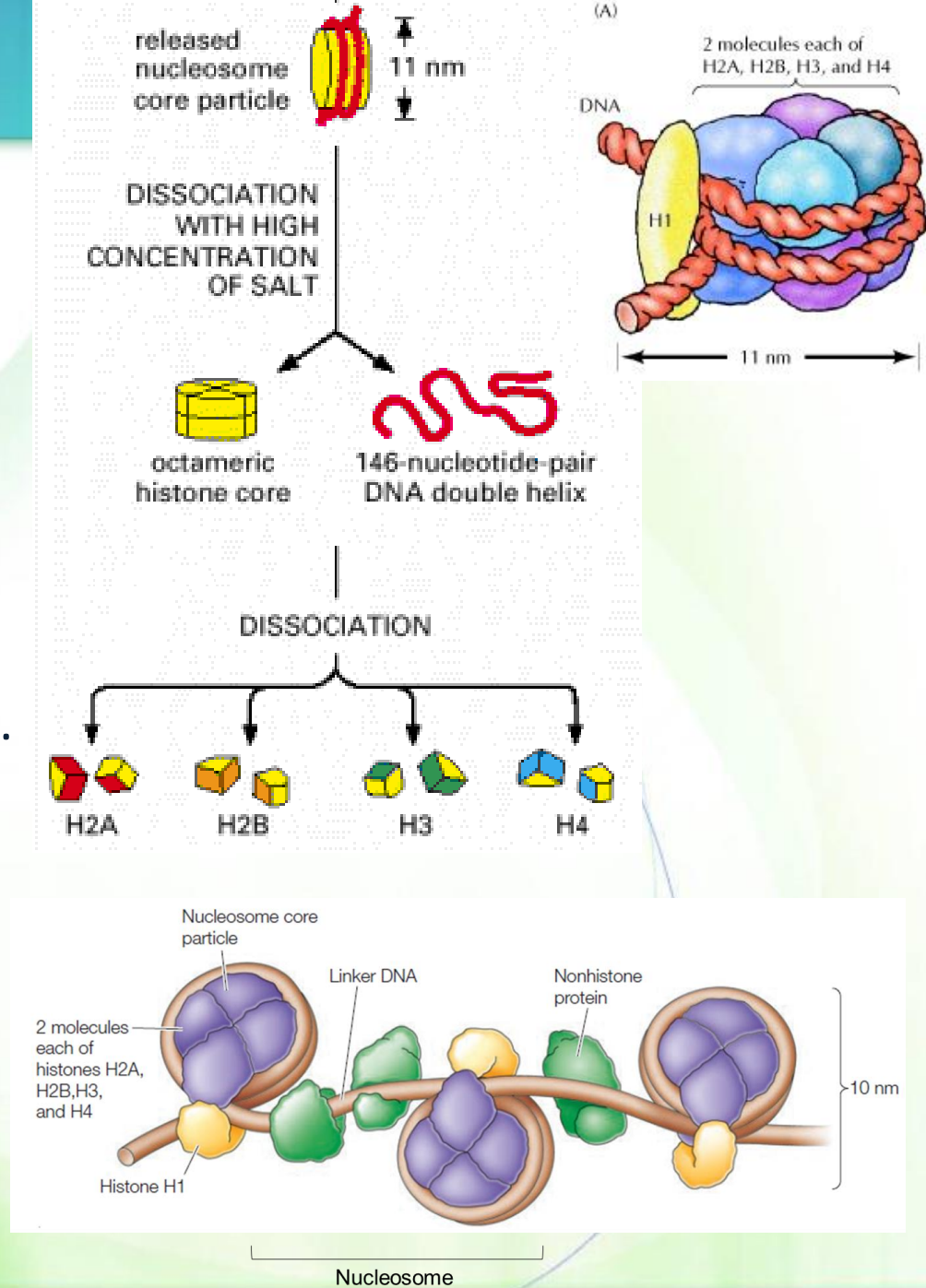


- In eukaryotes, DNA is coiled to package the large DNA.
- Eukaryotic DNA is complexed with a number of proteins, principally histones, which package DNA.
- Chromatin = DNA molecule + proteins.
- The basic structural unit of chromatin is known as a nucleosome.



Nucleosomes

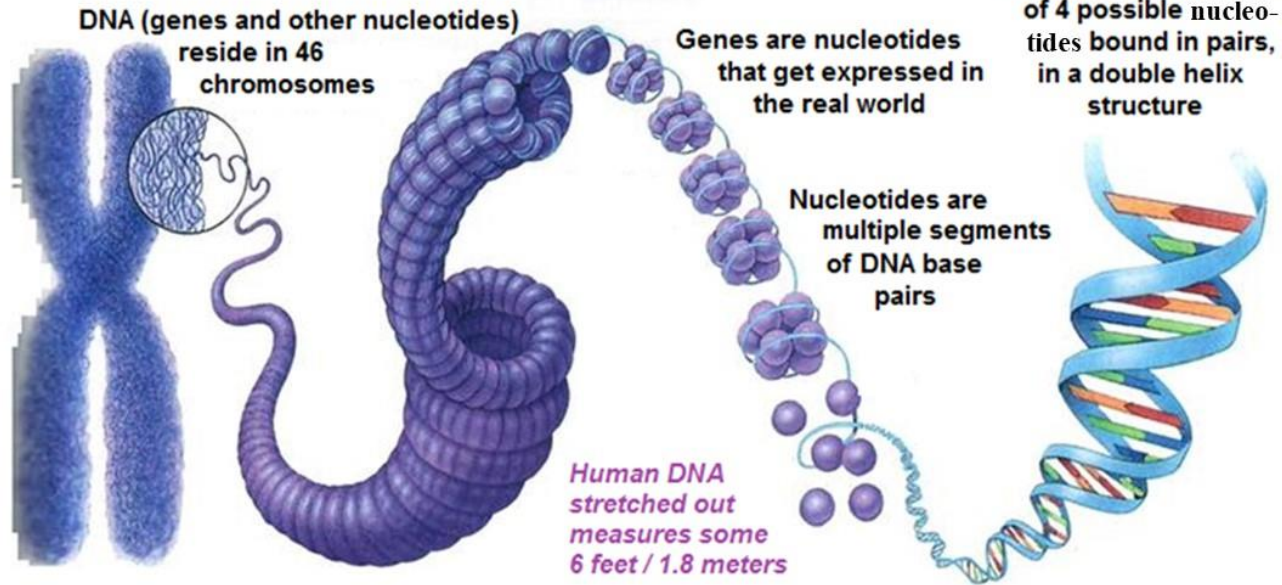
- A **nucleosome** consists of DNA wrapped around a nucleosome core particle, linker DNA, and histone H1.
- The histone core particle is an octamer (two molecules of histones H2A, H2B, H3, and H4) and the DNA wrapped around it.
- A linker DNA connects two nucleosome core particles.
- Histone H1 is bound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



Histones package chromosomes



The Hierarchical Structure of DNA through to the Chromosome



Euchromatin



+ Histone H1

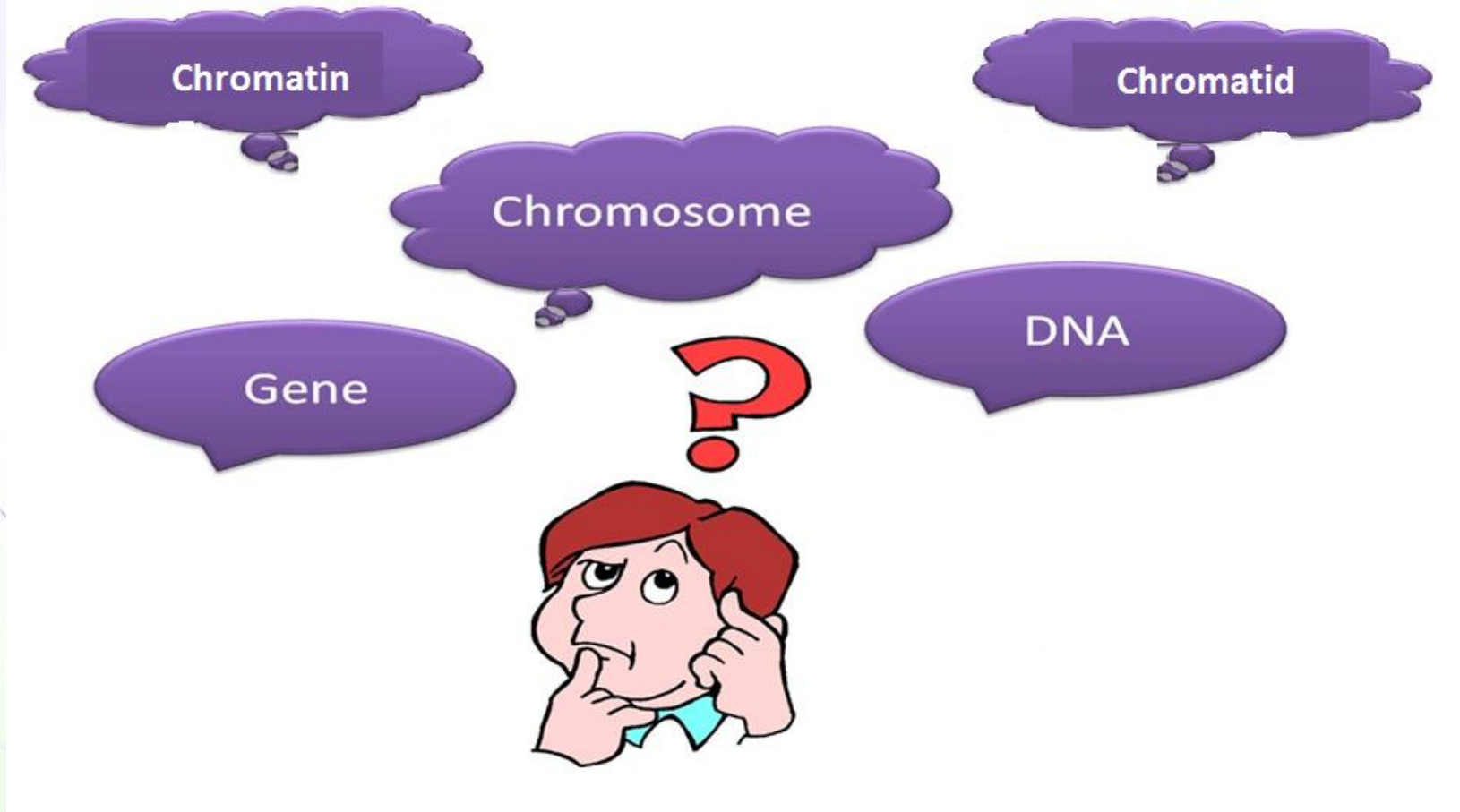


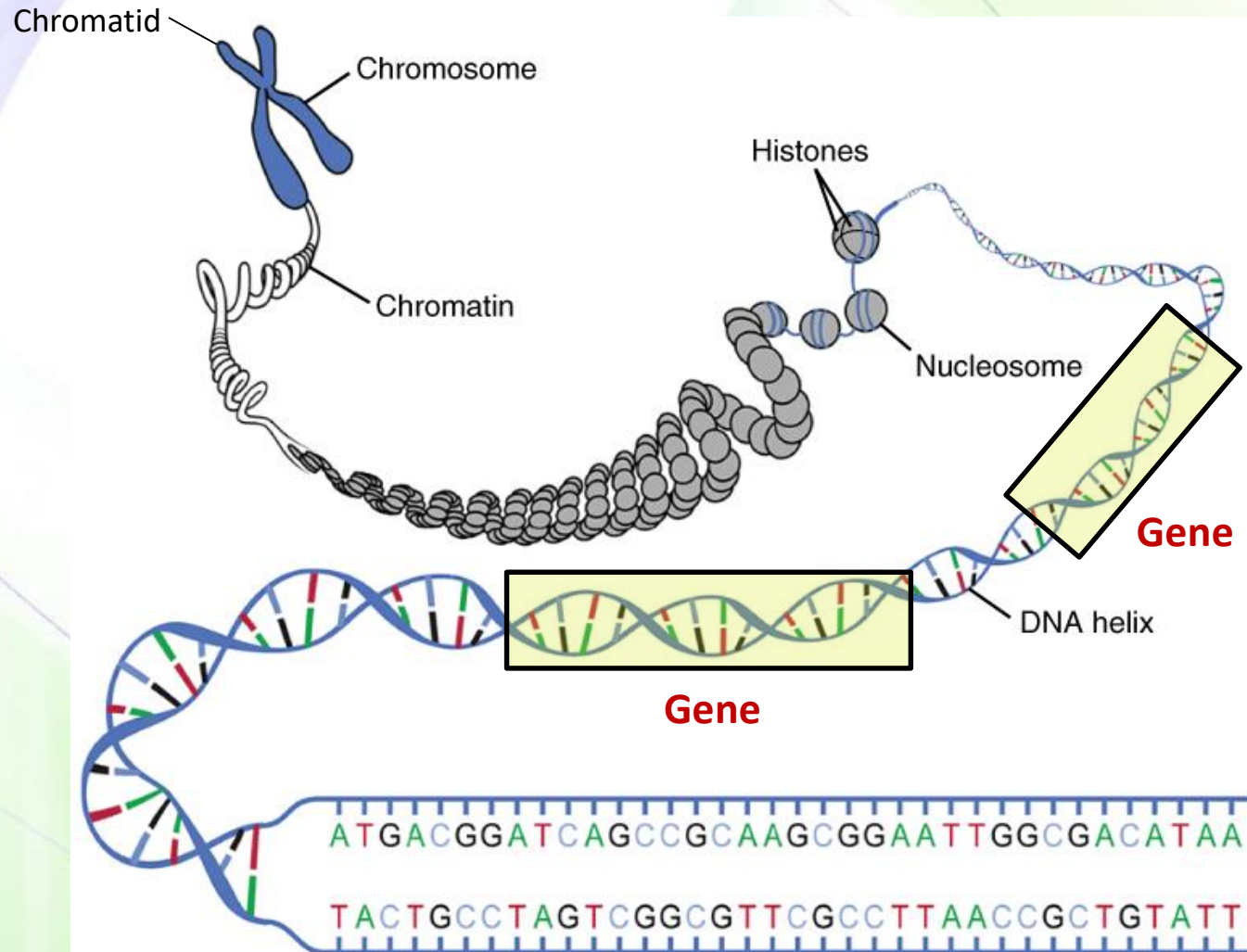
- Histone H1

Heterochromatin



Terms to know



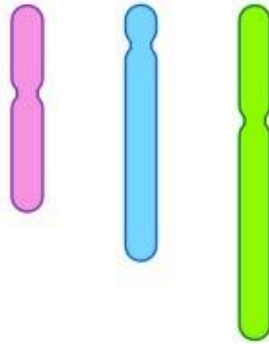


Remember...we are diploid



Haploid (n)

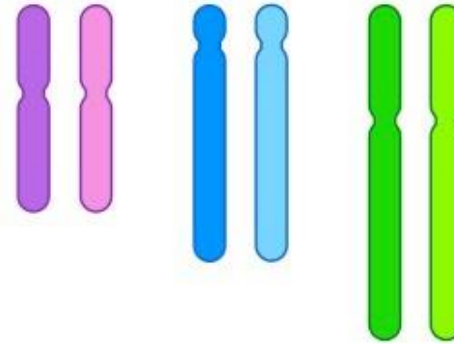
One copy of each chromosome



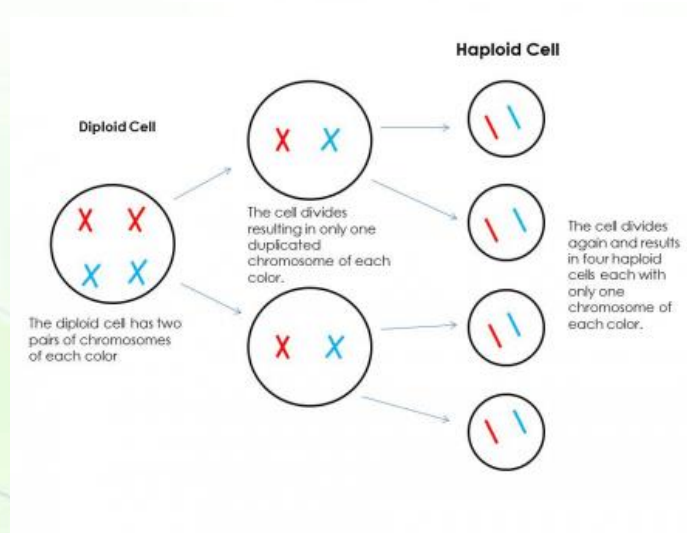
Three non-homologous chromosomes

Diploid (2n)

Two copies of each chromosome



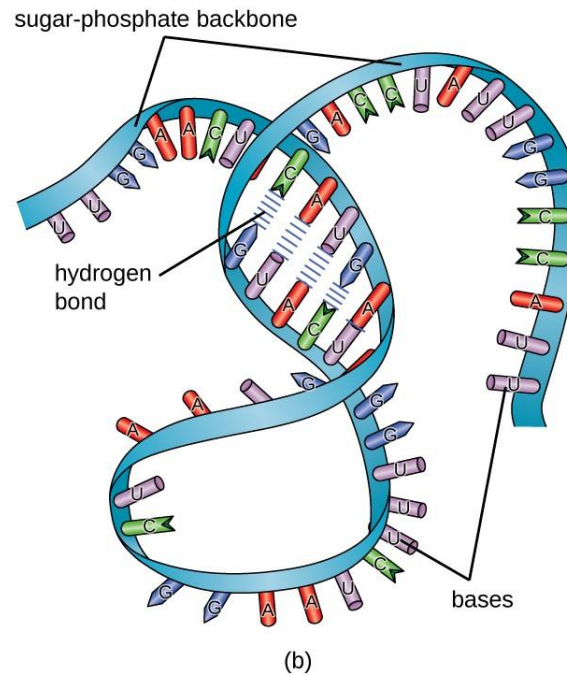
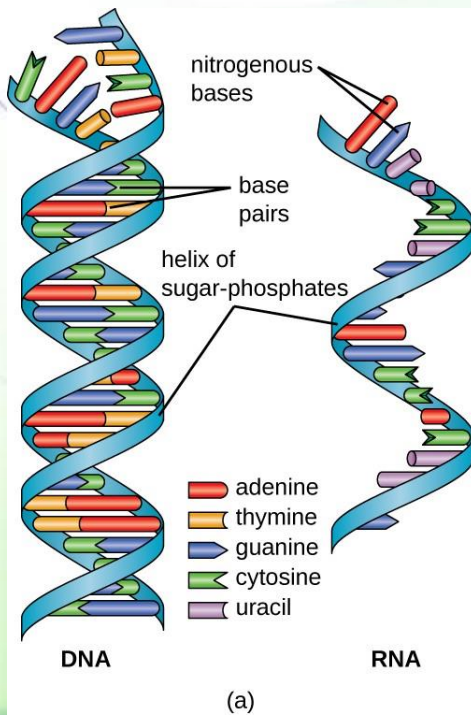
Three pairs of homologous chromosomes
(of maternal and paternal origin)



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).



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

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