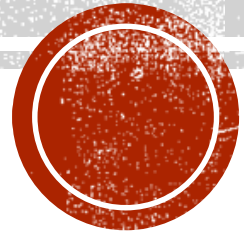
NUCLEIC ACIDS

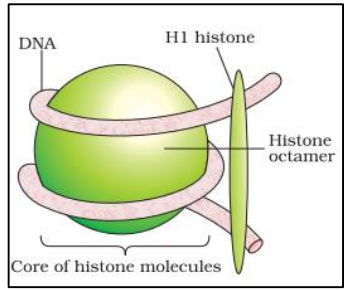
Prof. Nafez Abu Tarboush

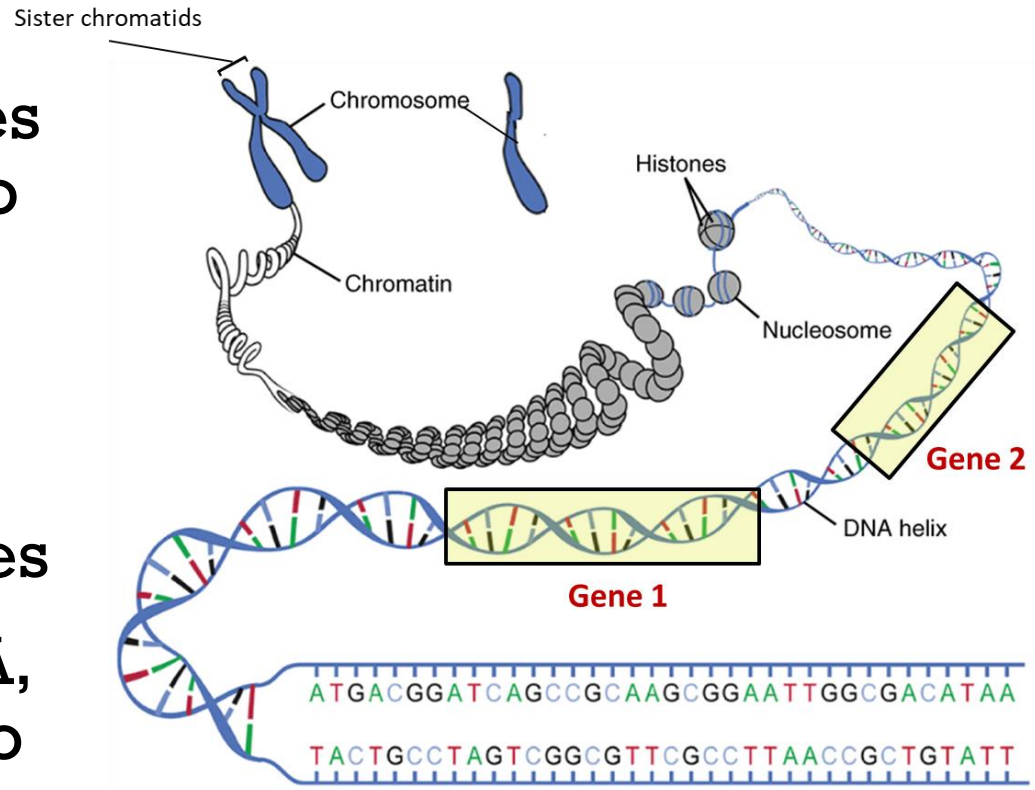


TERMS

- DNA and RNA: nucleic acids; polymers of nucleotides
- Gene: continuous sequence of nucleotides that is transcribed (codes for or is used to make RNA)
- A nucleosome: a short sequence of DNA wrapped around proteins called histones
- Chromatin is a stretch of DNA and histones
- Chromosome is a whole molecule of DNA, which can consist of one chromatid or two identical chromatids, called sister chromatids

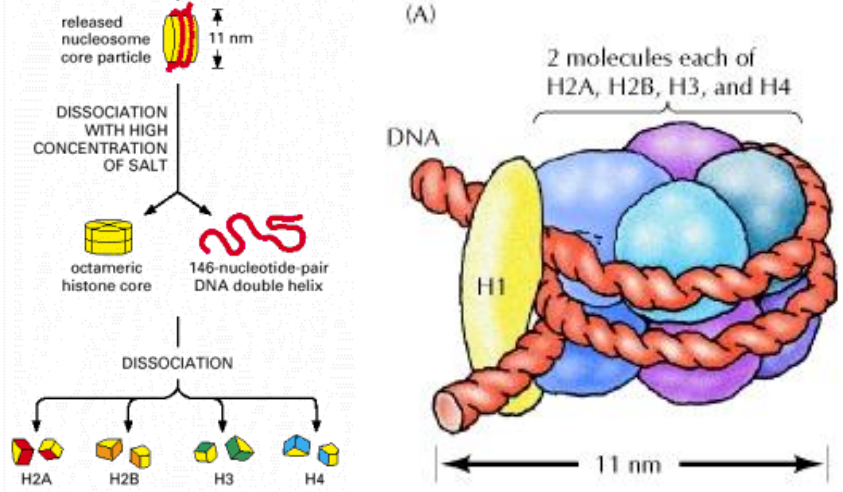
Nucleosome

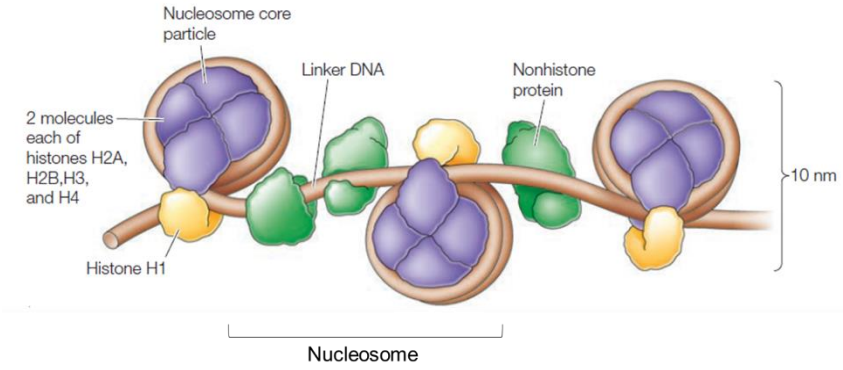


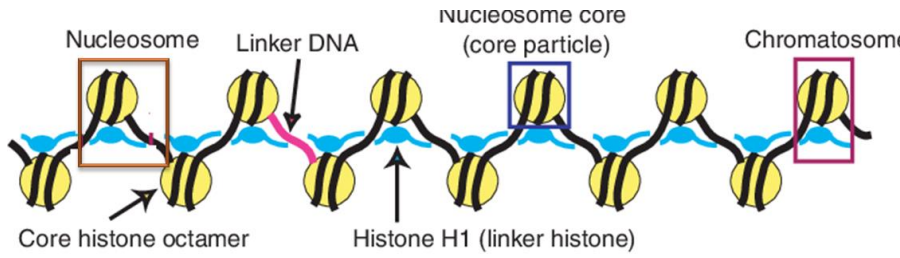


NUCLEOSOMES

- DNA wrapped around a 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**

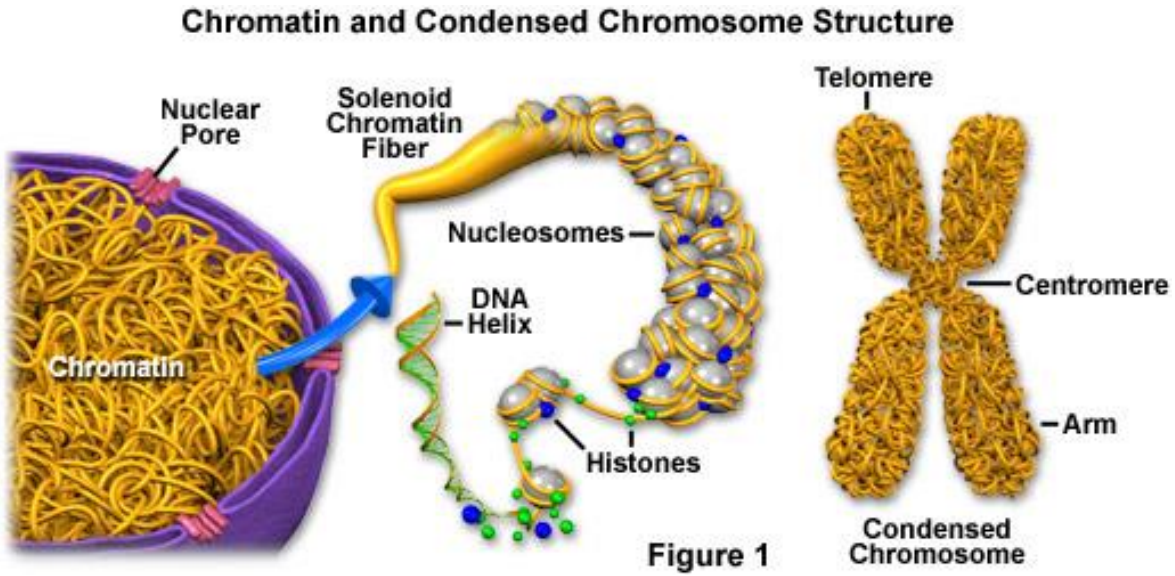


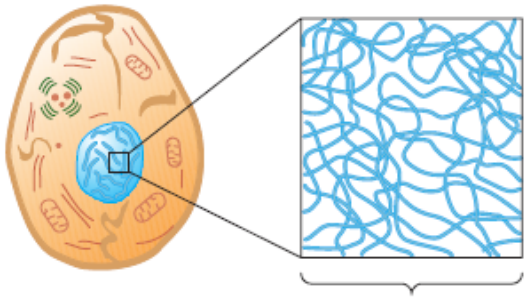


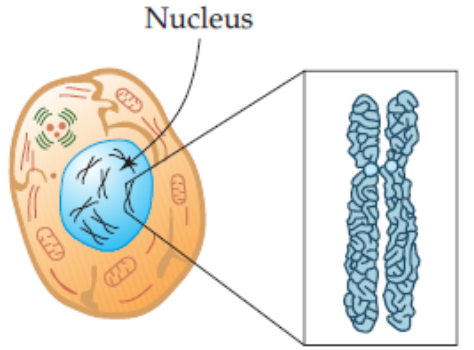


CHROMOSOME VS. CHROMATIN

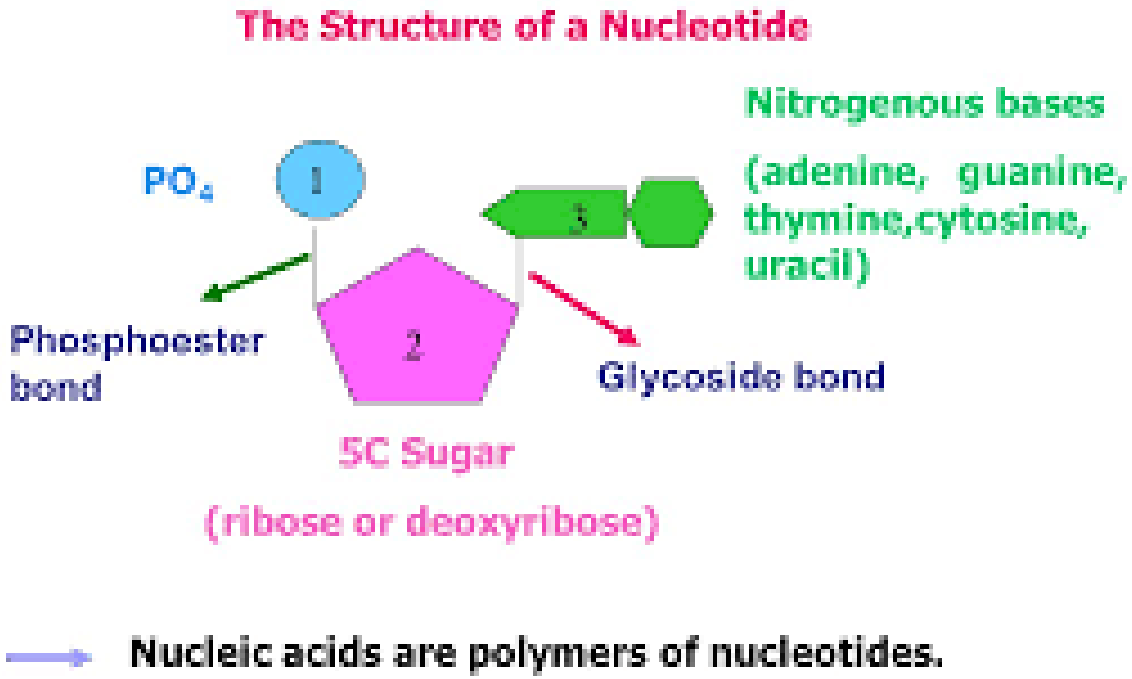
- In non-dividing cells, the chromatin of chromosomes is not condensed (uncoiled) and cannot be distinguished from each other before cell division (like a spaghetti plate).
- At cell division, chromosomes become condensed (coiled) DNA molecules that can be distinguished from other chromosomes.





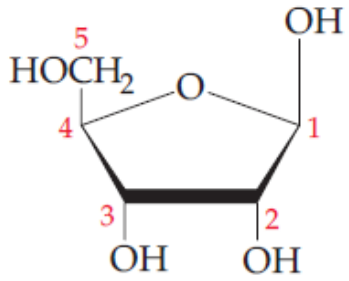


NUCLEOTIDES IN DNA AND RNA

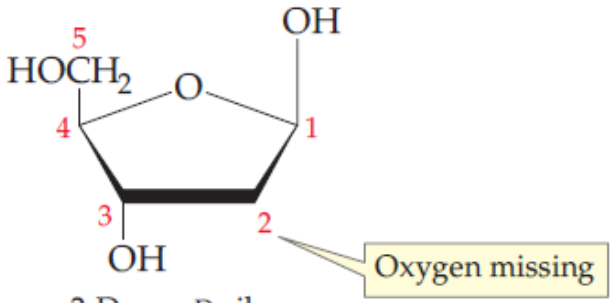


Nucleic acids are polymers of nucleotides.

- All nucleotides have a common structure:
  1. a phosphate group linked by a phosphoester bond to a pentose.
  2. The pentose is linked to a nitrogenous base via a glycosidic bond.
  3. A nucleotide can have one, two, or three phosphate groups linked to each.



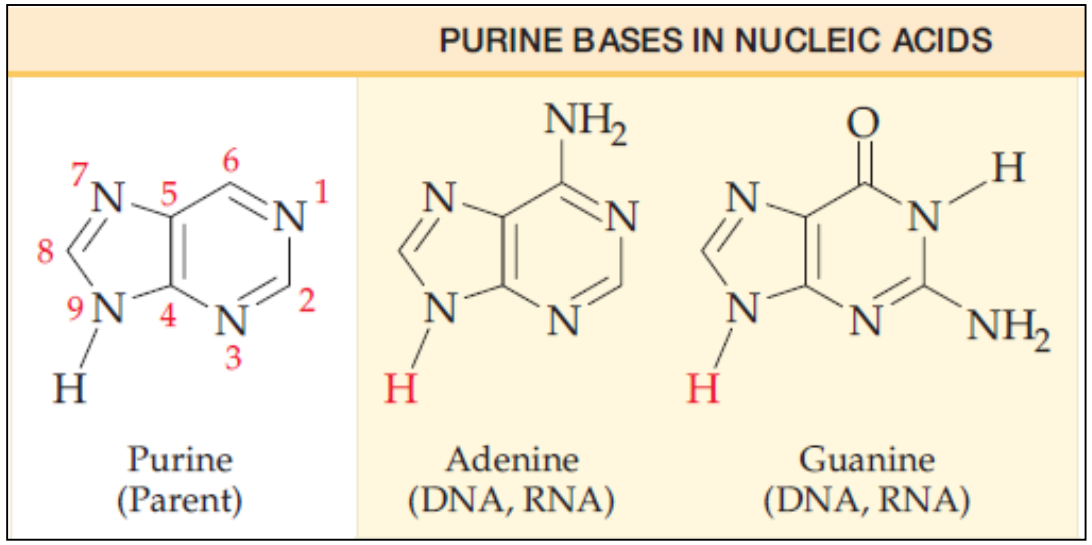
D-Ribose
(in RNA)

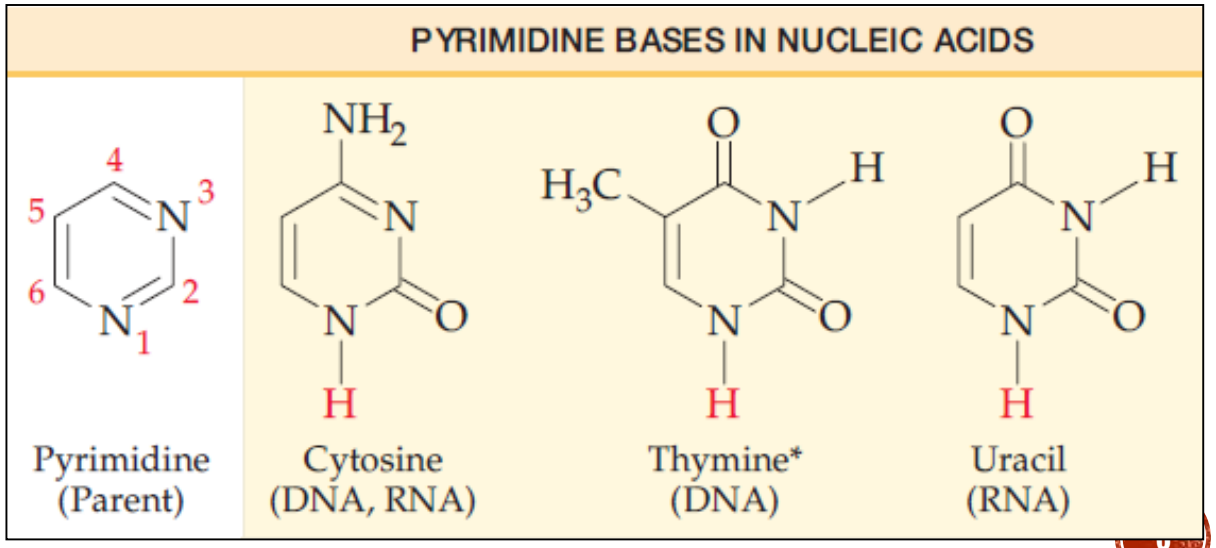


2-Deoxy-D-ribose
(in DNA)

NITROGENOUS BASES

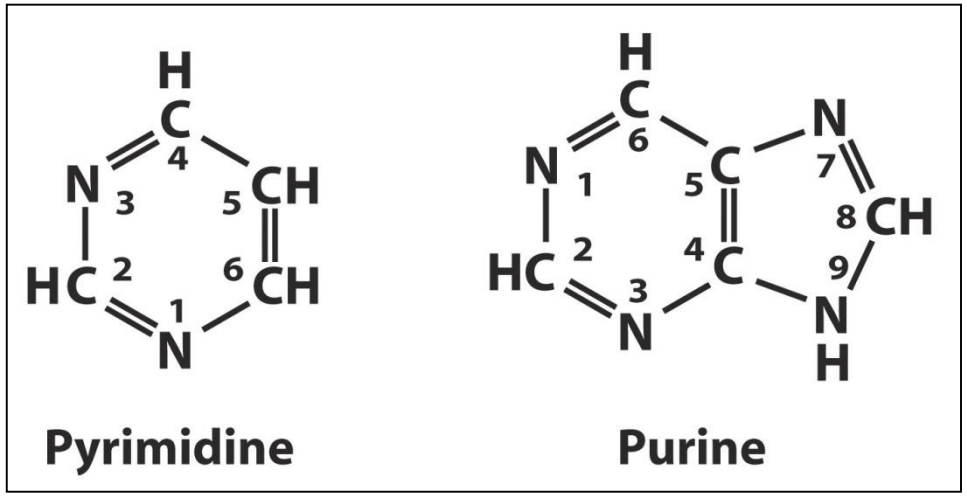
- DNA and RNA consist of only four different nucleotides of two classes: purines and pyrimidines.
- Purines are adenine and guanine, and pyrimidines are cytosine, thymine (DNA), and uracil (RNA).
- The bases are abbreviated A, G, C, T, and U, respectively

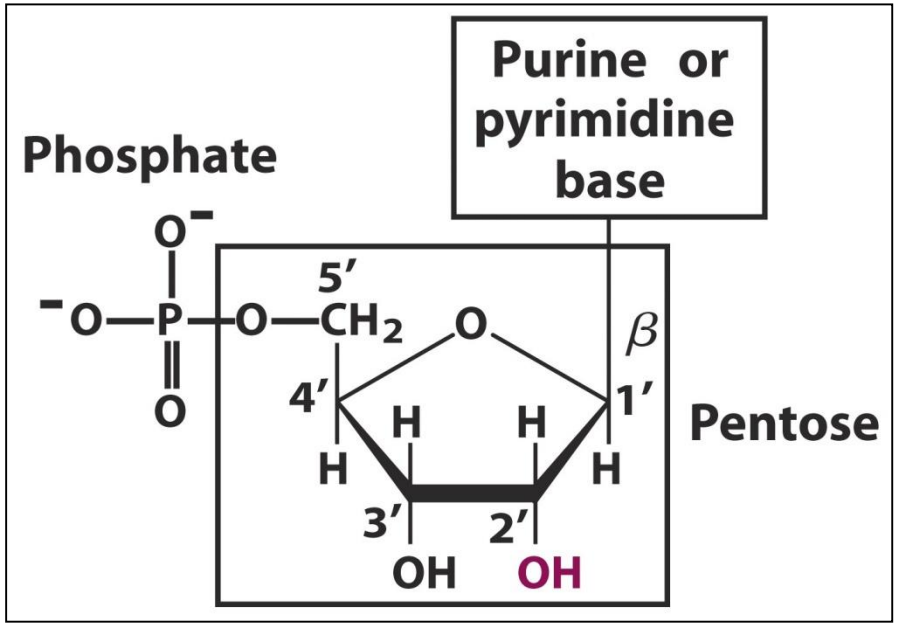




HOW ARE BASES CONNECTED TO RIBOSE?

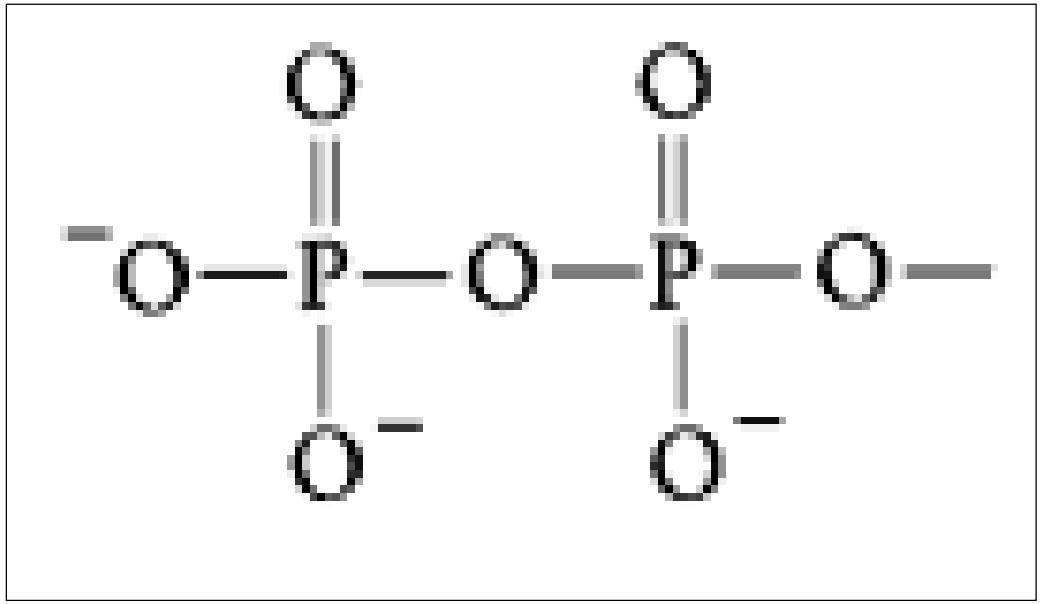
- In nucleotides, the 1 carbon atom of the sugar (ribose or deoxyribose) is attached to the nitrogen.





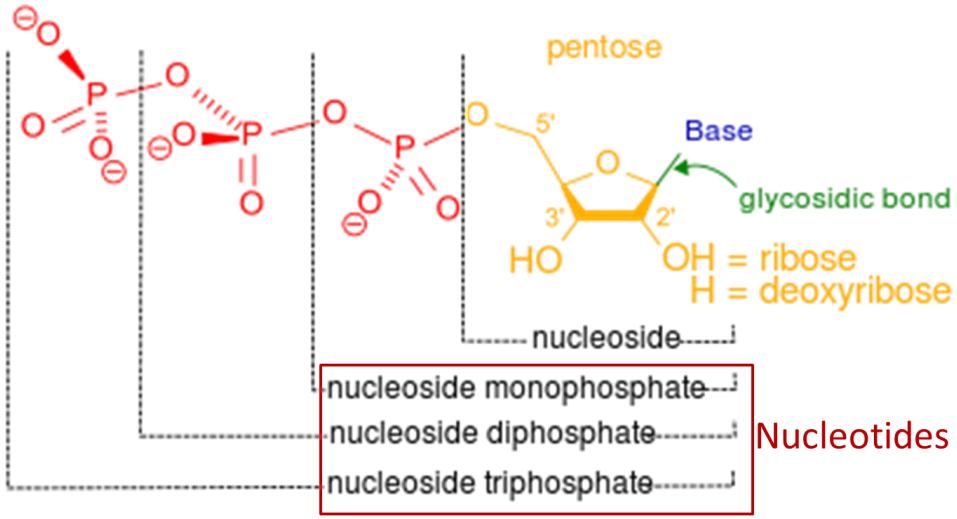
NUCLEOTIDES ARE ACIDIC

- Due to the presence of phosphate, which dissociates protons at physiological pH inside cells, freeing hydrogen ions and leaving the phosphate negatively charged

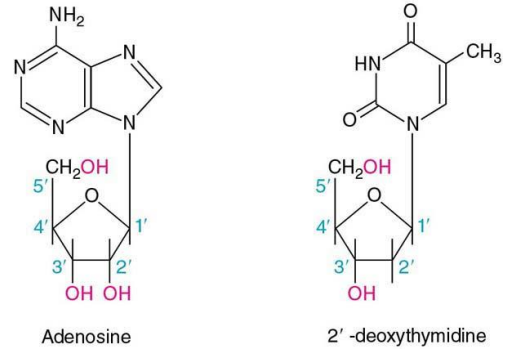


NUCLEOTIDES VS. NUCLEOSIDES

- Nucleosides are combinations of a base and a sugar without a phosphate
- Nucleotides are nucleosides that have one, two, or three phosphate groups esterified at the 5' hydroxyl
- Nucleoside monophosphates have a single esterified phosphate
  - diphosphates contain a two-phosphate group
  - triphosphates have three phosphates



NAMING OF NUCLEOTIDES



Adenosine

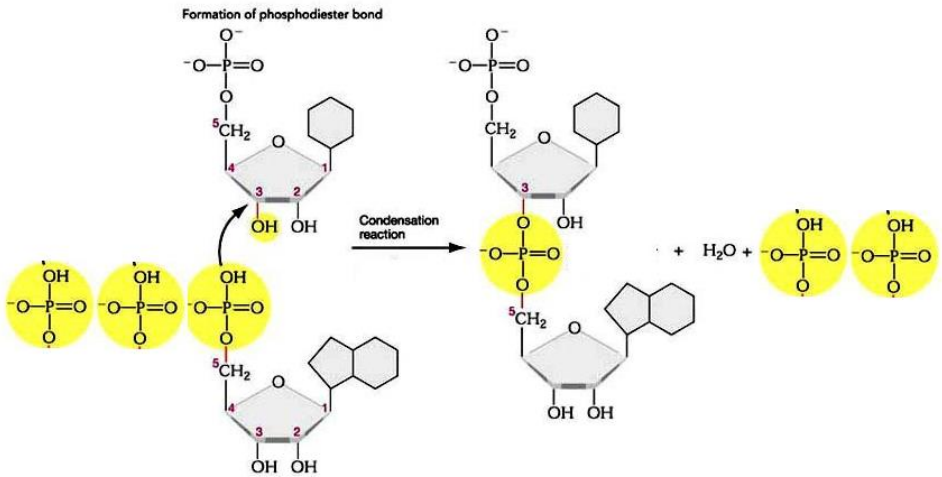
2′ -deoxythymidine

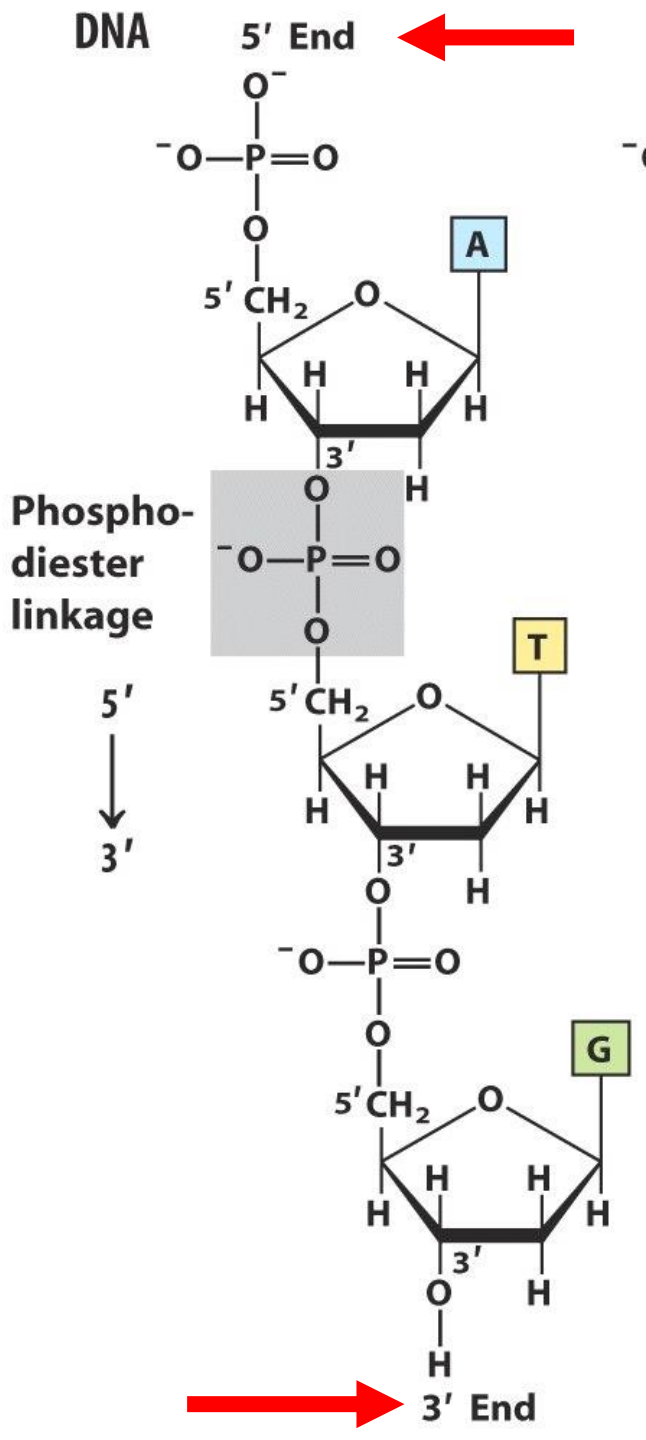
BASES	NUCLEOSIDES	NUCLEOTIDES*
DNA		
	Deoxyribonucleosides	**Deoxyribonucleotides**
Adenine (A)	Deoxyadenosine	Deoxyadenosine 5′-monophosphate (dAMP)
Guanine (G)	Deoxyguanosine	Deoxyguanosine 5′-monophosphate (dGMP)
Cytosine (C)	Deoxycytidine	Deoxycytidine 5′-monophosphate (dCMP)
Thymine (T)	Deoxythymidine	Deoxythymidine 5′-monophosphate (dTMP)
RNA		
	Ribonucleosides	**Ribonucleotides**
Adenine (A)	Adenosine	Adenosine 5′-monophosphate (AMP)
Guanine (G)	Guanosine	Guanosine 5′-monophosphate (GMP)
Cytosine (C)	Cytidine	Cytidine 5′-monophosphate (CMP)
Uracil (U)	Uridine	Uridine 5′-monophosphate (UMP)

1. Look for the phosphate
    1. No: nucleoside
    2. Yes: nucleotide
2. Look at C2 of the sugar
    1. H: deoxyribose
    2. OH: Ribose
3. Look at the base
    1. Single ring (pyrimidine): C, T, or U
    2. Double ring (purine): A or G

NUCLEIC ACID POLYMER

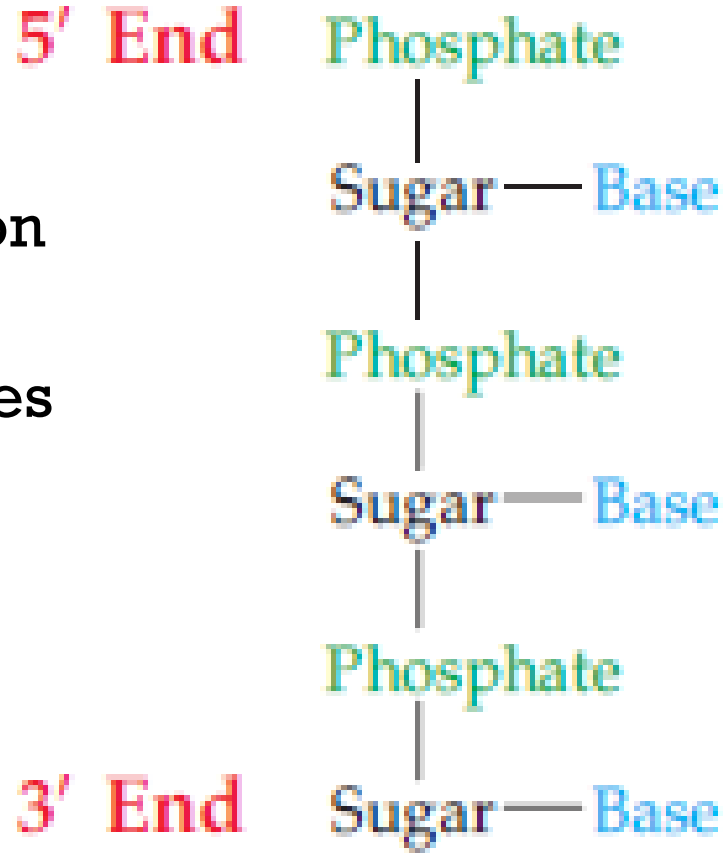
- Hydroxyl group attached to the 3’ carbon of a sugar of one nucleotide forms a bond to the phosphate of another nucleotide.
- A single nucleic acid strand is a phosphate-pentose polymer (a polyester) with purine and pyrimidine bases as side groups.
- The links between the nucleotides are called phosphodiester bonds.





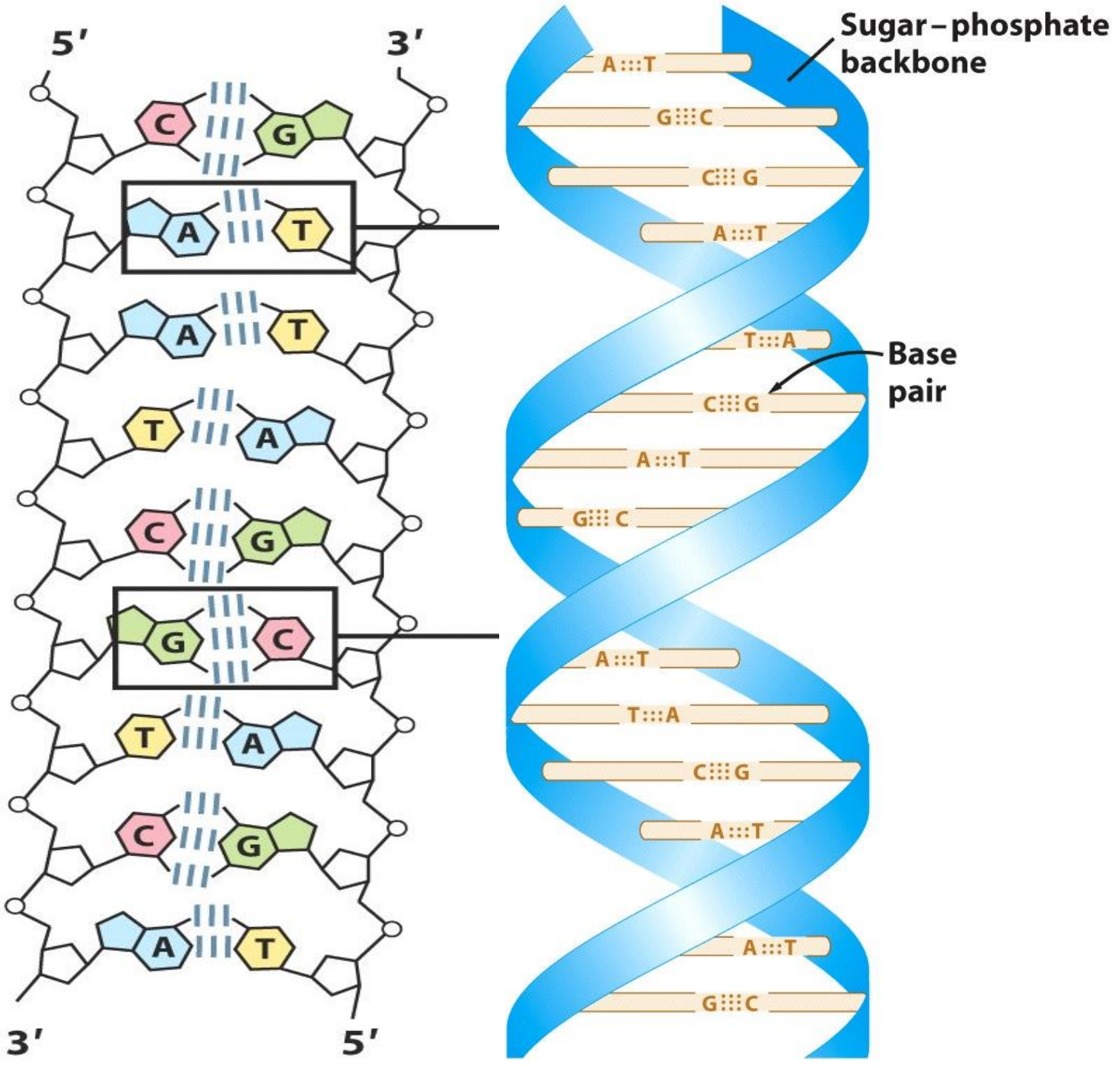
DIRECTIONALITY

- A nucleic acid strand has an end-to-end chemical orientation:
  - The 5’ end has a free phosphate group on the 5’ carbon
  - The 3’ end has a free hydroxyl group on the 3’ carbon
  - This directionality has made polynucleotide sequences written and read in the 5'→3' direction (from left to right).
  - Example: the sequence AUG is assumed to be (5')AUG(3’).



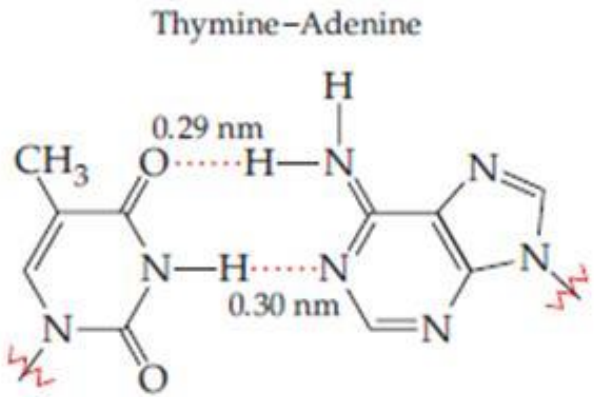
DNA STRUCTURE

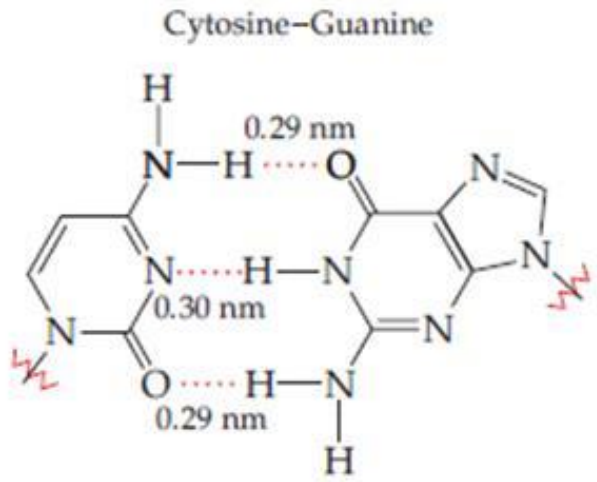
- Two associated polynucleotide strands that wind together (double helix)
- The sugar-phosphate groups are on the outside
- The bases project into the interior
- The sugar-phosphate groups are termed backbone
- The orientation of the two strands is antiparallel



BASE PAIRING

- In DNA, the larger purines (A or G) must pair with a smaller pyrimidines (C or T).
- A always hydrogen bonds with T and G with C, forming A·T and G·C base pairs.
- A is paired with T through two hydrogen bonds; G is paired with C through three hydrogen bonds.

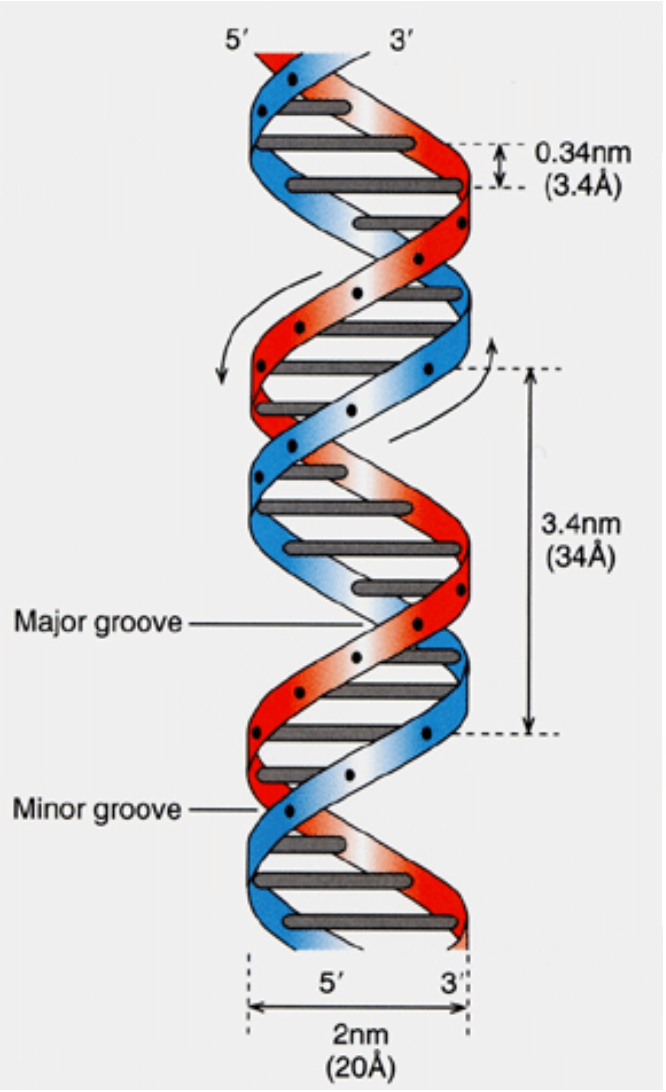


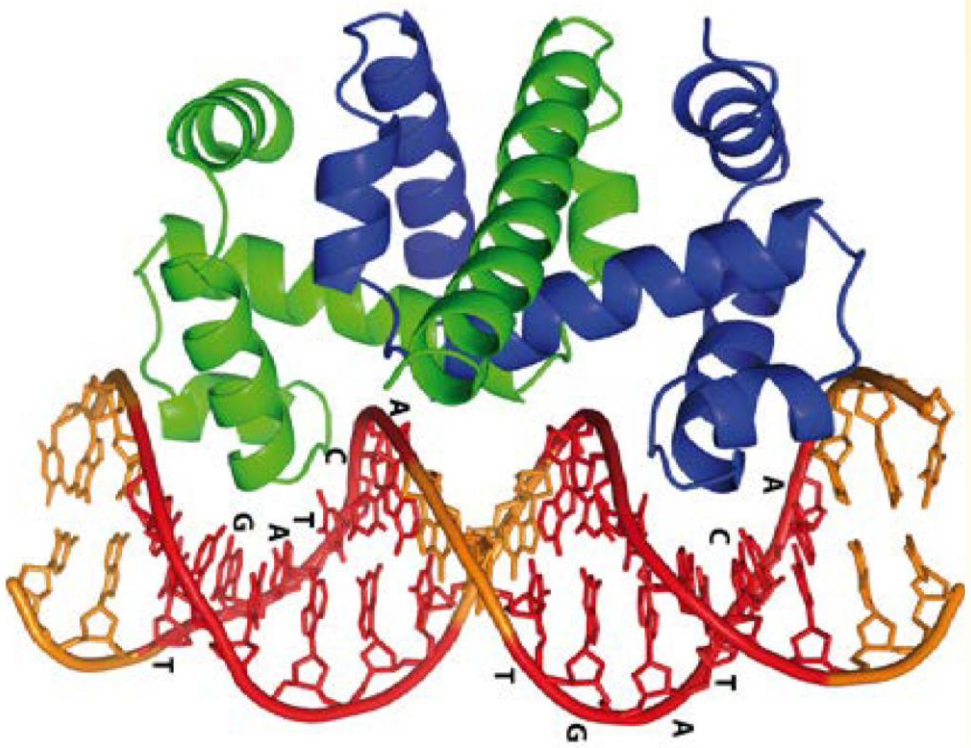


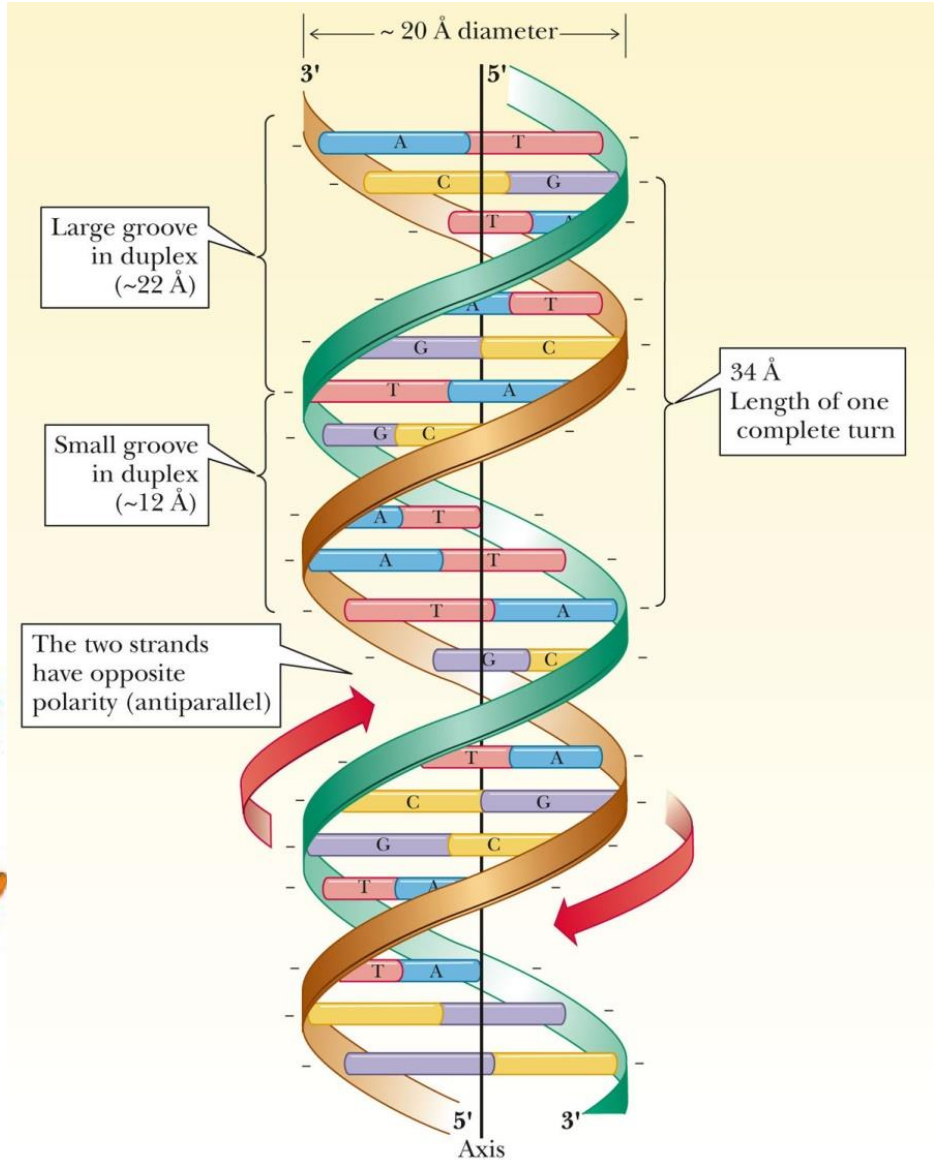
Chargaff's rules

Pyrimidines (T + C) always equals purines (A + G).
T always equals A.
C always equals G.
A + T is not necessarily equal to G + C.

DNA GROOVES

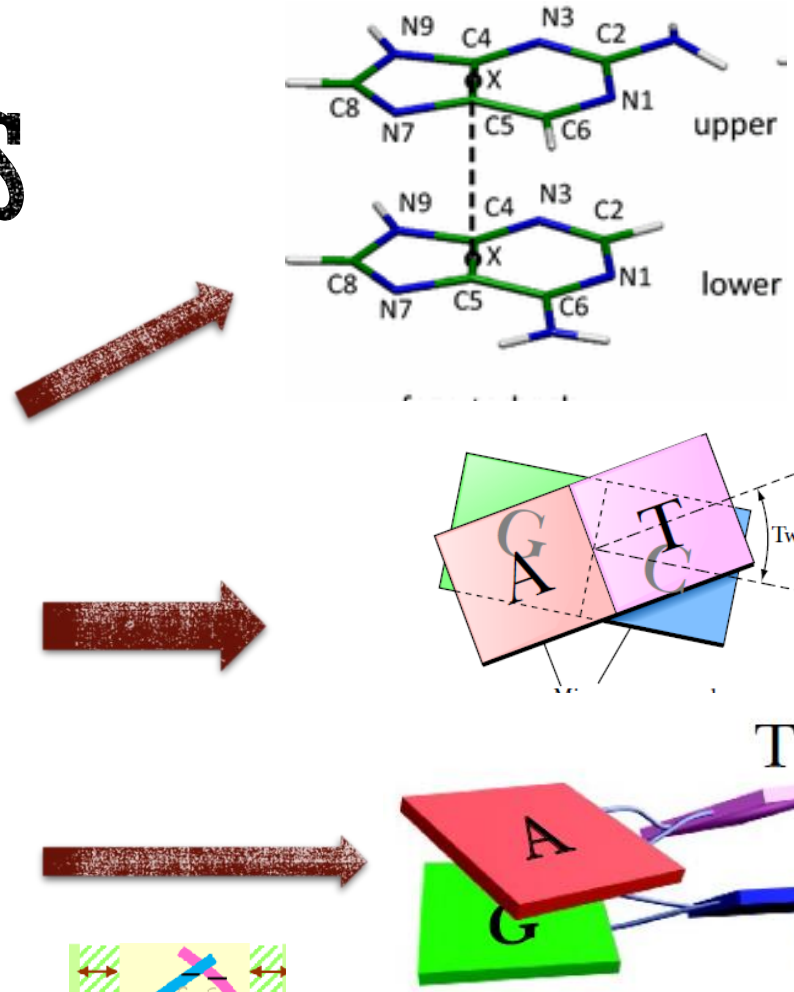

5′
3′
0.34nm
(3.4Å)
3.4nm
(34Å)
Major groove
Minor groove
5′
3′
2nm
(20Å)




~ 20 Å diameter
3′
5′
Large groove
in duplex
(~22 Å)
Small groove
in duplex
(~12 Å)
34 Å
Length of one
complete turn
The two strands
have opposite
polarity (antiparallel)
5′
3′
Axis

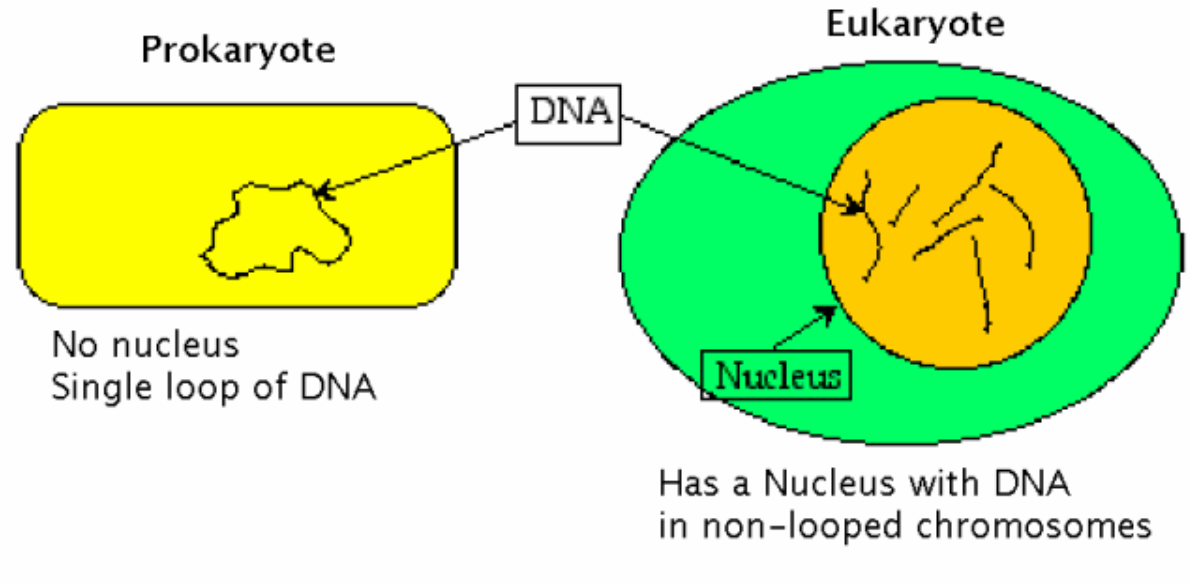
DNA-STABILIZING FORCES

- Hydrogen bonds
- Hydrophobic stacking: 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



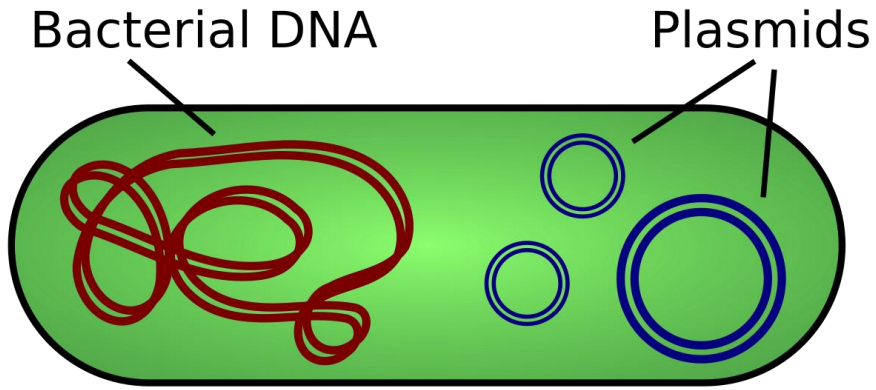
THE GENOME OF PROKARYOTES VERSUS EUKARYOTES

- 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

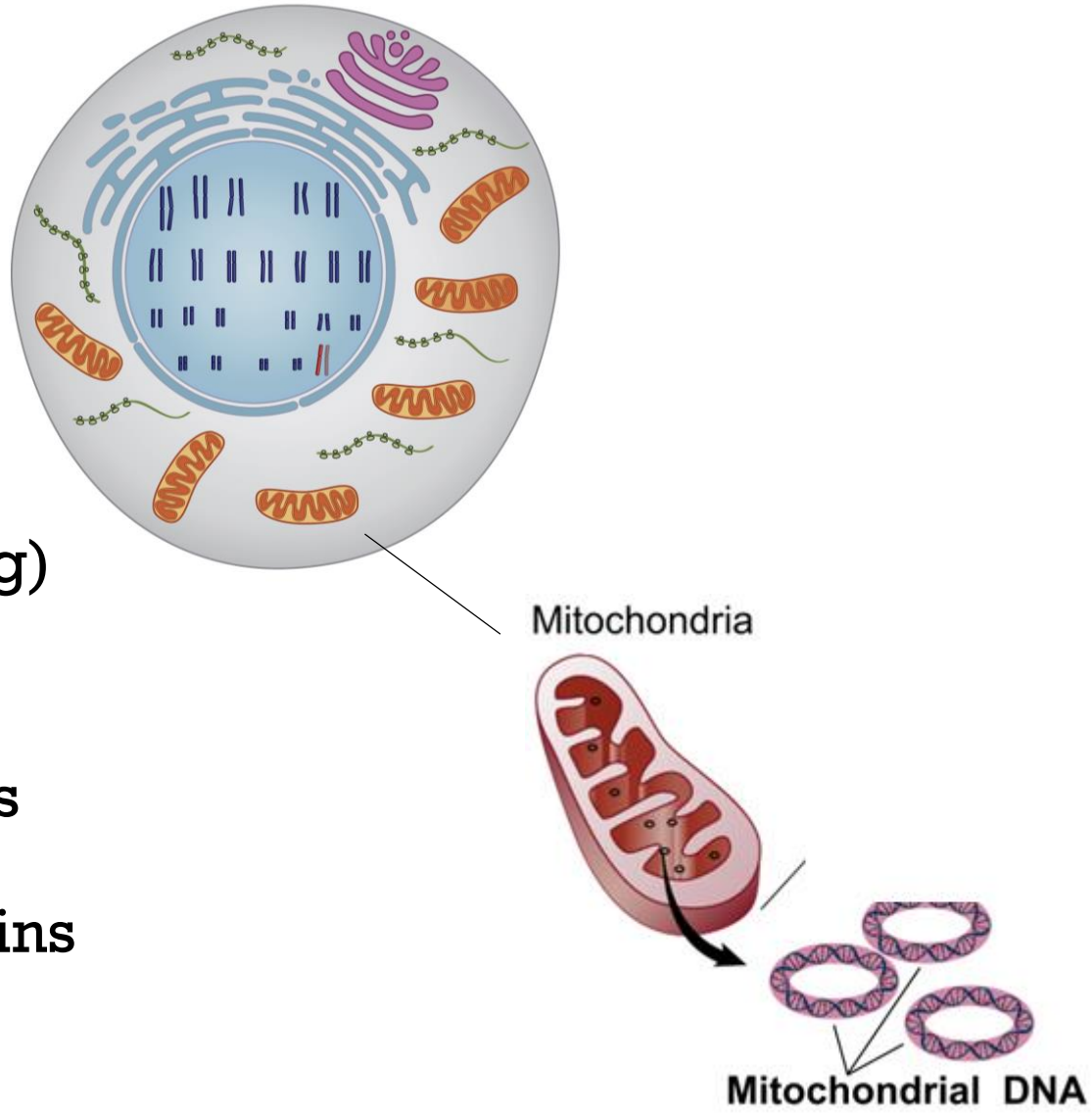
- The genetic materials of bacteria are of 2 types:
- 1. The chromosome: One circular chromosome of double-stranded DNA.
  - E.g. *Escherichia coli* contains > 4 × 10^6 bp (length of 2 mm) carrying 4200 genes.



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

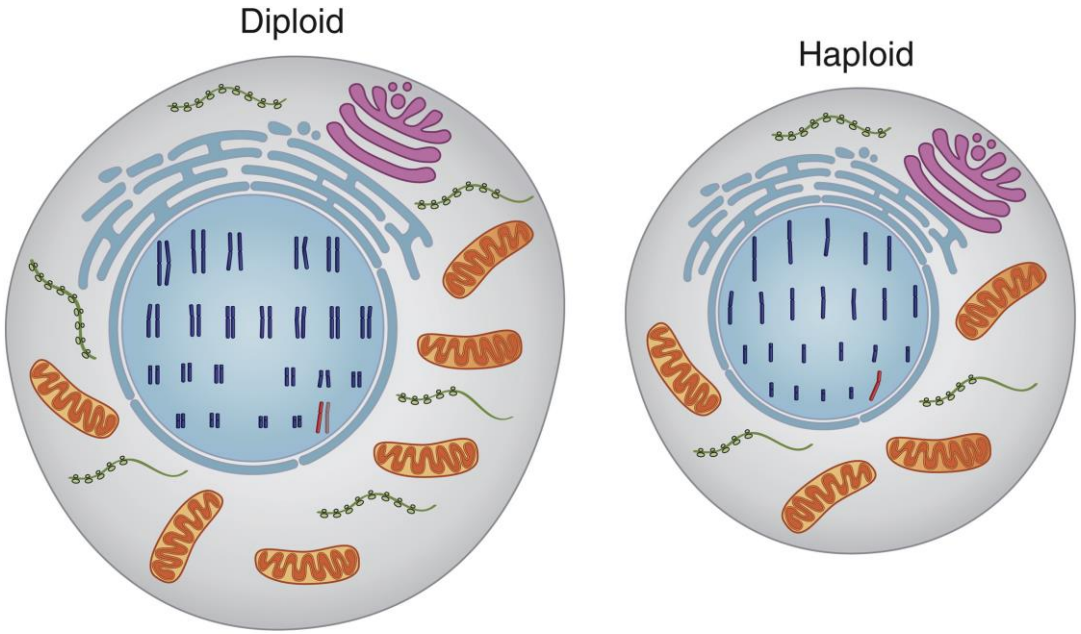
THE HUMAN GENOME

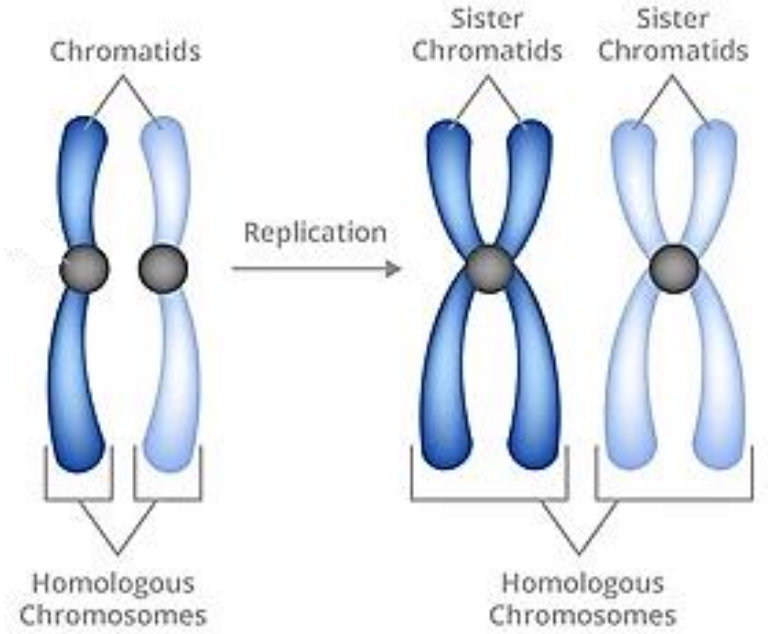
- The genetic material of humans is of 2 types:
- The nuclear genome: organized as linear chromosomes that consist of ~$3x10^9$ nucleotides in germline cells (sperm and egg) with a length of 1m per cell and that carry ~20000 genes
- The mitochondrial genome, which constitutes less than 0.1% of the total DNA in a cell (~16500 bp) and encodes 37 genes for proteins involved in the respiratory chain reaction



MORE EUKARYOTIC TERMS

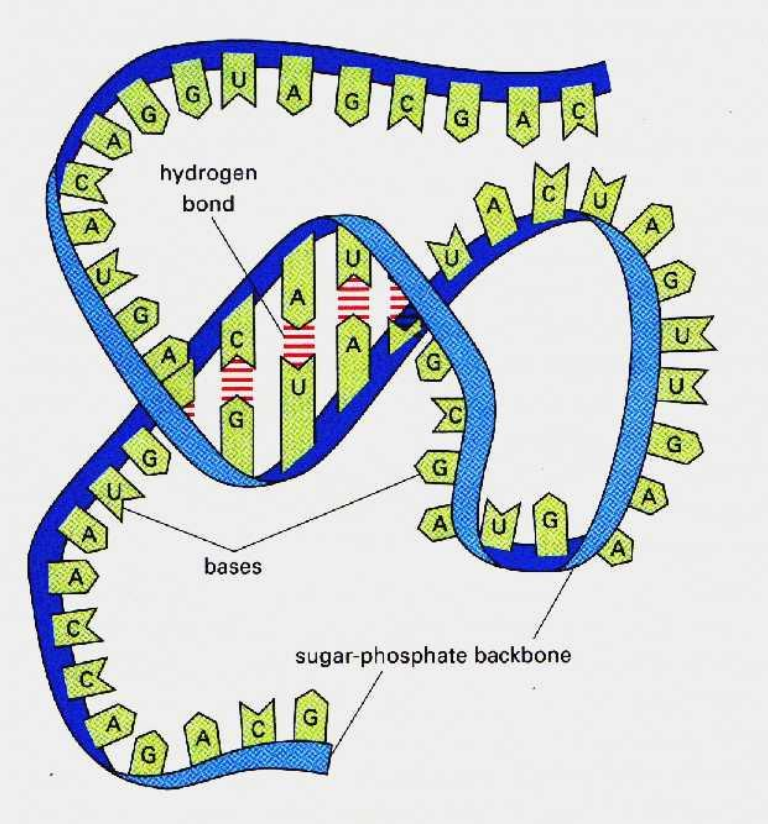
- Germline cells are haploid cells having one copy of every chromosome (either maternal or paternal)
- Somatic cells are diploid having two copies of every chromosome (maternal AND paternal) called homologous chromosomes
- Each chromosome can be made of one chromatid or sister chromatids





RNA STRUCTURE

- Note: RNA is usually single-stranded and does not have a specific structure



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