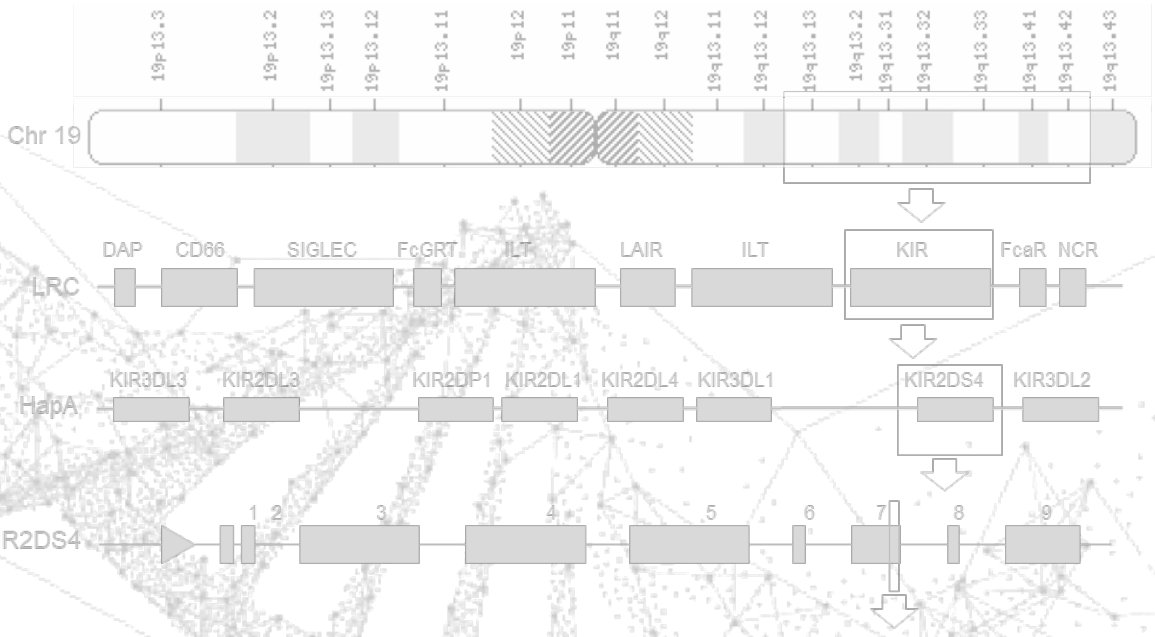


Nucleic acid biochemistry

San Luis Potosi State University (UASLP) Mexico
Molecular Biology Course, Faculty of Medicine post-graduate program

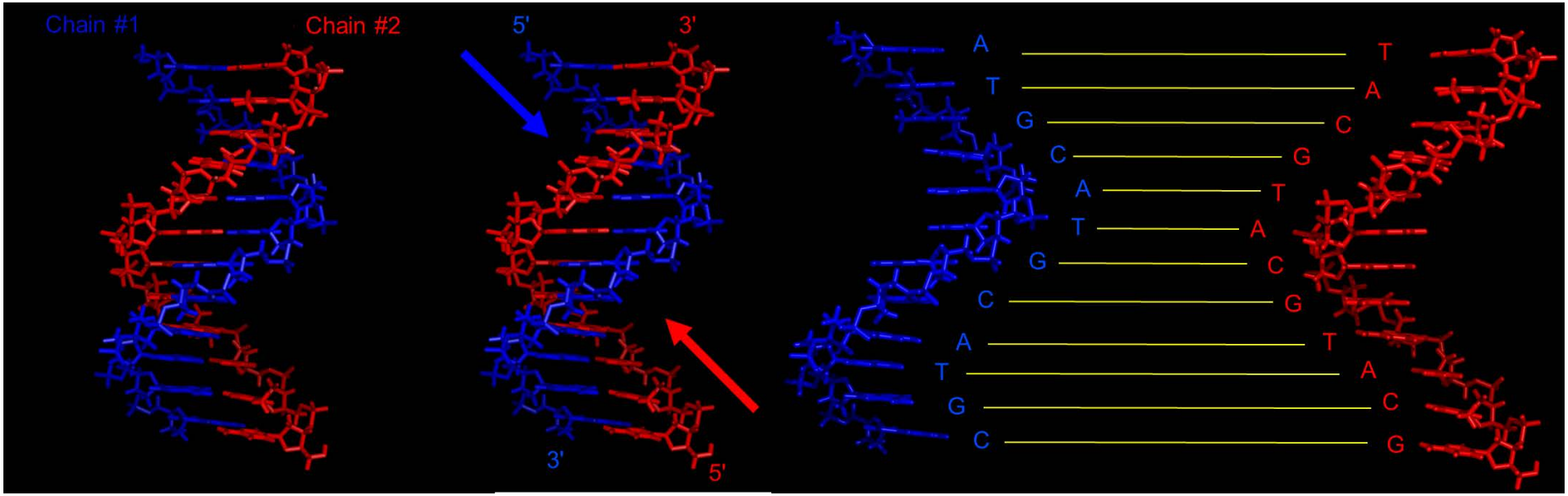
Dr. Christian A. García-Sepúlveda

Viral & Human Genomics BSL-3 Laboratory

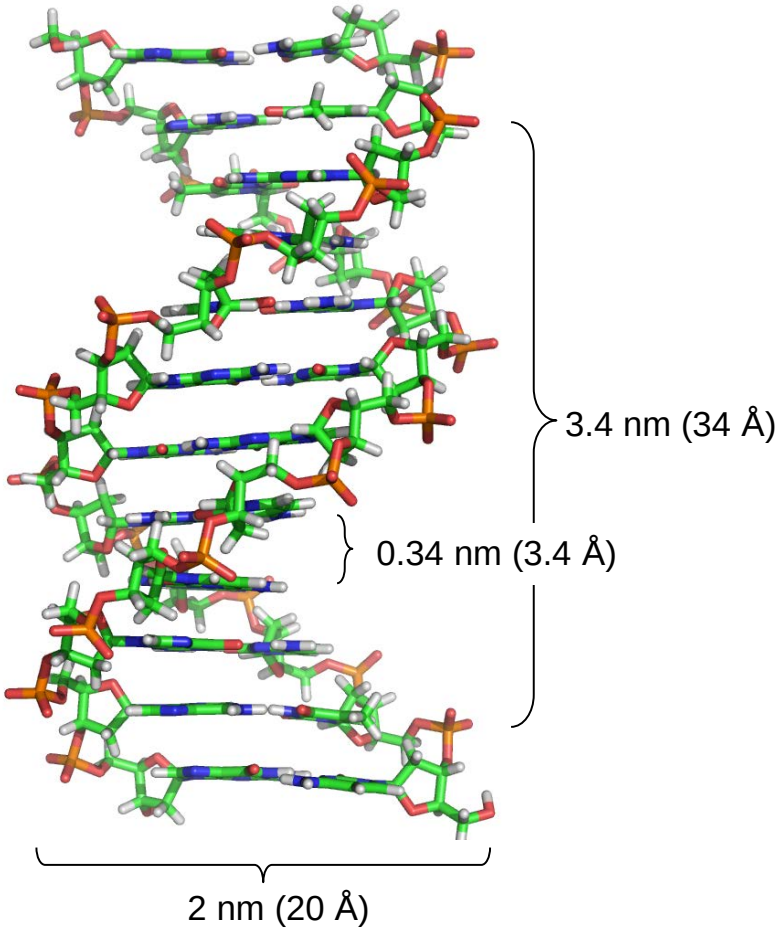
Last updated October 21, 2024 v1

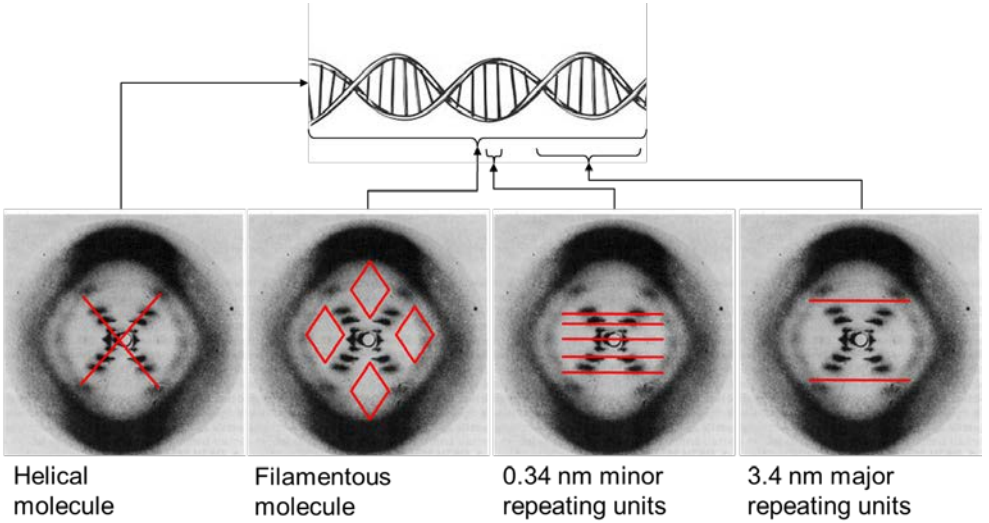
Deoxyribonucleic acid (DNA)

DNA is a double-stranded (duplex), antiparallel and complementary molecule.



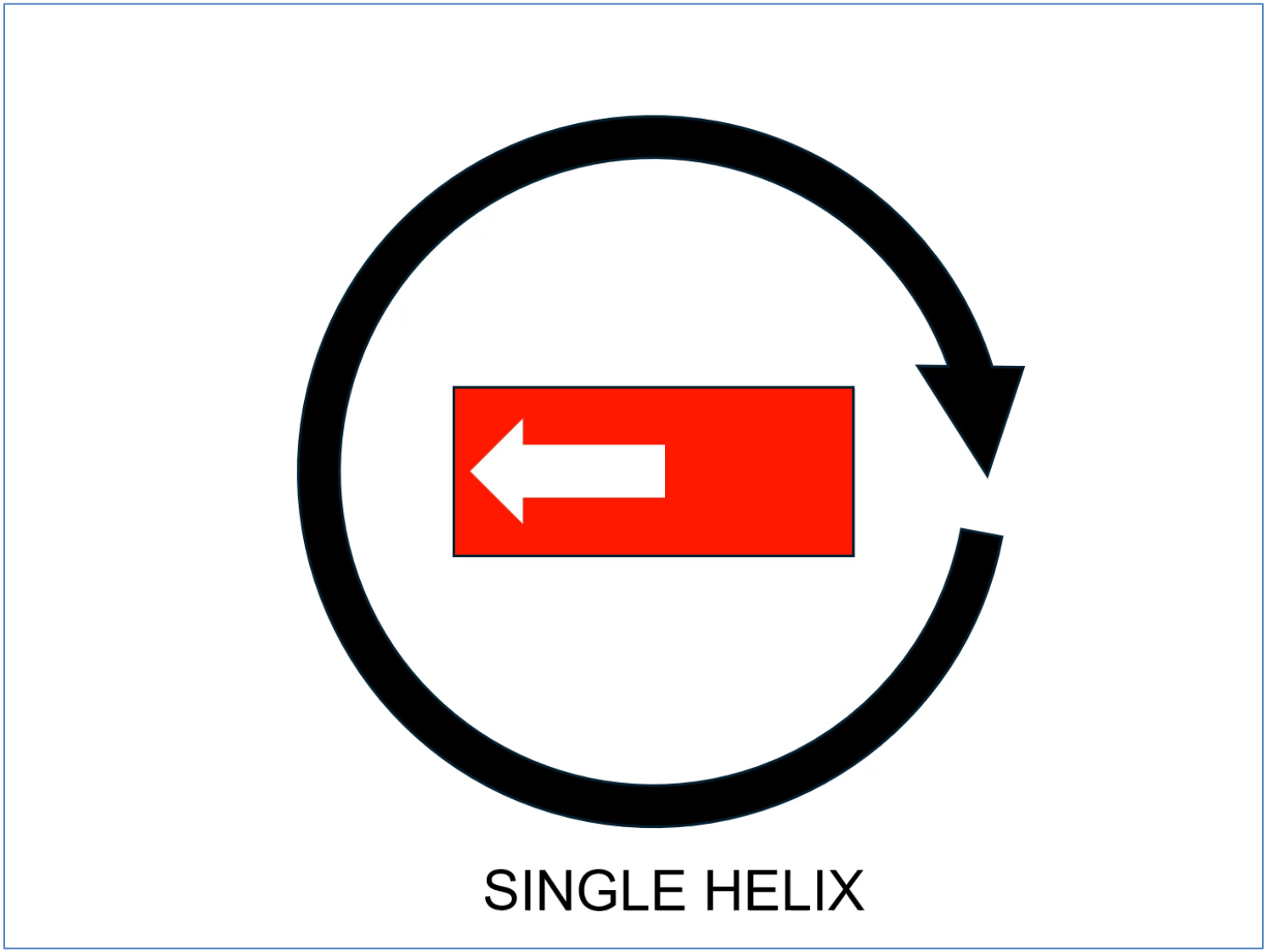
Deoxyribonucleic acid (DNA)



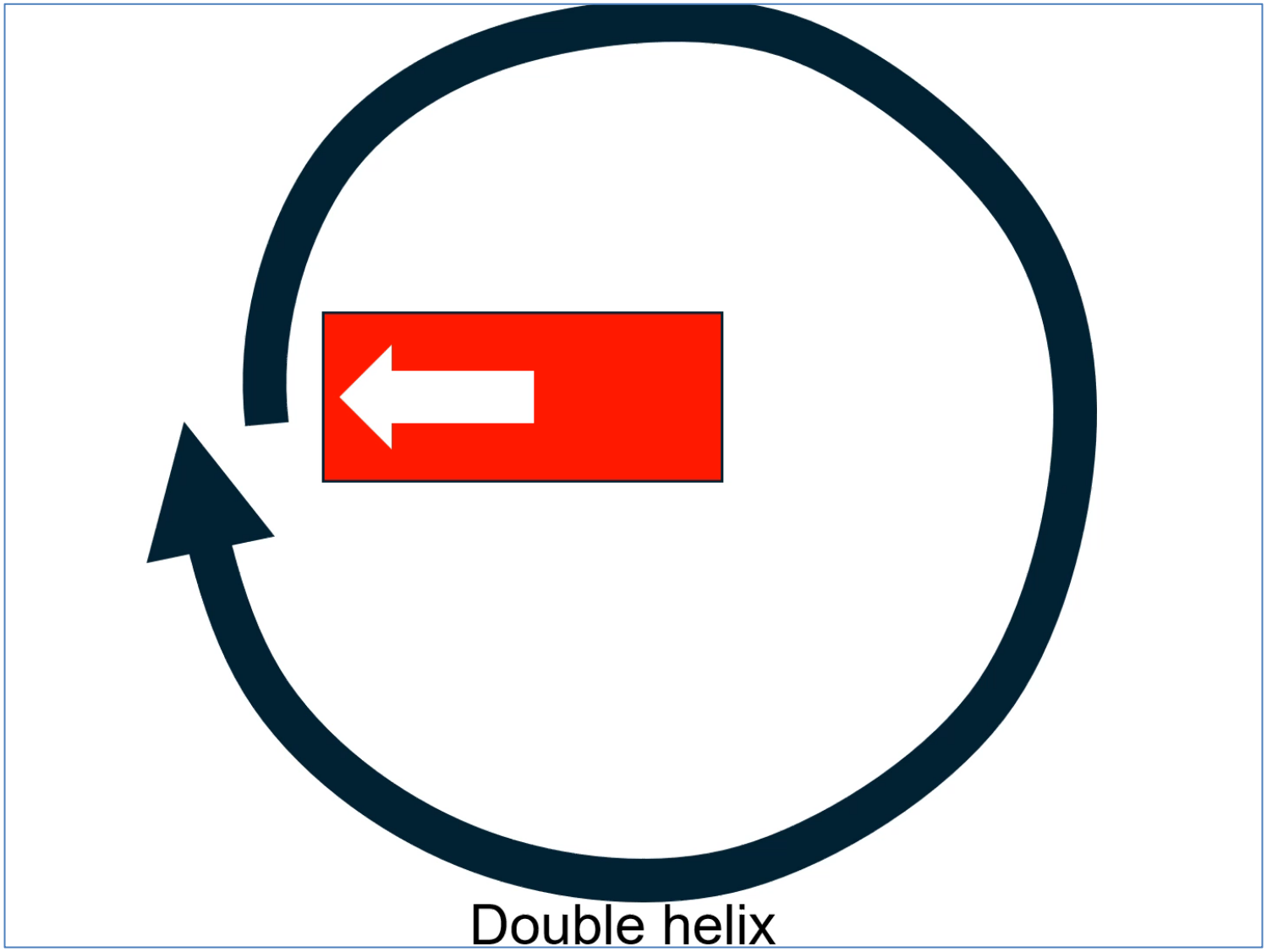


- Helical structure
- Filamentary shape (large molecule)
- Small units every 0.34 nm (3.4 Å)
- Large unit every 3.4 nm (34 Å)
- 1 Ångström = 0.1 nanometer

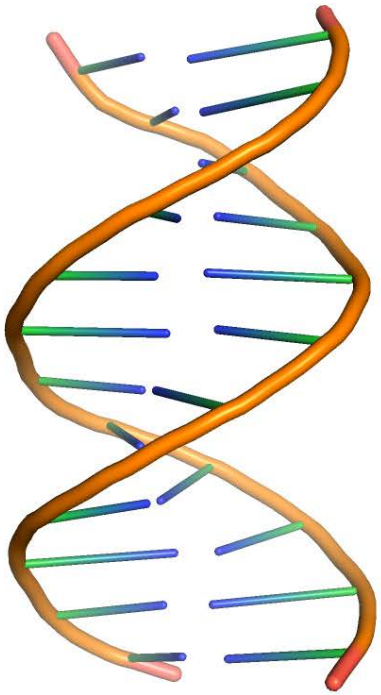
Deoxyribonucleic acid (DNA) is a double helix



Deoxyribonucleic acid (DNA) is a double helix

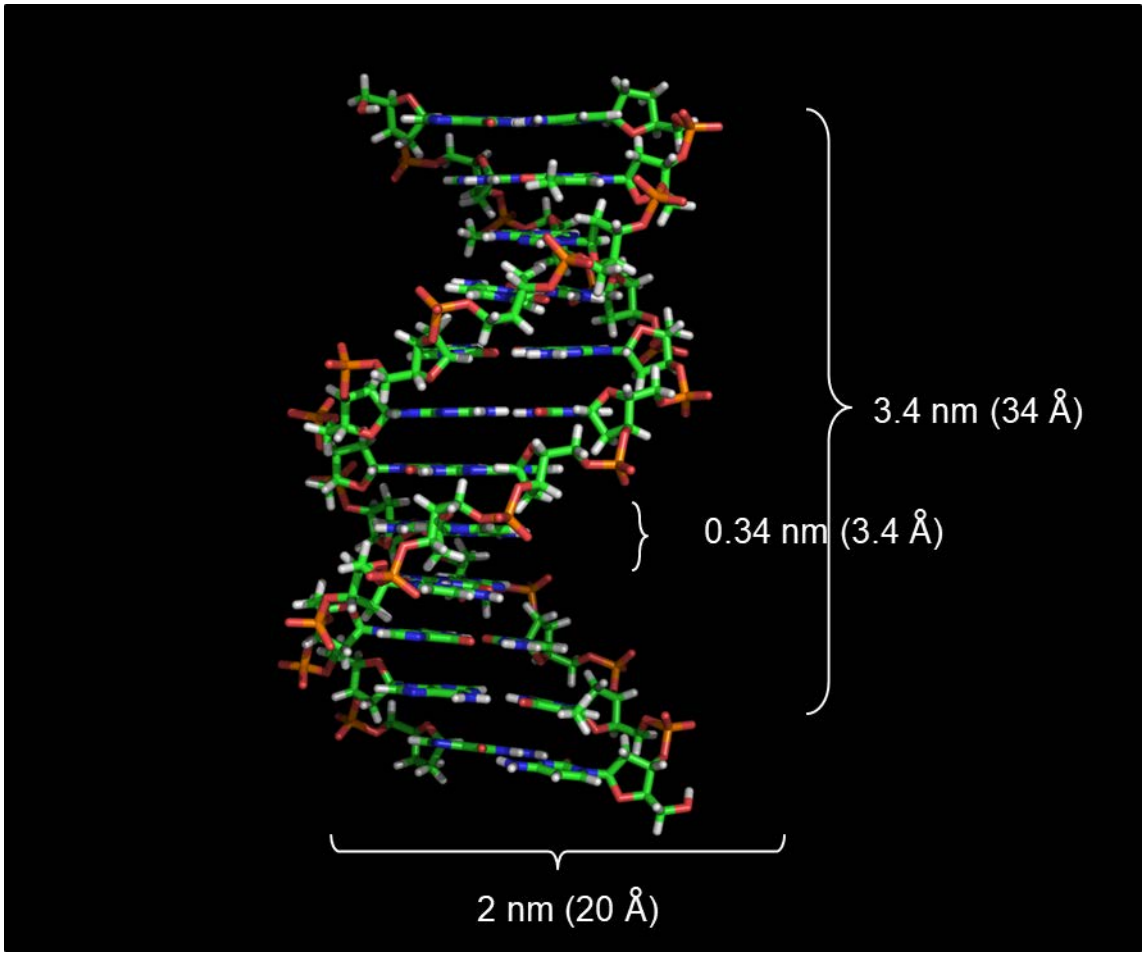


Deoxyribonucleic acid (DNA) is a double helix



DNAs dimensions

DNA in B conformation is 2 nm x 3.4 nm per turn (10 bases).



DNAs surface topology

The major groove and minor grooves have different widths and depths.

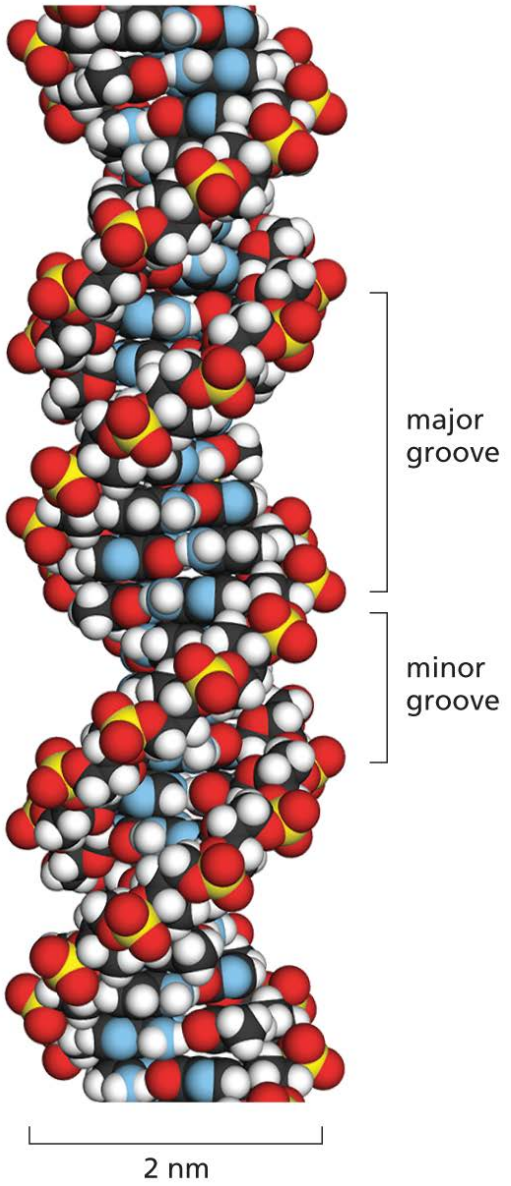
Each groove has unique functional implications in biological processes, especially in how proteins and molecules interact with DNA.

The major groove provides more accessible chemical information to proteins and other molecules.

Allows proteins, like transcription factors, to recognize and bind to specific DNA sequences with high affinity.

Proteins can "read" the DNA sequence without unwinding it.

The minor groove is narrower, less accessible and provides fewer distinguishing features for proteins to recognize specific sequences.



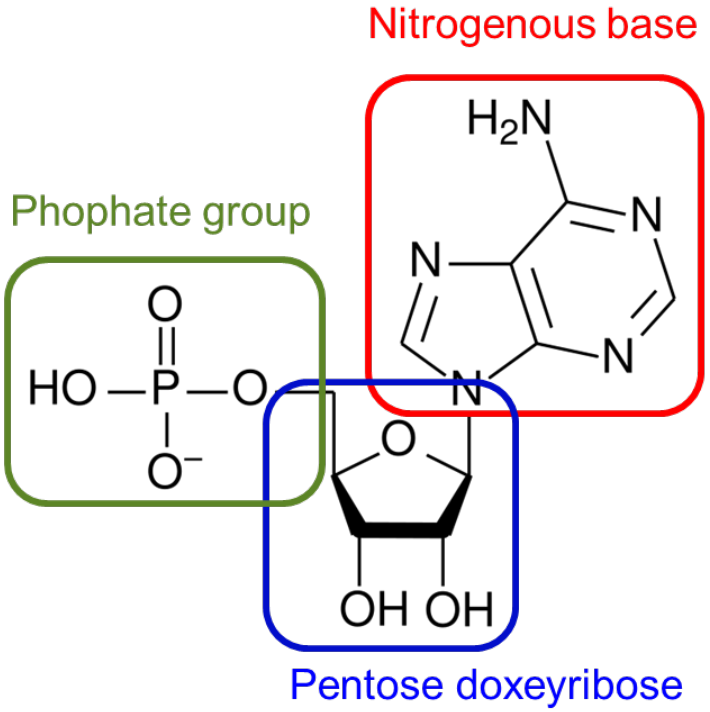
Nucleotides

Nucleotides are the building blocks of DNA and essential for genetic information storage and transmission.

Each nucleotide has a nitrogenous base (adenine, thymine, cytosine, or guanine).

A pentonse deoxyribose sugar that stabilizes the DNA structure.

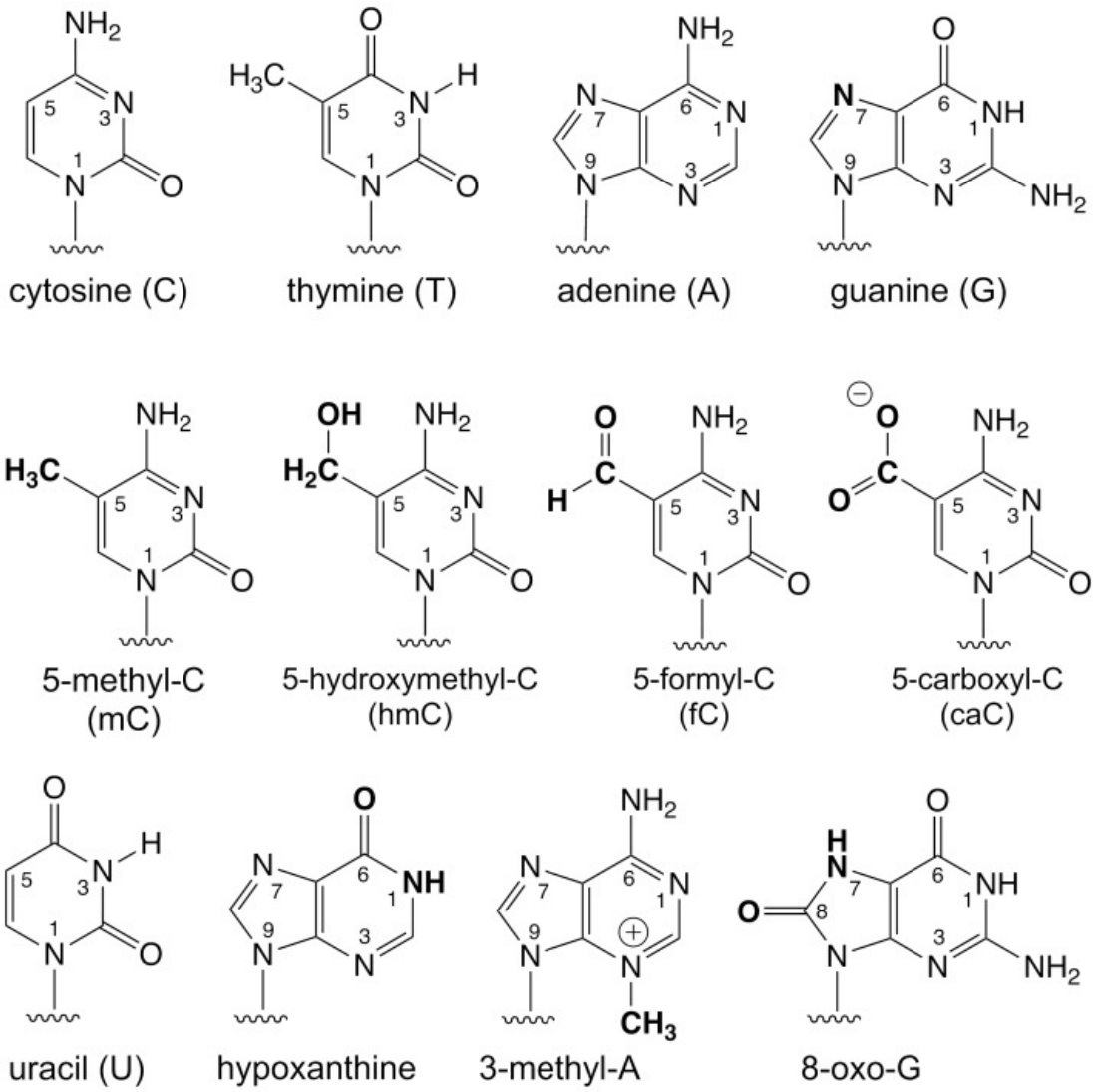
A phosphate group that forms the DNA backbone through phosphodiester bonds.



Nitrogenous bases

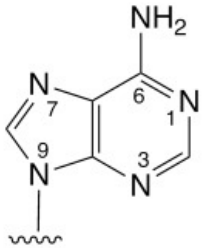
Adenine (A)
Thymine (T)
Cytosine (C)
Guanine (G)

5-Methylcytosine (5mC)
5-Hydroxymethylcytosine (5hmC)
N^6-Methyladenine (6mA)
7-Deazaguanine

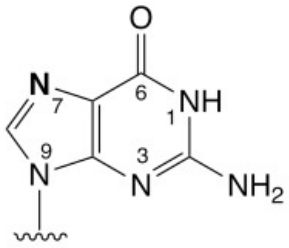


Nitrogenous bases

Purines
2 rings (Pyrimidine and imidazole)
A is similar to NH group in form
G is similar to O group in form
Attach to pentose via Nitrogen #9

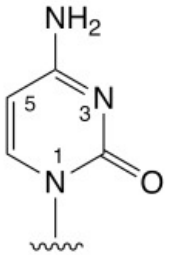


adenine (A)

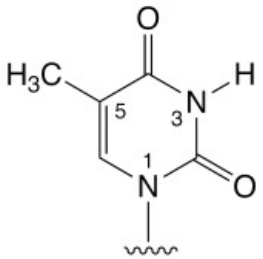


guanine (G)

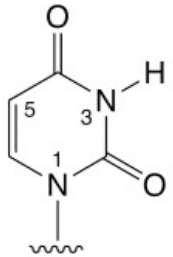
Pyrimidines
Single pyrimidine ring
Look like letter “i”
Have mane “i’s” in name (in Spanish at least)
Attach to pentose via Nitrogen #1



cytosine (C)



thymine (T)

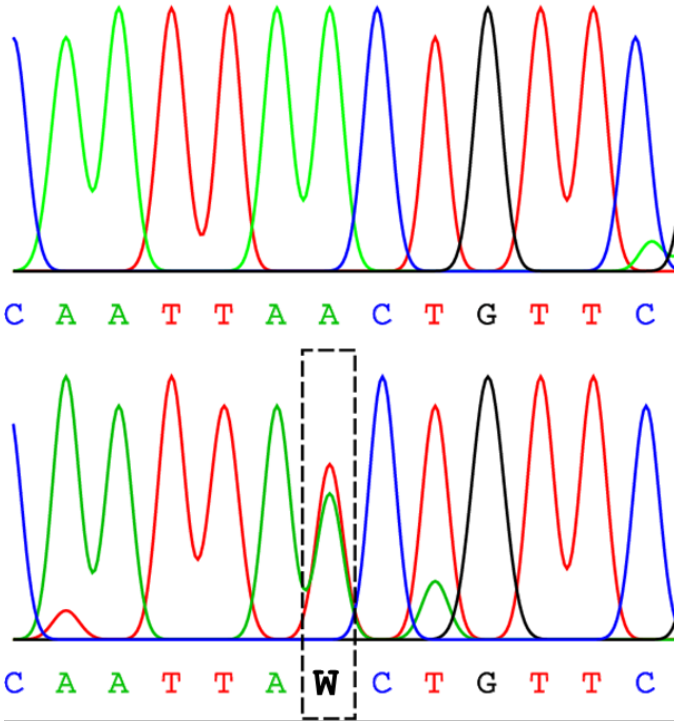


uracil (U)

Contrary to purines:
C is NOT similar to NH group
T is not similar to O group
Uracil present only in RNA
Uracil is not methylated, thymine is.

IUPAC nucleotide ambiguity codes

Symbol	Bases	Description
A	A	Adenine
C	C	Cytosine
G	G	Guanine
T (or U)	T (or U)	Thymine (or Uracil)
W	**A** or **T**	Weak
S	**C** or **G**	Strong
M	**A** or **C**	aMino
K	**G** or **T**	Keto
R	**A** or **G**	puRine
Y	**C** or **T**	pYrimidine
B	C or G or T	not A (B comes after A)
D	A or G or T	not C (D comes after C)
H	A or C or T	not G (H comes after G)
V	A or C or G	not T (V comes after T and U)
N	any base	any Nucleotide (not a gap)



Pentose relevance

Carbons labelled ‘ (prime) to distinguish from atoms of nitrogenous base.

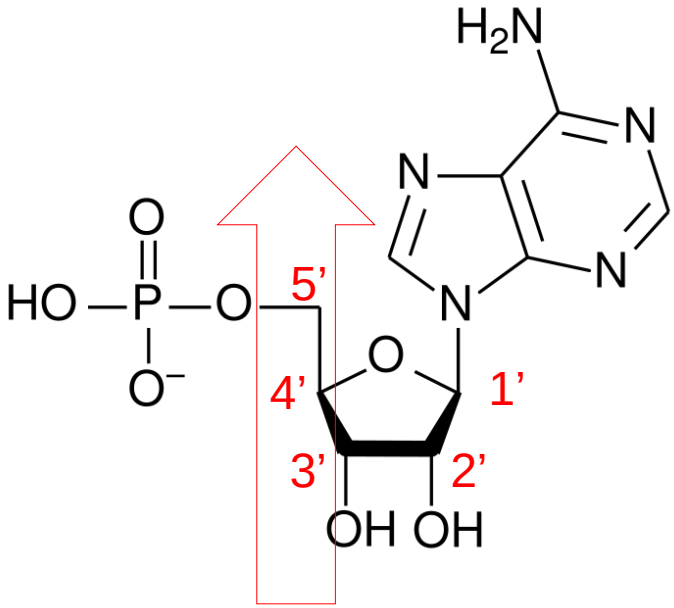
Carbon 1’ attaches to nitrogenous base.

Carbon 2’ distinguishes DNA (deoxydized) from RNA (oxydized).

Carbon 3’ and 5’ establish polarity.

Carbon 5’ attaches to phosphate group.

Polymerases attach nucleotides to 3’-OH group (extensible 3’-OH).



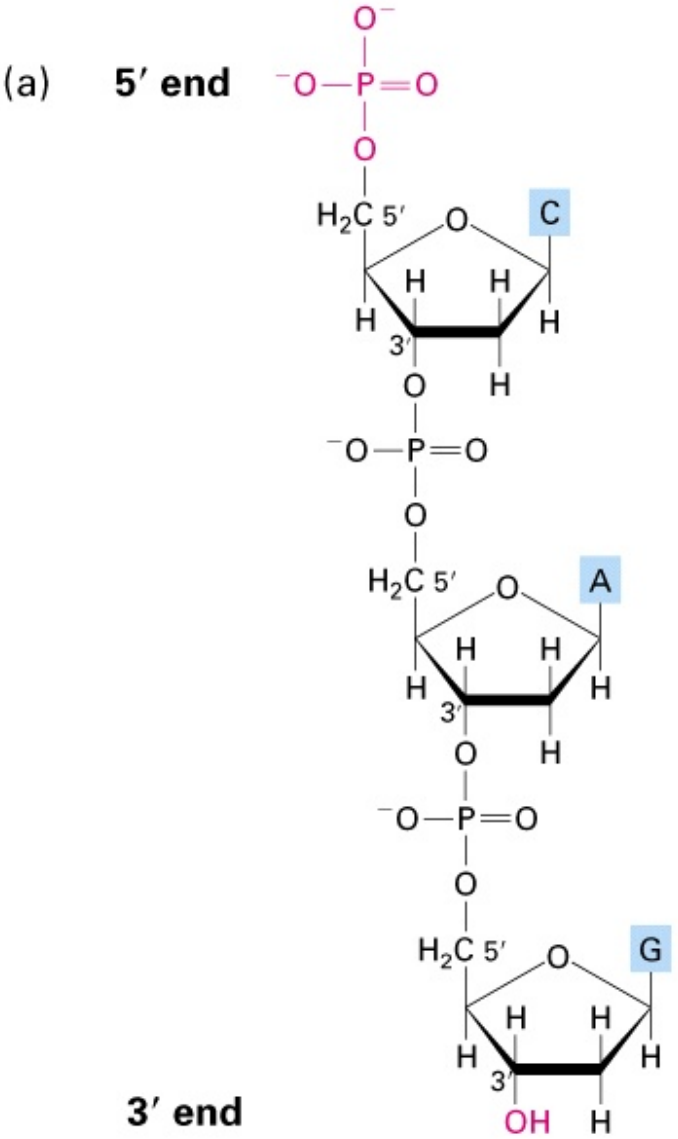
(a)

DNA and RNA polymerization

Polymerases attach nucleotides to 3’-OH group (extensible 3’-OH).

During DNA and RNA synthesis, the 3' hydroxyl group of one nucleotide reacts with the 5' phosphate group of the incoming nucleotide through a phosphodiester bond.

Without the 3' hydroxyl group, the chain cannot extend, halting DNA or RNA synthesis exploited by Chain Termination in Sanger DNA Sequencing.



Nomenclature

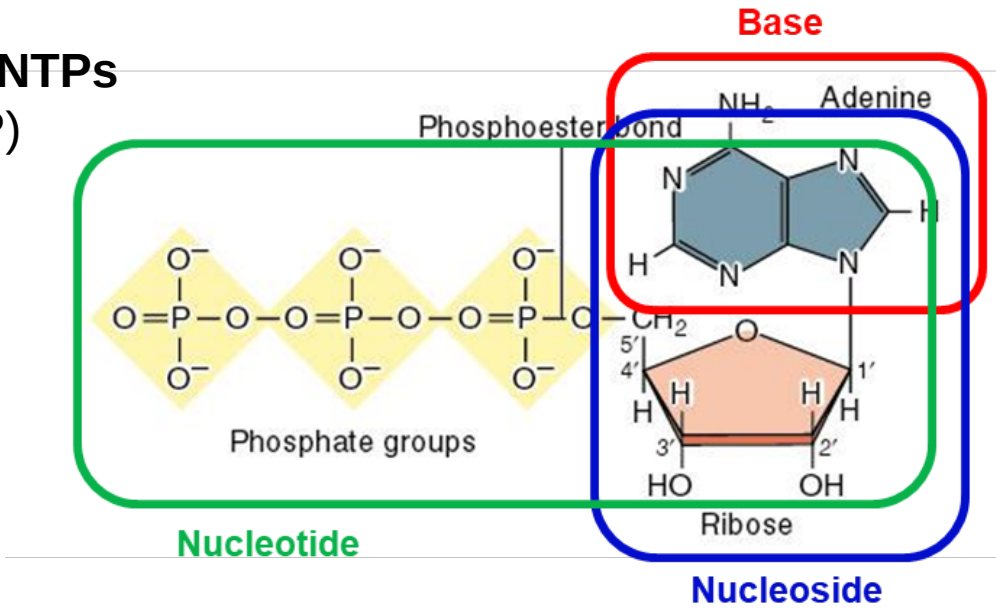
Distinguishes between nitrogenous bases, nucleosides, nucleotides, RNA and DNA.

In RNA nucleotides are known as NTPs

Adenine, Adenosine, Adenosimonophosphate (AMP), ADP and ATP.
Guanine, Guanosine , Guanosindiphosphate (GMP), GDP and GTP.
Cytosine, Cytidine, Cytidintriphosphate (CMP), CDP and CTP.
Thymine,Thymidine, Thymidintriphosphate (TMP), TDP and TTP
Uracil, Uridine, Uridintriphosphate (UMP), UDP and UTP

In DNA nucleotides are known as dNTPs

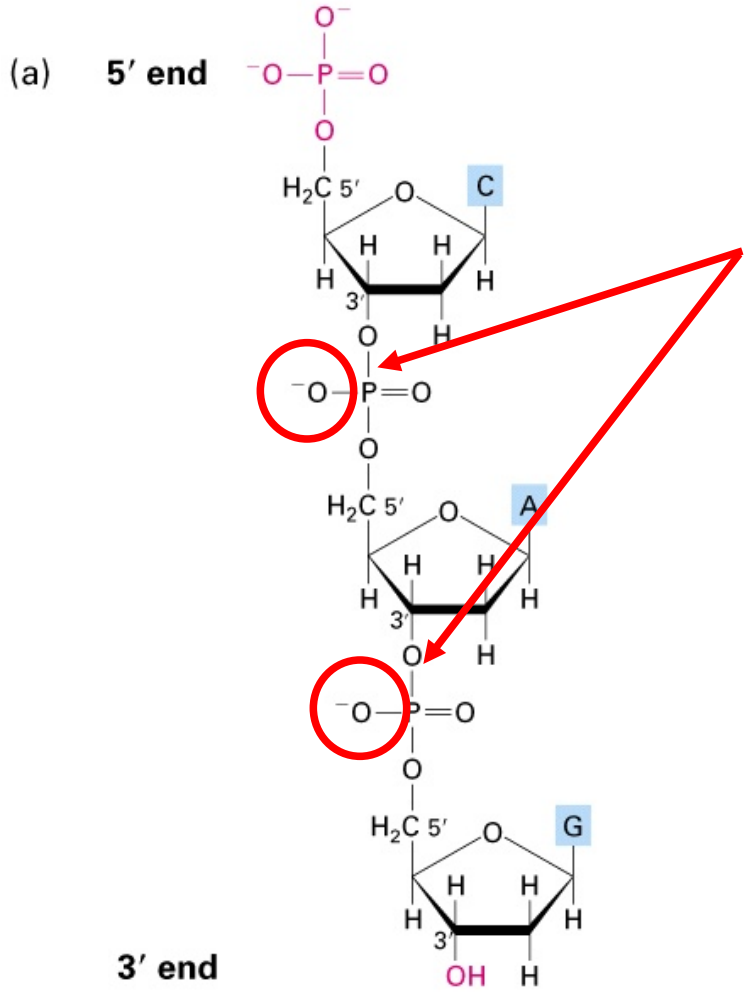
Deoxyadenosimonophosphate (dAMP)
Deoxyguanosindiphosphate (dGMP)
Deoxycytidintriphosphate (cCMP)
Deoxythymidintriphosphate (dTMP)



Fosfatos

Text here

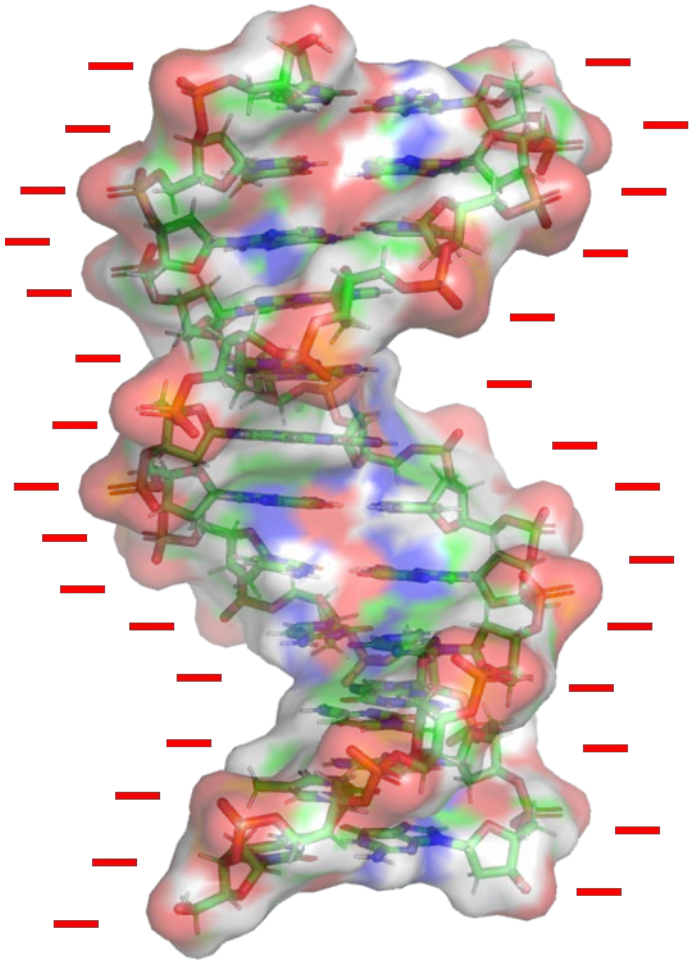
- Fosfatos y enlaces fosfodiester = Polimerización de ácidos nucléicos

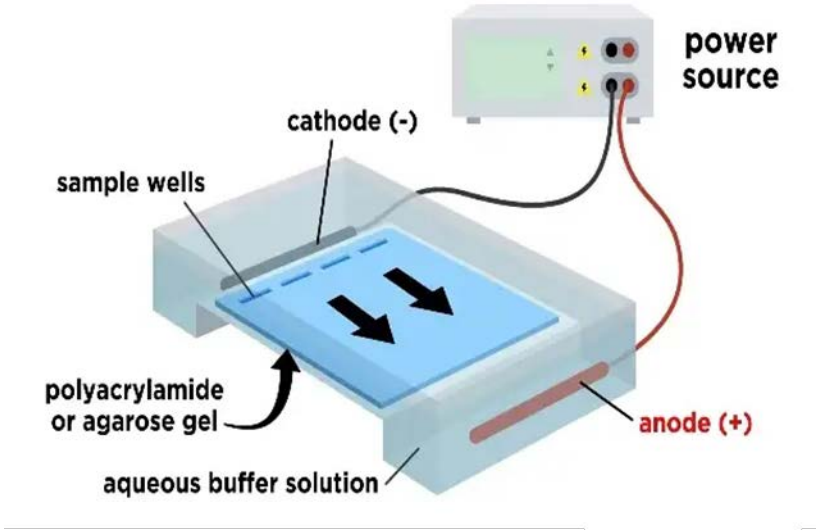


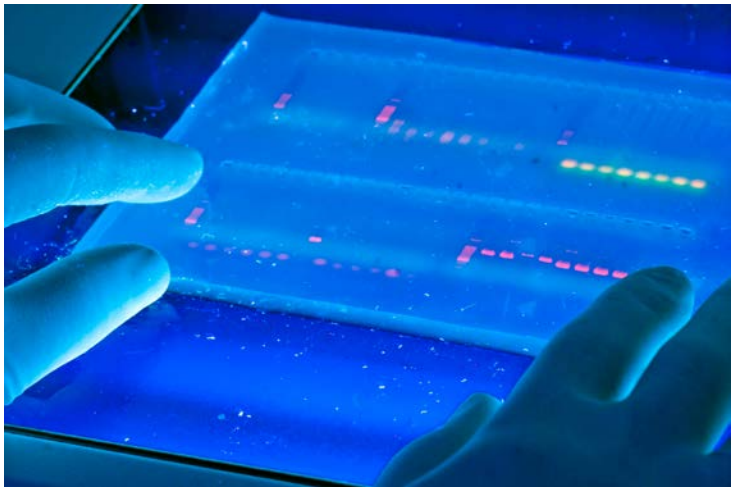
Cada enlace fosfodiester conlleva una carga electroestática de -1 por lo cual la carga neta del polímero de nucleótidos (DNA) es negativa.

Phosphate groups

DNA backbone has an overall negative charge due to phosphate groups.

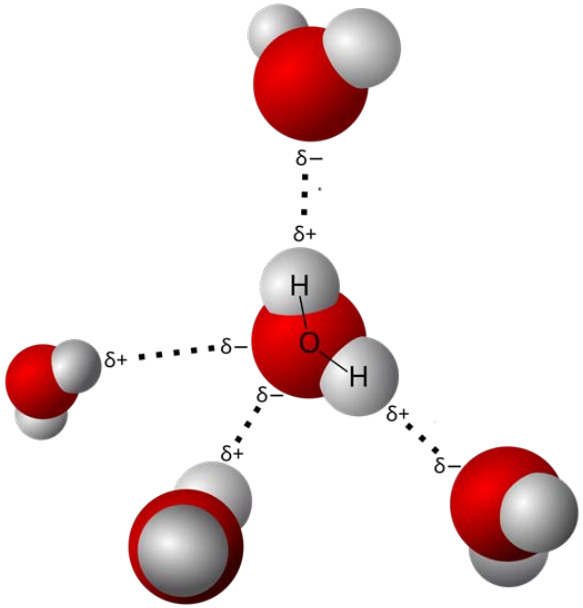




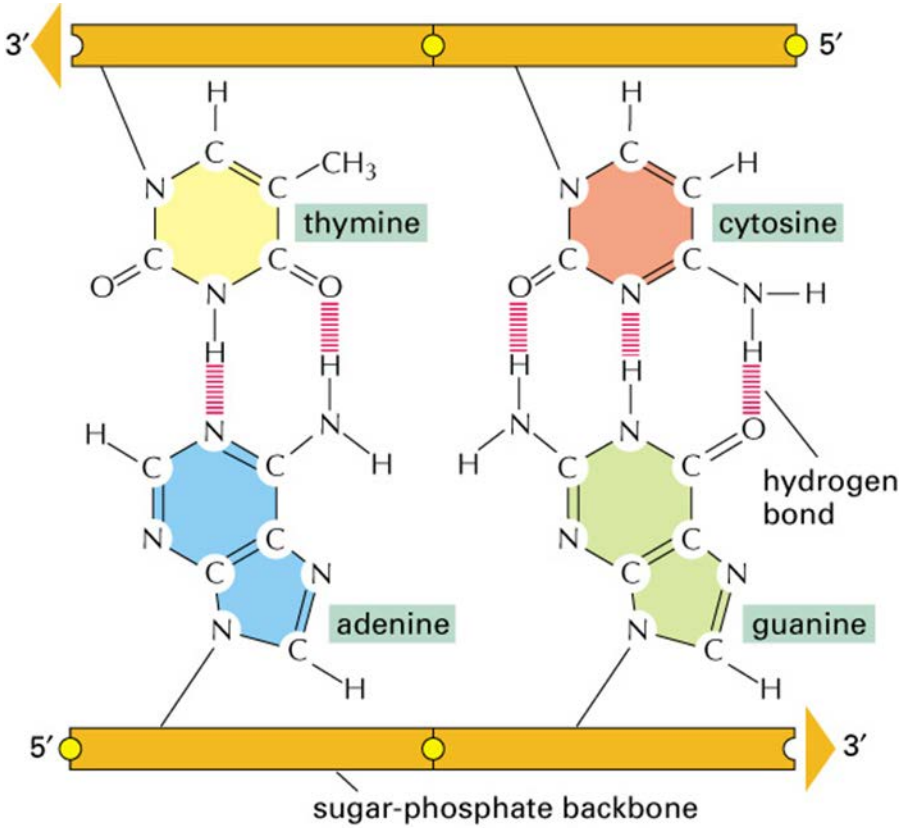


Hydrogen bonds

An electrostatic force of attraction between a hydrogen (H) atom covalently bonded to an electronegative "donor" atom (δ+), and another electronegative atom bearing a lone pair of electrons (δ-).



Hydrogen bonds between water molecules.



Molecular Biology of the Cell, 4th Edition.

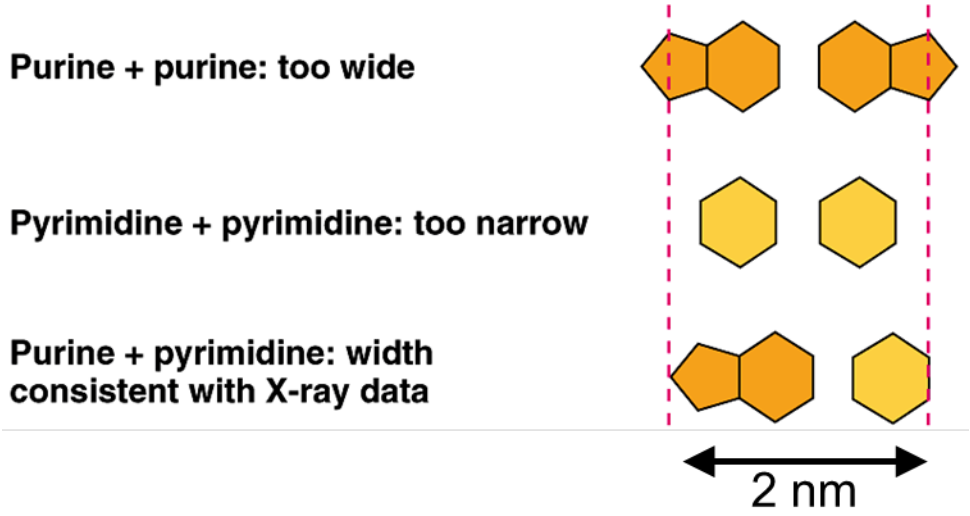
Watson–Crick base pairing

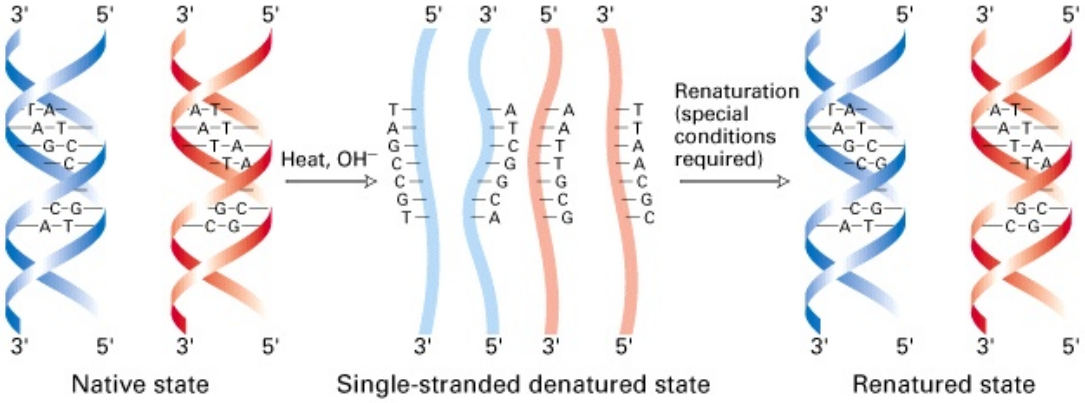
Specific hydrogen bonding patterns allow for "Watson–Crick" (or "Watson–Crick–Franklin") base pairing.

G≡C and A=T

The complementary nature of these base pairs provides a redundant copy of the genetic information in each strand of DNA.

Paired DNA & RNA molecules are stable at room temperature but separate above a melting point determined by the length of the molecules and the GC content.





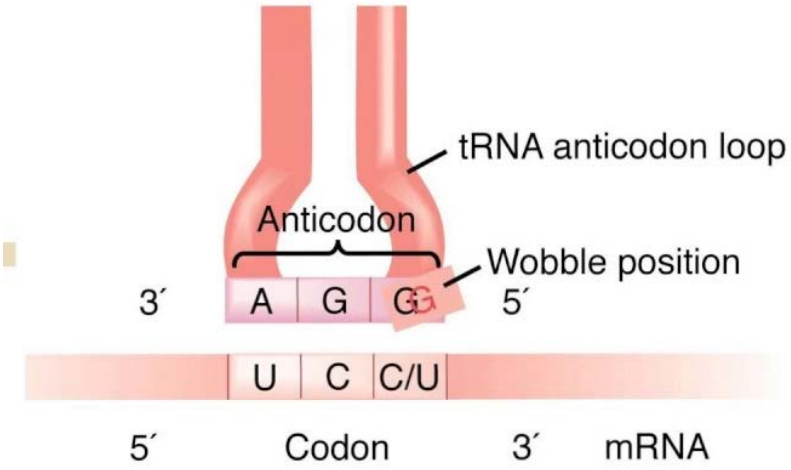
Molecular Biology of the Cell, 4th Edition.

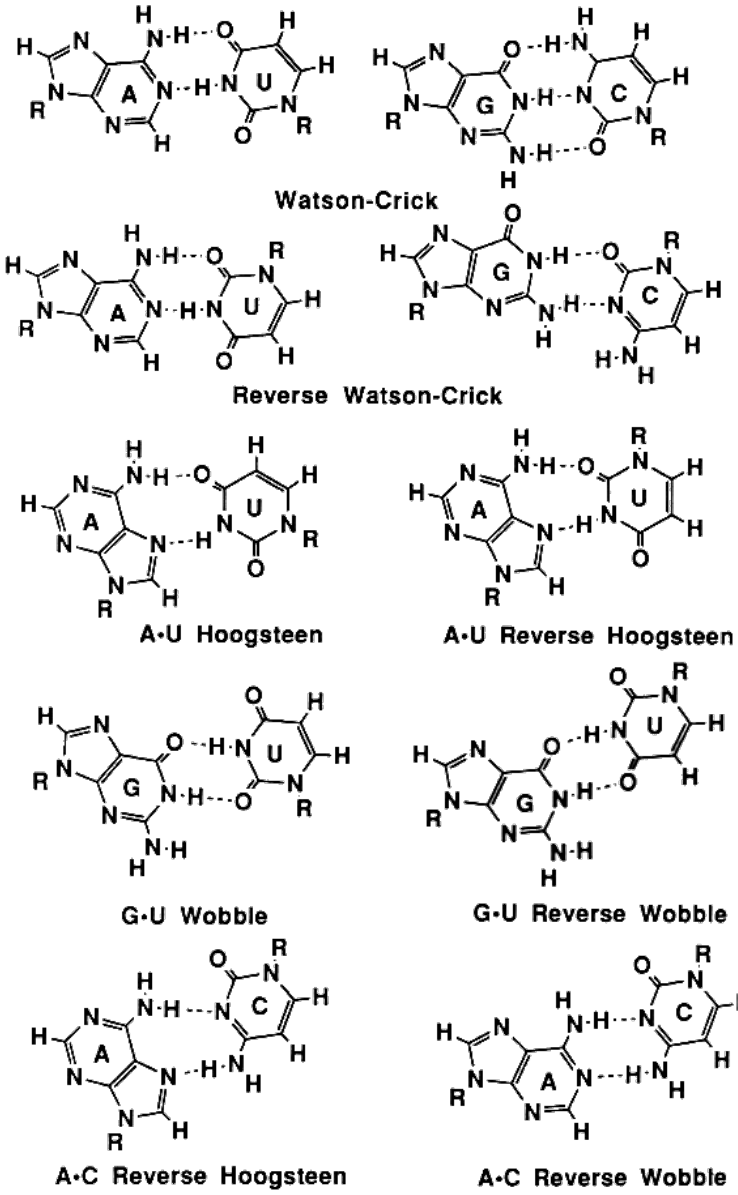
Non-canonical base pairing

Base-pairing with alternative base orientation, and number and geometry of hydrogen bonds.

Accompanied by alterations to the local backbone shape.

Wobble base pairing that occurs between tRNAs and mRNAs at the third base position of many codons during transcription.





A, B and Z DNA conformation

DNA can adopt several conformations, with three primary forms known as A-DNA, B-DNA, and Z-DNA.

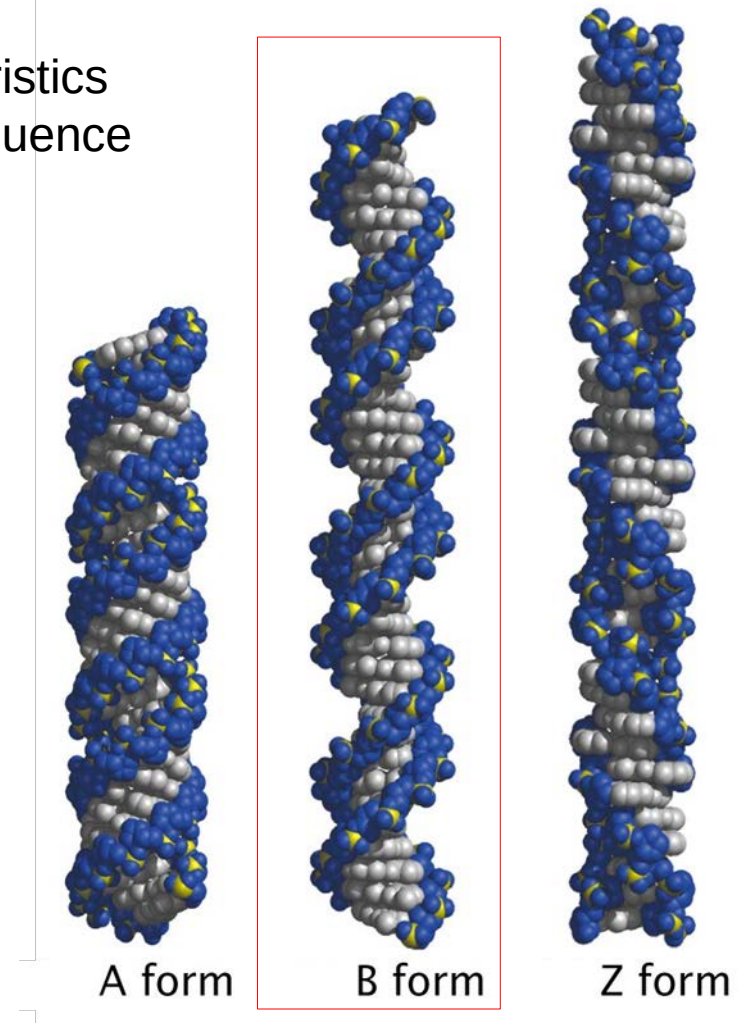
Each conformation has unique structural characteristics and is influenced by environmental conditions, sequence composition, and biological function.

B-DNA

Most common and biologically relevant form of DNA in cells.

Right-handed double helix with 10.5 bp/turn

Its major and minor grooves allow proteins to interact with specific sequences, making B-DNA ideal for genetic information storage and protein binding.



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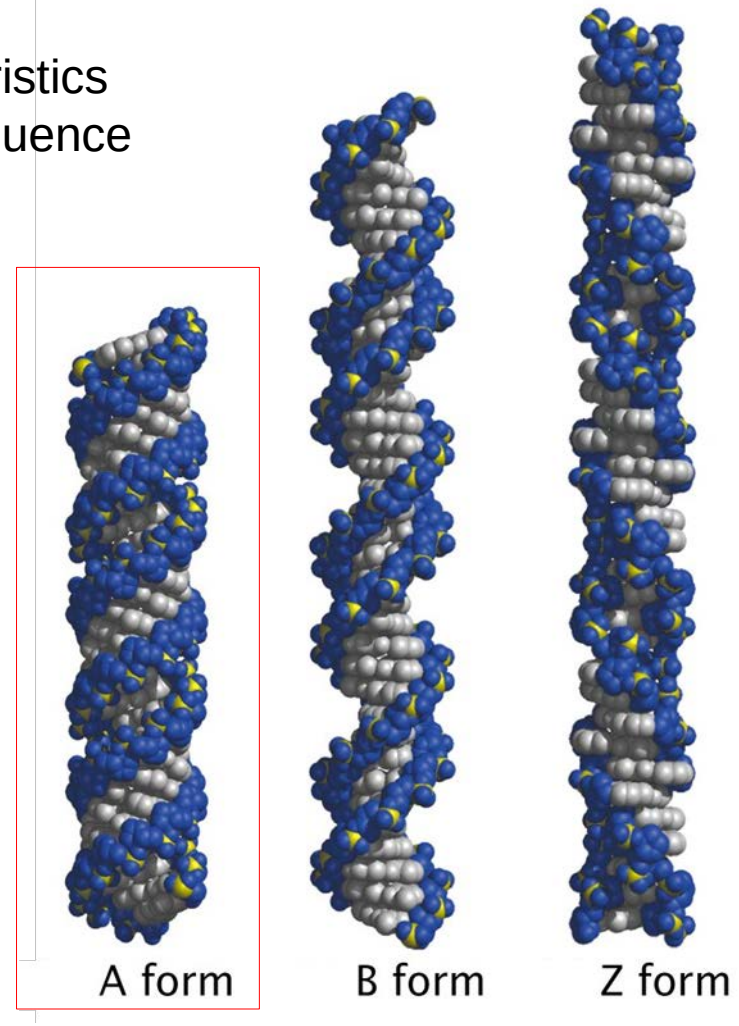
A-DNA
A right-handed helix more compact than B-DNA.

11 base pairs per turn.

Found under dehydrated conditions or in double-stranded RNA and DNA-RNA hybrids.

Its wider and shallower grooves make it less accessible to proteins, but it's still structurally stable.



A, B and Z DNA conformation

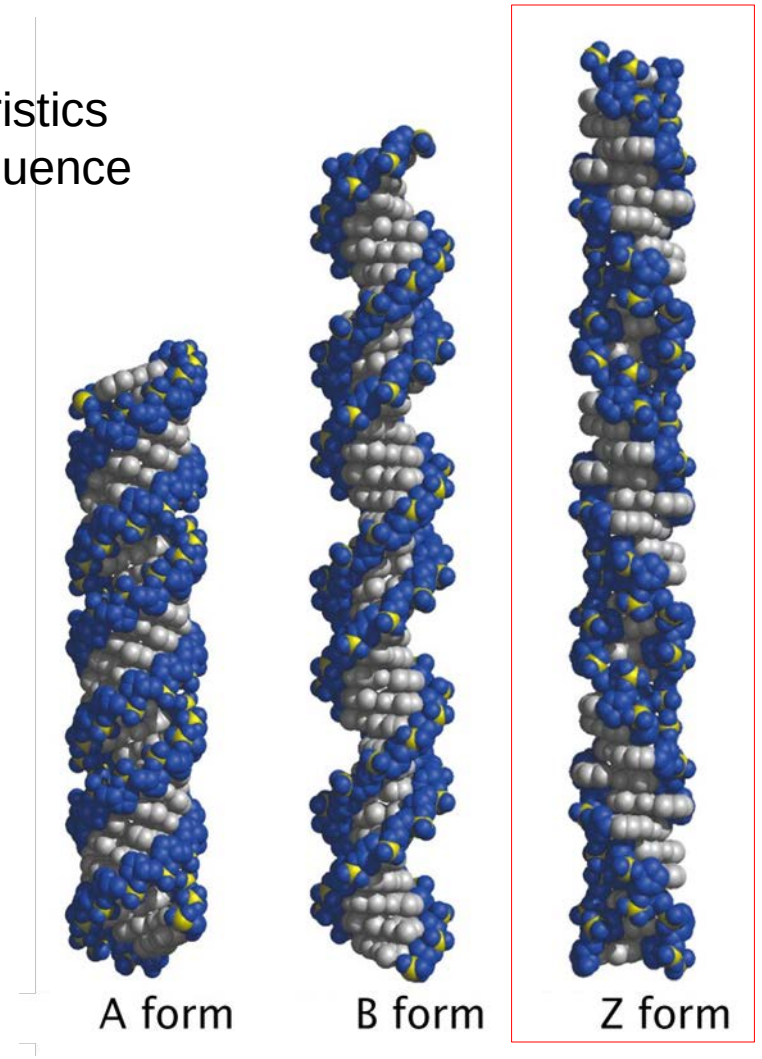
DNA can adopt several conformations, with three primary forms known as A-DNA, B-DNA, and Z-DNA.

Each conformation has unique structural characteristics and is influenced by environmental conditions, sequence composition, and biological function.

Z-DNA
Left-handed helical form has a zigzag backbone, hence the name "Z-DNA."

It occurs in regions with alternating purine-pyrimidine sequences (like CG repeats) and may form transiently during active transcription.

Z-DNA is thought to play a role in gene regulation and is recognized by specific proteins.



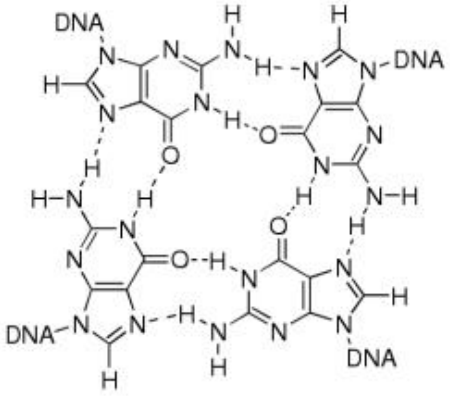
DNA tetrads and G-quadruplexes

Consist of four guanine bases that hydrogen bond together in a square planar structure called a G-tetrad.

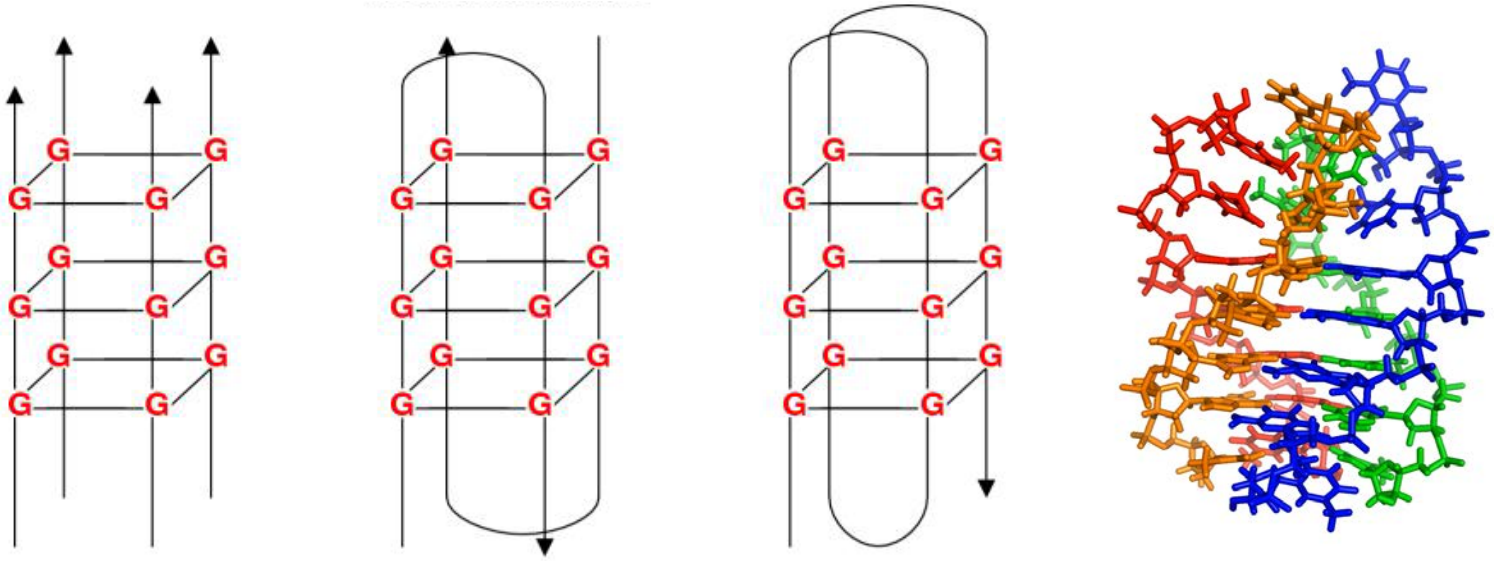
Multiple g-tetrads stack on top of each other to stabilize the structure, often held together by cations.

Formation in guanine-rich regions, such as telomeric regions, promoter regions, and regulatory areas of the genome.

Can be parallel, antiparallel, or mixed.



A. G-tetrad structure



DNA tetrads and G-quadruplex roles

In telomeres protect chromosome ends and regulate telomerase activity.

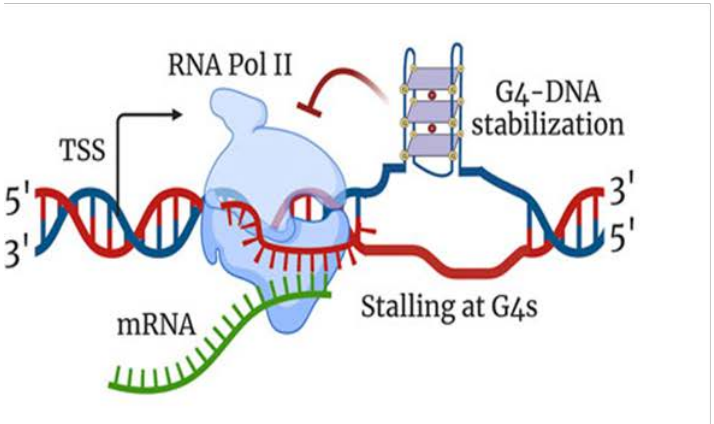
In promoters influence gene expression as physical barrier to transcription.

Serve as regulatory checkpoints or pause sites for replication.

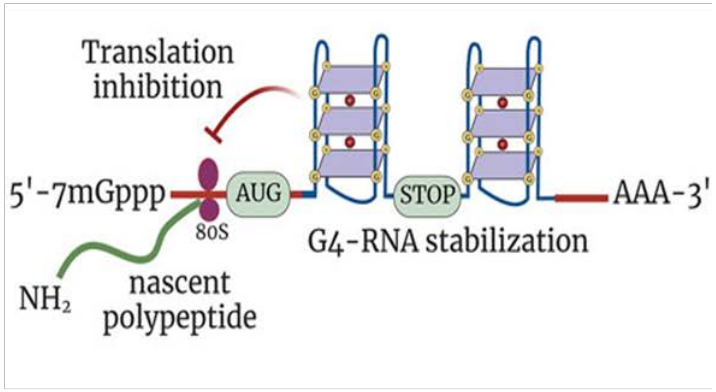
Are therapeutic targets for roles in cancer and aging (telomerase regulation),

Overall, DNA tetrads or G-quadruplexes play significant roles in cellular processes, especially in genome stability, regulation, and telomere function.

Tetrads regulating transcription



Tetrads regulating translation



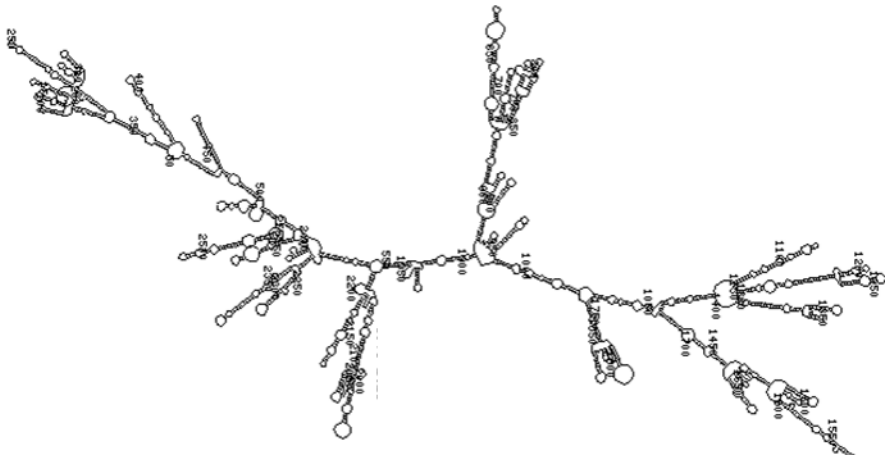
mRNA biochemistry

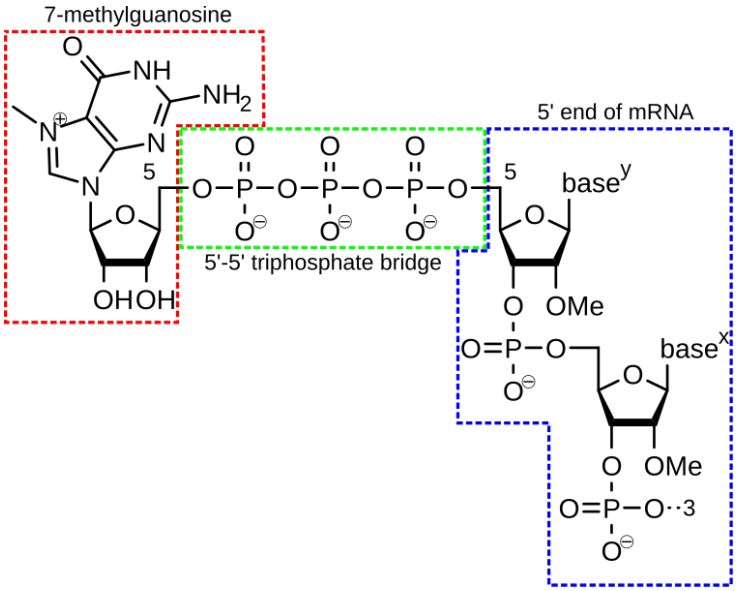
Single-stranded RNA (ssRNA) written from a DNA gene by RNA polymerase II that is translated by a ribosome to a protein.

mRNA uses uracil (U) instead of thymine (T).

5’ end is stabilized with an antiparalell 7-methylguanosine (m7G cap) through a 5'-5'-triphosphate bond.

Stabilized through secondary structure (hairpins, stems and loops).





tRNA biochemistry

Small ssRNA molecule that transfers specific amino acids to the ribosome, where they are assembled into proteins according to the mRNA codon sequence.

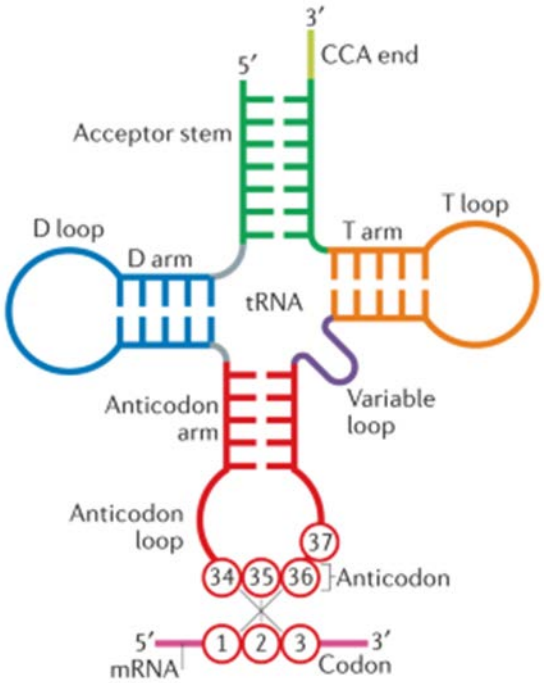
tRNA has a characteristic cloverleaf secondary structure with four main regions:

Acceptor stem where an amino acid is covalently attached, always ends in CCA

D loop contains dihydrouridine, which provides flexibility.

Anticodon loop contains anticodon which base-pairs with the complementary codon on the mRNA.

TψC loop contains pseudouridine, and helps in tRNA stability and proper positioning within the ribosome.



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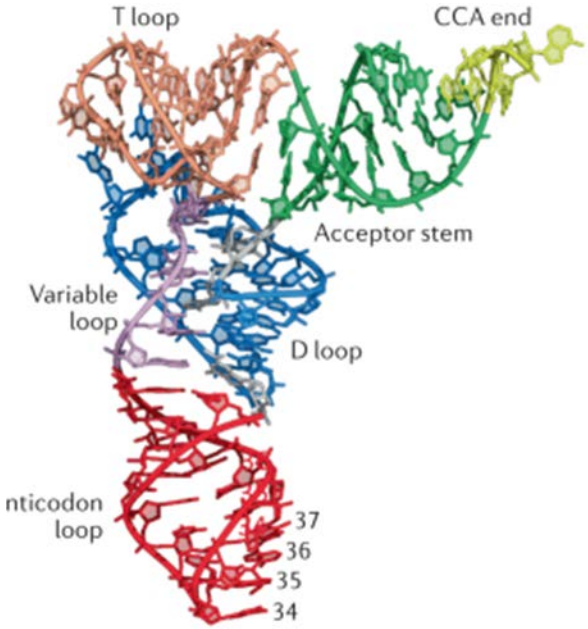
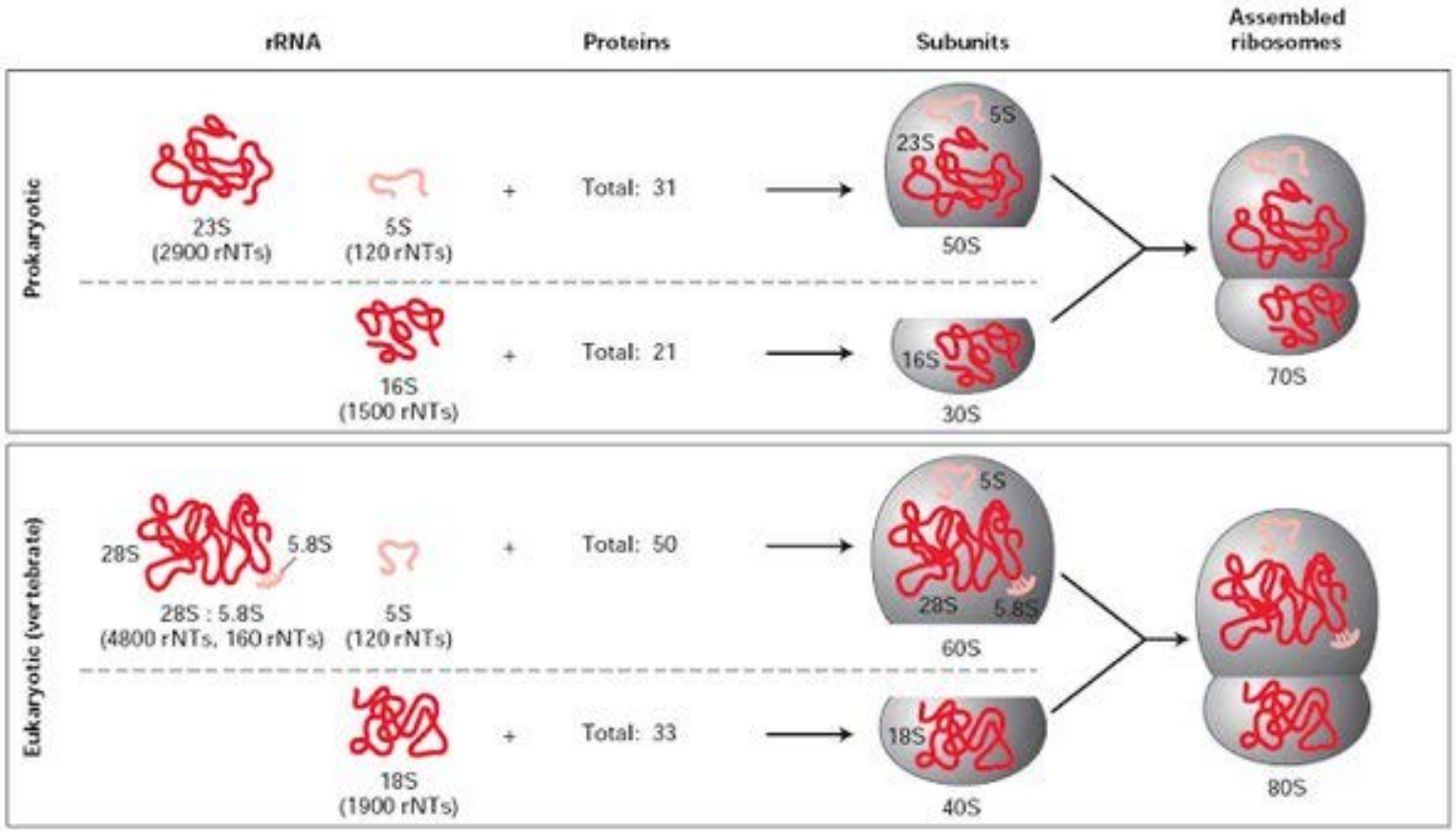
TψC loop contains pseudouridine, and helps in tRNA stability and proper positioning within the ribosome.

Also stabilized through secondary structure (Stem loops).



rRNA biochemistry

Complex of small ssRNA molecules and proteins involved in providing a niochemically secluded environment for tRNA-mRNA interactions and translation of RNA into proteins.



Laboratorio de Genómica Viral y Humana

Instalaciones de Alta Contención Biológica Nivel de Bioseguridad 3 (BSL-3) CDC-certificadas

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