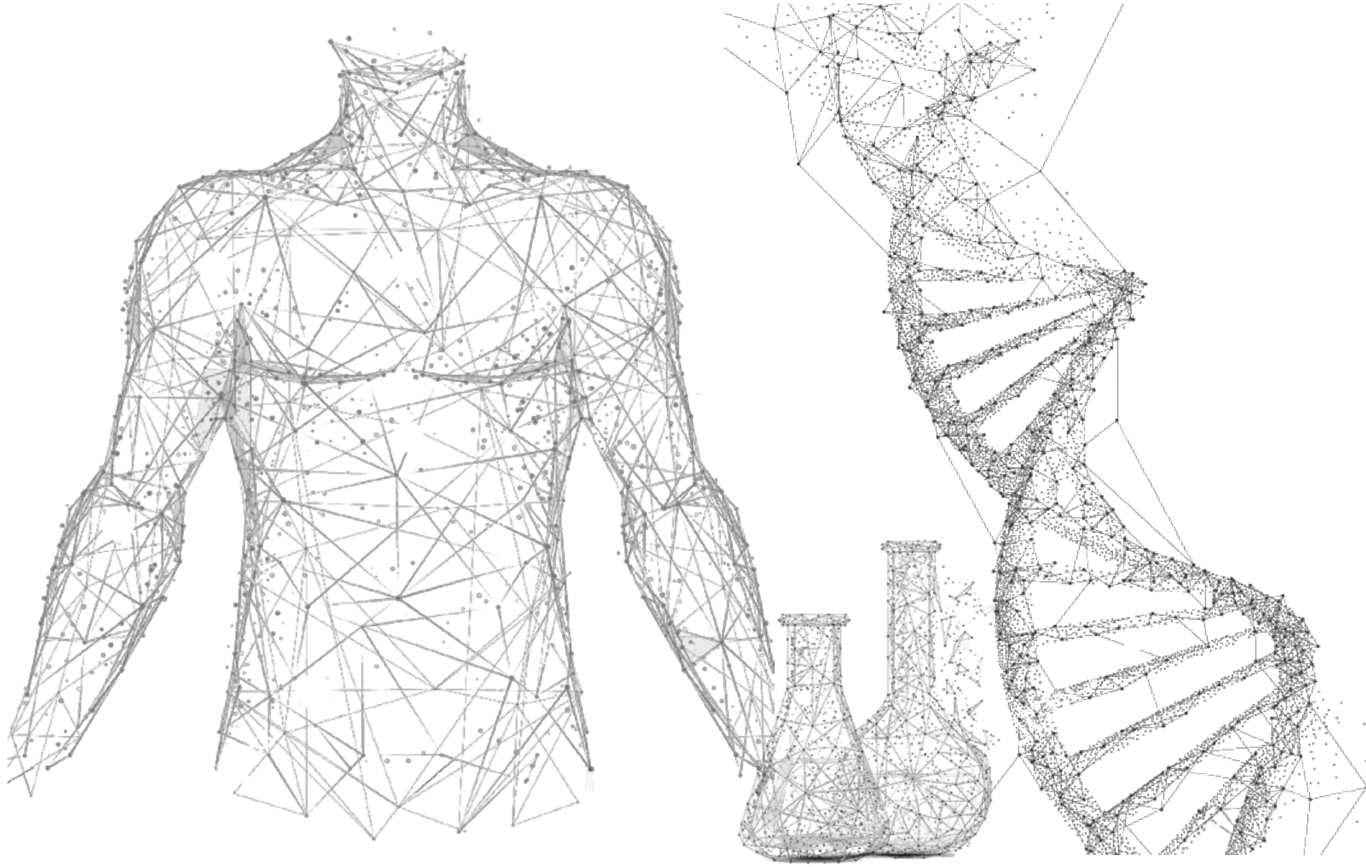


Molecular Structure of DNA

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

Dr. Christian A. García-Sepúlveda

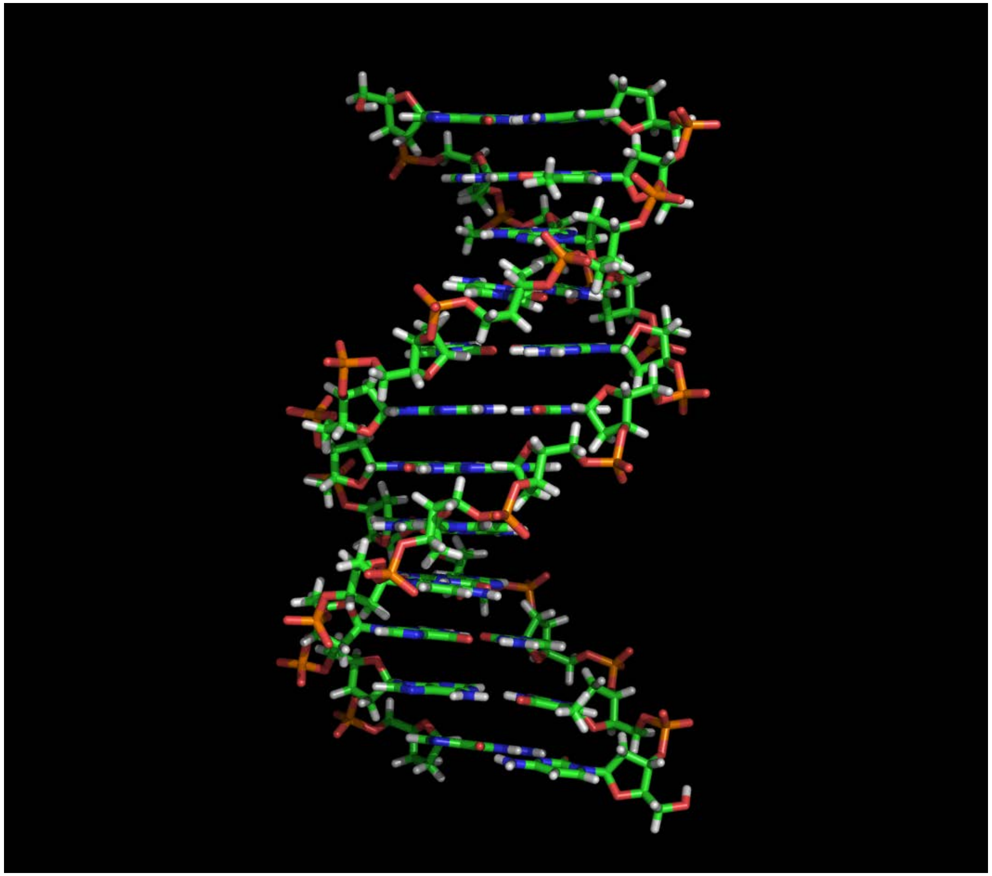
Viral & Human Genomics BSL-3 Laboratory

Last updated January 22, 2025 v3

DNA ultrastructure

What is DNA?

A bicatenary, antiparallel and complementary molecule encoding genetic information of most, but not all living organisms.



DNA genomes
10,000 bacterial species
500 archaeal species
611,000 fungal species, including yeasts
298,000 plant species
7.8 million animal species.
58,000 to 77,000 viral species

RNA genomes
161,979 RNA virus species
44 viroids

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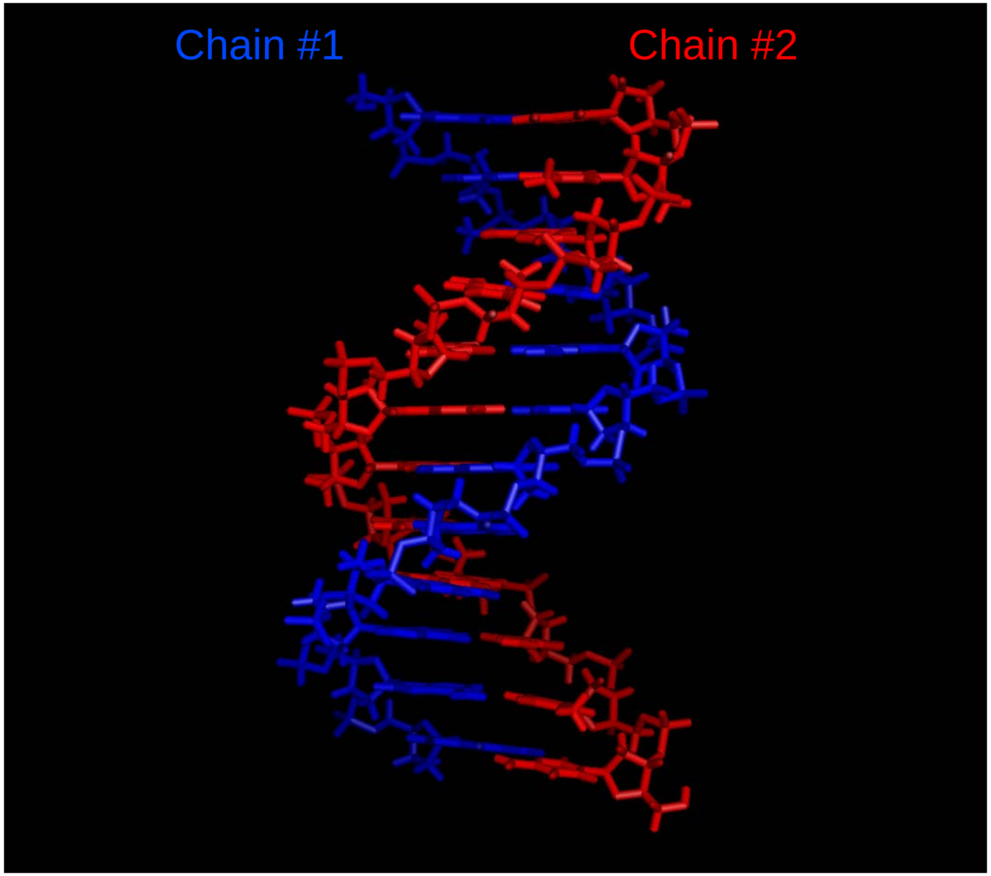

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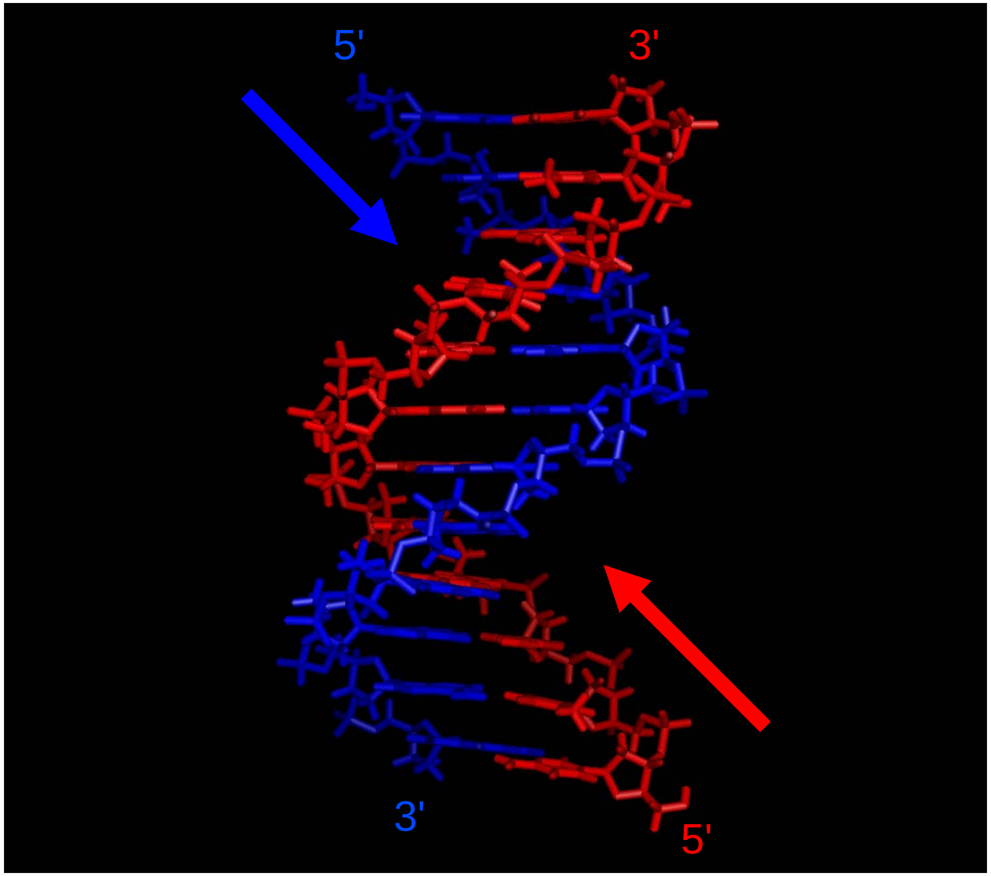
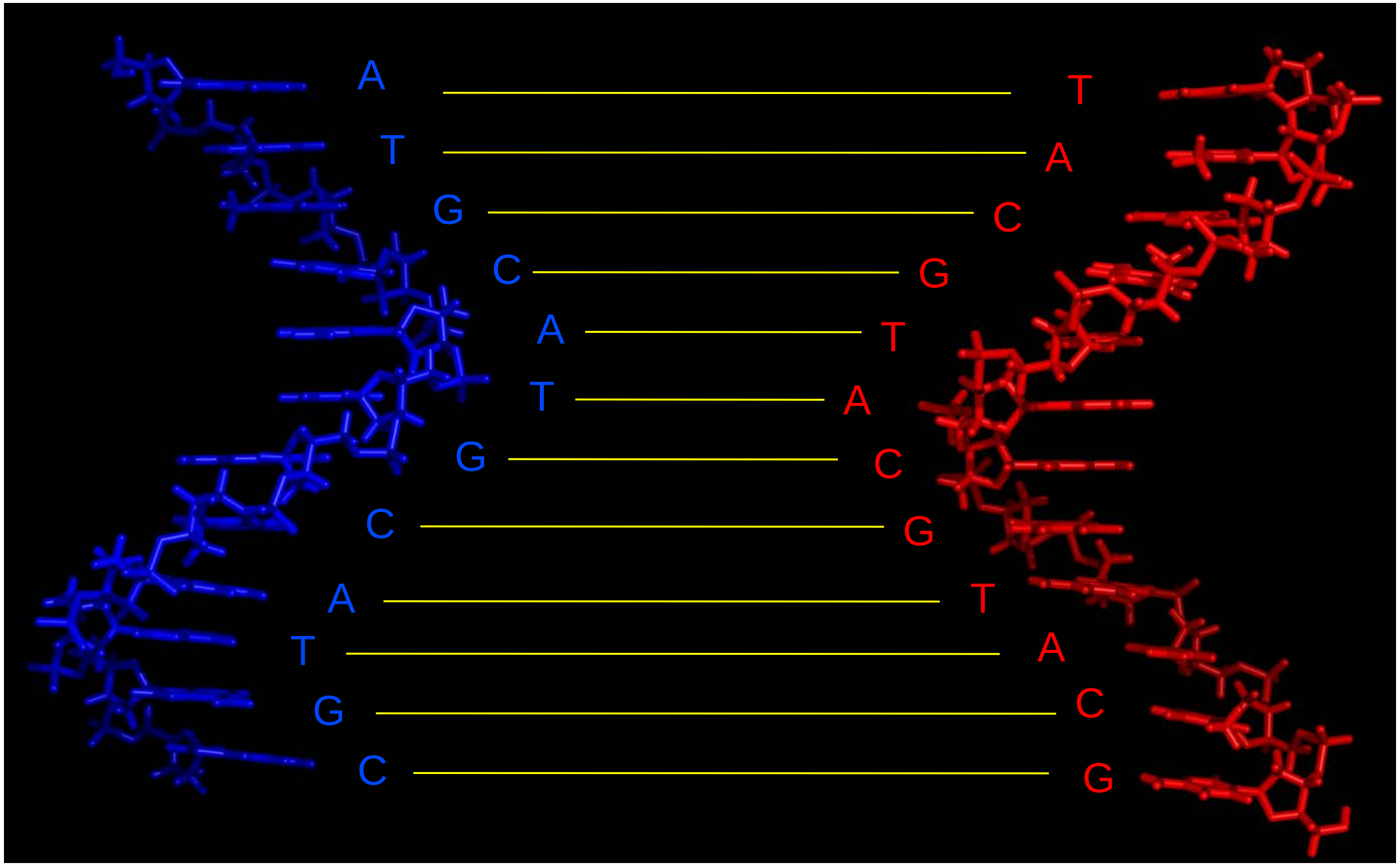


Each DNA chain has a 5' end and a 3' end (depending on the orientation of the deoxyribose).

DNA ultrastructure

What is DNA?

A bicatenary, antiparallel and complementary molecule encoding genetic information of most, but not all living organisms.

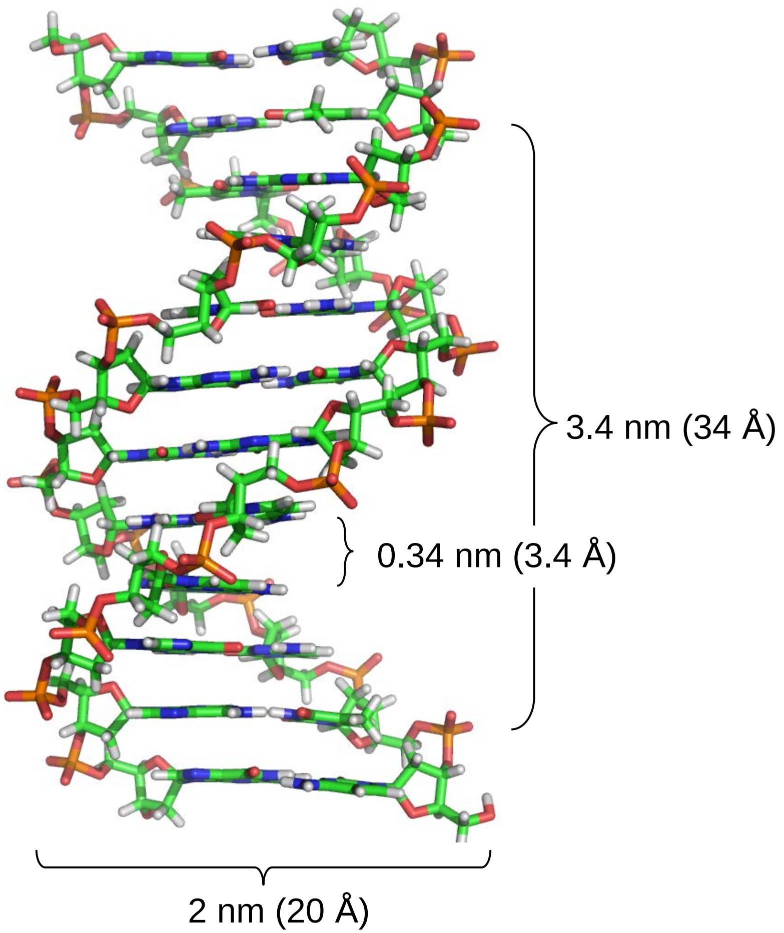


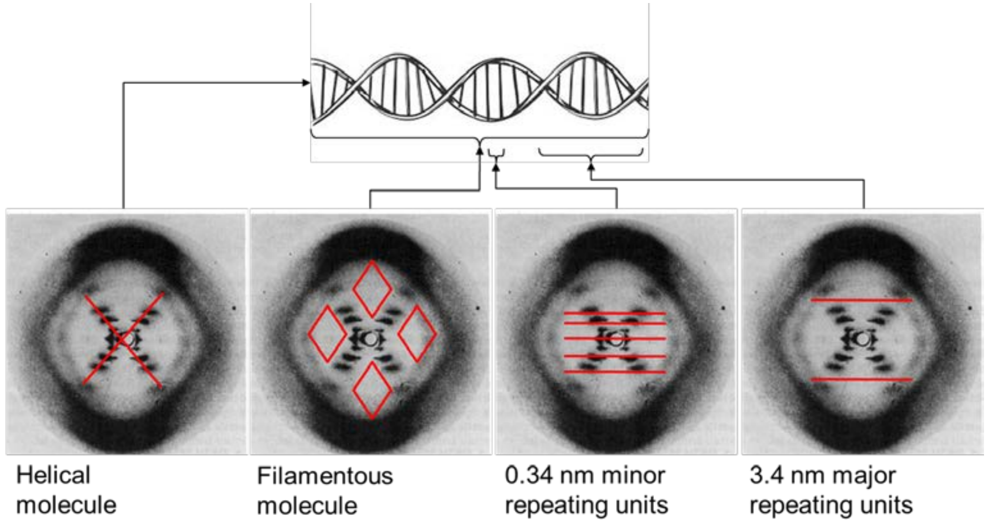
dsDNA
When chains are part of a duplex.

ssDNA
When chains are isolated and not part of a duplex.

ccdsDNA
Covalently closed circular double-stranded DNA (plasmids, virus, mitochondrial genome).

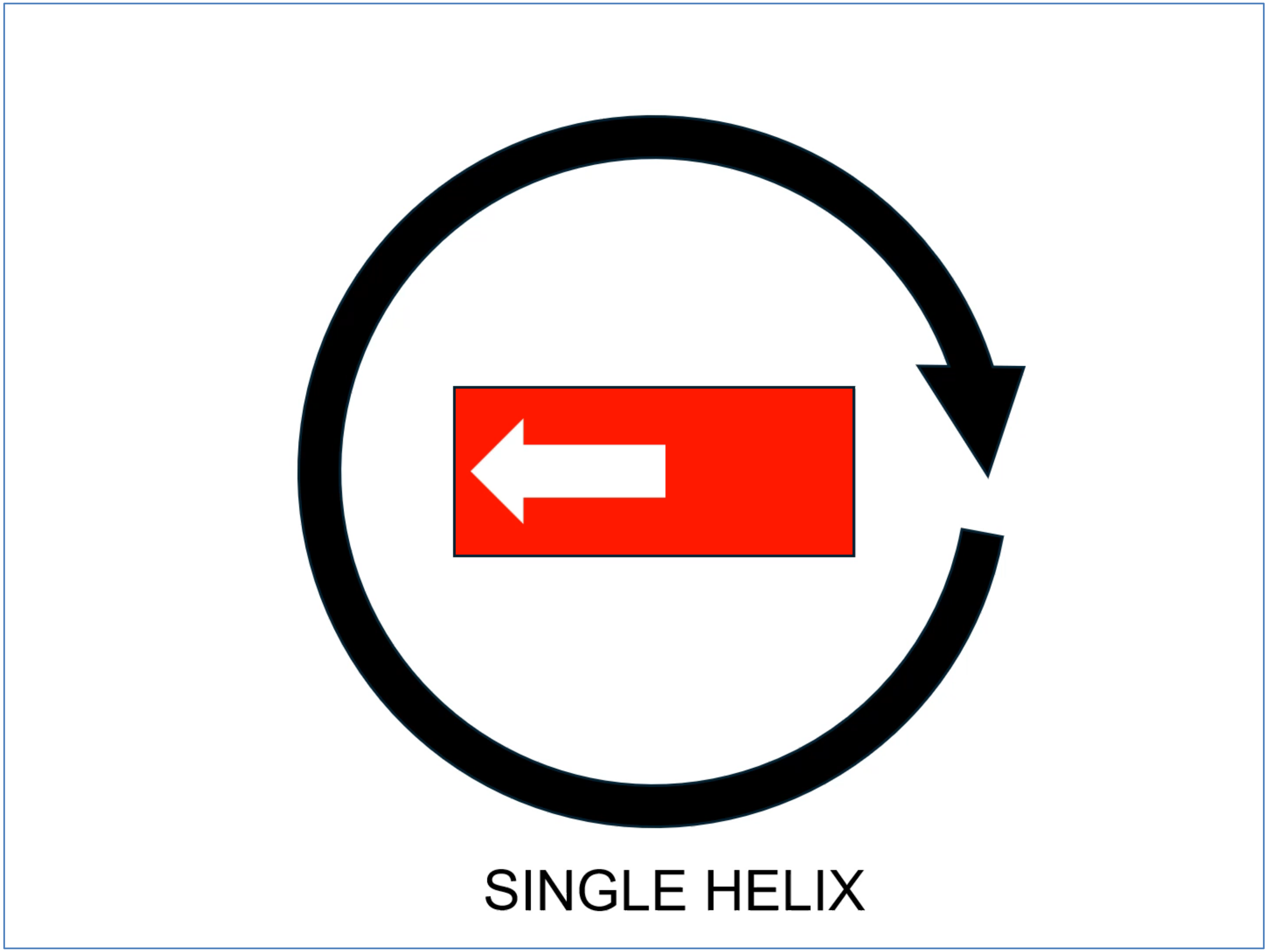
DNA ultrastructure



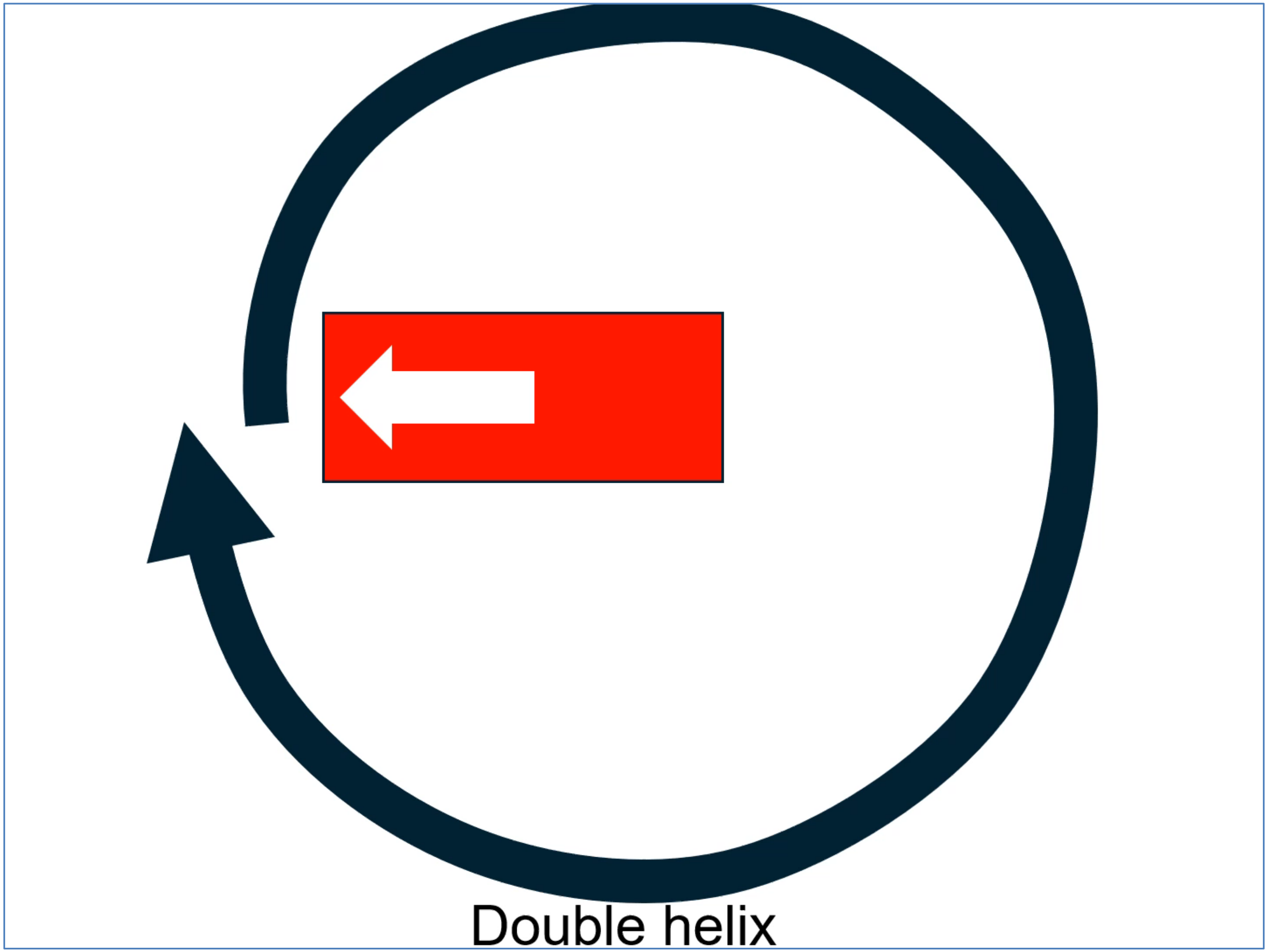


- Helical structure
- Filamentary shape (large molecule)
- Small units every 0.34 nm (3.4 Å)
- Large unit every 3.4 nm (34 Å)
- 1 Ångström = 0.1 nanometer

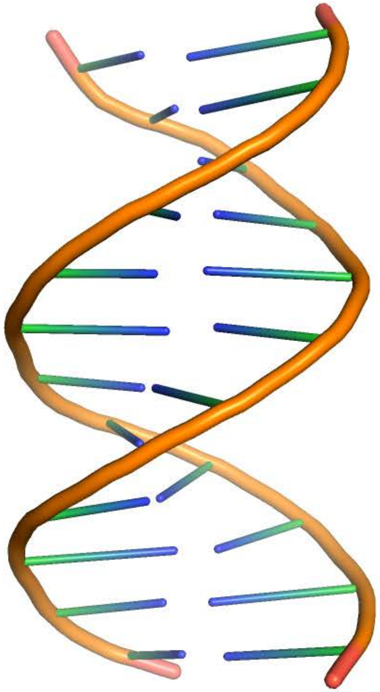
Double helix



Double helix



Double helix



DNA Surface topology

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

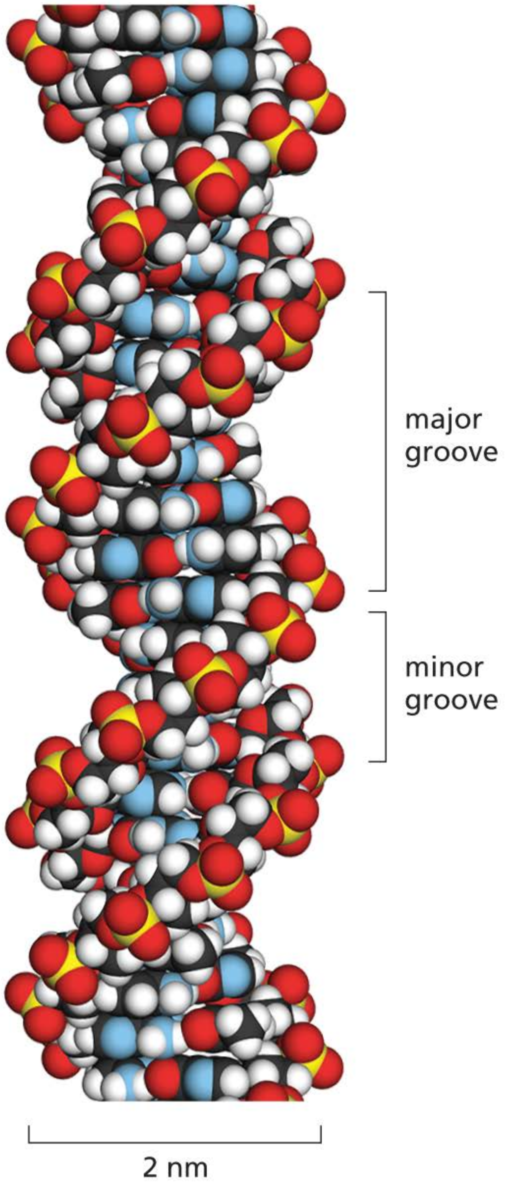
Each groove has unique functional implications in biological processes, especially in how proteins and molecules interact with DNA.

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.



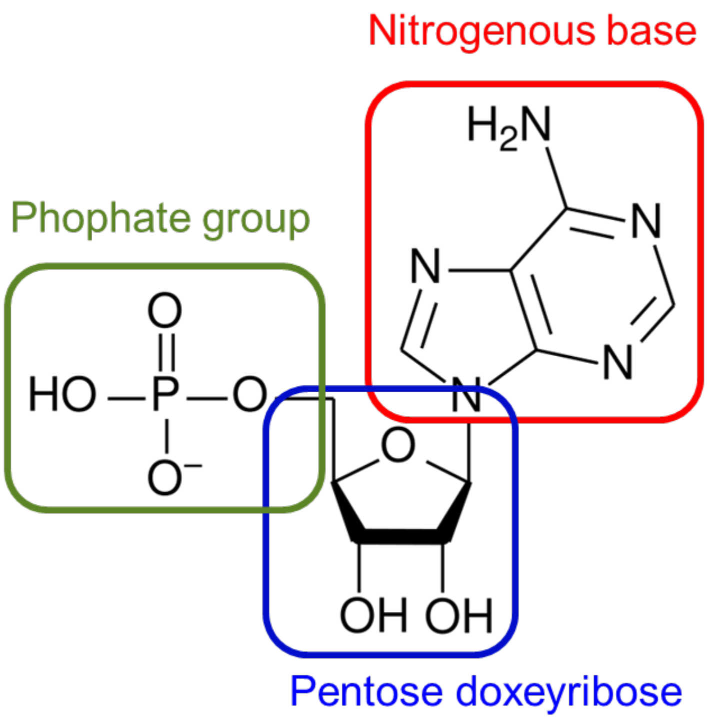
Nucleotides

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.

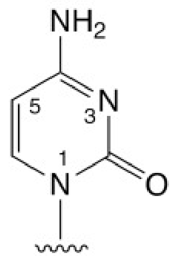
A phosphate group that forms the DNA backbone through phosphodiester bonds.



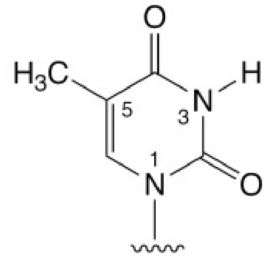
Nitrogenous bases

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

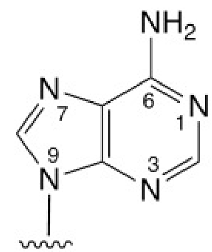
5-Methylcytosine (5mC)
5-Hydroxymethylcytosine (5hmC)
N^6-Methyladenine (6mA)
7-Deazaguanine



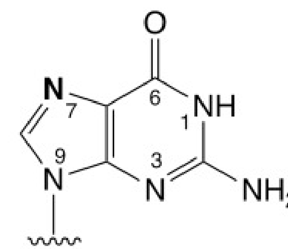
cytosine (C)



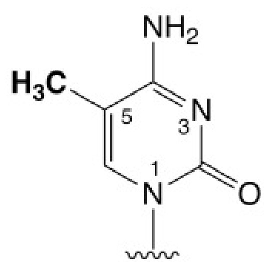
thymine (T)



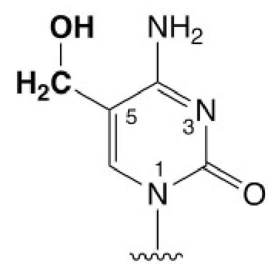
adenine (A)



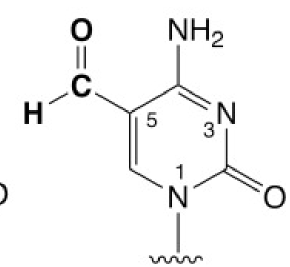
guanine (G)



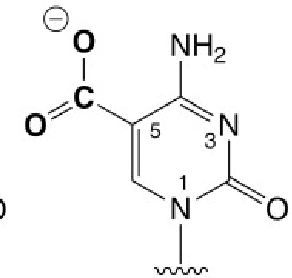
5-methyl-C (mC)



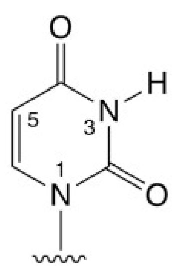
5-hydroxymethyl-C (hmC)



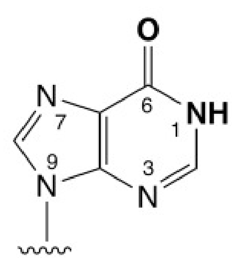
5-formyl-C (fC)



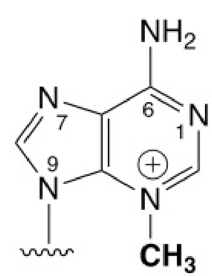
5-carboxyl-C (caC)



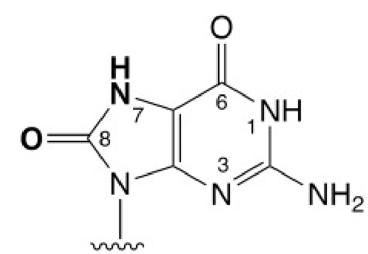
uracil (U)



hypoxanthine



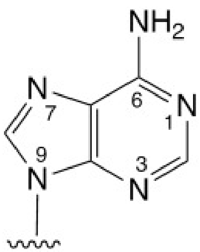
3-methyl-A

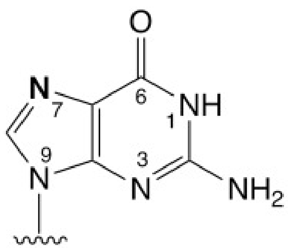


8-oxo-G

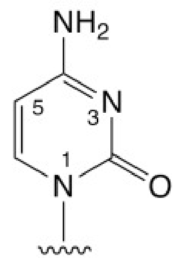
Nitrogenous bases

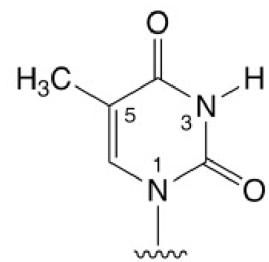
Purines
2 rings (Pyrimidine and imidazole)
A is similar to NH group in form
G is similar to O group in form
Attach to pentose via Nitrogen #9

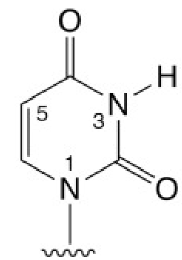

adenine (A)


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.

Pentose relevance

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

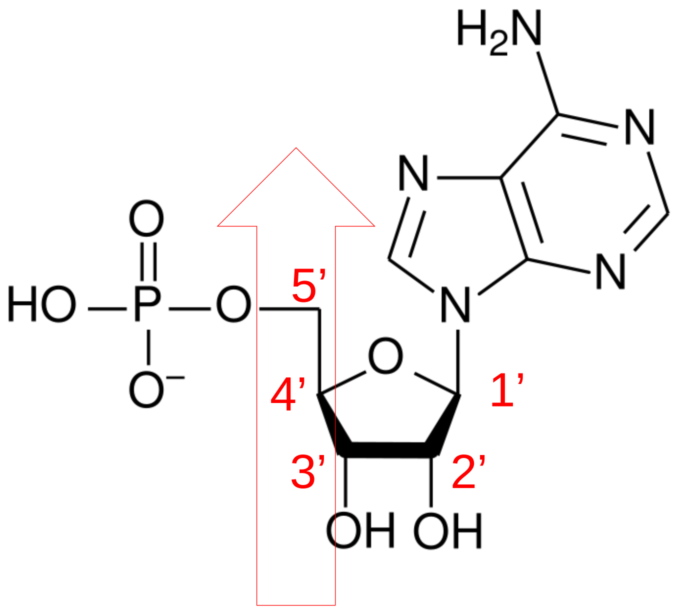
Carbon 1’ attaches to nitrogenous base.

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).

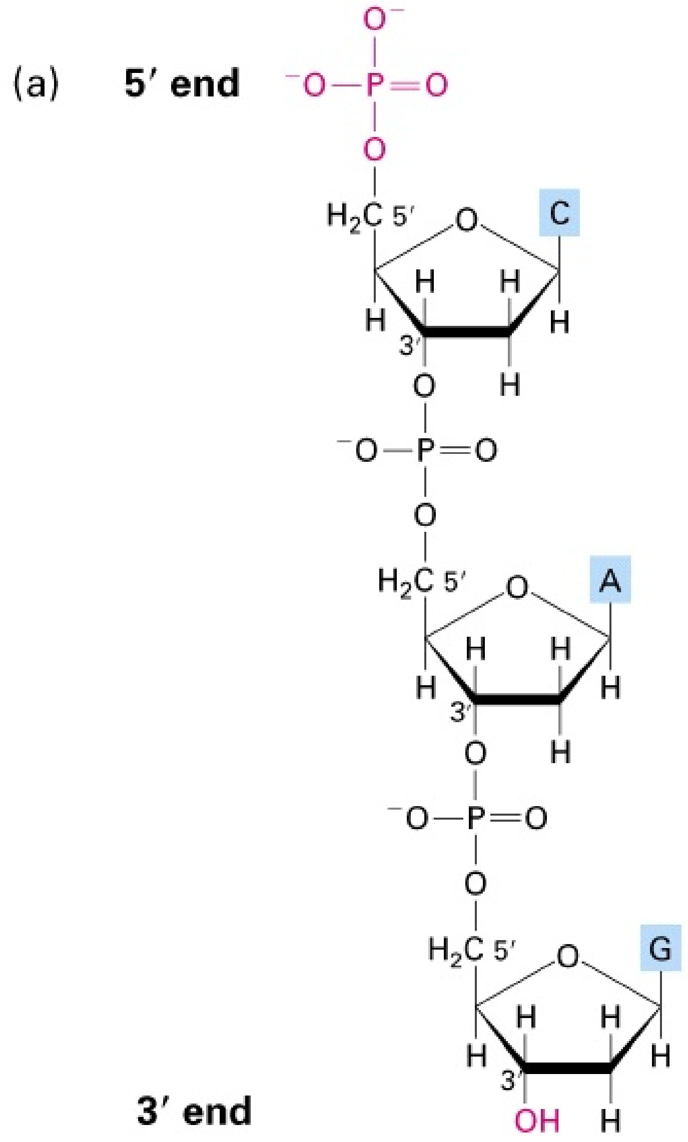


DNA and RNA polymerization

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.

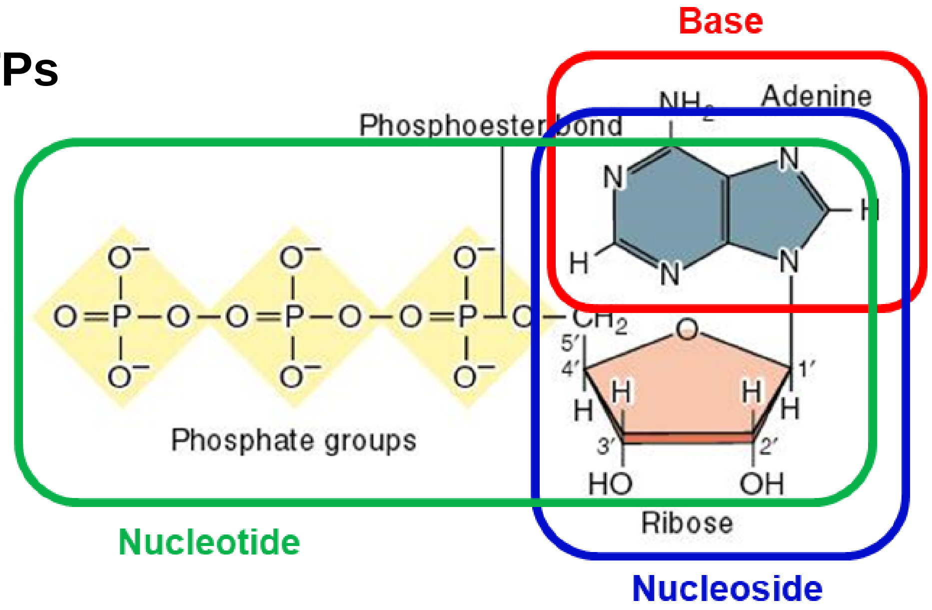


Nomenclature

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

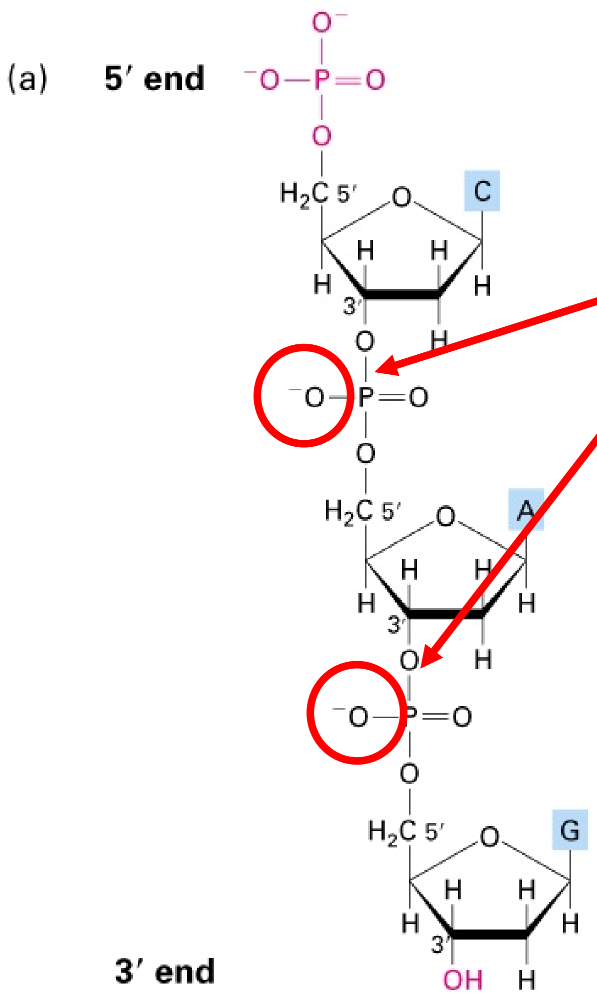
In RNA nucleotides are known as NTPs
Adenine, Adenosine, Adenosimonophosphate (AMP), ADP and ATP.
Guanine, Guanosine , Guanosindiphosphate (GMP), GDP and GTP.
Cytosine, Cytidine, Cytidintriphosphate (CMP), CDP and CTP.
Thymine,Thymidine, Thymidintriphosphate (TMP), TDP and TTP
Uracil, Uridine, Uridintriphosphate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

In DNA nucleotides are known as dNTPs
Deoxyadenosimonophosphate (dAMP)
Deoxyguanosindiphosphate (dGMP)
Deoxycytidintriphosphate (cCMP)
Deoxythymidintriphosphate (dTMP)



Phosphate groups

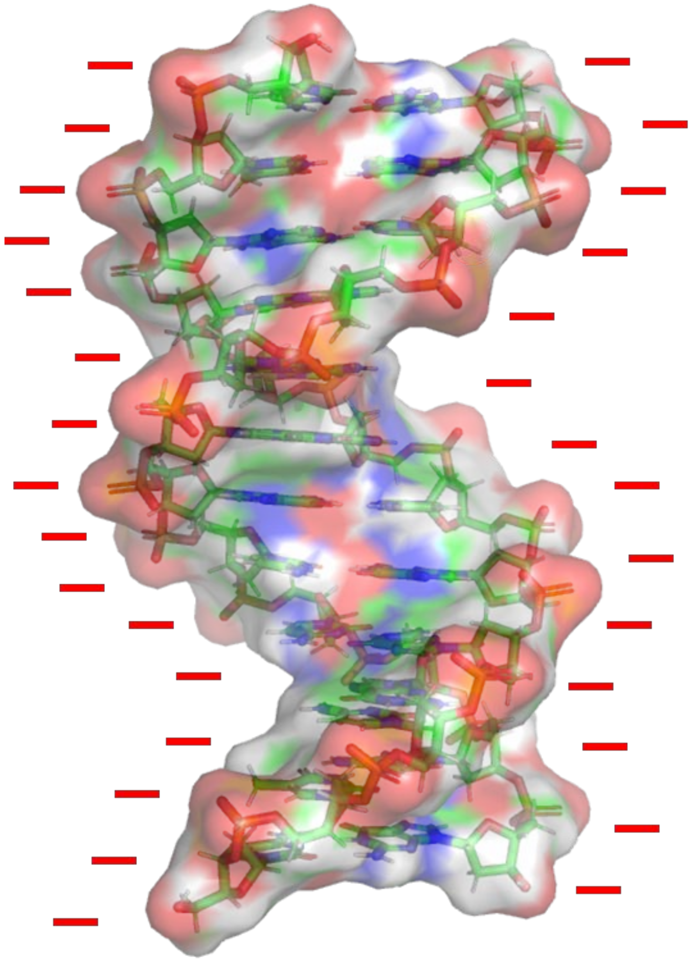
Phosphates and phosphodiester bonds = Polymerization of nucleic acids

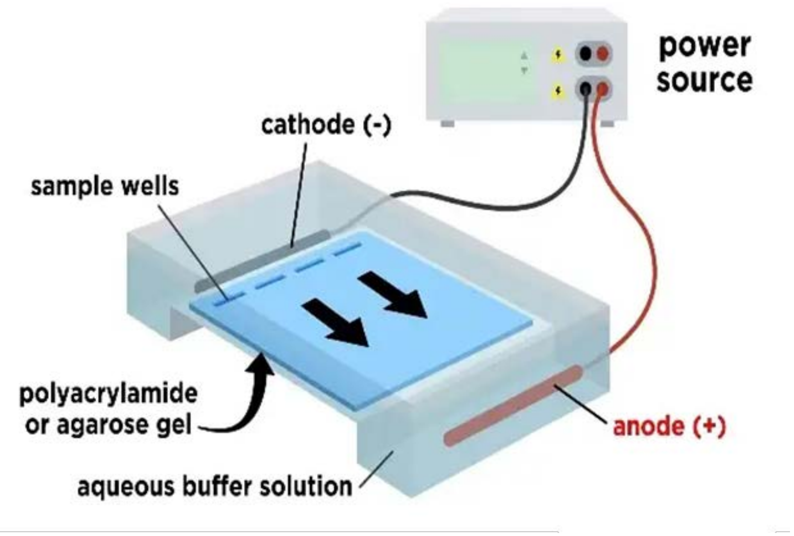


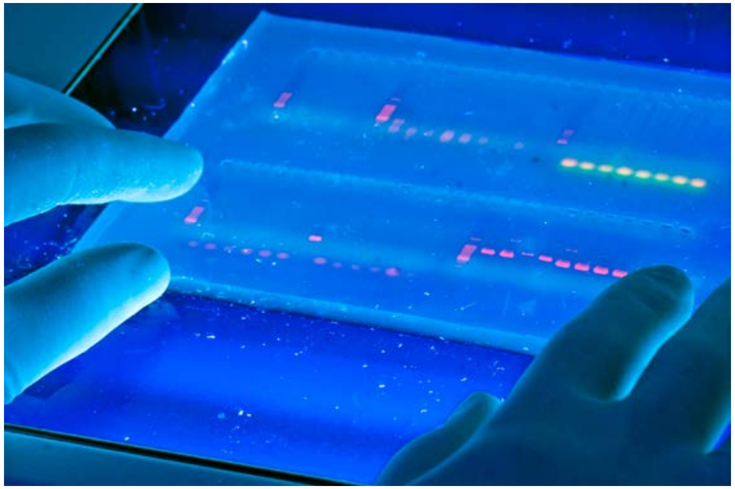
Each phosphodiester bond carries an electrostatic charge of -1 so the net charge of the nucleotide polymer (DNA) is negative.

Phosphate groups

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

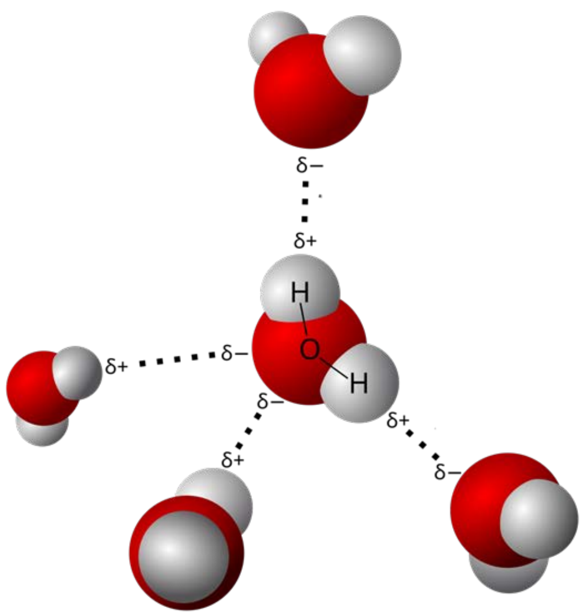




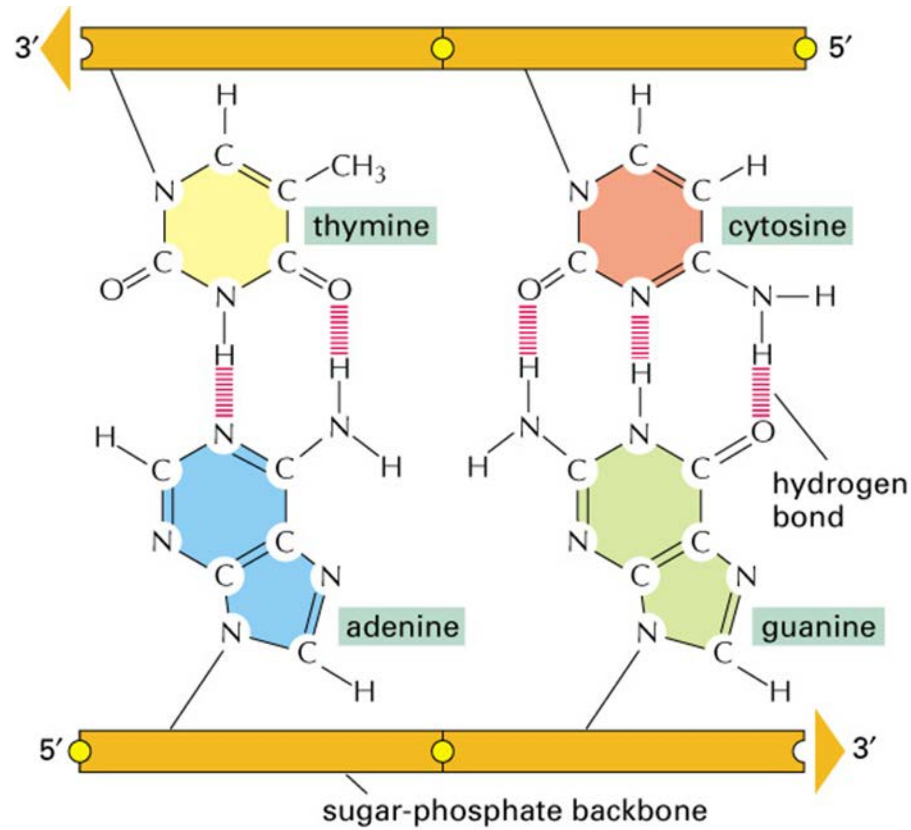


Hydrogen bonds

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.

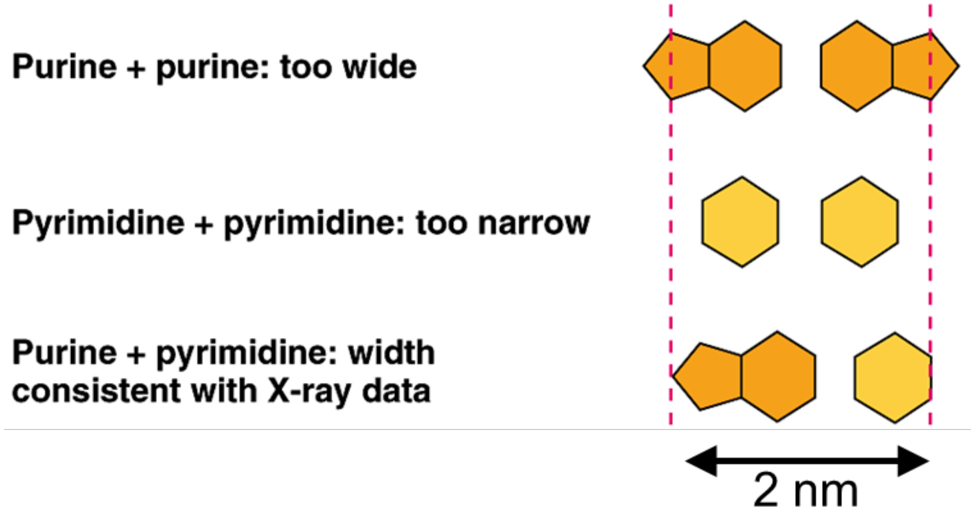
Watson–Crick base pairing

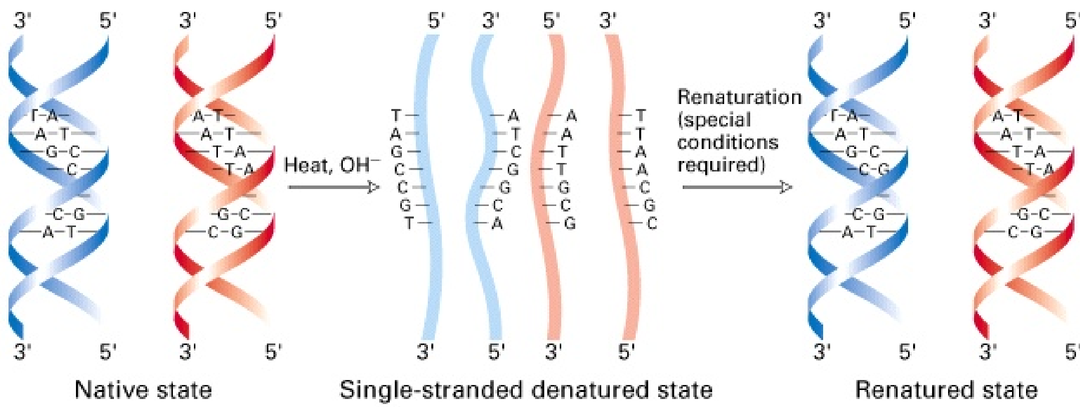
Specific hydrogen bonding patterns allow for "Watson–Crick" (or "Watson–Crick–Franklin") base pairing.

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.

Applications of nucleic acid hybridization

Southern blotting

Microarrays

Fluorescent in situ hybridization (FISH)

Dot blot hybridization

Colony hybridization

Northern blotting (for RNA detection)

DNA:RNA hybridization assays

PCR-SSP

PCR-SSO

Reverse dot blot hybridization**

Array-based Comparative Genomic Hybridization (aCGH)**

Quantitative Fluorescent In Situ Hybridization (Q-FISH)**

Tissue Microarrays (TMA)**

Stringent DNA Probe Hybridization**

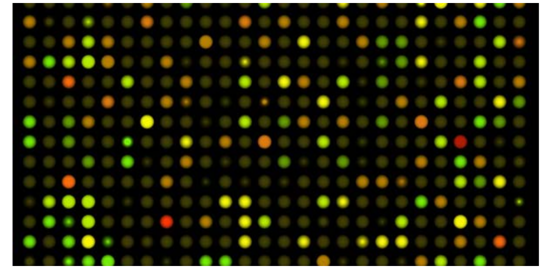
Padlock Probes**

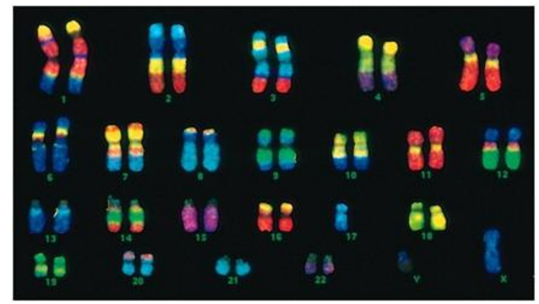
Hybridization Chain Reaction (HCR)**

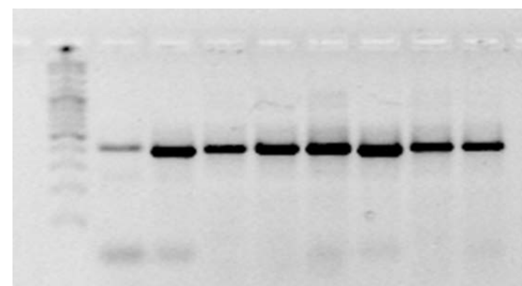
Electrochemical DNA Hybridization Assays**

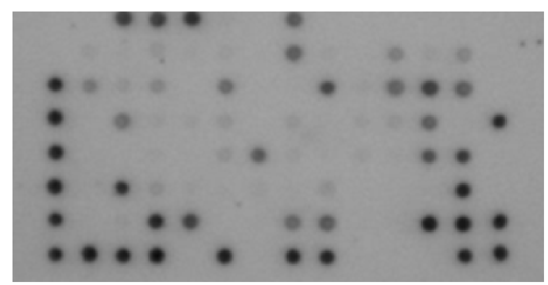
Bead-based Hybridization Assays**

Dual-labeled Probe Hybridization (e.g., TaqMan probes)**







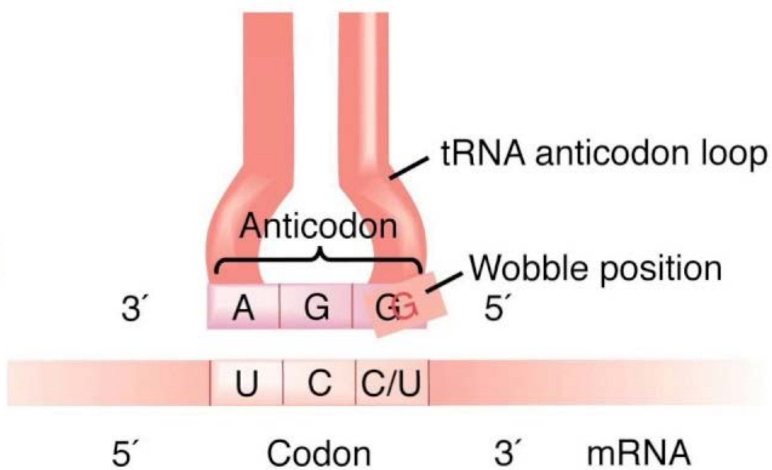


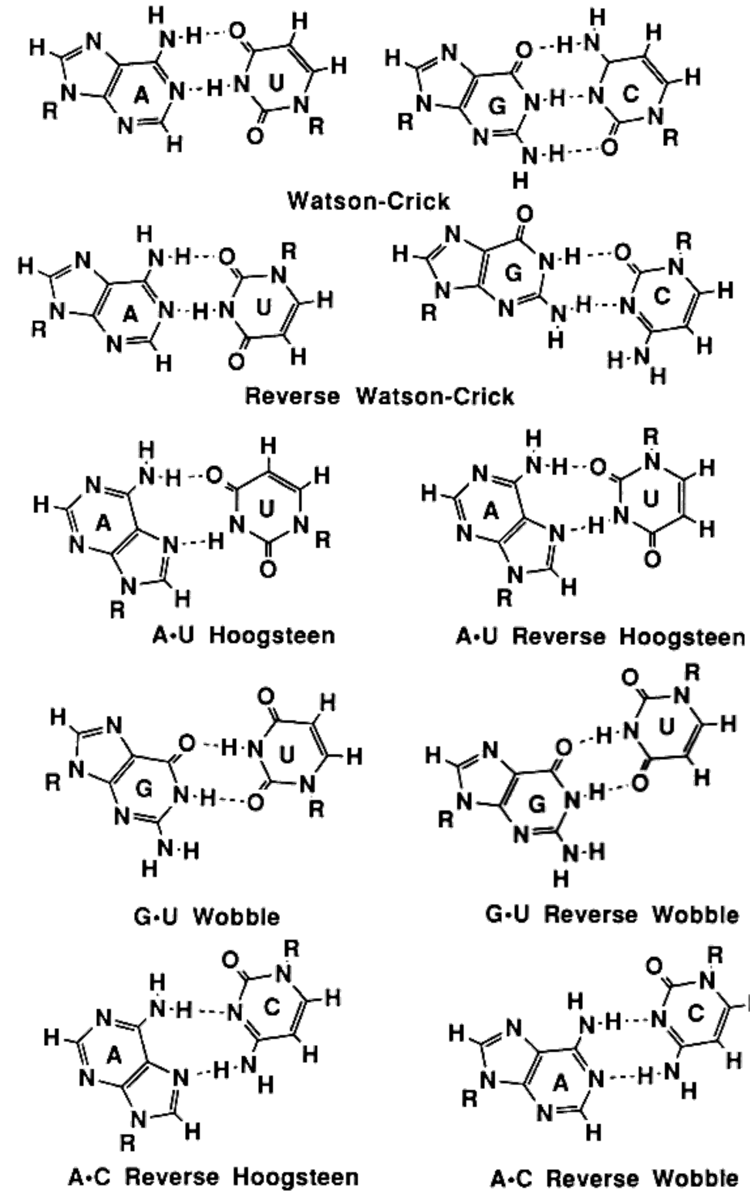
Non-canonical base pairing

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.

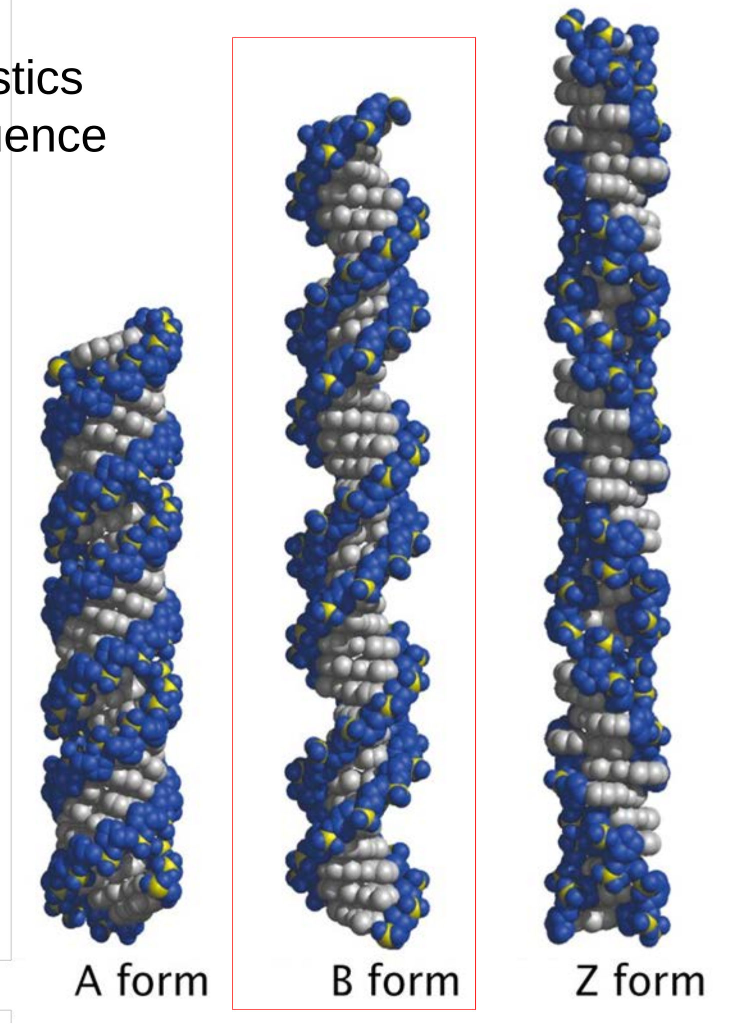
Each conformation has unique structural characteristics and is influenced by environmental conditions, sequence composition, and biological function.

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.



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.

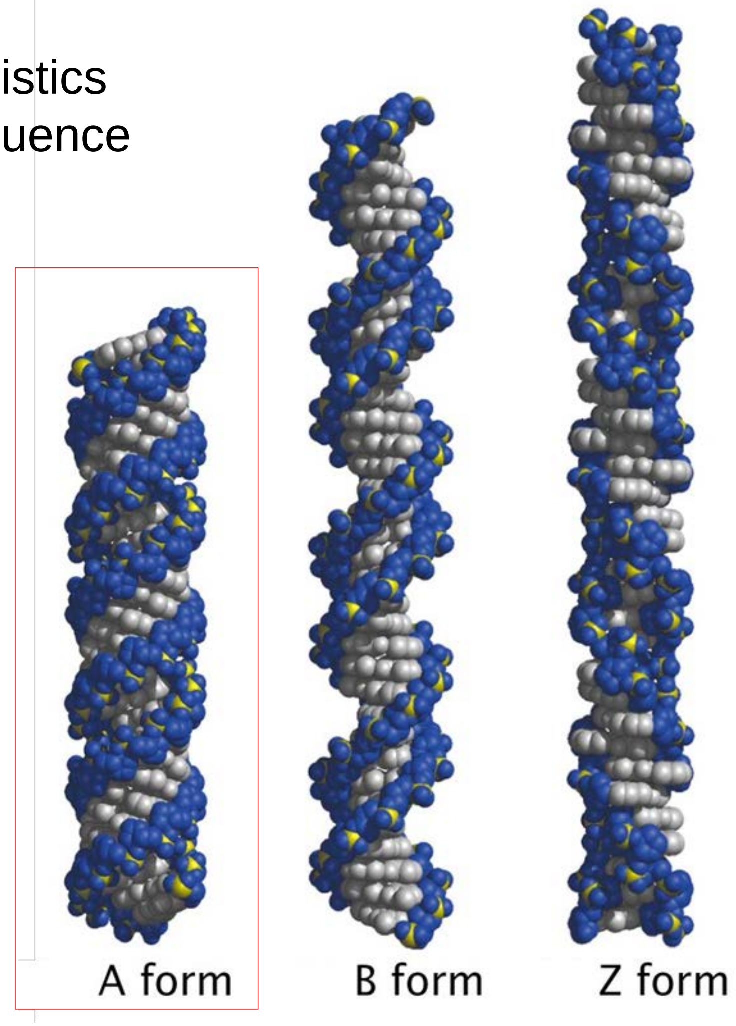
A-DNA

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

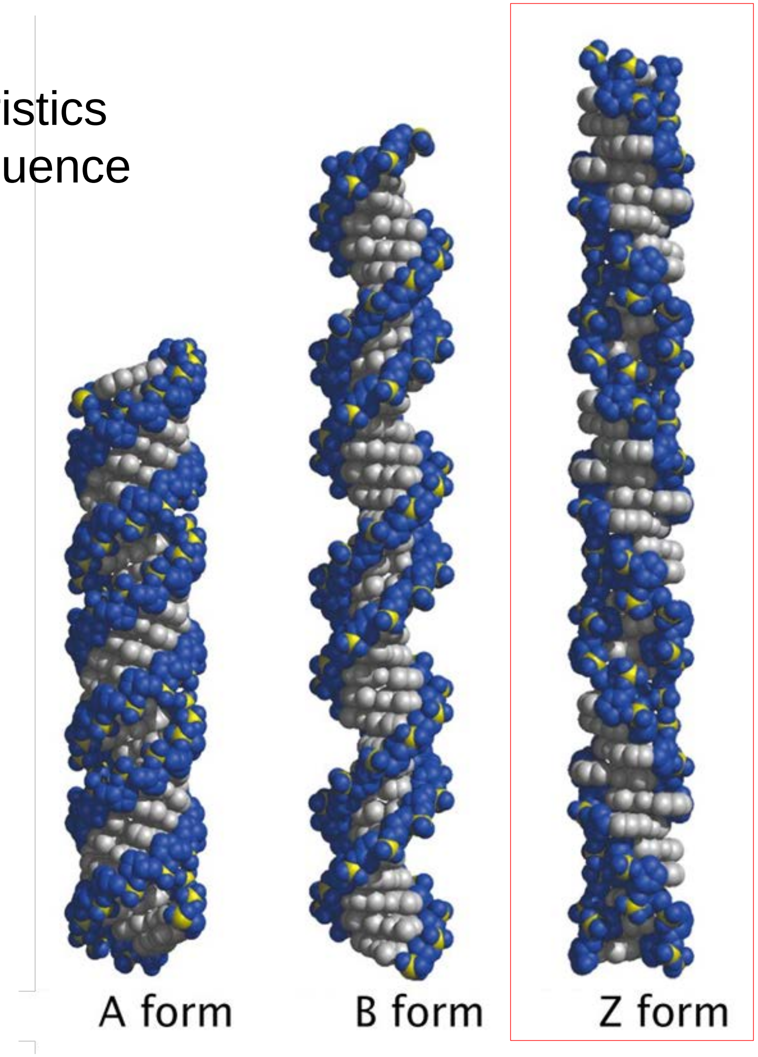
DNA can adopt several conformations, with three primary forms known as A-DNA, B-DNA, and Z-DNA.

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.

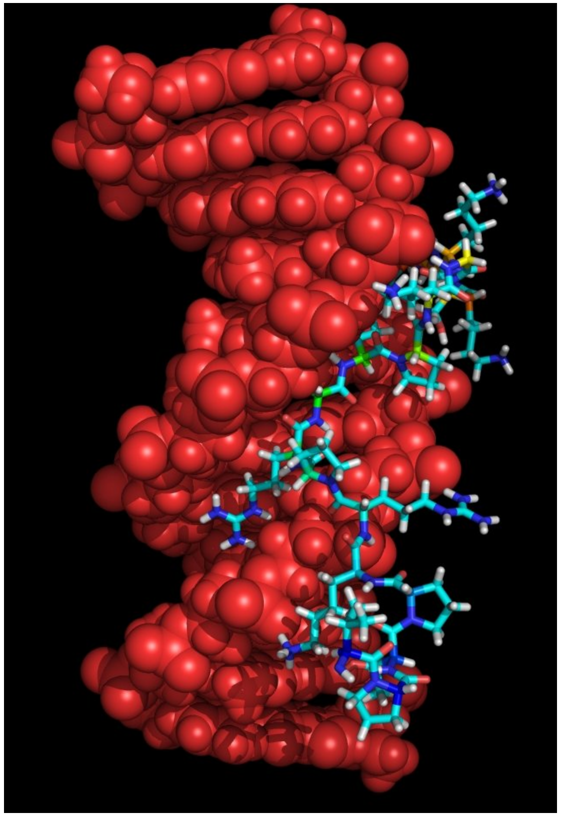
Z-DNA is thought to play a role in gene regulation and is recognized by specific proteins.

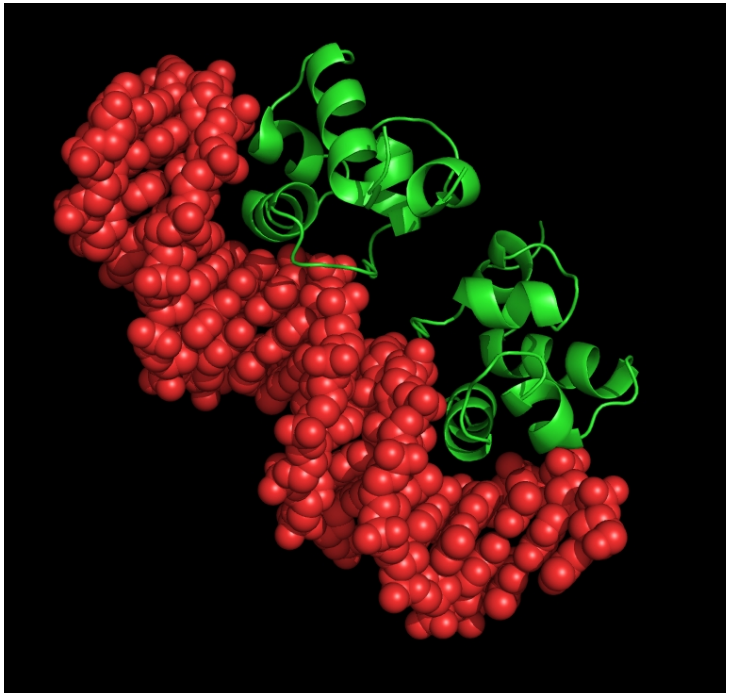


Functional relevance of DNA topology

DNA conformation affects the physicochemical properties of the molecule and therefore the type of interactions it can have with proteins.

Interferon Beta promoter being recognized by transcription factor with affinity for the minor cleft.





Transcription factor CRO 434 recognizing the OR1 operator of phage 434

Laboratorio de Genómica Viral y Humana

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

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