
# Introduction to Molecular Biology

Lecture .1

By

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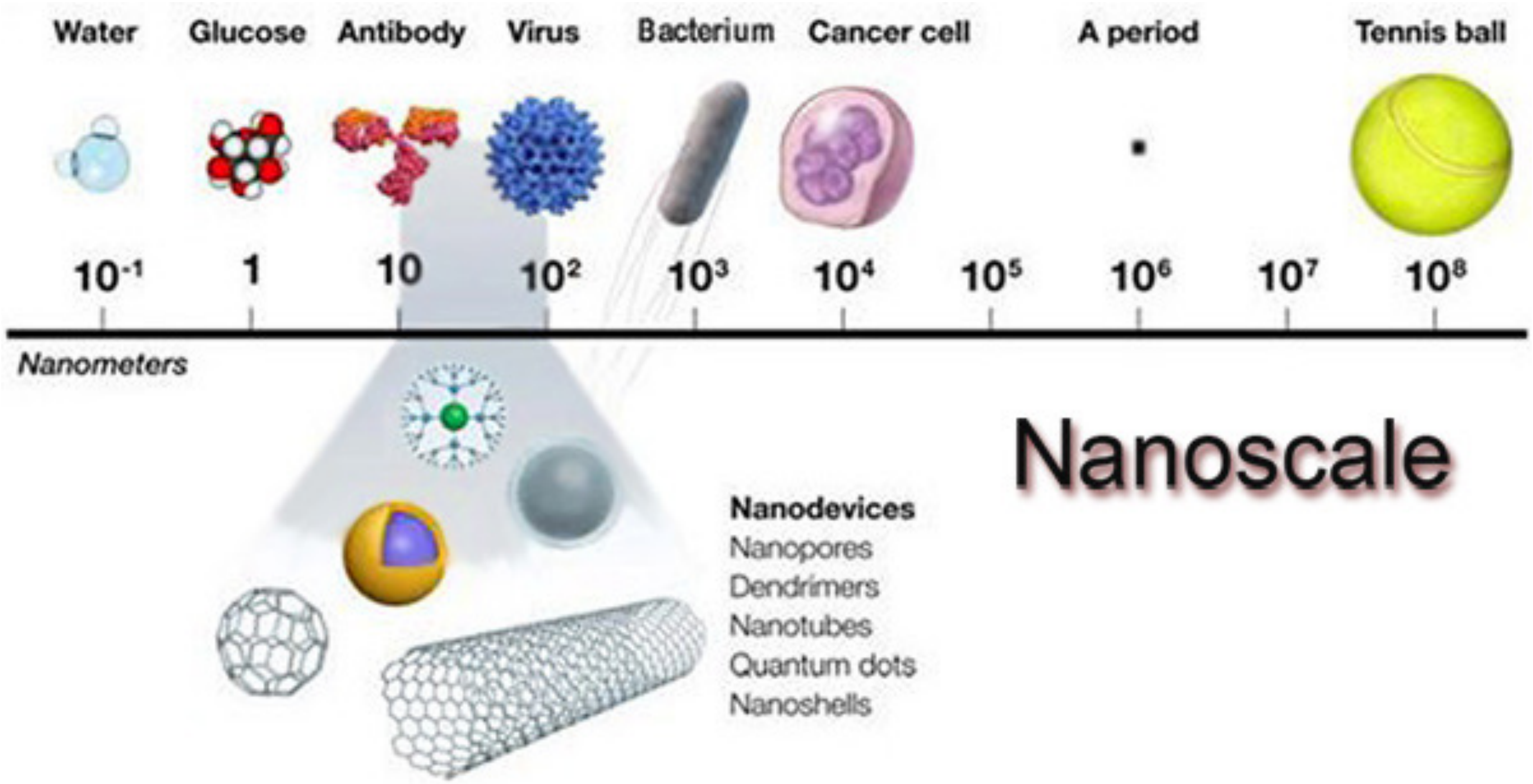
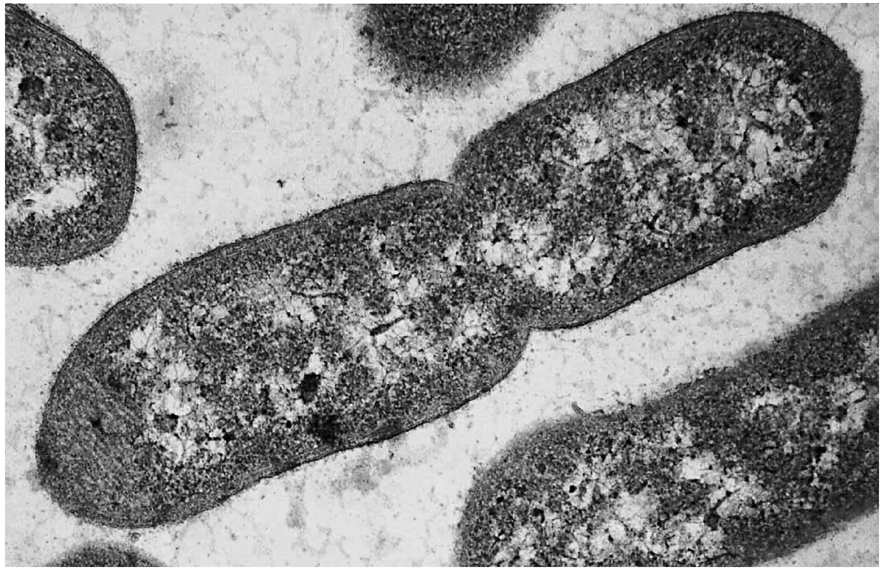
MSc. In Molecular Biology

# Objectives:

- To give an overview on Molecular biology and it’s contributions.
- Discuss and clarify the genetic martial.
- Explaining Griffith's experiment.
- Figure out the DNA structure, some properties, and types.

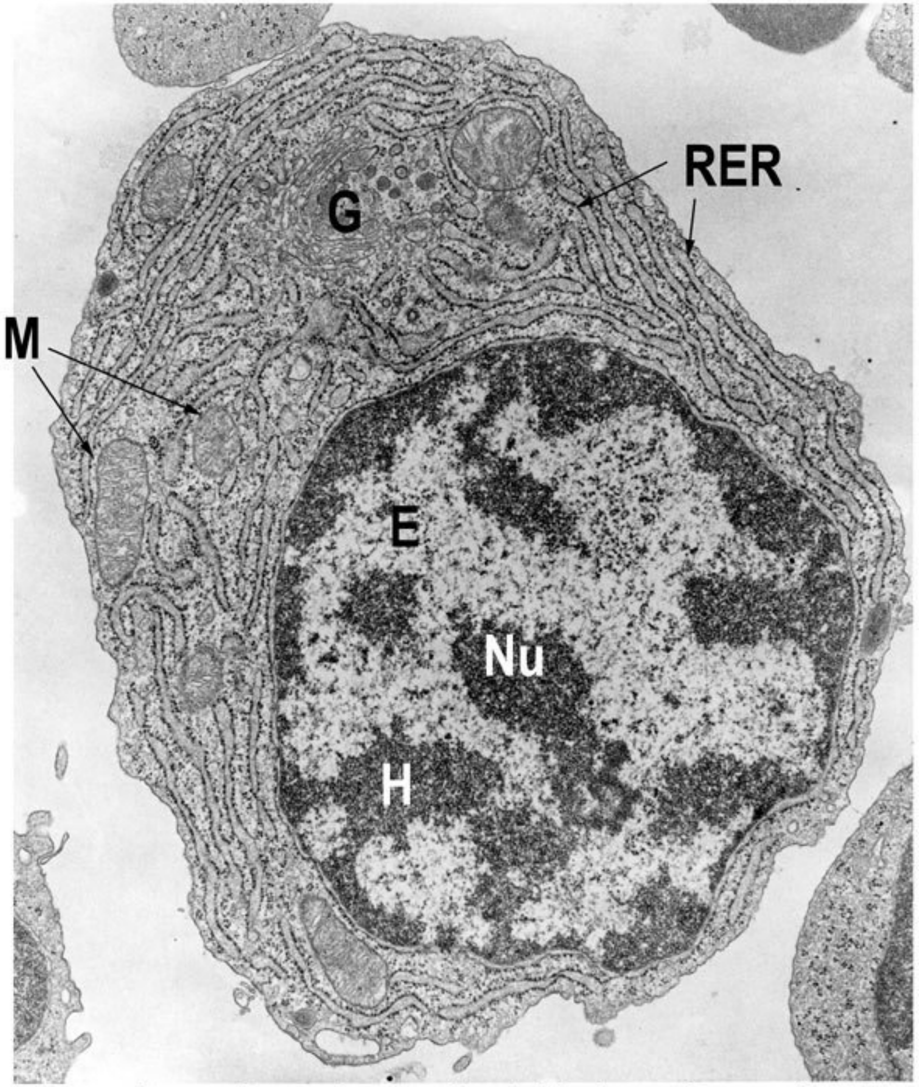
How small is small?!



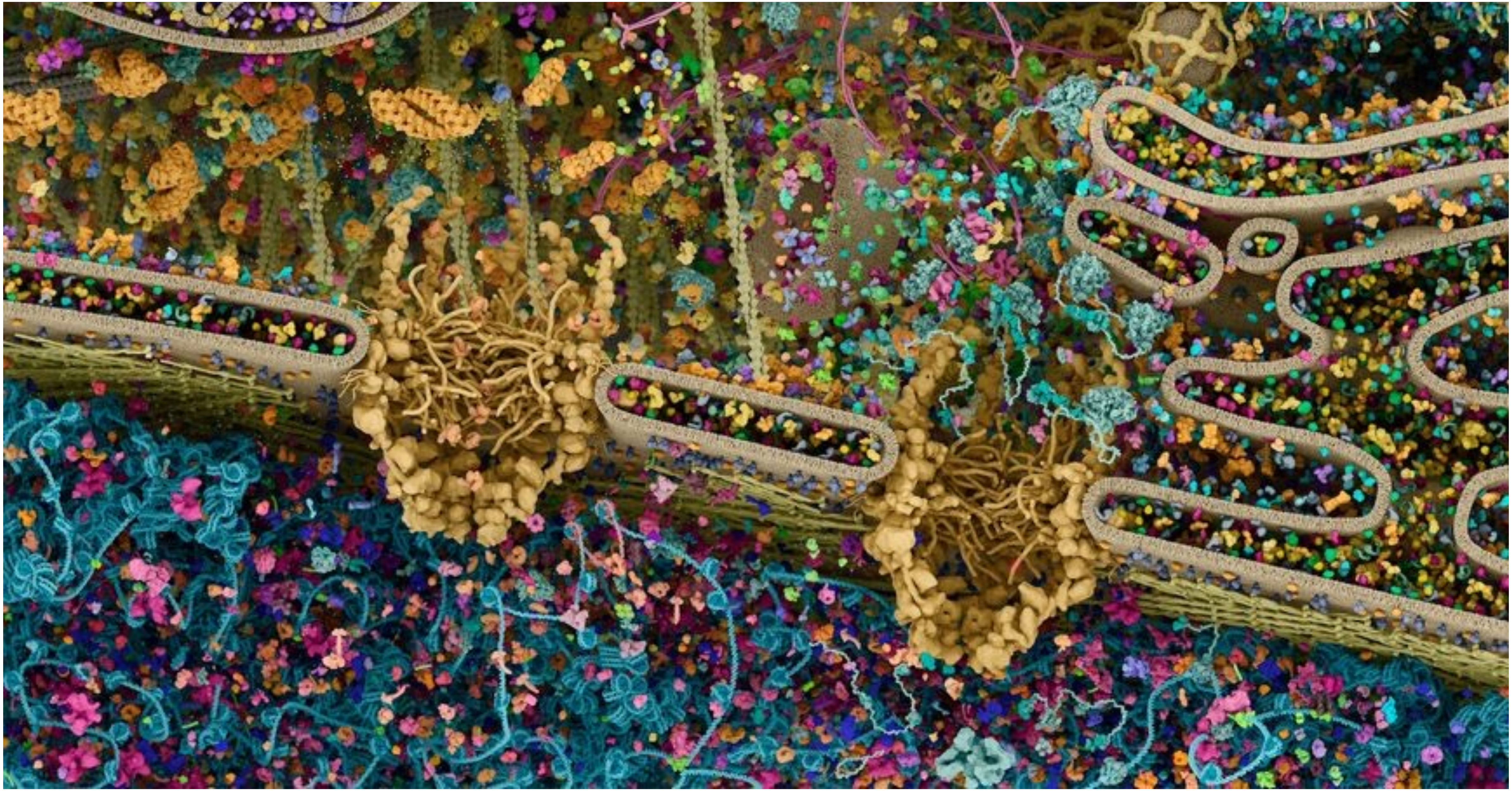


A bacterial Cell

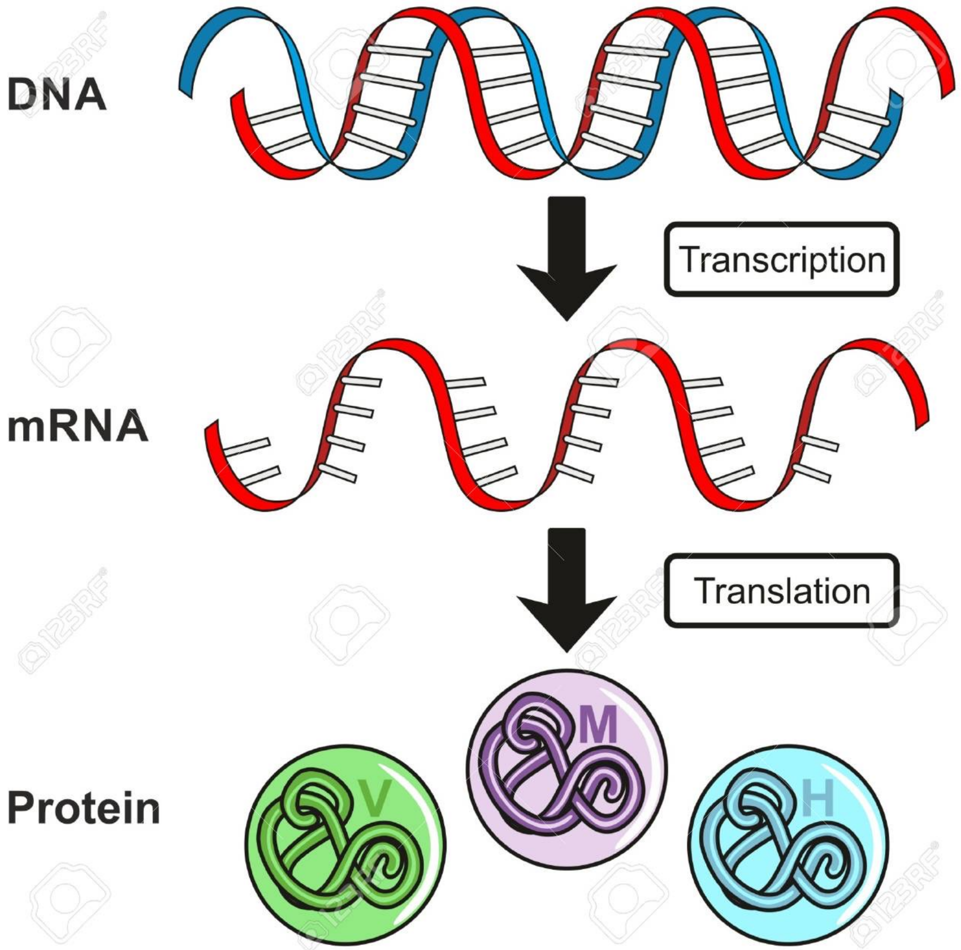
An animal cell




Nu-nucleus, E-euchromatin, H-heterochromatin, M-mitochondria, RER-rough endoplasmic reticulum, G-golgi complex



# Central Dogma of Molecular Biology



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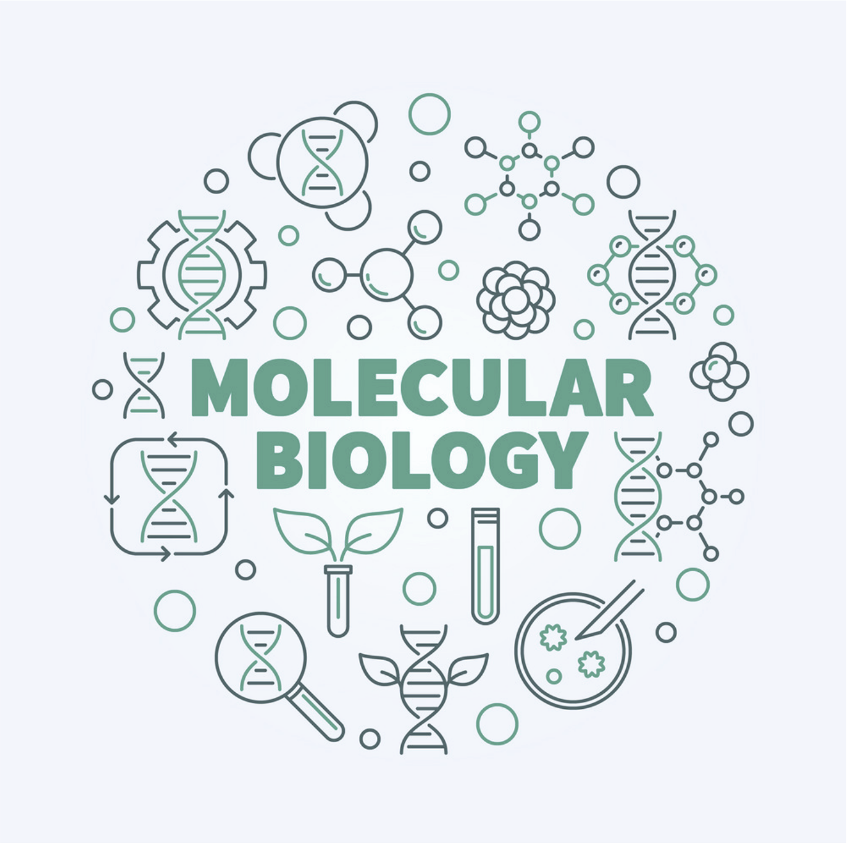
# Molecular Biology

- Is the branch of biology that deals with the molecular basis of biological activity.

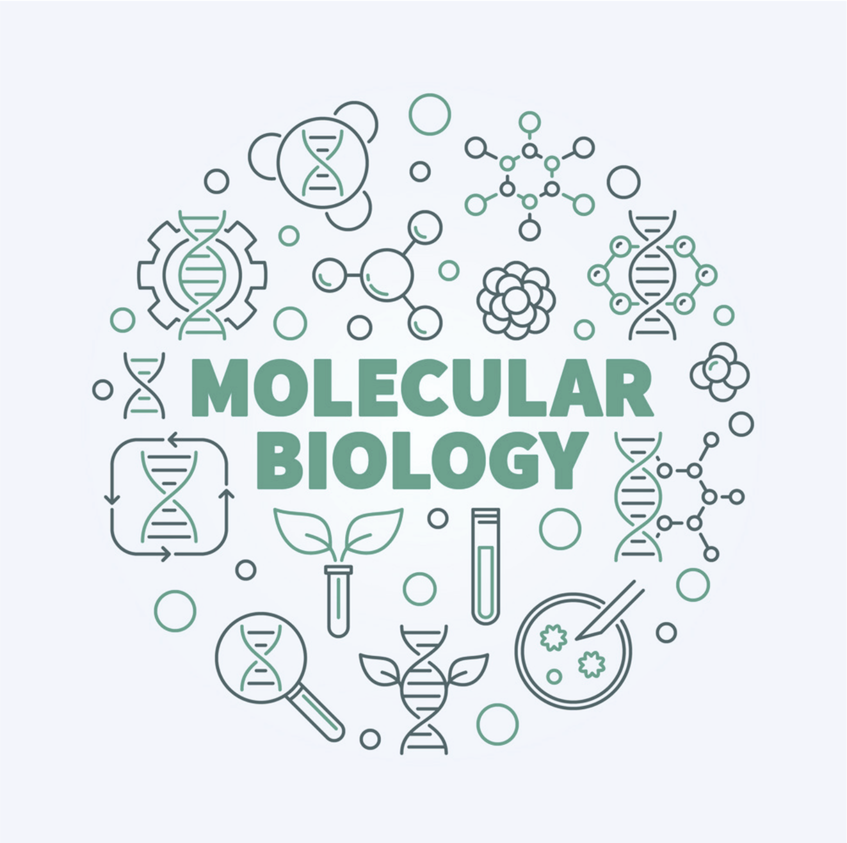
- This field overlaps with other areas of biology and chemistry, particularly **cell biology, genetics and biochemistry**.

✓ **"The biochemistry of genes and their products"**



# Molecular Biology

- The term of “Molecular Biology” was coined by Warren Weaver in 1938, the director of Natural Science division of Rockerfeller Foundation.
- The term firstly used by William Asbury in 1945 to study the chemical and physical structure of biological macromolecules.



# Molecular Biology contributions

## BIOCHEMISTRY

- **First biochemical experiment in 1897 by Edward Buchner**,sugar fermentation *in vitro* using cell-free extract.
- Decoding of metabolic pathways like Glycolysis,TCA cycle,etc., in the first half of twentieth century.
- The term "**macromolecule**" was introduced by German chemist,**Hermann Staudinger**(1922) to describe biomolecules of the cell.

## GENETICS

- **Archibald Garrod** (1902) described the first precise relationship between genes and metabolism
- In 1941, **George Beadle** and **Edward Tatum** demonstrated that genes control enzyme synthesis in *Neurospora*. They proposed **'One gene one enzyme theory'**.
- **Avery, Macleod** and **McCarty** in 1944 discovered the chemical nature of gene.
- **Watson** and **Crick** in 1953 described the double helical structure of DNA based on X-ray diffraction studies made by **M. H. F. Wilkins** and **Rosalind Franklin.**

## PHYSICS

- Physicist, **Szilard**, developed technique for the analysis of gene regulation in bacteria.
- **George Gamow** (1954) deciphered the genetic code to explain relationship between sequences of nitrogenous bases in DNA and amino acids in the polypeptide chain.

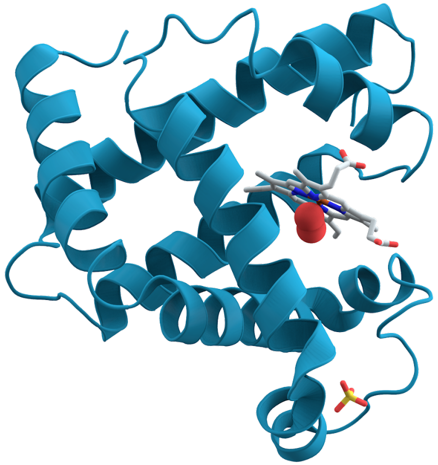
## INSTRUMENTATION and BIOLOGICAL TECHNIQUES

- **Theodor Svedberg**(1920) developed analytical centrifuge that is used to determine the molecular weight of macromolecules and small cell organelles or their parts.
- **Knoll** and **Ruska** (1930) invented the electron microscope to study the structural details of viruses, macromolecules and various cell organelles.
- **Mikhail Tswett** in 1906 developed simple column chromatography.

# Molecular Biology

## Classical Molecular Biology

- Science of observation
- Centered on protein
- Proteins with their three dimensional structure were considered to be specific agents for biological processes.



## Modern Molecular Biology

- Science of intervention and action.
- Adopted an experimental approach.
- Concerned with determining the  sequences of nucleotides in genes and from deducing the sequence of amino acids in proteins.

# Milestone in the field of Molecular Biology

- 1953 James Dewey Watson(J.D.Watson) and Francis Harry Compton Crick(F.H.C.Crick) proposed the double helical model of DNA based on the studies of Maurice Wilkins and Rosalind Franklin.

Watson,Crick and Wilkins were awarded the Nobel Prize in 1962

James Watson

Francis Crick

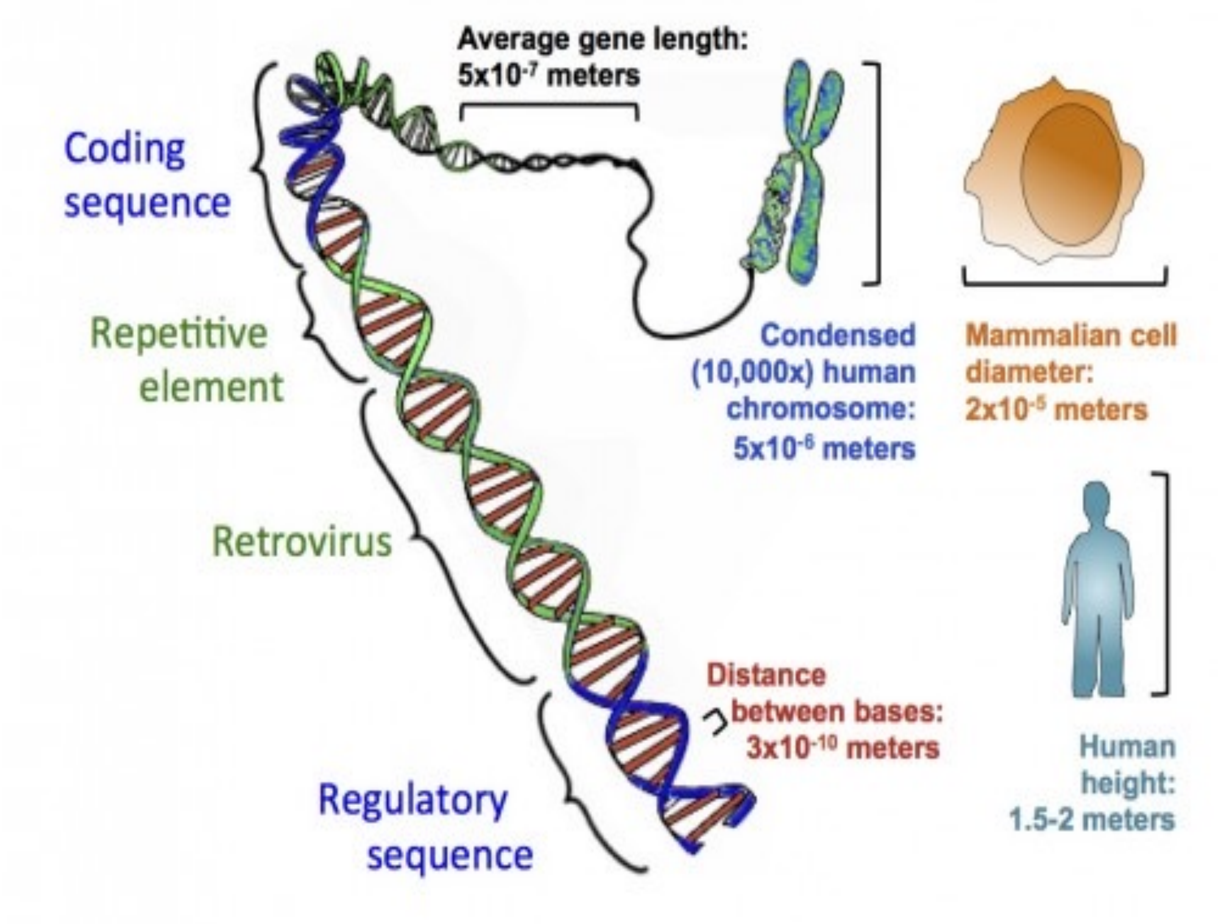
Maurice Wilkins

Rosalind Franklin

# Genetic Material

- Substance that stores information about structure, function and development of various characteristic of living thing.

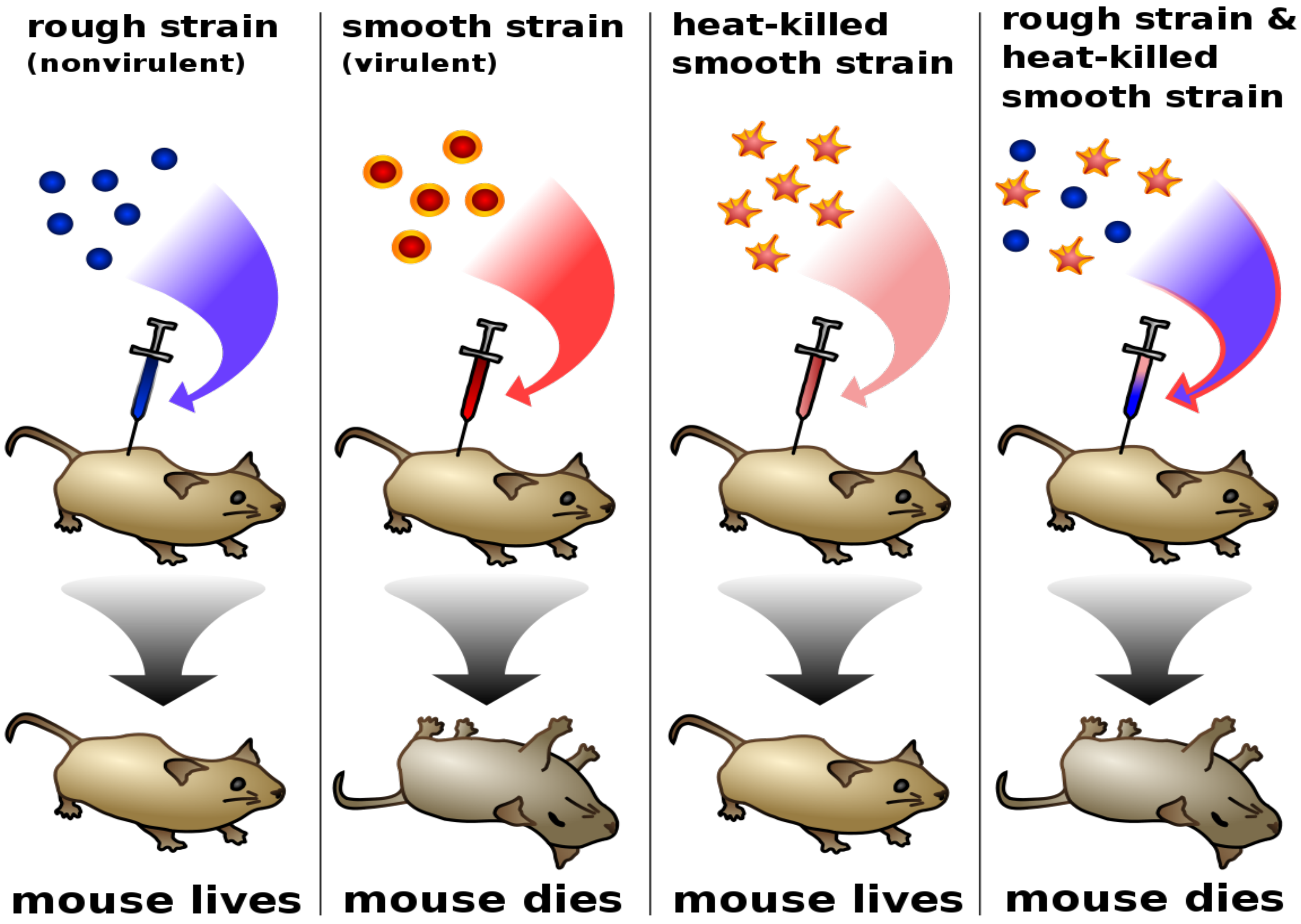
- The totality of genetic information of an organism which encodes in the DNA or RNA for some viruses is called **Genome**.



# Genetic Material

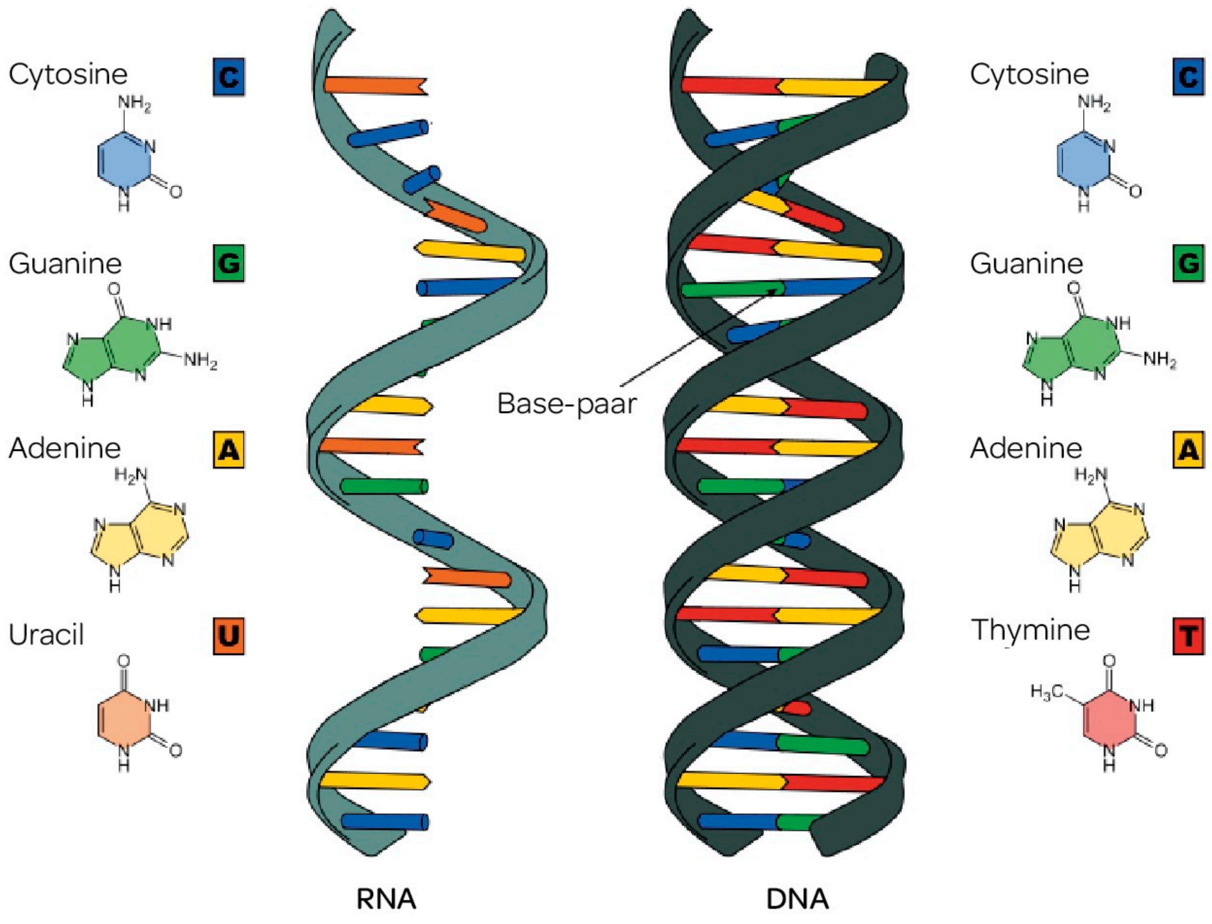
- It is responsible for **transmission of genetic information** for all the characteristics of living beings from parents to their progeny.
- Following the rediscovery of Mendel's laws, geneticists were able to conclude that:
  - Organism's characteristics are controlled by genes.
  - Genes are able to reproduce themselves or replicate without losing their information.
  - Genes are arranged on the chromosomes in a linear fashion.

# Griffith's experiment



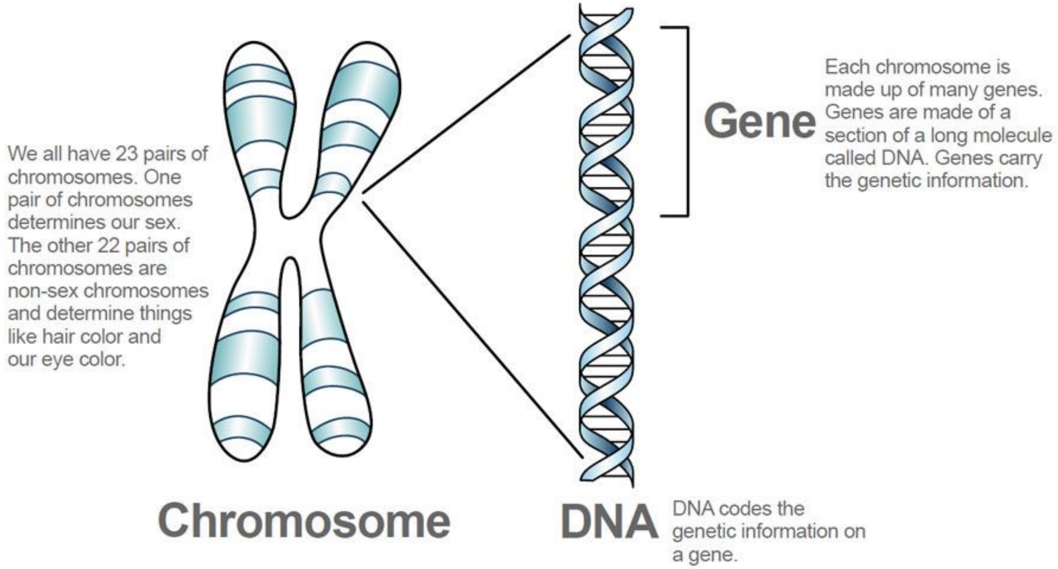
# Characteristic of genetic material:

- Storage of genetic information.
- Accurate Replication
- Accurate Transcription.
- Chemical Stability.
- Variation ability.



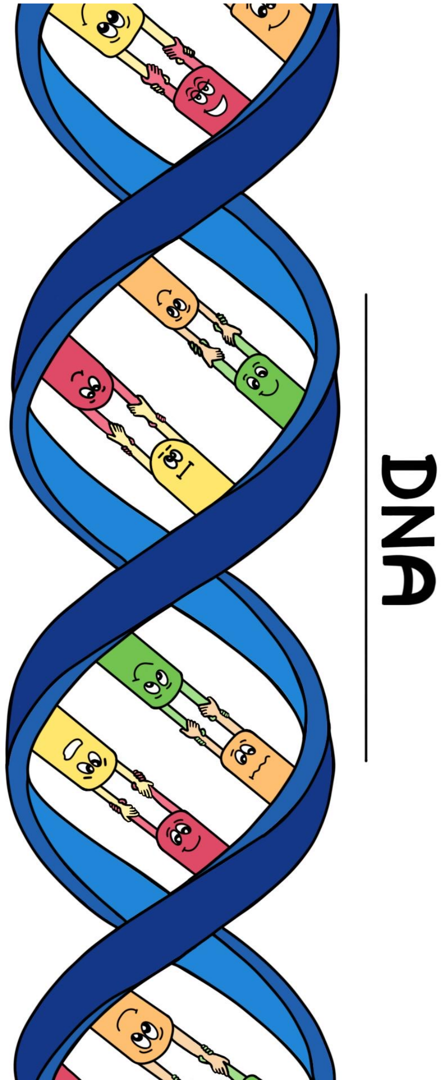
# Chromosome & Gene

- The storage place of all genetic information.
- The number of chromosome varies from one species to another.
- The DNA segments that carry this genetic information are called **genes**.



# Deoxyribonucleic acid (DNA)

- The **genetic instructions** used in the development and functioning of all known living organisms and some viruses.
- The main role of DNA molecules is the **long-term storage of information**.
- DNA is often compared to a set of blueprints or a recipe, or a code, since it contains the instructions needed to construct other components of cells, such as proteins and RNA molecules.

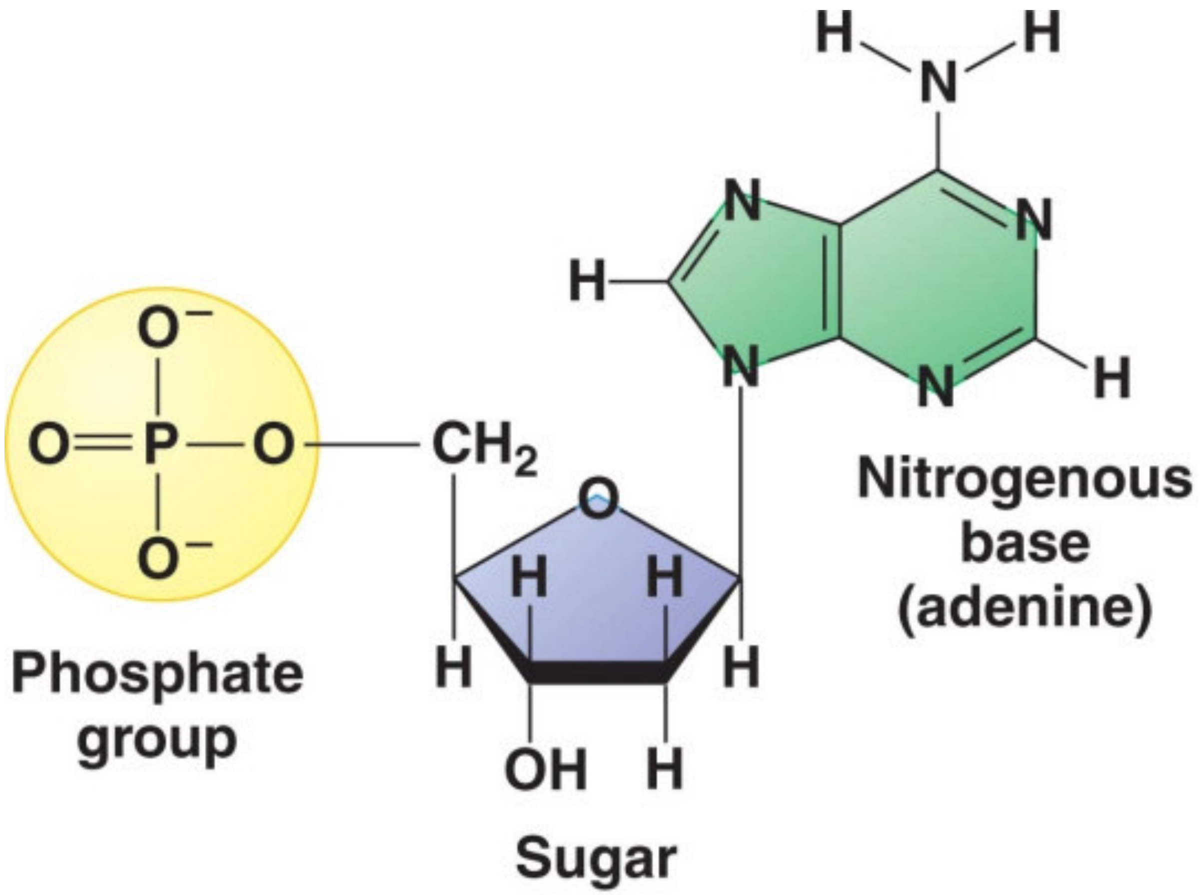


# General structure of nucleic acids:

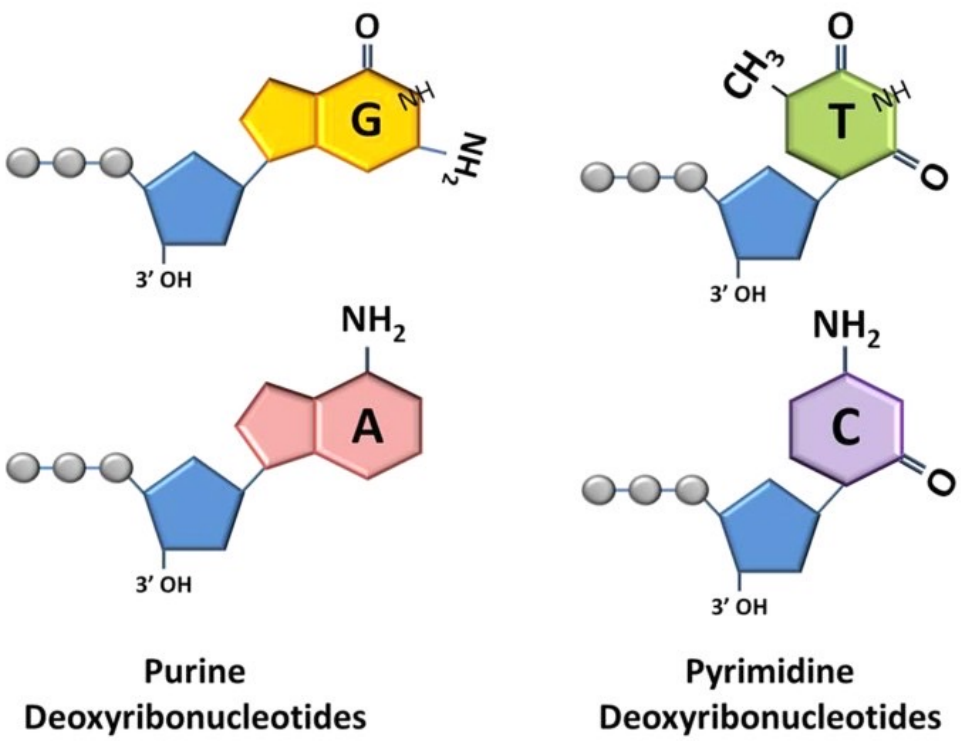
- DNA is a long polymer made from repeating units called nucleotides.
- The DNA chain is 22 to 26 Å wide (2.2 to 2.6 nano.), and one nucleotide unit is 3.3 Å (0.33 nm) long. Although each individual repeating unit is very small, DNA polymers can be very large molecules containing millions of nucleotides.
- Human chromosome number 1, is approximately 220 million base pairs long.

# Building Blocks - Nucleotides

- A nucleotide is composed of three parts: **sugar** ( Ribose in RNA and Deoxy ribose in DNA), **base** and **phosphate** group. If all phosphate groups are removed, a nucleotide becomes a nucleoside.



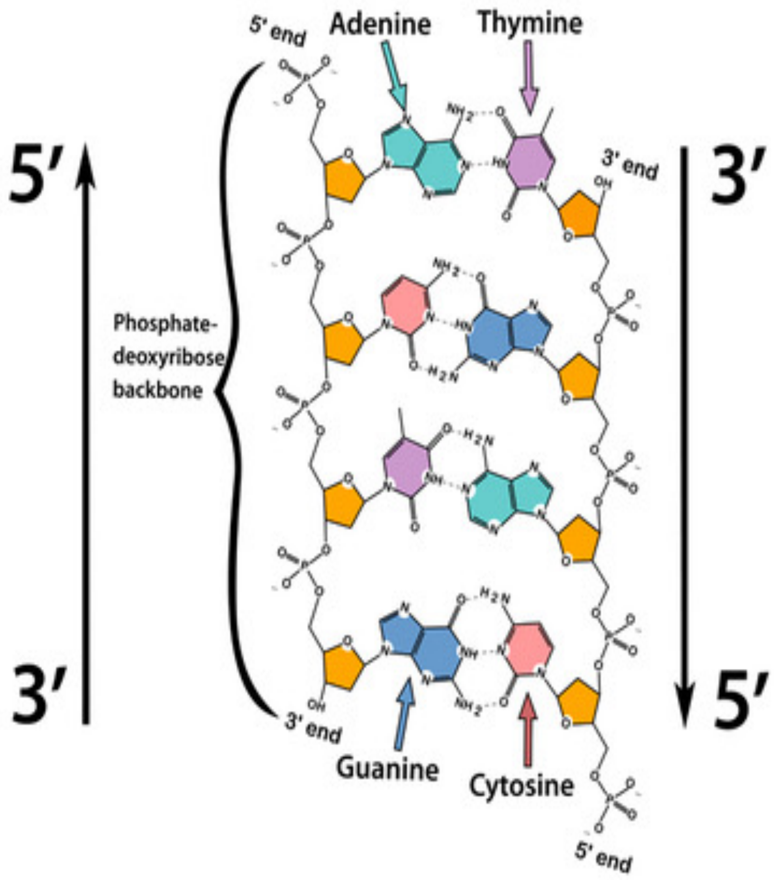
## The four bases found in DNA are:




- Adenine (A),
- Cytosine (C),
- Guanine (G) and
- Thymine (T).
- A fifth pyrimidine base, called uracil (U), usually takes the place of thymine in RNA and differs from thymine by lacking a methyl group on its ring.
- These bases are classified into two types; adenine and guanine are fused five- and six-membered heterocyclic compounds called purines,
- While cytosine and thymine are six-membered rings called pyrimidines.

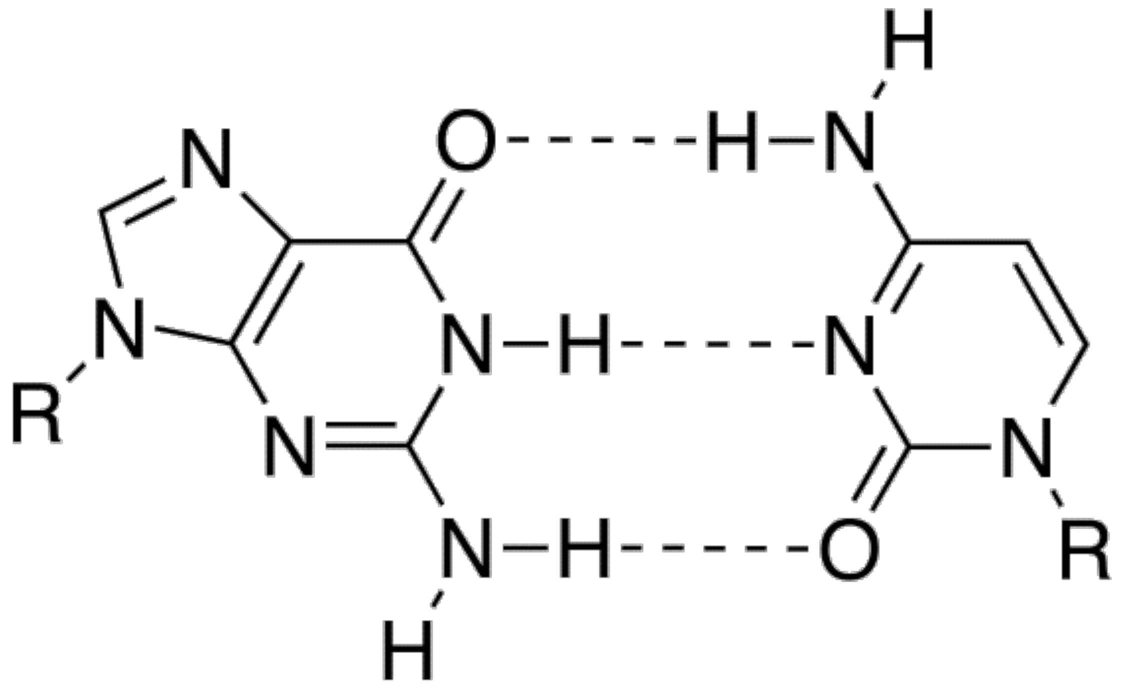
# Properties of DNA:

- In living organisms, DNA does not usually exist as a single molecule, but instead as a pair of molecules that are held tightly together.
- In a double helix the direction of the nucleotides in one strand is opposite to their direction in the other strand (**antiparallel**).
- The asymmetric ends of DNA strands are called the 5′ (five prime) and 3′ (three prime) ends, with the 5' end having a terminal phosphate group and the 3' end a terminal hydroxyl group.

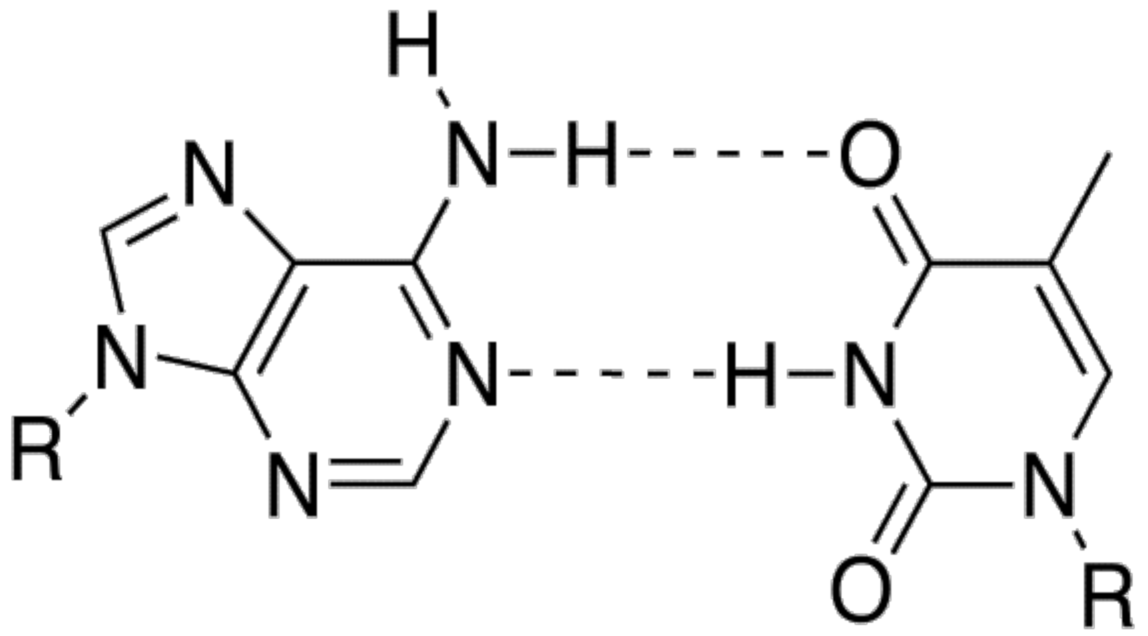


# Base pairing

- Each type of base on one strand forms a bond with just one type of base on the other strand. This is called complementary base pairing. Here, purines form hydrogen bonds to pyrimidines, with A bonding only to T, and C bonding only to G.
- This arrangement of two nucleotides binding together across the double helix is called a base pair. As hydrogen bonds are not covalent, they can be broken and rejoined relatively easily.

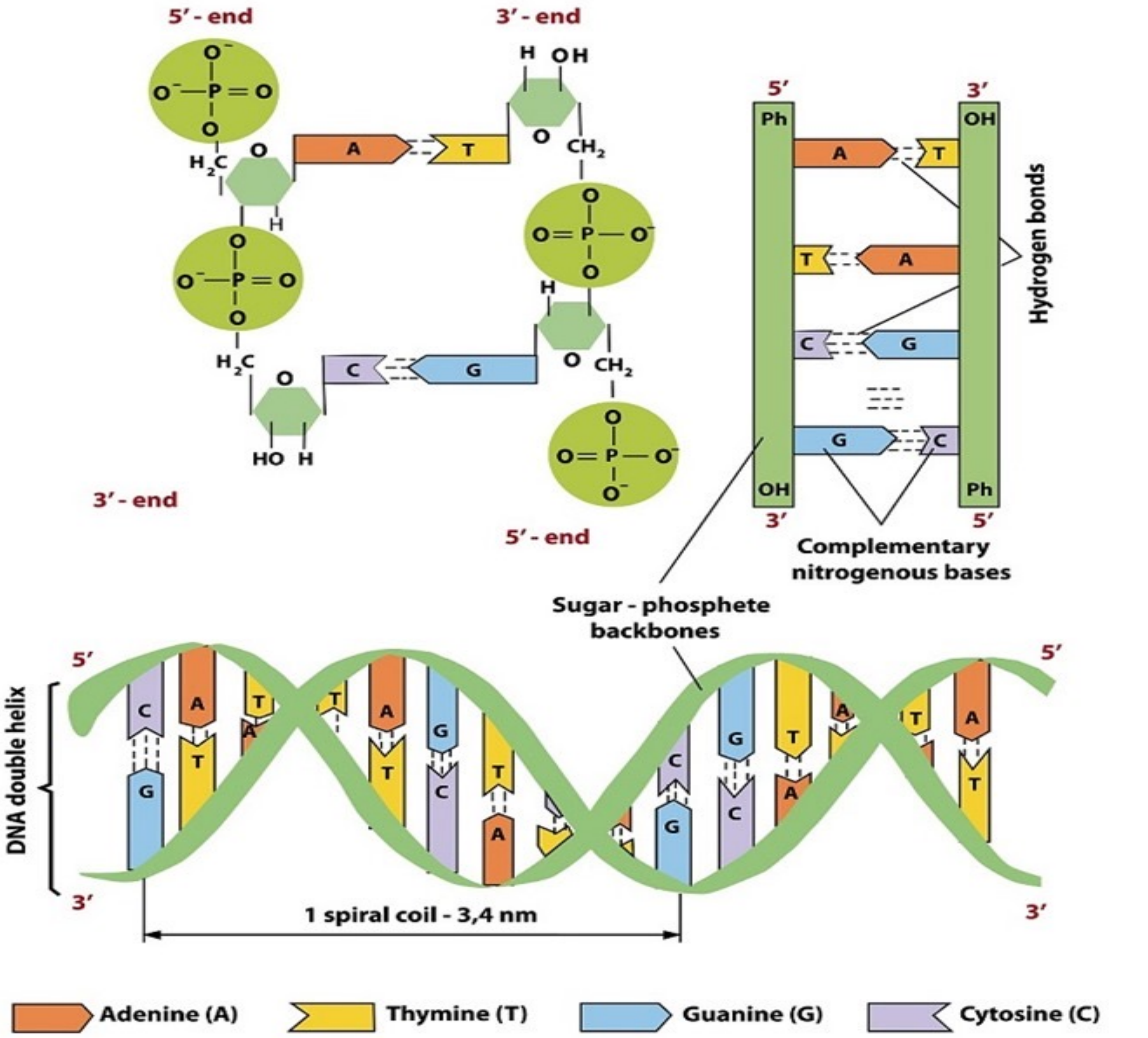


Guanine Cytosine



Adenine Thymine

# DNA Structure

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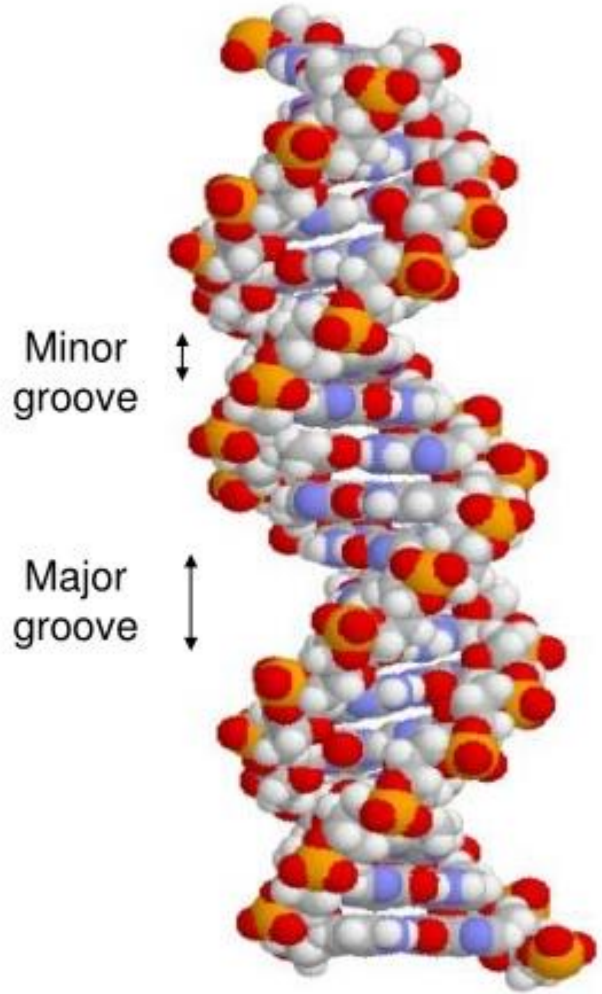
- Due to the specific base pairing, DNA's two strands are complementary to each other. Hence, the nucleotide sequence of one strand determines the sequence of another strand. For example, the sequence of the two strands can be written as
- 5'-ACT-3'
- 3'-TGA-5'
- Note that they obey the (A:T) and (C:G) pairing rule. If we know the sequence of one strand, we can deduce the sequence of another strand. For this reason, a DNA database needs to store only the sequence of one strand. By convention, the sequence in a DNA database refers to the sequence of the 5' to 3' strand (left to right).

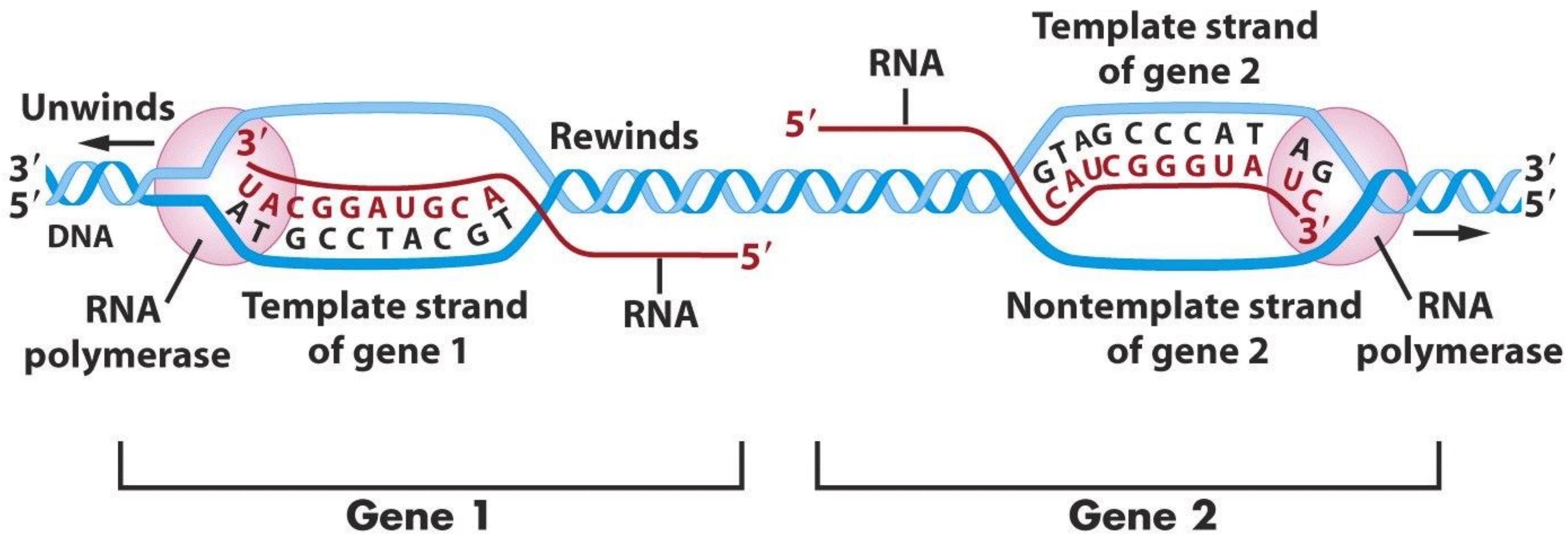
# Grooves

- Twin helical strands form the DNA backbone. Another double helix may be found by tracing the spaces, or grooves, between the strands. As the strands are not directly opposite each other, the grooves are unequally sized. One groove, the **major groove, is 22 Å** wide and the other, **the minor groove, is 12 Å** wide.



# Sense and antisense

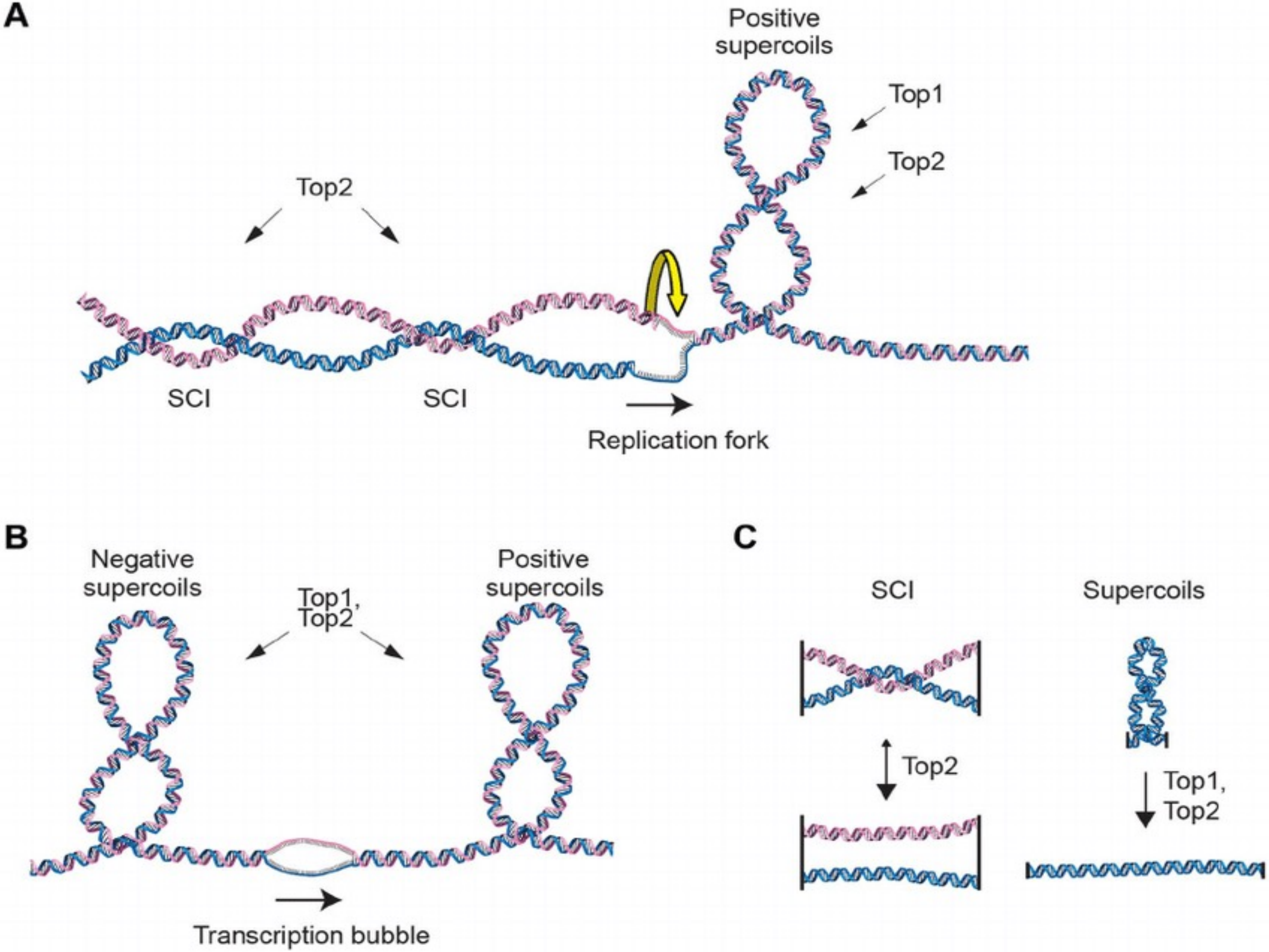
- A DNA sequence is called "sense" if its sequence is the same as that of a messenger RNA copy that is translated into protein. The sequence on the opposite strand is called the "antisense" sequence. Both sense and antisense sequences can exist on different parts of the same strand of DNA (i.e. both strands contain both sense and antisense sequences). In both prokaryotes and eukaryotes, antisense RNA sequences are produced, but the functions of these RNAs are not entirely clear.



# Supercoiling

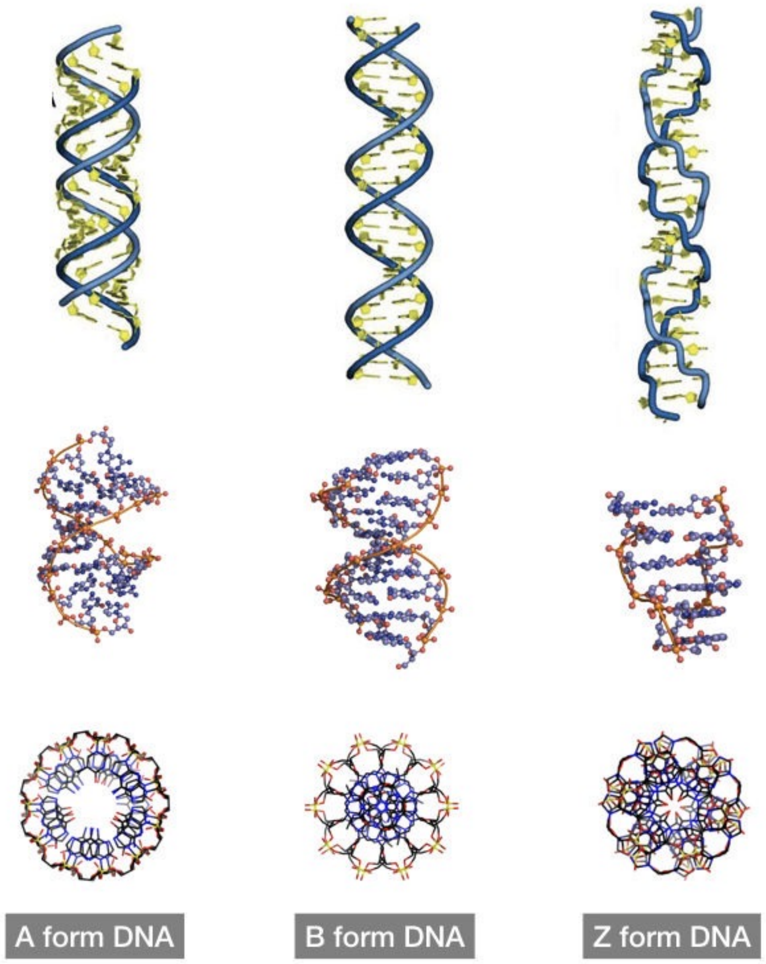
- DNA can be twisted like a rope in a process called DNA supercoiling. With DNA in its "relaxed" state, a strand usually circles the axis of the double helix once every 10.4 base pairs.
- If the DNA is twisted in the direction of the helix, this is positive supercoiling, and the bases are held more tightly together.
- If they are twisted in the opposite direction, this is negative supercoiling, and the bases come apart more easily.
- In nature, most DNA has slight negative supercoiling that is introduced by enzymes called topoisomerases.

https://www.youtube.com/watch?v=DXznYpXZu3M


A
Positive supercoils
Top1
Top2
Top2
SCI
SCI
Replication fork
B
Negative supercoils
Top1, Top2
Positive supercoils
Transcription bubble
C
SCI
Supercoils
Top2
Top1, Top2

# Alternate DNA structures

- DNA exists in many possible conformations that include A-DNA, B-DNA, and Z-DNA forms, although, only B-DNA and Z-DNA have been directly observed in functional organisms.



# References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- Lodish, H., Berk, A., Kaiser, C. A., Krieger, M., Scott, M. P., Bretscher, A., ... & Matsudaira, P. (2008). *Molecular cell biology*. Macmillan.