Nucleic Acids

Introduction

Nucleic acids are the most vital macromolecules for the continuity of life, serving as the **storage and expression vehicles for genetic information**. They dictate the synthesis of proteins and, through them, the structure and function of the entire organism. Deoxyribonucleic acid (**DNA**) and Ribonucleic acid (**RNA**) are the two primary types of nucleic acids, built from monomers called nucleotides.

- Nucleic acids carry the **hereditary information** (DNA) and are central to the process of **protein synthesis** (RNA).
- The flow of genetic information from DNA to RNA to protein defines the **Central Dogma of Molecular Biology**.
- Molecular tools based on nucleic acids, like **PCR** and **cloning**, have revolutionized biotechnology and medicine.

Learning Objectives

By the end of this module, you will be able to:

- Describe the chemical components (bases, sugars, phosphate) that constitute **nucleotides** and **nucleic acids**.
- Differentiate the structures of **DNA** and **RNA**.
- Outline the three major processes of the Central Dogma: **replication**, **transcription**, and **translation**.
- Classify and explain different types of **mutations** and **DNA repair systems.**
- Explain the principles and applications of **basic recombinant DNA technology**, including cDNA synthesis and PCR.

Key Concepts and Definitions

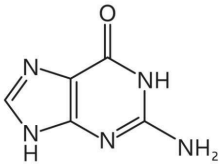
Term	Definition
Nucleotide	The monomer unit of a nucleic acid, consisting of a **nitrogenous base**, a **pentose sugar** (ribose or deoxyribose), and one or more **phosphate groups**.
Nucleoside	A subunit consisting only of a **nitrogenous base** attached to a **pentose sugar** (lacks the phosphate group).
Purine	A double-ringed nitrogenous base found in nucleic acids: **Adenine (A)** and **Guanine (G).**
Pyrimidine	A single-ringed nitrogenous base found in nucleic acids: **Cytosine (C), Thymine (T)** (in DNA), and **Uracil (U)** (in RNA).
Central Dogma	The foundational principle of molecular biology stating that genetic information flows from **DNA** → **RNA** → **Protein**.
Gene Expression	The process by which the information encoded in a gene is used to synthesize a functional gene product (protein or functional RNA).
Mutagen	A physical or chemical agent that causes genetic mutations by changing the DNA structure.
Recombinant DNA	A DNA molecule created in a laboratory by joining DNA fragments from different biological sources.

Detailed Discussion

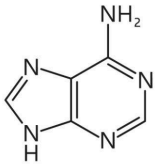
General Properties and Structures of Nucleic Acid Components

Nucleic acids (DNA and RNA) are polymers made of repeating nucleotide monomers.

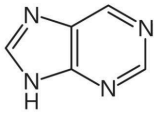
a. Nitrogenous Bases. The bases are aromatic, nitrogen-containing ring structures. They are the information-carrying part of the nucleotide.



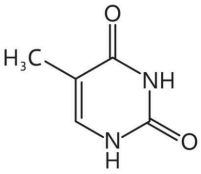
GUANINE



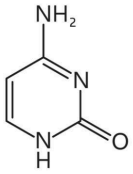
ADENINE



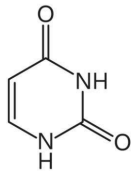
PURINE



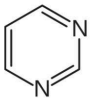
THYMINE



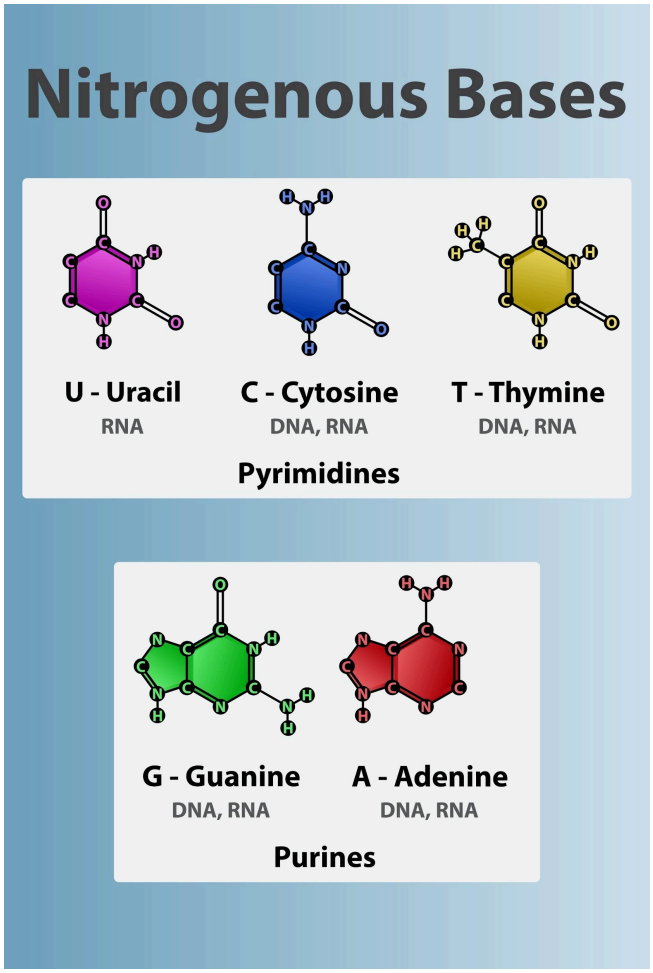
CYTOSINE



URACIL



PYRIMIDINE



Base Type	Examples	Description	Found In
Purines	Adenine (A), Guanine (G)	Double-ringed structure.	DNA & RNA
Pyrimidines	Cytosine (C), Thymine (T), Uracil (U)	Single-ringed structure.	C in DNA & RNA; T in DNA only; U in RNA only

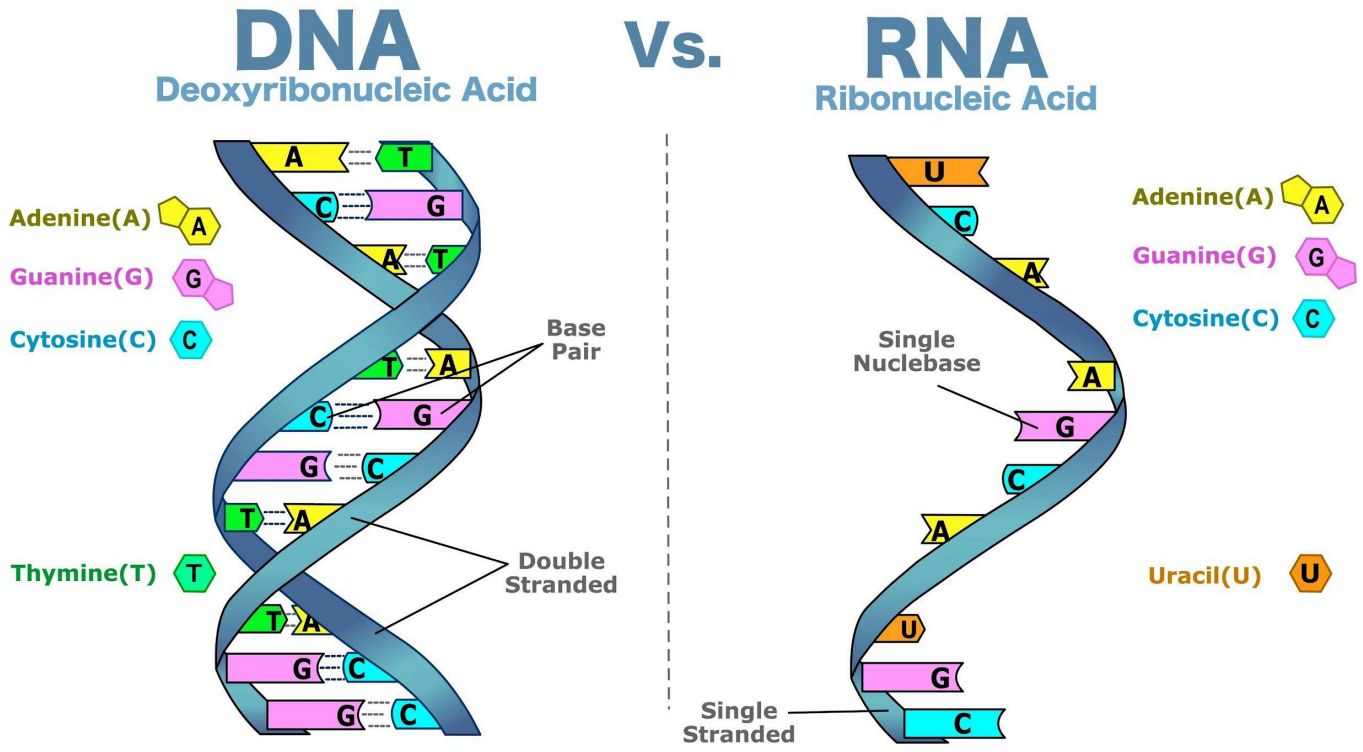
b. Nucleosides and Nucleotides

- **Nucleoside**: Base + Sugar (e.g., Adenosine, Guanosine).
- **Nucleotide**: Base + Sugar + Phosphate Group(s) (e.g., ATP, dGTP).
- **Backbone**: Nucleotides link together via a **phosphodiester bond** between the phosphate group on the 5' carbon of one sugar and the hydroxyl group on the 3' carbon of the next sugar. This creates a chain with inherent **directionality** (5' end to 3' end).

c. Nucleic Acid Structure (DNA vs. RNA)

Feature	Deoxyribonucleic Acid (DNA)	Ribonucleic Acid (RNA)
Sugar	Deoxyribose (lacks an -OH group at 2' carbon)	Ribose (has an -OH group at 2' carbon)
Bases	A, G, C, T	A, G, C, U
Structure	Double helix (two anti-parallel strands)	Usually single-stranded
Function	Long-term genetic information storage	Protein synthesis (mRNA, tRNA, rRNA) and gene regulation

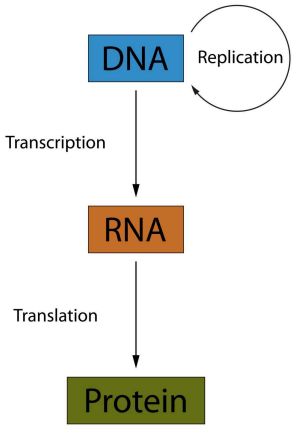
DNA exists as a **double helix**, where two strands of nucleotides coil around each other. The strands are **antiparallel** and held together by **hydrogen bonds** between complementary bases: **A pairs with T** (two H-bonds) and **G pairs with C** (three H-bonds). RNA, being typically single-stranded, can leave the nucleus and perform various functional roles in the cytoplasm.



The Central Dogma of Molecular Biology

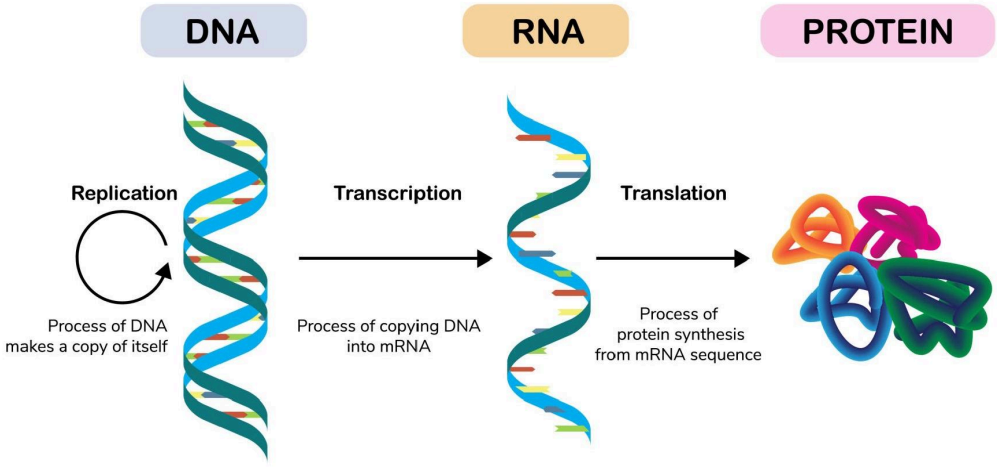
The flow of genetic information in a cell is fundamentally: $\text{DNA} \xrightarrow{\text{Replication}} \text{DNA} \xrightarrow{\text{Transcription}} \text{RNA} \xrightarrow{\text{Translation}} \text{Protein}$

The central dogma of molecular biology



BIOLOGY

Central Dogma



- **DNA Replication**:
  - **Goal**: To duplicate the entire genome before cell division.
  - **Process**: **Semi-conservative**. The double helix unwinds, and each parental strand serves as a template for the synthesis of a new, complementary daughter strand. The enzyme **DNA polymerase** carries out this synthesis.
  - **Example**: When a cell in your liver divides, its entire ~3 billion base pair genome must be accurately copied.
- **Transcription**:
  - **Goal**: To synthesize an **RNA** copy of a specific **gene** sequence.
  - **Process**: The enzyme **RNA polymerase** binds to a promoter region on the DNA, unwinds the helix, and synthesizes a complementary RNA strand (mRNA, tRNA, or rRNA) using the DNA as a template.
  - **Example**: A gene for insulin is transcribed into an insulin mRNA molecule.
- **Translation**:
  - **Goal**: To synthesize a **protein** (polypeptide chain) using the information encoded in mRNA.
  - **Process**: Occurs on the **ribosome**. The mRNA sequence is read in triplets called codons. Transfer RNA **(tRNA)** molecules, each carrying a specific amino acid, match their anticodons to the mRNA codons, adding the amino acid to the growing polypeptide chain.
  - **Example**: The mRNA codon 5'-AUG-3' signals the start of translation and codes for the amino acid Methionine.
- **Regulation of Gene Expression:**
  - Cells control which genes are transcribed and translated and at what rate. This control can occur at multiple stages.
  - **Example (Eukaryotes**): **Chromatin remodeling** (making DNA accessible), **transcription factor binding** (controlling RNA Polymerase activity), and **RNA splicing/stability control.**
  - **Example (Prokaryotes**): The **lac operon** system controls the expression of lactose-metabolizing enzymes based on the presence of lactose and glucose.

Mutation, Repair, and Carcinogenesis

- **Mutation**: Any change in the nucleotide sequence of DNA.
  - **Types of Mutation:**
    - **Point Mutations (Small Scale):**
      - **Silent**: Change in a codon, but the same amino acid is coded (no effect).

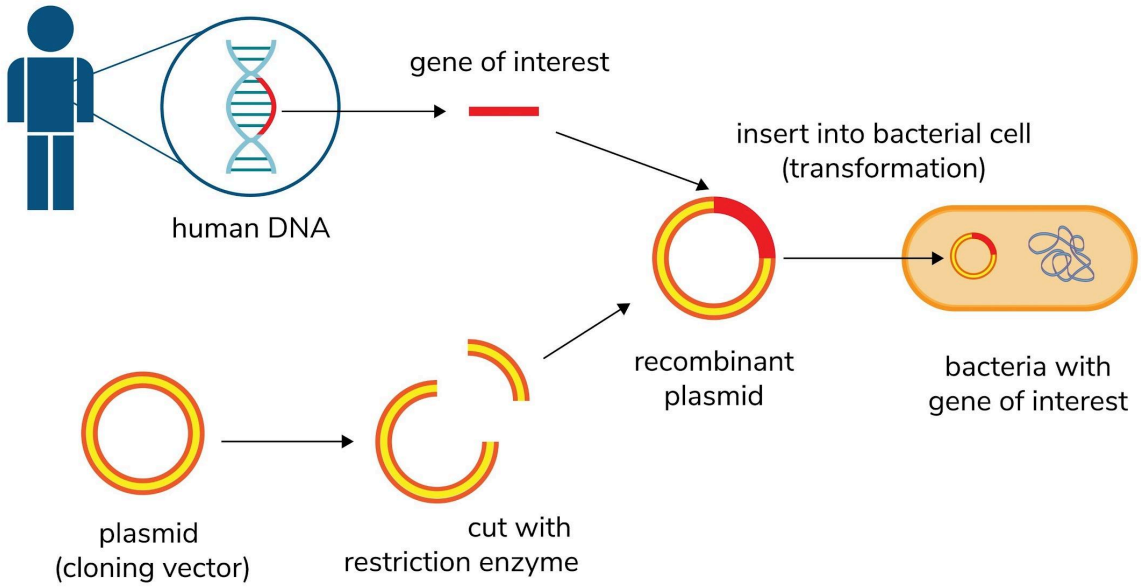
        - **Missense**: Change in a codon, resulting in a different amino acid (e.g., Sickle Cell Anemia).
        - **Nonsense**: Change resulting in a premature **stop codon** (usually severe).
    - **Frameshift Mutations**: Insertion or deletion of nucleotides that shifts the reading frame of the ribosome, severely altering the resulting protein.
  - **Types of Mutagens**: Agents that increase the rate of mutation.
    - **Physical**: UV radiation (causes pyrimidine dimers, especially thymine dimers), Ionizing radiation (causes single and double-strand breaks).
    - **Chemical**: Base analogs (mimic normal bases), **Intercalating agents** (insert into DNA helix, causing frameshifts), and certain environmental chemicals (e.g., components in tobacco smoke).
- **DNA Repair Systems**: Cells have evolved complex enzymatic systems to correct DNA damage.
  - **Base Excision Repair (BER):** Corrects small damage like altered bases (e.g., oxidative damage) by removing the base, then the sugar-phosphate, and filling the gap.
  - **Nucleotide Excision Repair (NER):** Corrects large, helix-distorting lesions, such as pyrimidine dimers caused by UV light.
  - **Mismatch Repair (MMR)**: Corrects errors introduced during DNA replication that were missed by the DNA polymerase proofreading.
- **Mutagenesis and Carcinogenesis**:
  - Damage to DNA that is not repaired leads to **mutagenesis** (the creation of mutations).
  - If these mutations occur in genes controlling cell growth (**proto-oncogenes** and **tumor suppressor genes**), it can lead to uncontrolled cell division and accumulation of damage, a process called **carcinogenesis** (the initiation of cancer).

Basic Recombinant Technology

Recombinant DNA Technology (RDT) involves combining genetic material from different sources to create a new DNA molecule.

BIOLOGY

Recombinant DNA technology



- **Basic Cloning:**

1. Obtain the **Gene of Interest** (Insert) and a self-replicating DNA molecule (**Vector**, usually a plasmid).
2. Use **Restriction Enzymes** (molecular scissors) to cut both the insert DNA and the vector at specific sequences, creating compatible "sticky ends."
3. Use **DNA Ligase** (molecular glue) to join the insert and the vector, creating a recombinant plasmid.
4. Introduce the **recombinant plasmid** into a host organism (e.g., E. coli) via **transformation**.
5. Select host cells containing the plasmid (e.g., using antibiotic resistance). The host cell replicates the recombinant DNA along with its own DNA.

- **cDNA (Complementary DNA):**
  - **Definition**: A double-stranded DNA molecule synthesized from a messenger RNA **(mRNA)** template.
  - **Synthesis**: The enzyme **Reverse Transcriptase** uses the mRNA as a template to create a single strand of DNA (cDNA), and then a DNA polymerase makes the complementary strand.
  - **Importance**: Eukaryotic genes contain non-coding regions **(introns)**, which are removed in mature mRNA. cDNA lacks these introns, making it ideal for expressing eukaryotic genes in prokaryotic cells (like bacteria) for research or biopharmaceutical production (e.g., recombinant insulin).

- **Polymerase Chain Reaction (PCR):**
  - **Goal**: **Rapidly amplify** (make millions of copies of) a specific DNA sequence in vitro (in a test tube).
  - **Basic Steps (Thermocycling):**
    i. **Denaturation** (~95° C): Heat separates the double-stranded DNA template into single strands.
    ii. **Annealing** (~50–65° C): Short, synthetic **primers** bind (anneal) to the specific target sequences on the single strands.
    iii. **Extension** (~72° C): **Taq Polymerase** (a heat-stable DNA polymerase) extends the primers, synthesizing new complementary DNA strands.
    iv. **Application**: Forensics, medical diagnostics (e.g., detecting viral DNA), and molecular biology research.

References

1. Watson, J. D., & Crick, F. H. C. (1953). Molecular structure of nucleic acids: A structure for deoxyribose nucleic acid. Nature, 171(4356), 737–738.
2. Nelson, D. L., & Cox, M. M. (2021). Lehninger principles of biochemistry (8th ed.). W. H. Freeman.
3. Brown, T. A. (2020). Gene cloning and DNA analysis: An introduction (8th ed.). Wiley-Blackwell.