Nucleic Acids: Structure, Base Pairing, and DNA Topology

Learning objectives of the lecture

By the end of this lecture, you should be able to:

1. Distinguish structurally and functionally between DNA and RNA.
2. Explain hydrogen bonding and complementary base pairing in nucleic acids and how this supports faithful information transfer.
3. Define DNA supercoiling (positive vs negative) and describe how it arises in cells.

1. DNA vs RNA: Structural and functional comparison

1.1 Basic definition

- DNA (deoxyribonucleic acid) and RNA (ribonucleic acid) are polymers of nucleotides.
- Each nucleotide =
  - Sugar (pentose)
  - Phosphate group(s)
  - Nitrogenous base

1.2 Sugar component

- **DNA**:
  - Sugar = **2'-deoxyribose** (no OH group at 2' carbon).
- **RNA**:
  - Sugar = **ribose** (has **2'-OH group**).

Functional implication of 2'-OH in RNA:

- The 2'-OH enables base-catalyzed hydrolysis by attacking the phosphodiester bond within the molecule.
- RNA is chemically less stable than DNA (more prone to degradation).
- DNA, lacking 2'-OH, is more resistant to hydrolysis → better for long-term information storage.

1.3 Nitrogenous bases

- **DNA bases**:
  - Adenine **(A)**, Guanine **(G)**, Cytosine **(C)**, Thymine **(T)**.
- **RNA bases**:
  - **A, G, C**, and **Uracil (U)** instead of T.
- **Base substitution in RNA:**
  - **U** pairs with **A** (analogous to T-A pairing in DNA).

1.4 Strand organization and higher-order structure

- **DNA**:
  - Typically, double-stranded in cells.

  - Two antiparallel strands form a right-handed double helix (B-DNA) under physiological conditions.
- **RNA**:
  - Usually single-stranded in cells.
  - Can adopt local secondary structures:
    - Hairpins
    - Internal loops
    - Short double helices

Functional consequences:

- **DNA double helix**
  - Bases are stacked and protected in the interior → enhanced chemical stability.
- **RNA single strand**
  - More exposed and structurally flexible → suitable for roles as messenger (mRNA), transfer (tRNA), and ribosomal component (rRNA)

1.5 Stability and biological roles

- **DNA**
  - Very stable chemically (no 2'-OH; double-stranded; hydrogen-bonded bases).
  - Designed for the efficient storage of hereditary information across extended periods.
- **RNA**
  - Less stable (2'-OH, often single-stranded).
  - Suited for transient roles:
    - Short-lived messages (mRNA)
    - Intermediate in gene expression
    - Catalytic activities (ribozymes, rRNA in ribosome).

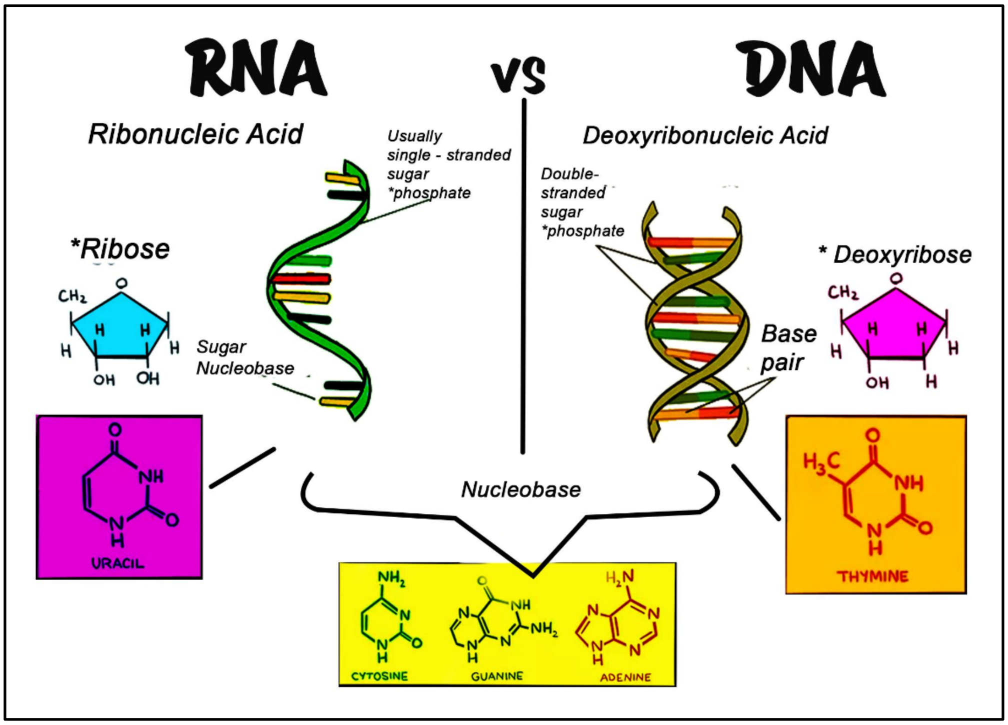

Figure 1: this diagram comparing RNA and DNA structures, highlighting sugar types, nucleobases, strand configuration, and differences between uracil and thymin.

2. Hydrogen Bonding and Base Pairing

2.1 Canonical Base Pairs

- In **DNA**:
  - **A–T** pair with **2 hydrogen bonds**.
  - **G–C** pair with **3 hydrogen bonds**.
- In **RNA**:
  - **A–U** pair with **2 hydrogen bonds**.
  - **G–C** still **3 hydrogen bonds**.

2.2 Structural consequences

- Base pairing is complementary and specific:
  - Purine (A or G) pairing with pyrimidine (T/U or C) ensures uniform helix width.
- Hydrogen bonds are individually weak, but collectively:
  - Stabilize the double helix (DNA) and helical regions in RNA.
  - Allow reversible strand separation (melting) when necessary.

2.3 Effects on Information Transfer

- Complementary base pairing ensures:
  - **Replication fidelity**:
    - Each base in a template strand specifies a unique complementary base in the daughter strand.
  - **Transcription accuracy**:
    - DNA template base specifies the RNA base (A ↔ U; T ↔ A; G ↔ C; C ↔ G).

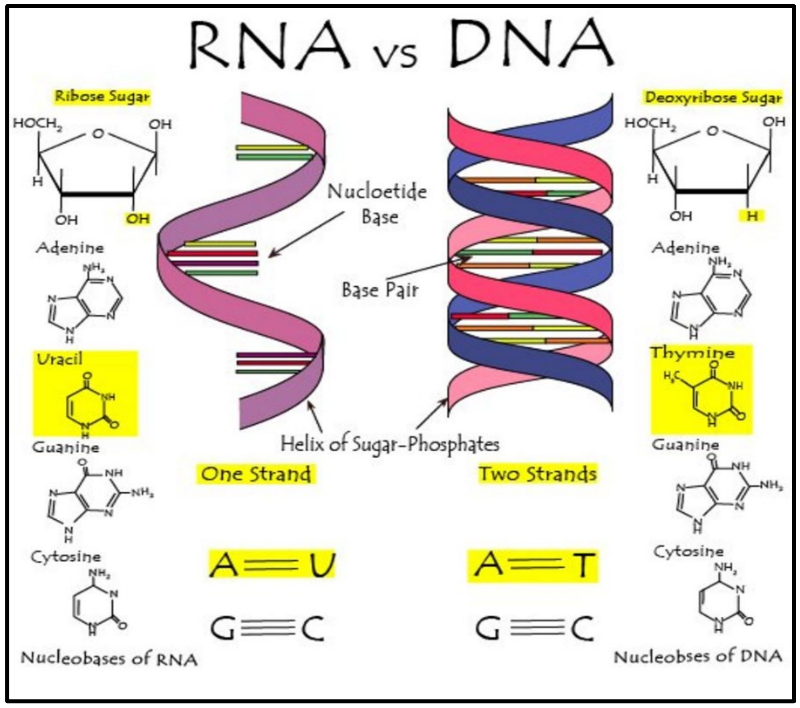

Figure 2: this diagram compares RNA and DNA structures, highlighting sugar differences, nucleotide bases, strand number, and base-pairing rules with annotated molecular illustrations.

3. DNA Supercoiling

3.1 Definition and terminology

- **DNA supercoiling** = additional coiling of the double helix on itself beyond the relaxed state.
- For **B-form DNA**, relaxed:
  - **~10.5 bp per helical turn**.

Types of supercoils:

- **Positive supercoils**
  - DNA is overwound (more turns than relaxed).
  - Helix becomes tighter; strand separation is more difficult.
- **Negative supercoils**
  - DNA is **underwound** (fewer turns than relaxed).
  - DNA tends to **writhe** to accommodate missing turns.