DNA, replication and protein synthesis

Nucleotides and the structure of DNA and RNA, semi-conservative replication and the Meselson-Stahl experiment, the genetic code, transcription and translation, and mutations.

Nucleotides and nucleic acids

A **mononucleotide** has three parts:

- a **pentose sugar**: **deoxyribose** in DNA, **ribose** in RNA,
- a **phosphate group**,
- a **nitrogenous base**: **adenine (A)**, **guanine (G)**, **cytosine (C)** and **thymine (T)** in DNA; **uracil (U)** replaces thymine in RNA.

Nucleotides join by **condensation reactions** between the phosphate of one and the sugar of the next, forming **phosphodiester bonds** and a **sugar–phosphate backbone**.

DNA

DNA is a **double helix** of two **antiparallel** polynucleotide strands. The bases pair by **complementary base pairing**: **A with T** (two hydrogen bonds) and **C with G** (three hydrogen bonds). The strands are held together by **hydrogen bonds** between the bases. DNA is stable, has a very large number of bases to store information, and its double strand lets it be **replicated** accurately.

	DNA	RNA
Sugar	Deoxyribose	Ribose
Bases	A, T, C, G	A, **U**, C, G
Strands	Two (double helix)	One
Length	Very long	Short
Role	Stores the genetic information	Copies and carries it (mRNA), translation (tRNA, rRNA)

DNA replication

DNA replicates **semi-conservatively**: each new molecule has **one original strand** and **one new strand**.

1. **DNA helicase** unwinds the helix and breaks the hydrogen bonds between bases, exposing the two template strands.
2. Free **nucleotides** pair with their complementary bases on each template strand.

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3. **DNA polymerase** joins the nucleotides, forming phosphodiester bonds. It works in one direction only (5′ to 3′), so one strand is made continuously and the other in fragments, which are joined by **DNA ligase**.

Meselson and Stahl

They grew bacteria for many generations in a medium containing **heavy nitrogen (^{15}N)**, so all the DNA was heavy. They then transferred them to a medium with **light nitrogen (^{14}N)** and extracted the DNA after each generation, spinning it in a **density gradient** (centrifuge).

Generation	DNA band
0	One heavy band
1	One band of **intermediate** density
2	One intermediate and one **light** band

The first generation gave one intermediate band, which **rules out conservative replication** (that would give separate heavy and light bands). The second generation, with intermediate and light bands, **rules out dispersive replication** and supports **semi-conservative** replication.

The genetic code

A **gene** is a **sequence of bases on a DNA molecule** that codes for a **sequence of amino acids** in a polypeptide.

The code is:

- a **triplet code**: three bases (a **codon**) code for one amino acid (64 combinations, 20 amino acids),
- **non-overlapping**: each base is read once,
- **degenerate**: most amino acids have more than one codon,
- includes **start** (AUG, methionine) and **stop** codons (no amino acid),
- **universal** (almost the same in all organisms).

Protein synthesis

Transcription (in the nucleus)

1. **DNA helicase** (or RNA polymerase itself) unwinds the section of DNA for the gene.
2. **RNA polymerase** binds to the **template (antisense) strand**, and joins free RNA nucleotides that pair with the template bases (U with A), forming **pre-mRNA**.

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3. The mRNA is **complementary** to the template strand and has the same sequence as the coding (sense) strand, with U for T.
4. In eukaryotes, the pre-mRNA is **spliced** (introns removed) and the mature **mRNA** leaves the nucleus through a nuclear pore.

Translation (at the ribosome)

1. The mRNA binds to a **ribosome** (made of rRNA and protein).
2. A **tRNA** molecule with an **anticodon** complementary to the **codon** on the mRNA brings the matching amino acid (attached by an enzyme using ATP). The first codon is the **start codon** AUG.
3. Two tRNAs fit on the ribosome at a time. A **peptide bond** forms between the amino acids, and the ribosome moves along the mRNA one codon at a time.
4. The chain grows until a **stop codon** is reached, and the polypeptide is released.

> TRY IT
>
> The template strand reads TAC CGA. Give the mRNA codons and tRNA anticodons.

mRNA is complementary to the template: **AUG GCU**. The tRNA anticodons are complementary to the codons: **UAC CGA**.

Mutations

A **mutation** is a change in the base sequence of DNA. It can arise from errors in replication (a wrong base or a base added or lost), and is more likely in the presence of mutagens such as UV and some chemicals.

Type	Description	Effect
Substitution	One base replaced	May change one amino acid, or none (the code is degenerate), or create a **stop** codon
Insertion	A base added	A **frameshift**: all codons after the change are altered
Deletion	A base removed	A frameshift

Many mutations have **no observable effect** (a degenerate code, or a change outside the coding region), but some cause **genetic disorders** (e.g. cystic fibrosis, sickle cell anaemia) or lead to **cancer** if genes controlling cell division are changed. Mutations are the source of new alleles, and so of variation.

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