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TOPIC 2B: PROTEINS AND DNA

Comprehensive Advanced Level Study Notes

1. Introduction to Proteins & DNA

Proteins and nucleic acids are the essential molecular building blocks of life. A severe lack of dietary protein leads to medical deficiencies such as **kwashiorkor**, which affects millions of infants globally. Individuals with kwashiorkor may receive adequate total calories but lack fundamental protein, leading to physical wasting and a swollen abdomen because metabolic cellular processes fail without functional enzymes.

While proteins construct the cellular framework and act as metabolic biological catalysts, nucleotides (DNA and RNA) carry the fundamental genetic code required to manufacture these proteins and determine an organism's ultimate physical traits or phenotype.

2. Enzymes and Cellular Metabolism

Biological Catalysts

A **catalyst** is any substance that modifies and accelerates the rate of a chemical reaction without altering the end products generated or being permanently changed itself. At the end of a reaction, the catalyst remains intact and completely free to bind with new reactants.

Enzymes are complex biological catalysts composed of globular proteins. Cellular reactions must execute at bodily temperatures and physiological pH levels; without enzymes, these vital reactions would occur too slowly for biological life to exist. Enzymes control metabolic rates without shifting or disrupting the volatile internal physical conditions of the cellular cytoplasm.

Classification of Enzymes

- **Intracellular Enzymes:** Catalyse chemical reactions that happen strictly inside individual cells (e.g., *DNA polymerase* and *DNA ligase* involved in genetic replication).
- **Extracellular Enzymes:** Synthesised inside the cell but secreted outward to catalyse reactions outside the cell membrane (e.g., digestive enzymes like *pepsin* and *trypsin*, or *lysozyme* found within protective human tears).

Anabolism, Catabolism, and Metabolic Pathways

Cellular chemical reactions do not happen in isolation but occur as a tightly regulated series of linked steps called a **metabolic chain** or **metabolic pathway**. The entirety of these processes is termed **metabolism**, which is subdivided into two distinct arms:

- **Anabolic Reactions:** Processes that actively build up or synthesise complex new chemicals from simpler molecules (e.g., protein synthesis).
- **Catabolic Reactions:** Processes that systematically break down large molecules into smaller entities, releasing chemical energy (e.g., cellular respiration).

3. Mechanisms of Enzyme Action

Activation Energy Lowering

For a chemical reaction to successfully take place, colliding reactant molecules must possess a baseline quantity of kinetic energy to destabilise and break the initial chemical bonds holding them together. This barrier is termed the **activation energy**. Enzymes accelerate rates by dramatically lowering this required activation energy threshold, allowing reactions to rapidly cascade at baseline biological temperatures.

Uncatalysed Path: Requires high initial heat energy. *Transition State = High Energy*	→	**Catalysed Path:** Enzyme binds substrate, lowering the barrier. *Transition State = Lowered Energy*

Conceptual Diagram: Activation Energy Lowering via Enzyme-Substrate Complex

The Lock-and-Key vs. Induced-Fit Hypotheses

Historically, the **lock-and-key hypothesis** described enzymes as rigid structures where a specific molecule (the **substrate**) perfectly slots into a static **active site** on the enzyme, much like a physical key aligns into a door lock.

Modern structural analysis, including X-ray crystallography, reveals that active sites are actually highly dynamic and flexible. This gave rise to the universally accepted **induced-fit hypothesis**:

```
[ Substrate Molecule ] + [ Relaxed Enzyme Active Site ]
↓
[ Enzyme-Substrate Active Complex ]
(Active site alters its 3D conformation tightly around substrate, stressing bonds)
↓
[ Unchanged Free Enzyme ] + [ Altered Reaction Products ]
```

The Induced-Fit Sequence of Catalytic Conformation

The binding event causes the structural functional groups of the active site to morph precisely around the chemical substrate. This structural distortion applies mechanical and physical stress directly to the chemical bonds of the substrate, lowering the energy needed to split or combine molecules. Once the reaction finishes, the resulting products display an entirely different chemical shape, losing their physical affinity for the active site. They are ejected, and the enzyme returns to its relaxed, inactive state.

4. Environmental Factors Affecting Enzyme Kinetics

Because enzymes are highly complex structural globular proteins, their operational configuration relies on intricate intramolecular configurations. Any environmental variance alters the active site shape, modulating performance:

Environmental Variable	Kinetic & Structural Effect on Enzyme Action	Key Biological Metric / Example
Substrate Concentration	Increasing substrate concentration boosts reaction velocity as empty active sites become progressively occupied. Eventually, a plateau is reached when the enzyme saturates completely.	V_{max} (Maximum rate). Beyond saturation, only adding more enzyme increases the overall rate.
Temperature	Kinetic energy increases collision rates up to an *optimum temperature*. Beyond this point, thermal agitation tears apart fragile intramolecular bonds, causing structural collapse.	Q_{10} temperature coefficient. Denaturation typically begins above 40°C for humans. Thermophilic bacteria survive up to 85°C via dense disulfide networks.
pH Changes	Altering hydrogen ion levels disrupts delicate ionic and hydrogen bonds holding the tertiary/quaternary structure together, modifying the specific shape of the active site.	Pepsin works optimally at an acidic pH of ~2–3 (stomach), while trypsin works in alkaline ranges of pH ~8 (small intestine).

The effect of temperature can be quantified mathematically using the temperature coefficient, denoted as Q_{10}. Between 0°C and 40°C, the Q_{10} value for typical metabolic reactions is approximately 2, meaning the overall rate doubles for every 10°C rise:

$$Q_{10} = \frac{\text{Rate of reaction at } (x + 10)°C}{\text{Rate of reaction at } x°C}$$

5. Molecular Structure of Nucleic Acids (DNA & RNA)

Mononucleotides: The Structural Subunits

Nucleic acids are long polymers built out of individual repeating monomer units called **mononucleotides**. Every single mononucleotide is constructed via condensation reactions linking three distinct chemical components:

1. A 5-carbon pentose sugar (either **ribose** in RNA or **deoxyribose** in DNA). Deoxyribose has one fewer oxygen atom than ribose.
2. A negative, highly acidic inorganic **phosphate group** (-$\{PO_4\}^{3-}$).
3. A nitrogen-containing organic ring structure called a **nitrogenous base**.

Classification of Nitrogenous Bases

- **Purines (Double-Ring Structures):** Adenine (A) and Guanine (G).
- **Pyrimidines (Single-Ring Structures):** Cytosine (C), Thymine (T) [DNA only], and Uracil (U) [RNA only].

Polynucleotide Formation

Mononucleotides undergo systematic condensation reactions to assemble into long strands called **polynucleotides**. Strong covalent bonds called **phosphodiester bonds** link the pentose sugar of one nucleotide to the phosphate group of the adjacent nucleotide, generating a rigid structural sugar-phosphate backbone. Polynucleotide strands have a distinct structural orientation, featuring a free phosphate group at the 5' end and a free hydroxyl group at the 3' end.

Structural Character	Deoxyribonucleic Acid (DNA)	Ribonucleic Acid (RNA)
Pentose Sugar Type	Deoxyribose sugar	Ribose sugar
Nitrogenous Bases	Adenine, Thymine, Cytosine, Guanine	Adenine, Uracil, Cytosine, Guanine
Strand Architecture	Double-stranded helix layout	Single-stranded molecule

The Architecture of the Double Helix

A functional DNA molecule consists of two distinct polynucleotide strands winding symmetrically around each other to form a **double helix**. The sugar-phosphate backbones form the outside borders, while the nitrogenous bases point inward. The strands run in opposite directions, meaning they are structurally **antiparallel**.

The two strands are joined together through highly specific hydrogen bonding between complementary base pairs. A double-ring purine must always match with a single-ring pyrimidine to maintain a constant 2nm molecular width across the entire helix:

- **Adenine (A)** pairs exclusively with **Thymine (T)** via **two hydrogen bonds**.
- **Cytosine (C)** pairs exclusively with **Guanine (G)** via **three hydrogen bonds**.

6. Mechanisms of DNA Replication

To ensure accurate inheritance during cell division, DNA must copy itself perfectly. Historically, scientists debated whether replication followed a conservative or semiconservative pathway. In the 1950s, Matthew Meselson and Franklin Stahl definitively proved the **semiconservative replication model** using density-gradient centrifugation experiments with different isotopes of nitrogen (^{15}N and ^{14}N) in *E. coli* bacteria.

The Core Semiconservative Replication Steps

1. **Unwinding:** The enzyme **DNA helicase** breaks the hydrogen bonds holding the complementary base pairs together, unzipping the double helix into two separate strands that serve as templates.
2. **Complementary Alignment:** Free mononucleotides present in the nucleus line up along the exposed template strands according to strict base-pairing rules (A with T, C with G).
3. **Polymerisation:** The enzyme **DNA polymerase** links the aligned nucleotides together, catalysing the synthesis of a new complementary strand along each template.
4. **Ligation:** The enzyme **DNA ligase** seals any gaps in the sugar-phosphate backbone by catalysing the formation of covalent phosphodiester bonds, resulting in two identical double helices. Every new DNA molecule contains one conserved strand from the original parent molecule and one newly synthesised strand.

7. The Genetic Code and Protein Synthesis

The Nature of the Code

A **gene** is a specific sequence of bases along a DNA molecule that carries the instructions to build a corresponding sequence of amino acids in a polypeptide chain. Because cells use 20 standard amino acids, a single-base code (4 combinations) or a two-base code ($4 \times 4 = 16$ combinations) is mathematically insufficient. Therefore, life utilizes a **triplet code**, where a sequence of three bases (a **codon**) specifies a single amino acid, providing $4 \times 4 \times 4 = 64$ unique combinations.

The genetic code possesses two vital characteristics:

- **Non-overlapping Code:** Each triplet base sequence is read in a linear sequence. Adjacent codons do not share bases; a single mutation altering one base affects only one amino acid position.
- **Degenerate Code:** There are 64 possible codons but only 20 amino acids. Therefore, multiple distinct codons can code for the exact same amino acid, offering protection against point mutations.

The Two Stages of Protein Synthesis

Protein synthesis bridge the gap between nuclear DNA storage and functional cytoplasmic proteins through two highly coordinated stages:

1. **Transcription (Inside the Nucleus):**
   A section of the DNA double helix unwinds and unzips at a specific gene site. The **antisense strand** acts as the template, while the other strand is the sense strand. Free RNA nucleotides align along the antisense template strand via complementary base pairing, with **Uracil (U) replacing Thymine (T)** to pair with Adenine.

   The enzyme **RNA polymerase** links these RNA nucleotides together, creating a strand of **messenger RNA (mRNA)**. Once complete, the mRNA molecule detaches, moves out of the nucleus through a nuclear pore, and enters the cytoplasm.

2. **Translation (On the Ribosome Surface):**
   The mRNA strand binds to a **ribosome**, which reads the sequence one codon at a time. Molecules called **transfer RNA (tRNA)** bring specific amino acids from the cytoplasm to the ribosome. Each tRNA has a specific 3-base sequence called an **anticodon** that is perfectly complementary to an mRNA codon.

   When a tRNA anticodon binds to its matching mRNA codon, its amino acid is brought into close proximity with the adjacent amino acid. The ribosome catalyses a condensation reaction to form a **peptide bond** between the amino acids, systematically building a growing polypeptide chain. This process continues until a **stop codon** is reached, releasing the finished protein.

CORE VOCABULARY REFERENCE

Metabolism	The sum total of all the anabolic and catabolic chemical processes occurring inside a living cell.
Specificity	The property of an enzyme to catalyse only one specific reaction, determined by its 3D active site.
Mononucleotide	A molecular monomer subunit containing a pentose sugar, a phosphate group, and an organic base.
Phosphodiester Bond	The strong covalent bond linking the sugar of one nucleotide to the phosphate group of the next.
Antiparallel Strands	The parallel arrangement of the two DNA strands running in opposite molecular directions (5' to 3' vs. 3' to 5').
Transcription	The synthesis of an mRNA molecule from a complementary nuclear DNA antisense template strand.
Translation	The synthesis of a polypeptide chain on a ribosome by decoding an mRNA sequence using tRNA molecules.