CHAPTER 4: CELLULAR METABOLISM

I. METABOLIC PROCESSES

A. METABOLISM = the sum of an organism's chemical reactions.

1. Each reaction is catalyzed by a specific enzyme.
2. The reactions typically occur in pathways (i.e. in a sequence).
3. Reactions are divided into two major groups, anabolism and catabolism.

B. **ANABOLIC REACTIONS** = synthesis reactions:

1. building complex molecules from simpler ones; (i.e. monomers into polymers);
2. constructive, synthesis reactions;
3. Bonds are formed between monomers which now hold energy (= ENDERGONIC reactions);
4. Water is removed between monomers to build the bond, termed DEHYDRATION.
5. energy ↓ C + D ⟶ C---D ↓ water

$$C + D \xrightarrow[\downarrow \text{ water}]{\text{energy } \downarrow} C\text{---}D$$

6. Example is to build a protein (polymer) from individual amino acids (monomers).

C. **CATABOLIC REACTIONS** = decomposition reactions:

1. breaking complex molecules into simpler ones; (i.e. polymers into monomers);
2. degradation, destructive, decomposition, digestion reactions;
3. Bonds are broken between monomers releasing energy (= EXERGONIC reactions);
4. Water is used to break the bonds, termed HYDROLYSIS.
5. water ↓ A---B ⟶ A + B ↓ energy

$$A\text{---}B \xrightarrow[\downarrow \text{ energy}]{\text{water } \downarrow} A + B$$

6. Example is breaking a nucleic acid (polymer) into nucleotides (monomers).

II. CONTROL OF METABOLIC REACTIONS

Enzyme Action

1. Definition: Enzymes are biological, **protein catalysts** that **increase the rate of a chemical (metabolic) reaction** without being consumed by the reaction.
2. Enzymes are globular proteins.
3. Enzymes are **specific** for the substance they act upon (called a **substrate**).
   a. Only a specific region of the enzyme molecule actually binds the substrate. This region is called the **Active Site**.
   b. The enzyme and substrate fit together like a "Lock and Key" through the active site on the enzyme.
4. Enzymes are unchanged by the reaction they catalyze and can be **recycled**
5. **Factors affecting the rate of chemical reactions**:
   a. **Particle size**: The smaller the particle, the faster the reaction will occur.
   b. **Temperature**: The higher the temperature, the faster the reaction will occur (up to a point).
   c. **Concentration**: The greater number of particles in a given space, the faster the reaction.
   d. **Catalysts**: Enzymes in biological systems.
6. **Metabolic pathways** involve several reactions in a row, with each reaction requiring a specific enzyme.
7. Enzyme names are often derived from the substrate that they act upon (providing the root of enzyme name), and the enzyme names typically end in the suffix **-ase**:
   a. The enzyme sucrase breaks down the substrate sucrose;
   b. A lipase breaks down a lipid,
   c. The enzyme DNA polymerase allows for DNA to be synthesized from DNA nucleotides.

Factors that Alter Enzymes

1. Enzymes can become inactive or even denature in extreme conditions
   a. extreme temperatures
   b. extreme pH values
   c. harsh chemicals

III. ENERGY FOR METABOLIC REACTIONS

A. **Energy** is the capacity to do work.
   1. Common forms include heat, light, sound, electrical energy, mechanical energy, and chemical energy.
   2. Energy cannot be created or destroyed, but it changes forms.
   3. All metabolic reactions involve some form of energy.

B. Release of Chemical Energy

1. Most metabolic reactions depend on chemical energy.
    a. This form of energy is held within the chemical bonds that link atoms into molecules.
    b. When the bond breaks, chemical energy is released.
    c. This release of chemical energy is termed **oxidation.**
    d. The released chemical energy can then be used by the cell for anabolism.
2. In cells, enzymes initiate oxidation by:
    a. decreasing activation energy of a reaction or
    b. transferring energy to special energy-carrying molecules called coenzymes.

IV. CELLULAR RESPIRATION (CR)

Introduction:

1. CR is how animal cells use oxygen to release chemical energy from food to generate cellular energy (ATP).
2. The chemical reactions in CR must occur in a particular sequence, with each reaction being catalyzed by a different (specific) enzyme. There are three major series of reactions:
    a. glycolysis
    b. citric acid cycle
    c. electron transport chain
3. Some enzymes are present in the cell's cytoplasm, so those reactions occur in the cytosol, while other enzymes are present in the mitochondria of the cell, so those reactions occur in the mitochondria.
4. All organic molecules (carbohydrates, fats, and proteins) can be processed to release energy, but we will only study the steps of CR for the breakdown of glucose ($C_6H_{12}O_6$).
5. **Oxygen is required** to receive the maximum energy possible per molecule of glucose and products of the reactions include water, CO_2, and cellular energy (ATP).
    a. Most of this energy is lost as heat.
    b. Almost half of the energy is stored in a form the cell can use, as ATP.
        - For every glucose molecule that enters CR usually 36 ATP are produced, however, up to 38 ATP can be generated.

IV. CELLULAR RESPIRATION (CR)

ATP MOLECULES

1. Adenosine Triphosphate (ATP) is the immediate source that drives cellular work.

2. **Structure of ATP**:
   a. adenine,
   b. ribose sugar, and
   c. three phosphate groups;

3. The triphosphate tail of ATP is unstable.
   a. The bonds between the phosphate groups can be broken by hydrolysis releasing chemical energy (EXERGONIC);
   b. A molecule of inorganic phosphate (P_i) and ADP are the products of this REACTION:

   ATP $\longrightarrow$ **Adenosine Diphosphate (ADP) + P_i;**

4. The inorganic phosphate from ATP can now be transferred to some other molecule which is now said to be "phosphorylated";

5. ADP can be regenerated to ATP by the addition of a phosphate in a endergonic REACTION;

   Adenosine Diphosphate (ADP) + P_i $\longrightarrow$ **ATP**

6. ATP and ADP shuttle back and forth between the energy-releasing reactions of CR and the energy-utilizing reactions of the cell.

7. If ATP is synthesized by direct phosphate transfer the process is called **substrate-level phosphorylation**

IV. CELLULAR RESPIRATION (CR)

GLYCOLYSIS:

1. means "splitting of sugar";
2. A **6-carbon sugar** is split into **two 3-C pyruvate** molecules;
3. occurs in the **cytoplasm** of the cell;
4. Oxygen is **not** required (i.e. anaerobic);
5. Energy yield is :
   a. **2 Net ATP** per glucose molecule, substrate-level phosphorylation
   b. **2 NADH** (stored electrons for ETS).
6. Many steps are required, and each is catalyzed by a different, specific enzyme;

Anaerobic Reactions

Recall that glycolysis results in pyruvate. If oxygen is not present (i.e. under anaerobic conditions), pyruvate can ferment in one of two ways:

1. **Lactic Acid Fermentation**:
   a. Pyruvate is converted to lactic acid, a waste product;
   b. occurs in many animal muscle cells;
   c. serves as an alternate method of generating ATP when oxygen is scarce;
   d. accumulation causes **muscle soreness and fatigue**.

2. **Alcohol Fermentation**:
   a. Pyruvate is converted to ethanol;
   b. occurs in yeasts (brewing) and many bacteria.

Aerobic Reactions (of Cellular Respiration)

1. **Conversion of Pyruvate to Acetyl Coenzyme A (Acetyl CoA)**:

   Under **aerobic** conditions (when O_2 is present):
   a. Pyruvate enters the **mitochondrion**;
      - Usually requires 1 ATP per pyruvate
   b. Pyruvate (3-C) is converted to acetyl CoA (2-C);
      - The carbon is released as CO_2.
   c. Energy yield is 1 NADH per pyruvate in this step (i.e. **2 NADH** per glucose)

IV. CELLULAR RESPIRATION (CR)

Aerobic Reactions (of Cellular Respiration)

2. **CITRIC ACID (KREBS) CYCLE**
   a. occurs in the **mitochondrial matrix**;
   b. Acetyl CoA adds its 2 carbons to oxaloacetate (4C) forming citrate (6C);
   c. 2-CO_2s are released during the series of steps where citrate (6C) is converted back to oxaloacetate (4C);.
   d Energy yield is:
      - **6 NADH** per glucose,
      - **2 $FADH_2$** per glucose;
      - **2 ATP** per glucose. Substrate-level phosphorylation
   e. involves many steps, each catalyzed by a different enzyme.

3. **ELECTRON TRANSPORT CHAIN (ETC)**

   a. is located in the **inner mitochondrial membrane** (recall "cristae");
   b. During electron transport, these molecules alternate between reduced and oxidized states as they accept and donate electrons.
   c. The **final electron (**and H) **acceptor is oxygen** which forms water.
   d. Yield of energy (ATP) from the ETC is:
      - **3 ATP/NADH** and
      - **2 ATP/$FADH_2$**
      - Made by oxidative phosphorylation

4. **Overall ATP Yield From Glucose in CR:**
   a. **4 ATP** are generated directly:
      - 2 from glycolysis;
      - 2 from Krebs.
   b. The remaining ATP is generated indirectly through coenzymes:
      10 NADH are produced:
      - 2 from glycolysis,
      - 2 from conversion, &
      - 6 from Krebs
        - The yield from NADH is **30 ATP**.
      - **2 $FADH_2$** are produced in the Krebs Cycle
        - The yield from $FADH_2$ is **4 ATP**.
   c. The **maximum** net yield of ATP per glucose = **38 ATP**.
      *****Most of the time it takes 2 ATP to move the 2 pyruvates into the mitochondrion, so normal ATP production is 36ATP.**

Carbohydrate Storage
Carbohydrates from digested food may enter catabolic or anabolic pathways.

1. Catabolic Pathways
   a. Monosaccharides enter cells and are used in CR.
   b. The cell can use the ATP generated for anabolic reactions.
2. Anabolic Pathways
   a. Monosaccharides (when in excess) can be:
      - stored as glycogen
      - converted to fat or essential amino acids.

Metabolism of Lipids and Proteins:

1. When liver glycogen stores are deplenished, fats and proteins can be metabolized to generate ATP.
2. All organic molecules enter CR at some point in the pathway.
3. **Stored fats are the greatest reserve fuel in the body**.
4. The metabolism of an 18-C lipid will yield 146 ATP by a process called **Beta Oxidation**, while the metabolism of 3 glucoses (18-C) will yield 108 ATP.

V. NUCLEIC ACIDS AND PROTEIN SYNTHESIS

A. **Introduction**: Because enzymes regulate metabolic pathways that allow cells to survive, cells must have the information for producing these special proteins. Recall from Chapter 2, that in addition to enzymes, proteins have several important functions in cells, including structure (keratin), transport (hemoglobin), defense (antibodies), etc.

B. **Genetic Information**
1. DNA holds the genetic information which is passed from parents to their offspring.
2. This genetic information, DNA, instructs cells in the construction of proteins (great variety, each with a different function).
3. The portion of a DNA molecule that contains the genetic information for making one kind of protein is called a **gene.**
4. All of the DNA in a cell constitutes the **genome**.
   a. Over the last decade, researchers have deciphered most of the human genome (see chapter 24, The Human Genome Project).
5. In order to understand how DNA (confined to the nucleus) can direct the synthesis of proteins (which occurs at ribosomes in the cytoplasm or on rough endoplasmic reticulum), we must take a closer look at the structure of DNA and RNA molecules.

Deoxyribonucleic Acid: (DNA)

1. DNA is composed of **nucleotides**, each containing the following:
    a. a **pentose sugar** molecule (deoxyribose);
    b. a **nitrogen-containing base**;
        - a purine (double ring);
            - adenine (A) or
            - guanine (G);
        - a pyrimidine (single ring);
            - cytosine (C) or
            - thymine (T);
    c. a **phosphate group**.

2. Each DNA strand is made up of a backbone of deoxyribose sugars alternating with phosphate groups.
3. Each deoxyribose sugar is linked to one of four nitrogen-containing bases: A,G,C, or T.
4. Each DNA molecule consists of two parallel strands of nucleotides running in opposite directions.
5. The bases in these nucleotide strands are joined to a complement base on the opposite strand by hydrogen bonds forming:
    - **adenine bonds thymine** (through 2 hydrogen bonds) and
    - **guanine bonds cytosine** (through 3 hydrogen bonds).
6. The two strands are twisted into a **double helix**.

Genetic Code

1. Specified by sequence of nucleotides in DNA.
2. Each **triplet** (three adjacent nucleotides) "codes" for an amino acid.
3. Many triplets code for many amino acids, which are hooked together to form a polypeptide chain
4. RNA molecules facilitate the conversion of DNA triplets to an amino acid sequence.

RNA Molecules: (Ribonucleic Acid)

1. RNA (like DNA) is composed of nucleotides, each containing the following:
   a. a pentose sugar molecule (**ribose**);
   b. a nitrogen-containing base;
      - purine:
        - adenine (A) or
        - guanine (G).
      - pyrimidine:
        - cytosine (C) or
        - **uracil (U)**;
   c. a phosphate group.

2. Each RNA strand is made up of a backbone of ribose sugars alternating with phosphate groups.

3. Each ribose sugar is linked to either A, G, C, or U.

4. Each RNA molecule consists of a **single strand** of nucleotides.

5. **TYPES OF RNA:**
   There are three types of RNA molecules which assist the cell in protein synthesis:

   a. **Messenger RNA (mRNA)** carries the code for the protein to be synthesized, from the nucleus to the protein synthesizing machinery in the cytoplasm (i.e. ribosome).

   b. **Transfer RNA (tRNA)** carries the appropriate amino acid to the ribosome to be incorporated into the newly forming protein.

   c. **Ribosomal RNA (rRNA)** along with protein make up the protein synthesizing machinery, the ribosome.

Protein Synthesis:

Protein synthesis can be divided into two major steps, transcription and translation.

1. **TRANSCRIPTION**
   a. occurs in the **nucleus** of the cell,

   b. is the process of copying the information (for a particular protein) from a DNA molecule (gene), and putting it into the form of a **messenger RNA (mRNA)** molecule.

   c. The DNA strands unwind and the H-bonds between the strands are broken; Only one of the exposed templates of the DNA molecule (i.e. the gene) is used to build the mRNA strand.
   RNA polymerase (an enzyme) positions and links RNA nucleotides (within the nucleus) into a strand.

   d. The message (mRNA):
   • is **complementary** to the bases on the DNA strand (i.e. If DNA sequence is TACGATTGCCAA, then the mRNA sequence is AUGCUAACGGUU);
   • is in the form of a triple base code, represented by **codons** (i.e. AUG, CUA, ACG, GUU).
   Each codon on mRNA codes for one amino acid in the protein to be synthesized.
   • can now **leave the nucleus** and travel to the **ribosome,** the protein synthesizing machinery.

2. **TRANSLATION**:
   a. is the process by which the mRNA is "translated" into a protein.

   b. occurs at **ribosomes** that are either free in the **cytoplasm** or are attached to ER (as **RER**).

   c. can only start at the **start codon AUG,** which codes for methionine

   d. **Transfer RNA (tRNA)** molecules assist in translation by bringing the appropriate amino acid for each codon to the ribosome.
   - The tRNA molecule has an **anticodon** which is complementary to the codon on the mRNA strand.
   - If the codon for Glycine is GGG, then the anticodon on the tRNA molecule that carries Glycine to the ribosome is CCC.

e. Two codons of mRNA are read in the ribosome at the same time.
   - The tRNA molecules deliver their amino acids to the ribosome, and a **peptide bond** is formed between adjacent amino acids.
   - The mRNA molecule is read codon by codon, with each corresponding amino acid being added to the chain of amino acids.
   - A protein is synthesized.

f. The mRNA molecule is read until a **stop codon (UAA, UAG, UGA)** on the mRNA is reached:
   - The protein is released into the cytoplasm or RER;
   - The mRNA molecule can be read again and again

DNA REPLICATION:

1. Introduction: DNA holds the genetic code which is passed from parents to their offspring. **During interphase** of the cell cycle, our DNA is replicated or duplicated so each new daughter cell is provided with an identical copy of this genetic material.

2. **PROCESS OF DNA REPLICATION:**
   a. DNA uncoils, and unzips (hydrogen bonds are broken between A:T and G:C);
      - o Each free nucleotide strand now serves as a template (a set of instructions) for building a new complementary DNA strand.

   b. DNA nucleotides that are present in the nucleoplasm begin to match up with their complements on the templates.
      - o **DNA polymerase** (an enzyme) positions and links these nucleotides into a strand.

   c. This results in two identical DNA molecules, each consisting of one old and one newly assembled nucleotide strand.
      - o This type of replication is called **semi-conservative replication**.

VI. CHANGES IN GENETIC INFORMATION

A. Introduction

Definition: If there is an error in the DNA code (i.e. in a gene), this is called a **mutation.**

B. Nature of Mutations

1. DNA replication errors
   a. Proteins are altered
   b. Usually **repair enzymes** prevent mutations

SUMMARY OF CELLULAR RESPIRATION

	GLYCOLYSIS	CONVERSION STEP	KREBS CYCLE	ELECTRON TRANSPORT CHAIN
LOCATION	**cytoplasm**	**mitochondria**	**mito matrix**	**mito inner membrane**
Oxygen Required?	**no**	**yes**	**yes**	**yes**
Starting Product	**glucose** (6-C)	2 pyruvates (2 x 3C)	Acetyl CoA (2 x 2C)	10 NADH 2 $FADH_2$
End-Products	2 pyruvates (2 x 3-C) **2 ATP** 2 NADH	2 Acetyl CoA 2 NADH 2 CO_2	6 NADH 2 $FADH_2$ 2 ATP 4 CO_2	30 ATP 4 ATP 4 ATP 38 ATP
TOTAL		Minus 2 ATP for Pyruvate to enter mitochondria		**36 ATP**

PROTEIN SYNTHESIS SUMMARY TABLE

MAJOR STEP	**TRANSCRIPTION**	**TRANSLATION**
GENERAL DESCRIPTION	when the code (gene) for a protein to be synthesized is copied from the DNA and is put in the form of a Messenger RNA strand (mRNA)	when a strand of mRNA (carrying the code for the protein to be synthesized) is translated into a protein
LOCATION IN CELL	Nucleus	at a ribosome that is either free in the cytoplasm or on rough endoplasmic reticulum
MOLECULES INVOLVED AND HOW?	DNA: unwinds & unzips RNA Polymerase (an enzyme) positions the complementary RNA nucleotides along the DNA template and zips up their backbone.	mRNA carries the protein code to the ribosome. Ribosome is the protein synthesizing machinery. Transfer RNA (tRNA) brings the appropriate amino acid to the ribosome to be incorporated into the protein. Many enzymes.
OVERALL RESULT	A strand of mRNA	A protein