CBC NOTES COMPILED BY MODEST TRUST

CBC NOTES: RESPIRATION 2025

These notes are dedicated to all students and teachers in Uganda in efforts to promote teaching and learning of biology as a subject.

Disclaimer: ***These notes reflect my understanding and interpretation of respiration, based on trusted sources including Biological Science, Advanced Biology, Understanding Biology, Functional Approach, Campbell Biology, Biology in Context, and other reputable online resources. They are intended for educational use and may be subject to future updates or corrections. The notes have been focused on the current ADVANCED LEVEL CURRICULUM 2025. Please contact me for further clarifications or suggestions.***

- ✓ Hope you find this material useful

All living organisms require energy in order to remain alive. This energy comes initially from the **Sun** (or in a few instances from chemicals). Plants use solar energy to combine water and oxygen into complex organic molecules by the process of **photosynthesis**. Both plants and animals then break down these organic molecules to make **adenosine triphosphate (ATP)** that is used as the energy source to carry out processes that are essential to life.

RESPIRATION

This is the oxidation of organic substance to liberate energy in the body. Aerobic respiration requires oxygen whereas anaerobic respiration does not require oxygen.

Organic molecules (usually carbohydrate or fat) are broken down bond by bond, by a series of enzyme - controlled reactions. Each bond broken releases a small amount of energy converted to adenosine triphosphate (ATP). ATP is the immediate source of energy for cellular reactions.

Why do organisms need energy?

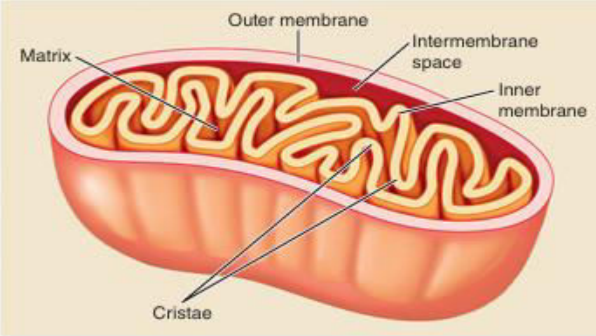
Without some input of energy, natural processes tend to break down in randomness and disorder. Living organisms are highly ordered systems that require a constant input of energy to prevent them becoming disordered – a condition that would lead to their death. More particularly energy is needed for:

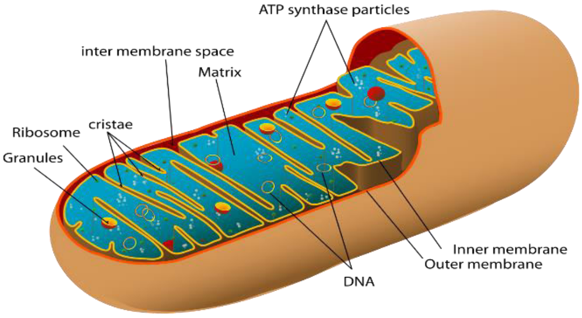
- **Anabolism**, in which smaller, more simple substances are built up into larger, more complex ones, e.g. during DNA replication, in which nucleotides are joined by condensation reactions to form polynucleotides, and protein synthesis, in which amino acids are joined together to form polypeptides.

- **Movement** both within an organism (e.g. circulation of blood) and of the organism itself (e.g. locomotion due to muscular contraction or movement of cilia and flagella).
- **Active transport** of ions and molecules against a concentration gradient across membranes, such as the cell surface membrane and the tonoplast, e.g. the **sodium-potassium pump**.
- **Maintenance, repair and division** of cells and the organelles within them.
- **Maintenance of body temperature** in birds and mammals. These organisms are **endothermic** and need energy to replace heat that lost as heat to the surrounding environment.

As discussed in cytology, the mitochondria is the power house of the cell

STRUCTURE OF THE MITOCHONDRIA





Mitochondria are compact organelles, typically measuring about **0.5–1.0** in diameter and **2–7micrometres** in length, presenting as spherical or rod-shaped bodies. Each is enclosed by **two phospholipid membranes**: the **outer membrane**, which is smooth and relatively permeable, and the **inner membrane**, which is extensively folded, forming projections called **cristae** that extend into the central space. This central space is the **matrix**, a dense, fluid-filled compartment housing key enzymes, **circular DNA**, **ribosomes**, and phosphate granules. The space between the two membranes is the **intermembrane space**. Critically, the number and shape of mitochondria vary widely depending on the cell's energy demands—**muscle cells have many**, whereas **red blood cells have none**.

FUNCTIONAL ADAPTATIONS FOR ENERGY SYNTHESIS

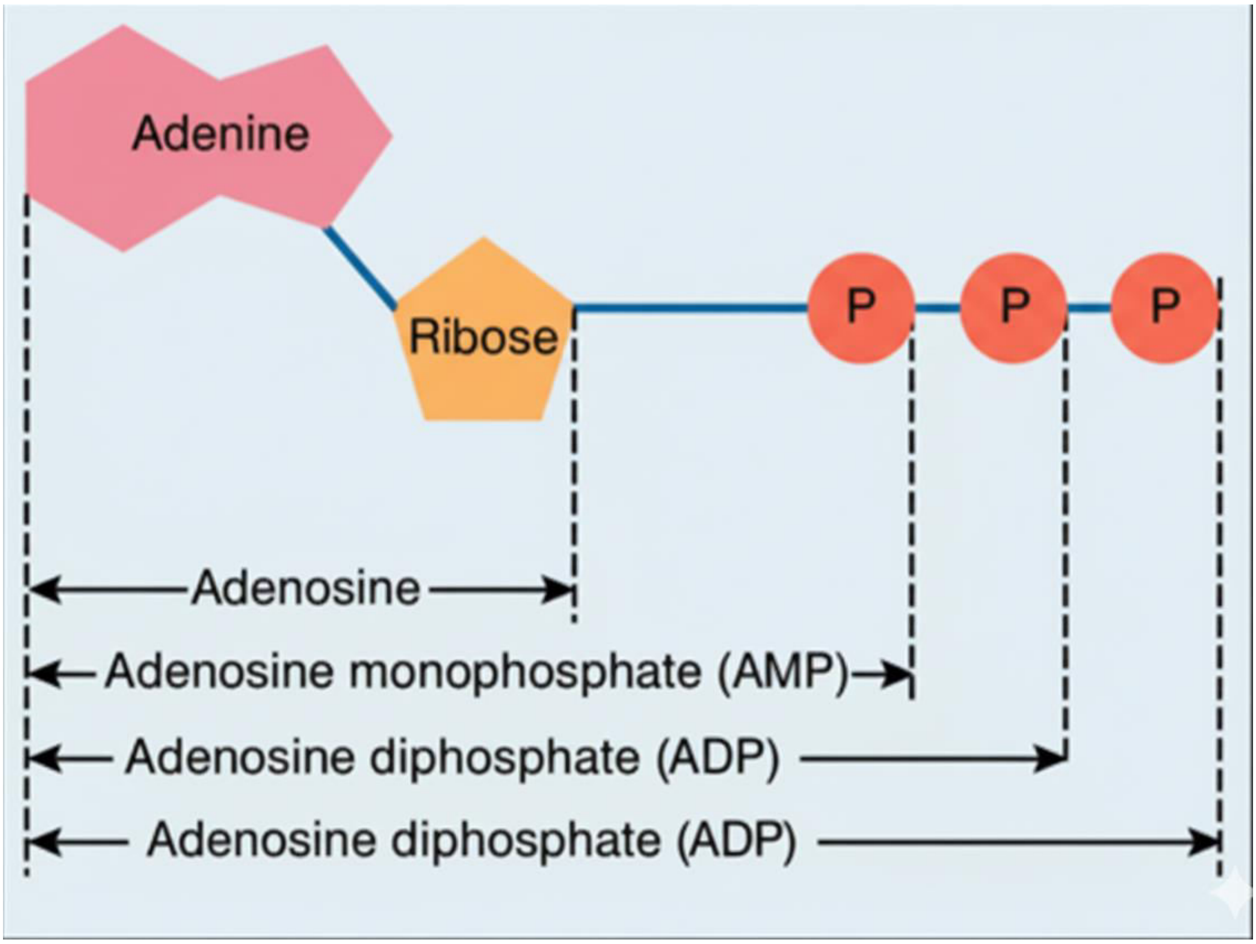
The structural components of the mitochondrion are perfectly adapted to ensure the highly efficient production of **ATP**:

- **Double membrane enclosure:** The presence of both membranes creates **compartmentalization**, effectively isolating respiration processes from the cytoplasm.

This is essential for the rapid establishment of the **ion gradients** necessary for ATP synthesis.

- **Small size and variable shape:** The compact size and flexible shape (spherical, rod-like, or filamentous) provide a **high surface area-to-volume ratio**, which facilitates the efficient uptake and release of **metabolites** required for respiration.
- **Folded inner membrane (Cristae):** The extensive folding into cristae dramatically **increases the available surface area**. This allows the membrane to accommodate a greater number of proteins for the **electron transport chain** and **ATP synthase**, substantially **enhancing ATP production** in active cells.
- **Narrow intermembrane space:** The thinness of this space allows a **steep proton concentration gradient** to be rapidly generated. This gradient powers **chemiosmosis**, driving highly efficient ATP synthesis.
- **Dense matrix:** The matrix is densely packed with enzymes for the **Krebs (citric acid) cycle**, as well as ribosomes and circular DNA. This ensures the **efficient processing of respiratory substrates** and allows for internal protein production, reducing reliance on cytoplasmic sources.
- **Autonomous genetic system:** The presence of **circular DNA and ribosomes** enables the mitochondria to synthesize critical proteins internally. This guarantees a **fast response to energy requirements** and provides genetic independence for core respiratory functions.
- **Membrane composition:** Differences in protein-to-lipid ratios (outer approx 50:50, inner approx 80:20) reflect specialized roles: the outer membrane's permeability for exchange versus the inner membrane's **high protein density** for electron transport and ATP production.
- **Variable abundance:** The number of mitochondria and the packing density of their cristae **adjust according to cell energy needs**. Energetically active cells, like muscle, possess many mitochondria with closely packed cristae for maximum ATP output, while inactive cells have few or none.

THE STRUCTURE OF ATP AND RELEASE OF ENERGY

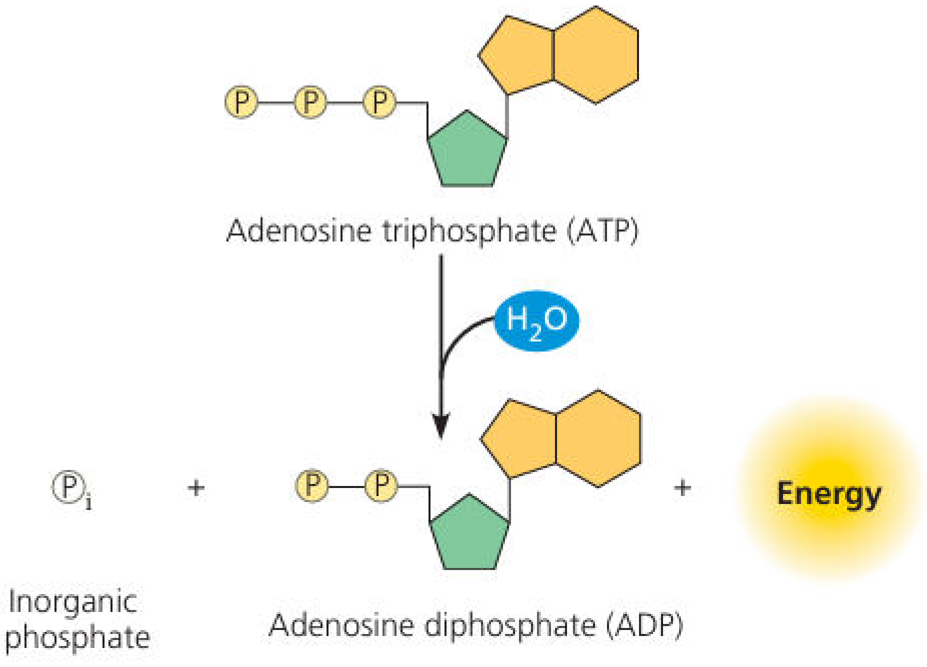


The universal energy currency of all cells is a molecule called adenosine triphosphate (ATP). Almost every energy-requiring process in cells uses ATP. It is a small water-soluble molecule and therefore easily transported around the cell. Some of the features that help to explain why ATP is suitable as the universal energy currency include:

- A one-step reaction provides an immediate source of energy
- It is easily hydrolysed to release energy
- A constant supply of ATP is possible as it is recycled from ADP, which is easily phosphorylated
- it is a relatively small molecule that can move around the cell with ease
- It is a water-soluble molecule so it can take part in metabolic reactions
- The quantity of energy released and the efficiency of recycling ATP means that the needs of the cell can be satisfied.

It is the phosphate groups in ATP that are the key to how ATP is the energy currency of the cell. Each one is very negatively charged and so they repel one another. The covalent bonds connecting each phosphate are rather unstable. These unstable covalent bonds have a low activation energy, which means they are easily broken and when they are, they release a considerable amount of energy – 30.5 kJ mol^{-1} for each of the first two phosphate groups and 14.2 kJ mol^{-1} for the removal of the final phosphate. The terminal phosphate is removed according to the enzyme-catalysed reversible equation:

$ATP + H_2O \rightarrow ADP + Pi + 30.5\ kJ$



(b) The hydrolysis of ATP. The reaction of ATP and water yields inorganic phosphate (P_i) and ADP and releases energy.

THE PRODUCTION OF ENERGY

The synthesis of ATP can be accomplished by two distinct mechanisms: one that involves chemical coupling with an intermediate bound to phosphate and another that relies on an electrochemical gradient of protons for the potential energy to phosphorylate ADP.

1. In substrate-level phosphorylation, ATP is formed by transferring a phosphate group directly to ADP from a phosphate-bearing intermediate, or substrate. During glycolysis, the initial breakdown of glucose, the chemical bonds of glucose are rearranged to produce intermediates that can transfer phosphate to ADP.

2. In oxidative phosphorylation, ATP is synthesized by the enzyme ATP synthase, using energy from a proton (H+) gradient. This gradient is formed by high-energy electrons removed by the oxidation of glucose passing down an electron transport chain. These electrons reach their lowest energy level when they are transferred to oxygen; hence the term oxidative phosphorylation. ATP synthase uses the energy from the proton gradient to catalyze the reaction:

ADP + Pi → ATP

Respiration in aerobic conditions can be divided into four stages:

1) Glycolysis – an enzyme-controlled pathway in which one molecule of 6-carbon glucose is converted into two 3-carbon pyruvate molecules.
2) Link reaction (pyruvate oxidation) – the 3-carbon pyruvate molecule is converted into carbon dioxide and a 2-carbon molecule called acetyl coenzyme A.
3) Krebs cycle – the introduction of acetyl coenzyme A into a cycle of eight enzyme-catalysed reactions that yield reduced coenzymes NAD and FAD and some ATP.
4) Oxidative phosphorylation (electron transport system) – oxidation of reduced NAD and FAD as part of an electron transport chain and ATP synthesis by chemiosmosis. Oxygen is required as a final electron acceptor and water is produced.

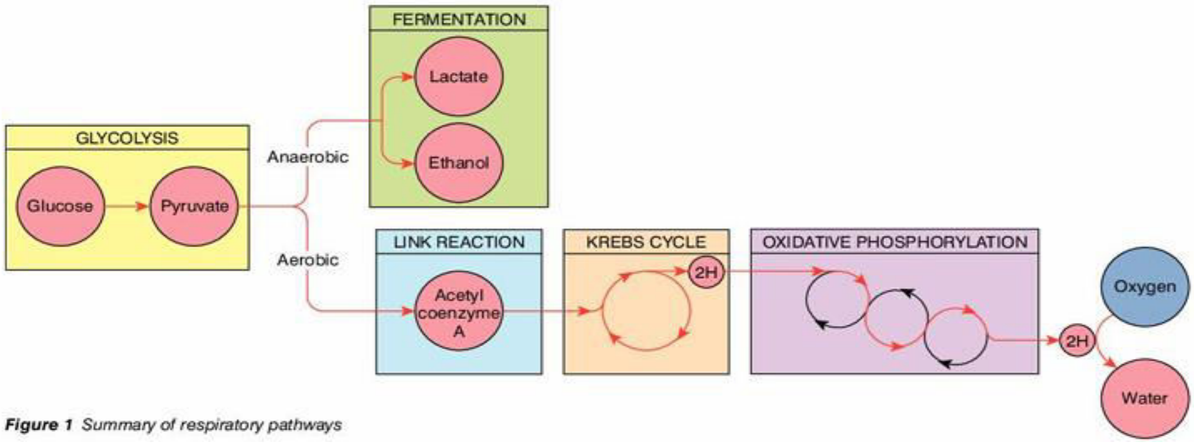
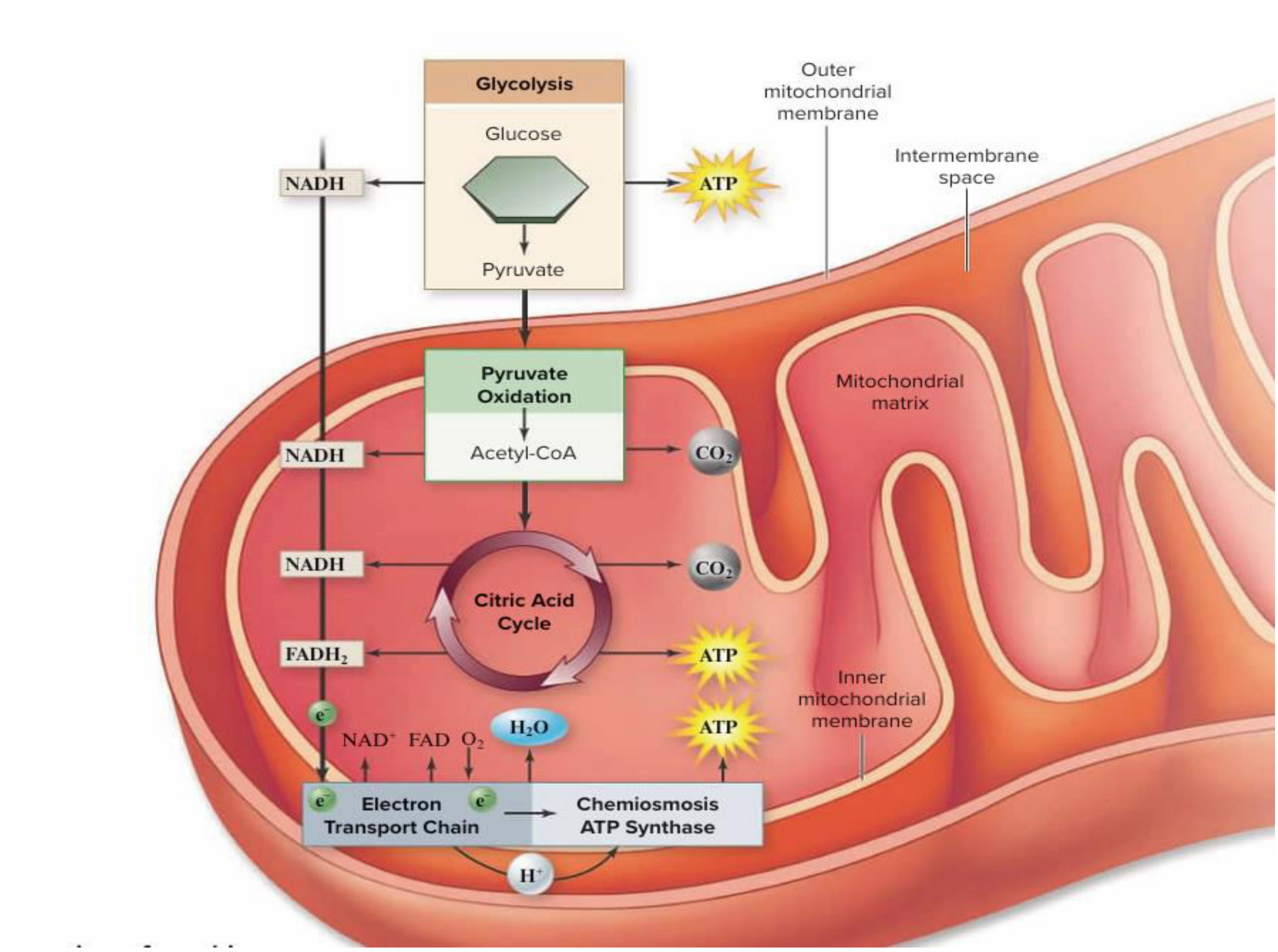


Figure 1 *Summary of respiratory pathways*



Each of the four processes consists of a distinctive starting molecule, a series of chemical reactions, and a characteristic set of products.

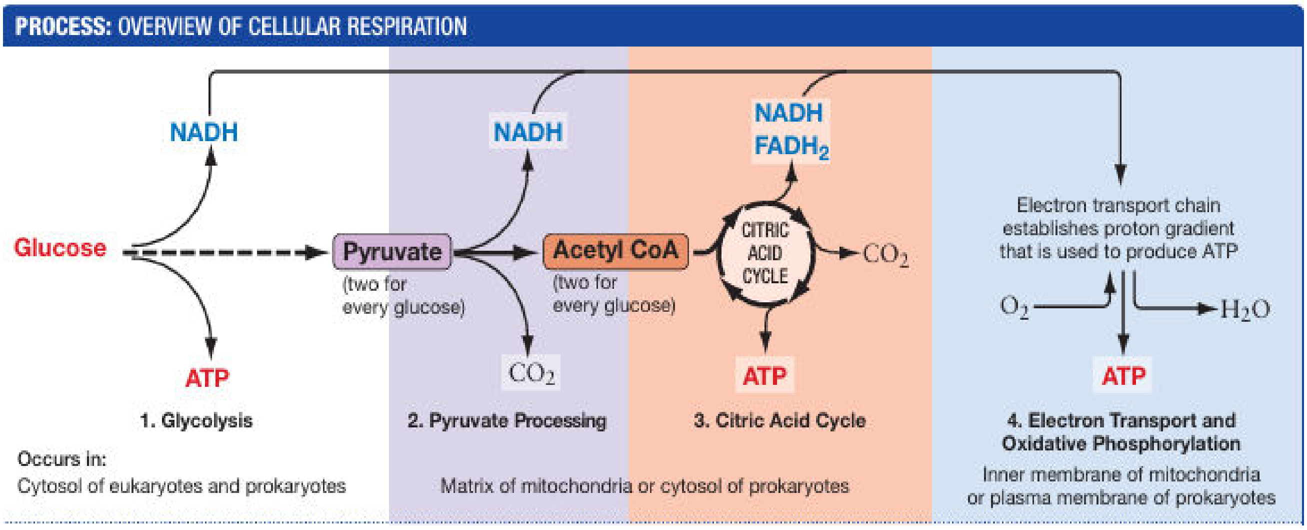
1. **Glycolysis:** In glycolysis, one six-carbon molecule of glucose is broken into two molecules of the three-carbon compound pyruvate. During this process, ATP is produced from ADP and Pi, and nicotinamide adenine dinucleotide is reduced to form NADH.

2. **Pyruvate processing**: Each pyruvate produced by glycolysis is processed to release one molecule of CO_2, and the remaining two carbons are used to form the compound acetyl CoA. The oxidation of pyruvate results in more NAD being reduced to NADH.

3. **Citric acid cycle**: The two carbons from each acetyl CoA produced by pyruvate processing are oxidized to two molecules of CO_2. During this sequence of reactions, more ATP and NADH are produced, and flavin adenine dinucleotide (FAD) is reduced to form FADH.

4. **Electron transport and oxidative phosphorylation**: Electrons from the NADH and FADH2 produced by pyruvate processing and the citric acid cycle move through a series of electron carriers that together are called an electron transport chain (ETC). The energy

obtained from this chain of redox reactions is used to create a proton gradient across a membrane; the ensuing flow of protons back across the membrane is used to make ATP. Because this mode of ATP production links oxidation of NADH and FADH2 with phosphorylation of ADP, it is called oxidative phosphorylation.



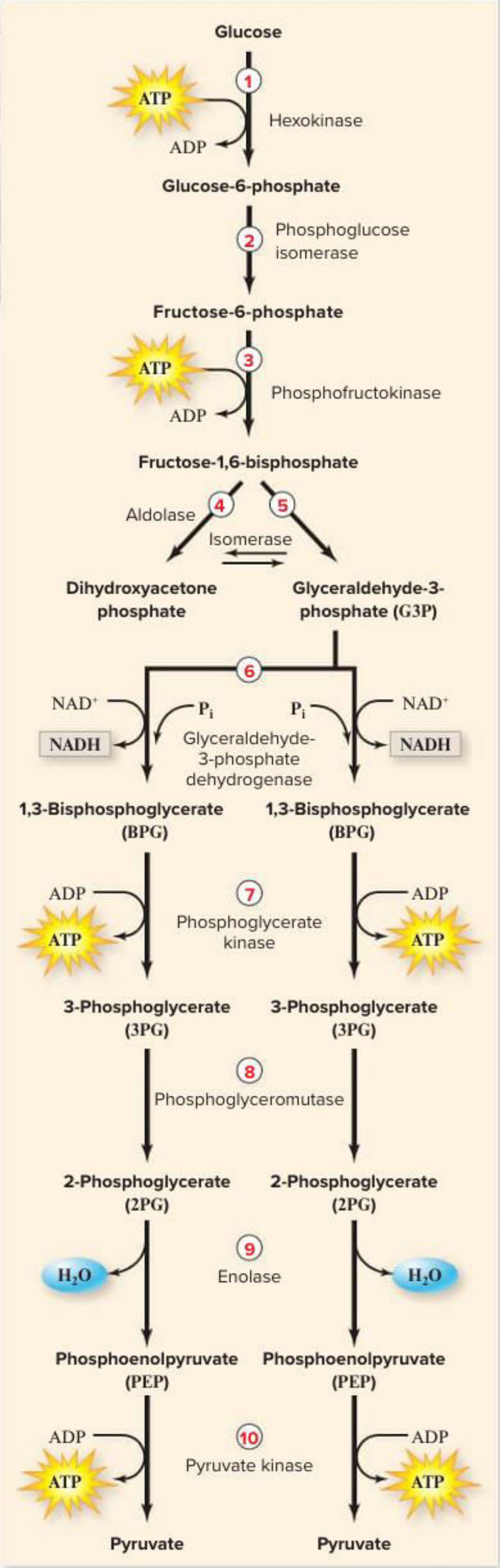
GLYCOLYSIS

This occurs in the cytosol of the cell. The word glycolysis means "sugar splitting," and that is exactly what happens during this pathway. Glucose, a six carbon sugar, is split into two three-carbon sugars. These smaller sugars are then oxidized and their remaining atoms rearranged to form two molecules of pyruvate. (Pyruvate is the ionized form of pyruvic acid.) Glycolysis can be divided into two phases: the energy investment phase and the energy payoff phase. During the energy investment phase, the cell actually spends ATP. This investment is repaid with interest during the energy payoff phase, when ATP is produced by **substrate-level phosphorylation** and NAD+ is reduced to NADH by electrons released from the oxidation of glucose. The net energy yield from glycolysis, per glucose molecule, is 2 ATP plus 2 NADH. All of the carbon originally present in glucose is accounted for in the two molecules of pyruvate; no carbon is released as CO_2 during glycolysis. Glycolysis **occurs whether or not O2 is present**. However, if O_2 is present, the chemical energy stored in pyruvate and NADH can be extracted by pyruvate oxidation, the citric acid cycle, and oxidative phosphorylation.

THE 10 STEPS OF GLYCOLYSIS

1) In the first step, hexokinase transfers a phosphate group from **ATP** to **glucose**, making **glucose-6-phosphate** and trapping the sugar inside the cell.
2) **Glucose-6-phosphate** is converted into **fructose-6-phosphate** through the action of **phosphoglucose isomerase**, changing the arrangement of its atoms.
3) Then, **phosphofructokinase** uses another **ATP** molecule to add a second phosphate group to **fructose-6-phosphate**, producing **fructose-1,6-bisphosphate** and committing the molecule to **glycolysis**.
4) In the fourth step, **aldolase** splits **fructose-1,6-bisphosphate** into two three-carbon molecules: **glyceraldehyde-3-phosphate (G3P)** and **dihydroxyacetone phosphate (DHAP)**.
5) **Isomerase** rapidly converts **DHAP** into **G3P**, ensuring that all products continue down the **glycolysis** pathway.
6) During the sixth step, **glyceraldehyde-3-phosphate dehydrogenase** catalyzes two reactions: **G3P** is oxidized and a phosphate group is added, forming **1,3-bisphosphoglycerate** and producing **NADH** from **NAD+**.
7) **Phosphoglycerokinase** then transfers a phosphate from **1,3-bisphosphoglycerate** to **ADP**, resulting in the formation of **ATP** and **3-phosphoglycerate**.
8) The enzyme **phosphoglyceromutase** relocates the phosphate group within **3-phosphoglycerate**, forming **2-phosphoglycerate**.
9) The enzyme **enolase** removing a water molecule from **2-phosphoglycerate**, resulting in the creation of **phosphoenolpyruvate (PEP)**, a molecule with very high energy potential.
10) Finally, **pyruvate kinase** transfers the phosphate group from **PEP** to **ADP**, forming **ATP** and **pyruvate**, thus completing the **glycolysis** pathway.

Glycolysis: The Reactions



1. Phosphorylation of glucose by ATP.

2–3. Rearrangement, followed by a second ATP phosphorylation.

4–5. The 6-carbon molecule is split into two 3-carbon molecules—one G3P, another that is converted into G3P in another reaction.

6. Oxidation followed by phosphorylation produces two NADH molecules and two molecules of BPG, each with a phosphate that can be transferred to ADP.

7. Transfer of two phosphate groups to two ADP molecules produces two ATP and two 3PG molecules.

8–9. Removal of water yields two PEP molecules, each with a phosphate group that can be transferred to ADP.

10. Transfer of two phosphate groups to two ADP molecules produces two ATP and two pyruvate molecules.

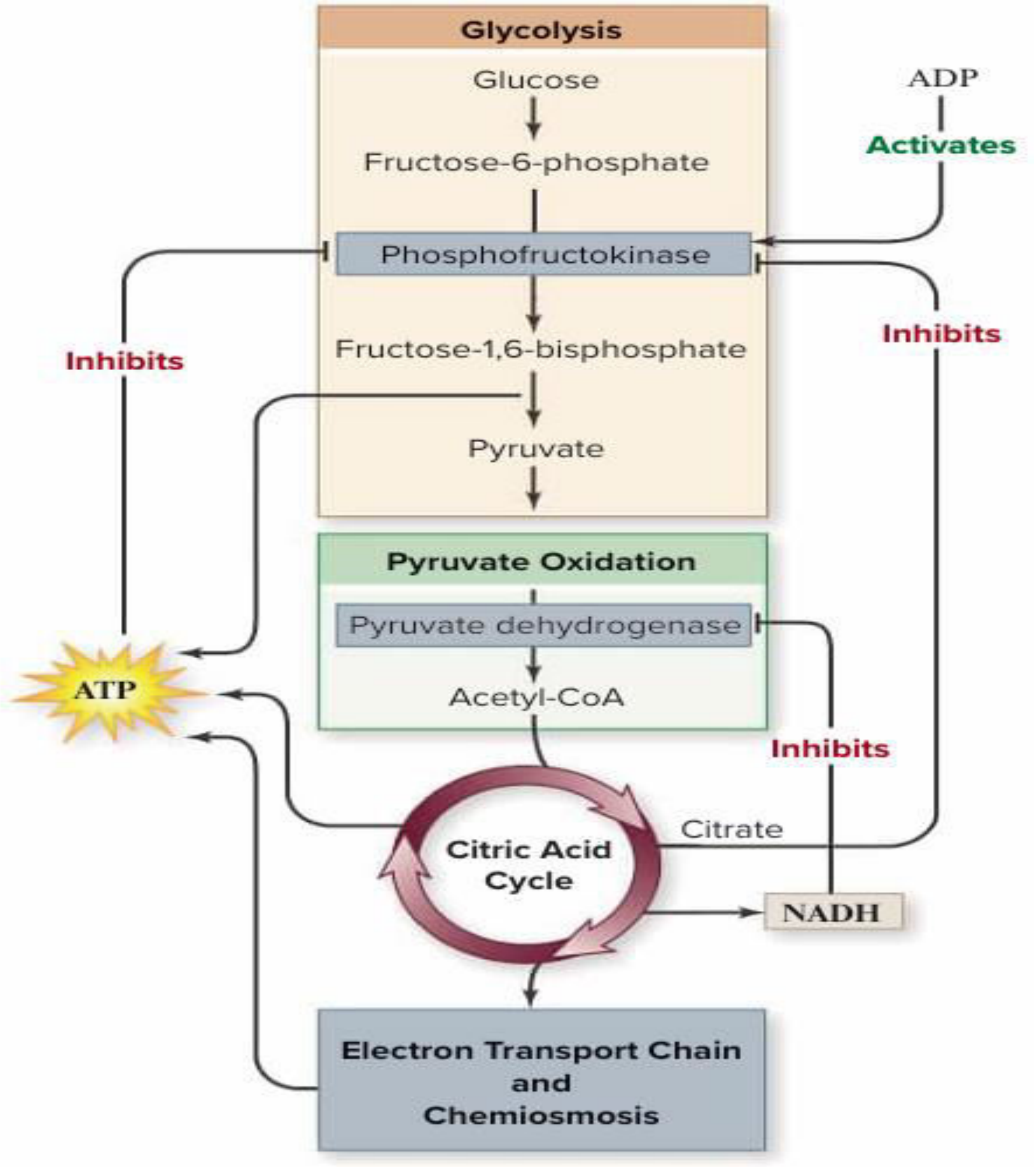
TABLE SUMMARISING GLYCOLYSIS

Step	**Enzyme**	**Key reaction and product**	**Energy or molecule involved**
1	**Hexokinase**	**Phosphorylation** of glucose at C6 to form Glucose-6-phosphate.	Consumes **1 ATP**; increases potential energy.
2	**Phosphoglucose isomerase**	**Isomerization** (rearrangement) of Glucose-6-phosphate to Fructose-6-phosphate.	None.
3	**Phosphofructokinase**	**Phosphorylation** of Fructose-6-phosphate at C1 to form Fructose-1,6-bisphosphate.	Consumes **1 ATP**; increases potential energy.
4	**Fructose-bis-phosphate aldolase**	**Cleavage** of Fructose-1,6-bisphosphate into two 3-carbon sugars: **DHAP** and **G3P**.	None.
5	**Triose phosphate isomerase**	**Interconversion** of DHAP into another molecule of **G3P**.	None. Favors G3P formation.
6	**Glyceraldehyde-3-phosphate dehydrogenase**	**Oxidation** of G3P and transfer of a phosphate (Pi) to form **1,3-bisphosphoglycerate**	Produces **1 NADH** (per G3P/per 3C molecule).
7	**Phosphoglycerate kinase**	**Substrate-level phosphorylation:** Transfers a phosphate from 1, 3-bisphosphoglycerate to ADP to make **3-phosphoglycerate**.	Produces **1 ATP** (per G3P/per 3C molecule).
8	**Phosphoglycerate mutase**	**Rearrangement** of the phosphate on 3-phosphoglycerate to form **2-phosphoglycerate**.	None.
9	**Enolase**	**Dehydration:** Removes a water molecule from 2-phosphoglycerate to form **Phosphoenolpyruvate (PEP)**.	None.
10	**Pyruvate kinase**	**Substrate-level phosphorylation:** Transfers a phosphate from PEP to ADP to make **Pyruvate**.	Produces **1 ATP** (per G3P/per 3C molecule).

REGULATION OF GLUCOSE METABOLISM

- Control of glucose catabolism occurs at two key points in the catabolic pathway, namely, at a point in glycolysis and at the beginning of the citric acid cycle. The control point in glycolysis is the enzyme phosphofructokinase, which catalyzes the conversion of fructose phosphate to fructose bisphosphate. This is the first reaction of glycolysis that is not readily reversible, committing the substrate to the glycolytic sequence. ATP itself is an allosteric inhibitor of phosphofructokinase, as is the citric acid cycle intermediate citrate. High levels of both ATP and citrate inhibit phosphofructokinase. Thus, under conditions when ATP is in excess, or when the citric acid cycle is producing citrate faster than it is being consumed, glycolysis is slowed.

- The main control point in the oxidation of pyruvate occurs at the committing step in the citric acid cycle with the enzyme pyruvate dehydrogenase, which converts pyruvate to acetyl-CoA. This enzyme is inhibited by high levels of NADH, a key product of the citric acid cycle.
- Another control point in the citric acid cycle is the enzyme citrate synthetase, which catalyzes the first reaction, the conversion of oxaloacetate and acetyl-CoA into citrate. High levels of ATP inhibit citrate synthetase (as well as phosphofructokinase, pyruvate dehydrogenase, and two other citric acid cycle enzymes), slowing down the entire catabolic pathway



THE LINK REACTION AND THE KREBS CYCLE

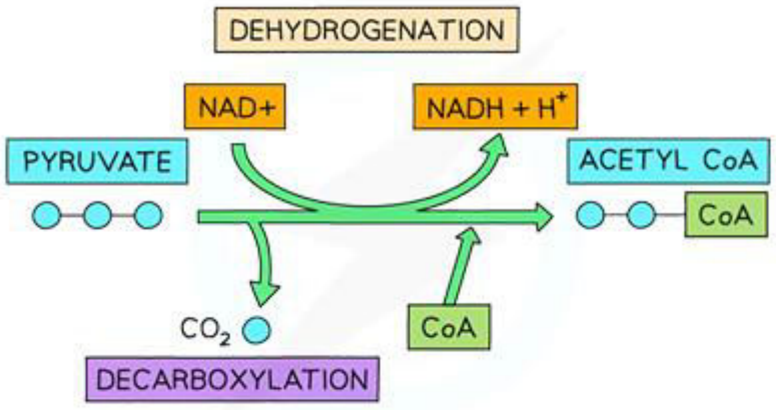
The pyruvate molecules produced during **glycolysis** possess potential energy that can only be released in a process called the **Krebs cycle**. Before they can enter the Krebs cycle, these pyruvate molecules must first be oxidized in a procedure known as the **link reaction**. In **eukaryotic cells** both the Krebs cycle and the link reaction take place exclusively inside **mitochondria** and these will only occur if oxygen is available.

THE LINK REACTION

The pyruvate molecules produced in the cytoplasm during glycolysis are actively transported into the **matrix of mitochondria**. Here pyruvate undergoes a complex series of oxidation-reduction reactions that are catalyzed by a multienzyme complex (pyruvate dehydrogenase). During these reactions the following changes take place:

- A carbon dioxide molecule is removed from each pyruvate (= **decarboxylation**) by means of the enzyme **pyruvate decarboxylase**.
- **Oxidation** of pyruvate results in the reduction of NAD to form **reduced NAD** (later used to produce ATP).
- The 2-carbon molecule that is formed is called an acetyl group and combines with a cofactor called **coenzyme A (CoA)** to produce a 2-carbon compound called **acetyl coenzyme A.**

The overall equation can be summarized as:

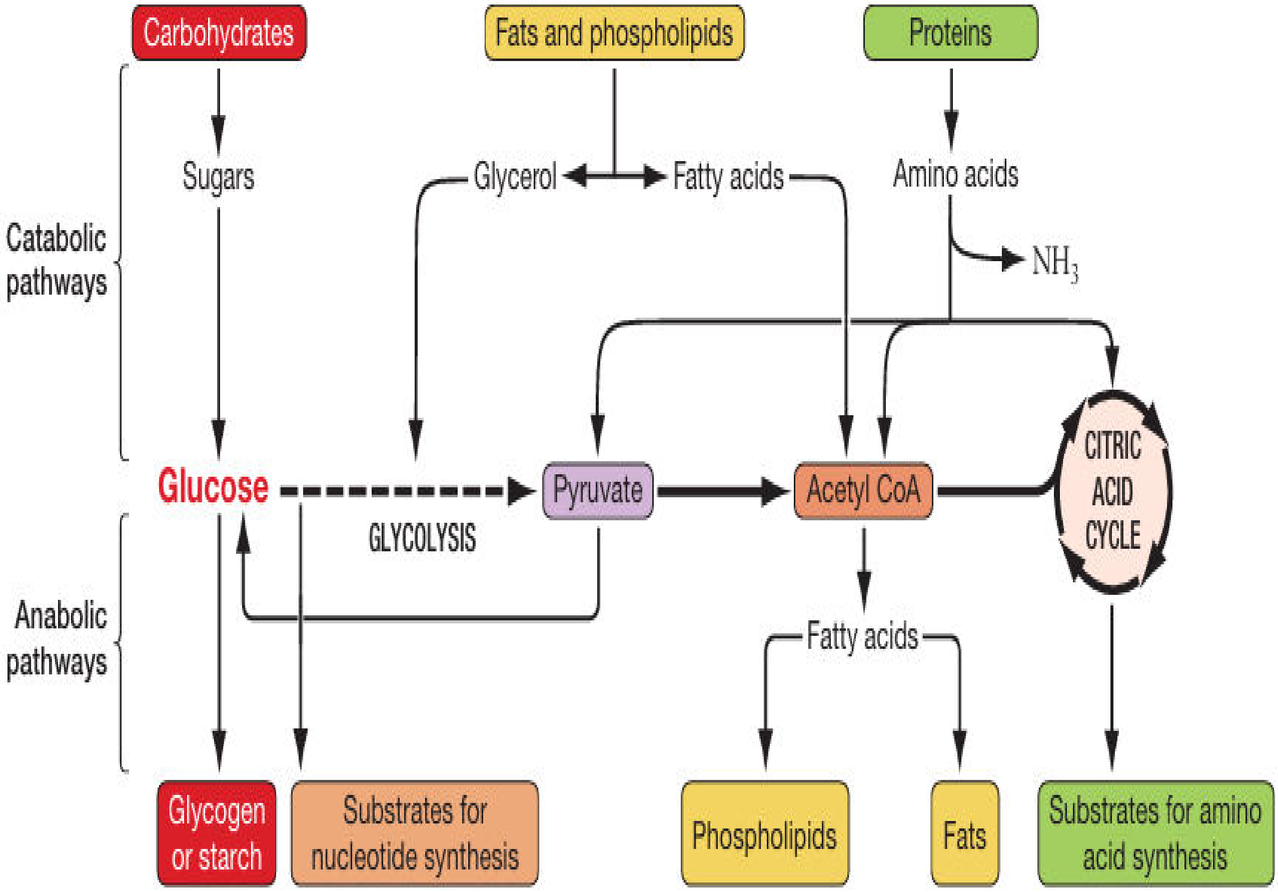


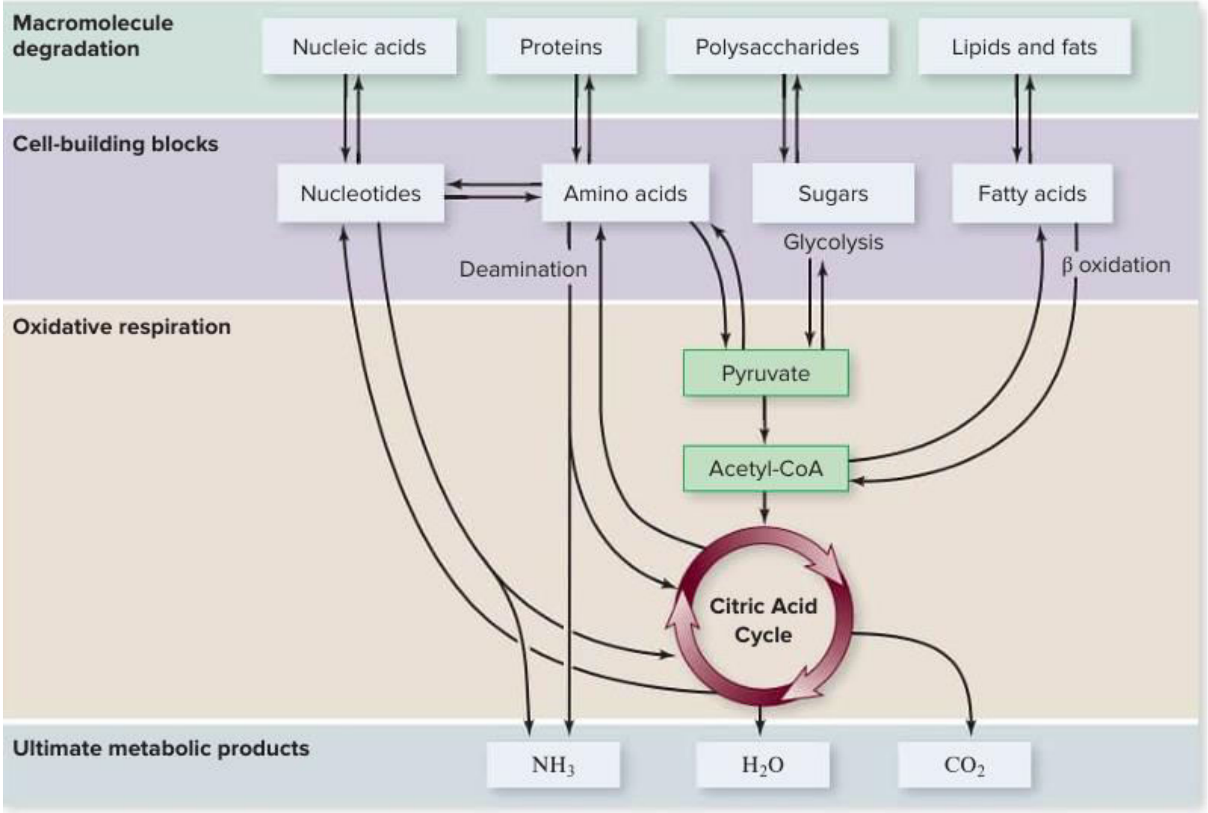
THE IMPORTANCE OF ACETYL COENZYME A IN CARBOHYDRATE, PROTEINS AND LIPID METABOLISM

A coenzyme is a molecule that helps an enzyme carry out its function but is not used in the reaction itselfCoenzyme A is made up of vitamin B_5, the organic base adenine and the sugar ribose. It carries the acetyl group made from pyruvate into the Krebs cycle in the form of acetyl coenzyme A. The acetyl coenzyme A molecule is important because most molecules that are used by living organisms for energy are made into acetyl coenzyme A before entering the Krebs cycle. Most carbohydrates and fatty acids can be metabolized into acetyl coenzyme A to release energy. In the case of fats, these are first hydrolyzed into glycerol and fatty acids. The glycerol can then be converted into triose phosphate that can be broken down during glycolysis, while the fatty acids are progressively broken down in the matrix of the mitochondria into 2-carbon fragments that are converted into acetyl coenzyme A. The reverse is also true, namely that excess carbohydrate can be made into fats via acetyl coenzyme A, making it a pivotal molecule in the interconversion of major substances in eukaryotic cells.

Carbohydrates are not the only important source of carbon compounds used in catabolic pathways, however. Fats are highly reduced macromolecules consisting of glycerol bonded to chains of fatty acids. In cells, enzymes routinely break down fats to release the glycerol and convert the fatty acids into acetyl-coA molecules. Glycerol can be further processed and enter glycolysis as an intermediate. Acetyl CoA enters the citric acid cycle.

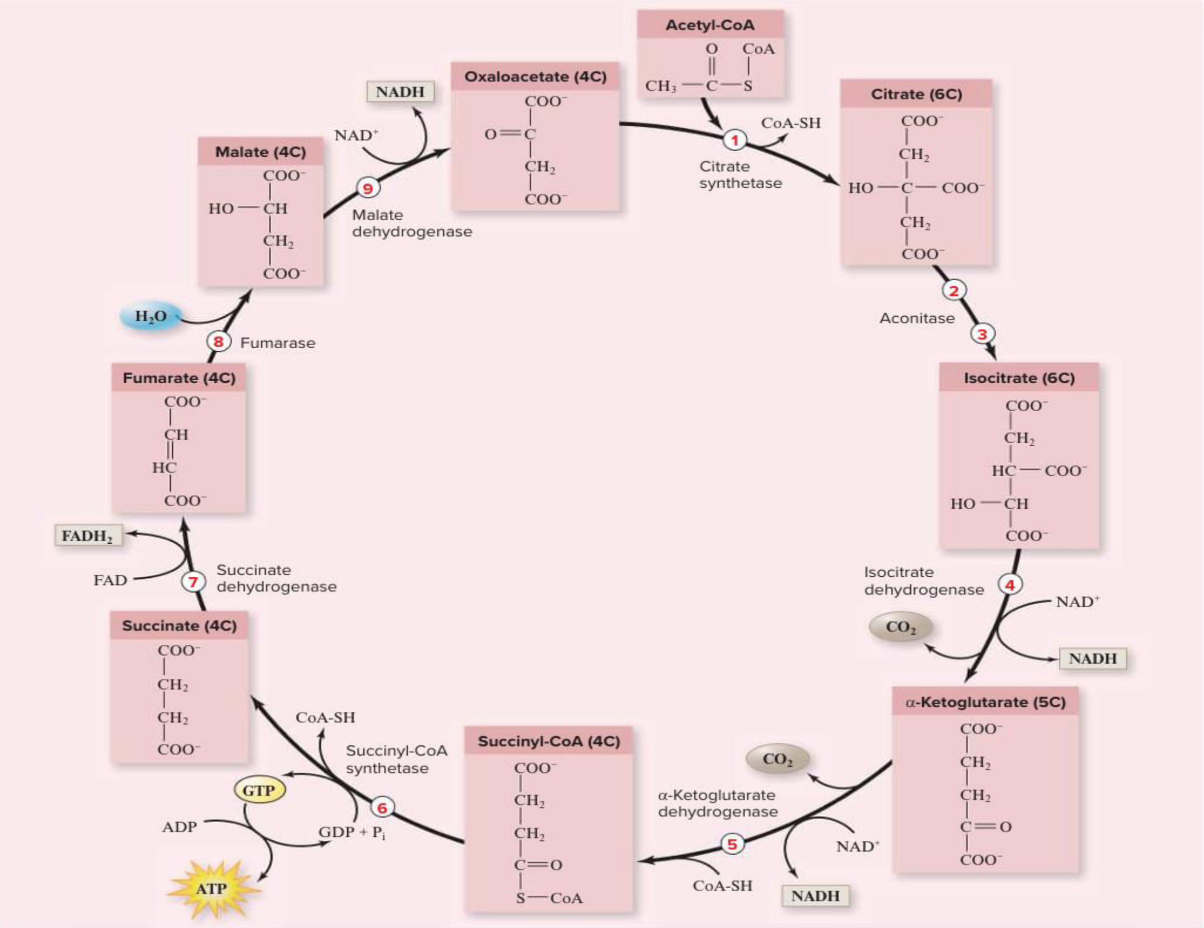
Proteins can also be catabolized, meaning that they can be broken down and used to produce ATP. Once they are hydrolyzed to their constituent amino acids, enzyme-catalyzed reactions remove the amino − (NH_2) groups (deamination). The amino groups are excreted in urine as waste, and the remaining carbon compounds are converted to pyruvate, acetyl CoA, or other intermediates in glycolysis and the citric acid cycle.





AEROBIC RESPIRATION: CITRIC ACID CYCLE (KREBS CYCLE)

The **Krebs cycle** (also known as the **Citric Acid Cycle** or **Tricarboxylic Acid (TCA) Cycle**) is a central metabolic pathway responsible for the final complete oxidation of glucose derivatives during cellular respiration. Named after its discoverer, Hans Krebs, this cyclic process involves **eight small carboxylic acids** that are oxidized in sequence. The cycle's critical feature is that the initial acceptor molecule, oxaloacetate, is **regenerated** after each turn. Located in the mitochondrial matrix of eukaryotes, the Krebs cycle is fueled by the 2-carbon **acetyl group** delivered by acetyl-coA (the product of pyruvate oxidation), ultimately yielding **three NADH, one FADH, and one ATP** per turn, driving the bulk of energy production for the cell.



The stages involved in the tricarboxyllic acid cycle

1) Acetyl CoA, a two-carbon molecule derived from pyruvate, combines with oxaloacetate, a four-carbon molecule, to form citrate, a six-carbon compound beginning the cycle under catalysis of **citrate synthase**.
2) Citrate is then rearranged into its isomer, isocitrate, through a process involving the removal and addition of a water molecule. In this step, the enzyme **aconitase** catalyses the isomerization of citrate to isocitrate.
3) Isocitrate undergoes oxidation, causing NAD to be reduced to **NADH**, and the molecule loses a carbon as CO_2, forming the five-carbon compound, alpha-ketoglutarate, under catalysis of **isocitrate dehydrogenase**.
4) Alpha-Ketoglutarate is then oxidized and loses another CO_2, while a second NAD is reduced to **NADH**; the resulting four-carbon molecule attaches to coenzyme A, creating succinyl CoA. Here, the enzyme **alpha-ketoglutarate dehydrogenase** catalyses this oxidative decarboxylation step.

5) The high-energy bond to CoA is displaced, and the released energy allows ADP to become quickly be converted to **ATP** by substrate-level phosphorylation, yielding succinate as the product under catalysis of **succinyl-CoA synthetase**.
6) Succinate is oxidized to fumarate, with two hydrogens transferred to FAD, forming **$FADH_2$**, another carrier of high-energy electrons. The enzyme **succinate dehydrogenase** catalyses this oxidation.
7) A water molecule is added to fumarate, rearranging its bonds and converting it into malate under catalysis of **fumarase**.
8) and 9 Finally, malate is oxidized, reducing NAD to **NADH**; this step regenerates oxaloacetate, which is then ready to combine with another acetyl-coA, ensuring the cycle continues. The enzyme **malate dehydrogenase** catalyses this final oxidation step.

Step	Enzyme	Reaction
1	**Citrate synthase**	Transfers the 2-carbon acetyl group from acetyl CoA to the 4-carbon molecule oxaloacetate to produce the 6-carbon molecule citrate.
2	**Aconitase**	Converts citrate to isocitrate by the removal of one water molecule and the addition of another water molecule.
3	**Isocitrate dehydrogenase**	Oxidizes isocitrate using the NAD+ coenzyme to produce **NADH** and release one CO_2, resulting in the formation of the 5-carbon molecule alpha-ketoglutarate.
4	**Alpha-Ketoglutarate dehydrogenase**	Oxidizes alpha-ketoglutarate using the NAD+ coenzyme to produce **NADH** and release one CO_2. The remaining 4-carbon molecule is added to coenzyme A(CoA) to form succinyl-CoA
5	**Succinyl-CoA synthetase**	Replaces CoA with an inorganic phosphate (Pi), converting succinyl-CoA to succinyl phosphate. This phosphate is then transferred to **ADP** to form **ATP**, or to **GDP** to form **GTP**, depending on the version of the enzyme. What remains after the transfer is succinate.
6	**Succinate dehydrogenase**	Oxidizes succinate by transferring two hydrogens to the coenzyme **FAD** to produce **$FADH_2$** resulting in the formation of fumarate.

7	**Fumarase**	Converts fumarate to malate by the addition of one water molecule.
8	**Malate dehydrogenase**	Oxidizes malate by using the NAD+ coenzyme to produce **NADH**, resulting in the regeneration of the oxaloacetate that will be used in step 1 of the cycle.

IMPORTANCE OF THE KREBS CYCLE

- It breaks down macromolecules into simpler ones; pyruvate is broken down into carbon dioxide.
- It is a source of intermediate compounds used by cells in the manufacture of other important substances such as fatty acids, amino acids and chlorophyll.
- It produces hydrogen atoms that are carried by **NAD** and **FAD** to the **electron transport chain** for **oxidative phosphorylation** and the production of **ATP** by chemiosmosis, which provides metabolic energy for the cell.
- It regenerates the starter material (**oxaloacetate**), which would otherwise be completely used up.

AEROBIC RESPIRATION: ROLE OF NAD AND FAD

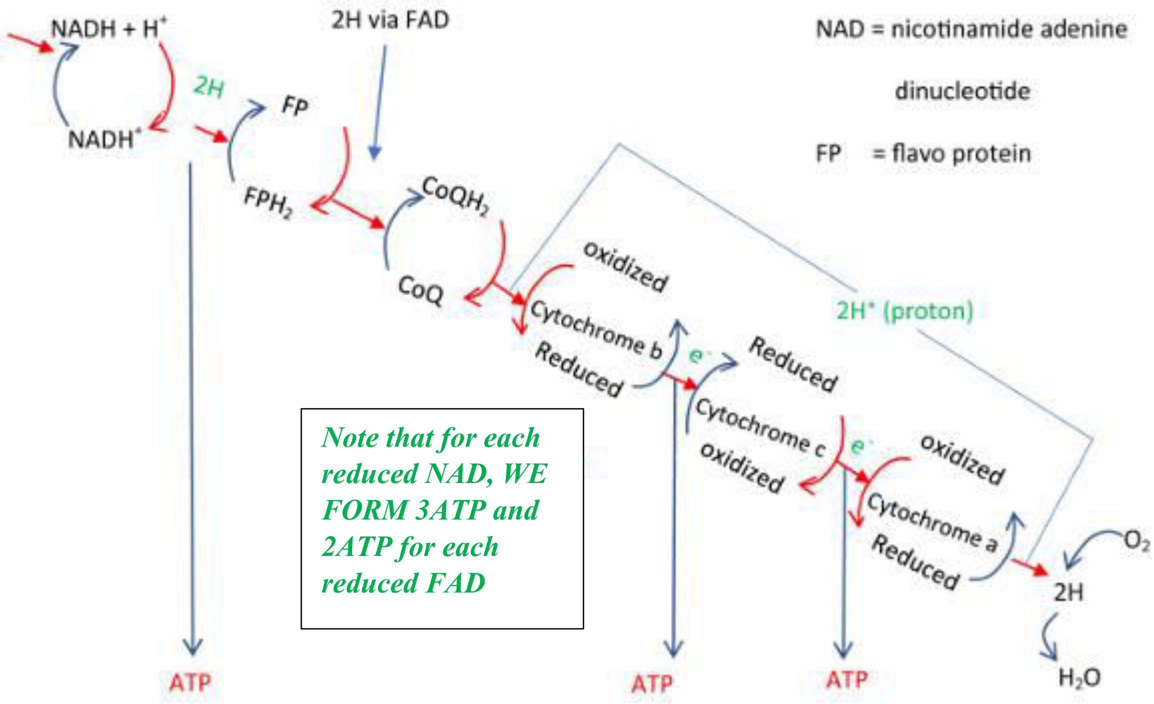
- Flavine adenine dinucleotide (FAD) has a similar function to NAD. Both are involved as coenzymes in the electron transport system, helping the enzyme dehydrogenase to transfer hydrogen from one molecule to another. Whereas NAD is made from niacin (also known as nicotinic acid or vitamin B_3), FAD is made from riboflavin (vitamin B_2). Riboflavin is obtained from a wide variety of foods including yeast, liver, eggs, and milk. It is quickly decomposed by heat, and when exposed to light, it is broken down into a substance called lumiflavin. Milk in bottles left in sunlight therefore loses much of its riboflavin. Riboflavin deficiency causes ariboflavinosis, characterised by cracked skin and eye problems.
- The coenzymes NAD and FAD play a critical role in aerobic respiration.
- When hydrogen atoms become available at different points during respiration NAD and FAD accept these hydrogen atoms.
- A hydrogen atom consists of a hydrogen ion and an electron
- When the coenzymes gain hydrogen they are ‘reduced’ **OIL RIG**: Oxidation Is Loss, Reduction Is Gain.

- Reduced NAD and reduced FAD transfer the hydrogen atoms (hydrogen ions and electrons) from the different stages of respiration to the electron transport chain on the inner mitochondrial membrane, the site where hydrogens are removed from the coenzymes
- When the hydrogen atoms are removed the coenzymes are 'oxidised'
- Hydrogen ions and electrons are important in the electron transport chain at the end of respiration as they play a role in the synthesis of ATP

THE ELECTRON TRANSPORT CHAIN

- Electron transport chain occurs in the membranes of the mitochondria. It is the means in by which the energy, in the form of hydrogen atom, from Krebs cycle, is converted to ATP. The hydrogen atoms attached to a hydrogen carriers NAD and FAD are transferred to a chain of other carriers at progressively lower energy levels (the carriers are situated at different energy levels).
- As the hydrogens pass from one carrier to the next, the energy released is used to produce ATP. The series of carrier is called respiration chain. The carriers in the chain include NAD, Flavo protein, coenzyme Q and iron-containing protein called cytochromes.
- Initially hydrogen atoms are passed along the chain, but latter split into their proton and electron and only the electron pass from carrier to carrier.
- At the end of the chain the protons and electrons **recombine**, and the hydrogen atoms create a link with oxygen to form water. This formation of ATP through the oxidation of the hydrogen atoms is called ***oxidative phosphorylation***. ***The role of oxygen is to act as the final electron acceptor.***
- The final redox reaction is catalysed by **cytochrome oxidase**. Some metabolic poisons such as cyanide inhibit the action of this enzyme, with potentially fatal results.

SUMMARY OF THE ETS



Note that for each reduced NAD, WE FORM 3ATP and 2ATP for each reduced FAD

CHEMIOSITIC THEORY OFATP SYNTHESIS

Suggested by peter Mitchell in 1961. It describes the generation of ATP from an electrochemical gradient established by transporting protons across the inner mitochondrial membrane.

The process is referred to as the **chemiosmotic theory of ATP synthesis.** Although it takes place in a similar way in both chloroplasts and mitochondria, the description below describes the process in mitochondria.

- Hydrogen atoms produced during respiration are carried to the electron transport chain where they are split into **protons** (hydrogen ions – H^+) and electrons.
- As electrons pass along the electron carriers of the electron transport chain, each one being at a lower energy level than the one before, the energy released is used to pump the protons (H^+) into the space between the inner and outer mitochondrial membranes.
- Protons accumulate (build up) in the inter-membranal space, leading to a concentration gradient of protons (H^+) between the space and the matrix. This also means that there is an electrochemical gradient between the inter-membranal space and the matrix.

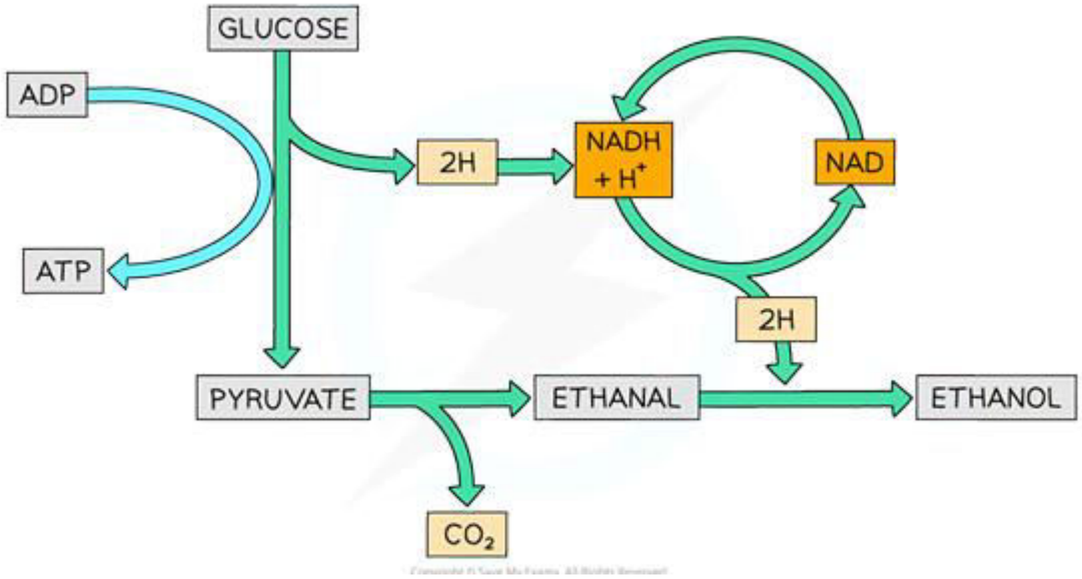
- As the inner mitochondrial membrane is almost impermeable to protons, they can only diffuse back through the **chemiosmotic channels** in the ATP synthase complexes.
- ***As protons flow through these channels their electrical potential energy is used to combine ADP with inorganic phosphate (P_i) to produce ATP.***
- The phosphorylation reaction is catalysed by **ATP synthase** found in the head piece of the ATP synthase complexes.
- Once in the matrix the protons recombine with the electrons on carriers on the inner membrane to form hydrogen atoms, which in turn combine with oxygen to form water.

ANAEROBIC RESPIRATION

Anaerobic respiration, also known as fermentation, is a process that allows cells to produce energy in the absence of oxygen. It begins with glycolysis, in which glucose is broken down into two molecules of pyruvate, yielding a small net gain of two molecules of ATP and two of NADH. Because there is no oxygen to serve as the final electron acceptor in the electron transport chain, the NADH produced during glycolysis must be oxidized back to NAD^+ through additional reactions. This regeneration of NAD^+ allows glycolysis to continue so that ATP can still be produced through substrate-level phosphorylation. Although fermentation yields far less ATP than aerobic respiration, it provides a vital backup energy pathway for many organisms and cells under oxygen-limited conditions.

ALCOHOL (ETHANOL) FERMENTATION

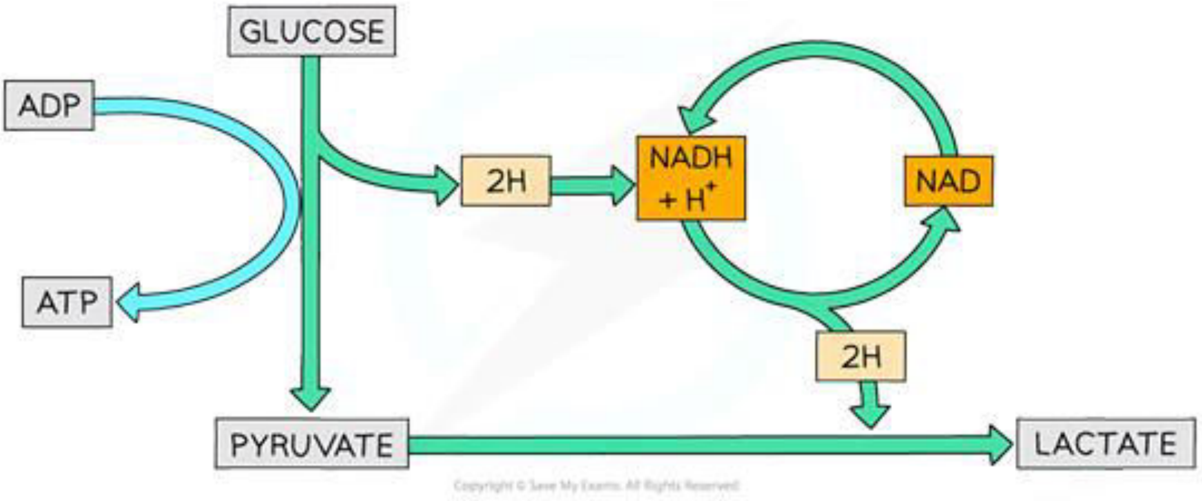
Alcohol fermentation occurs mainly in yeast and some types of bacteria. In this process, each pyruvate molecule produced by glycolysis is first converted into acetaldehyde through the removal of a molecule of carbon dioxide. The acetaldehyde (ethanal) then acts as an electron acceptor, being reduced by NADH to form ethanol, while NAD^+ is regenerated to sustain glycolysis.



The carbon dioxide produced in this process creates bubbles that cause bread to rise and give beer and champagne their fizz. Humans have exploited alcohol fermentation for thousands of years in baking, brewing, and winemaking. However, ethanol is toxic to yeast at concentrations around 12%, which limits the alcohol content of naturally fermented beverages.

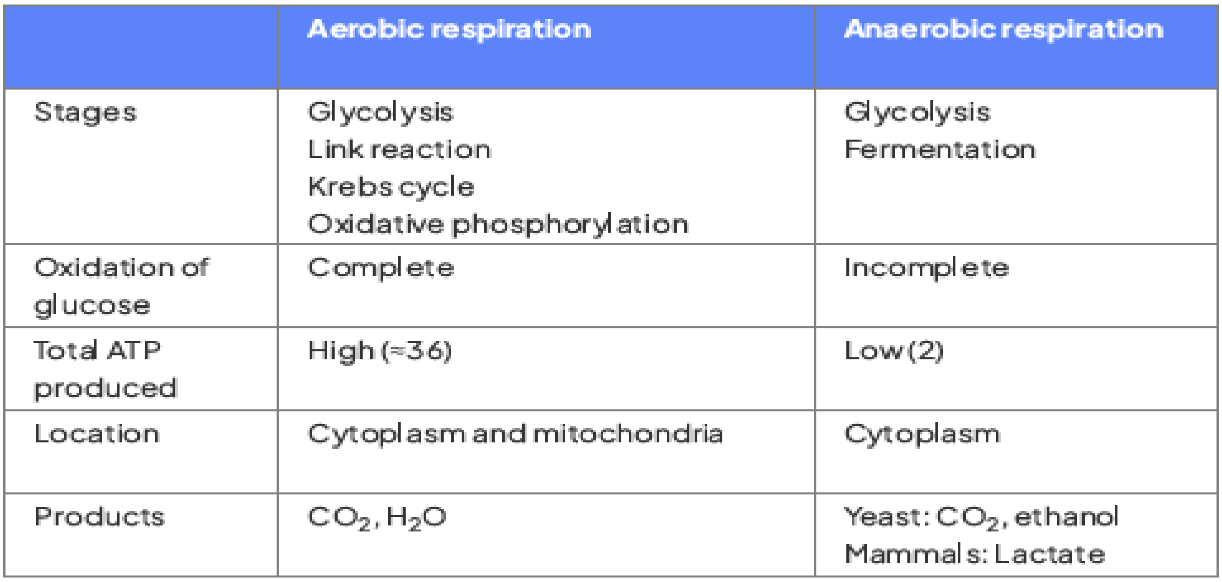
LACTIC ACID FERMENTATION

Lactic acid fermentation takes place in animal muscle cells and in certain bacteria and fungi. Here, pyruvate directly accepts electrons from NADH, forming lactate (the ionized form of lactic acid) and regenerating NAD$^+$.



Unlike alcohol fermentation, no carbon dioxide is released. In humans, this process occurs when oxygen is scarce, such as during intense exercise, allowing ATP production to continue for short periods. The lactate formed is later transported to other tissues like the liver, where it can be converted back into pyruvate or glucose once oxygen becomes available. Lactic acid fermentation is also used industrially in the production of yogurt, cheese, and other fermented foods. Although less efficient than aerobic respiration, it provides a rapid but temporary energy supply under anaerobic conditions.

COMPARISION OF AEROCIC AND ANAEROBIC RESPIRATION



	Aerobic respiration	Anaerobic respiration
Stages	Glycolysis Link reaction Krebs cycle Oxidative phosphorylation	Glycolysis Fermentation
Oxidation of glucose	Complete	Incomplete
Total ATP produced	High (≈36)	Low (2)
Location	Cytoplasm and mitochondria	Cytoplasm
Products	CO_2, H_2O	Yeast: CO_2, ethanol Mammals: Lactate

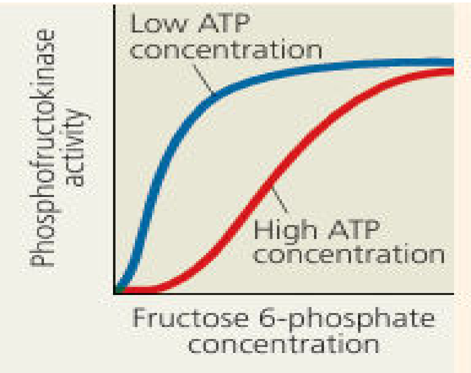
DIFFERENCES BETWEEN FERMENTATION AND AEROBIC RESPIRATION

Feature	**Fermentation**	**Aerobic Respiration**
Final e^- acceptor	Organic molecule (e.g., pyruvate, acetaldehyde)	Oxygen (O_2)
ATP yield (per glucose)	2	Up to 32–38
Site	Cytoplasm	Cytoplasm + mitochondria
Products	Ethanol + CO_2 or Lactate	CO_2 and H_2O

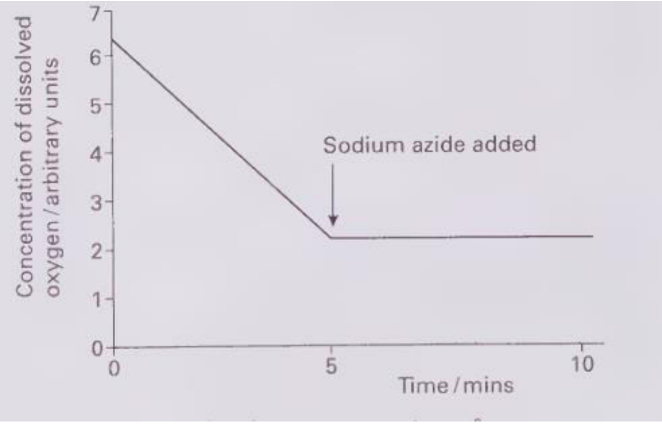
Feature	Fermentation	Aerobic Respiration
Electron transport chain	Absent	Present

SAMPLE QUESTIONS

1. Phosphofructokinase is an enzyme that acts on fructose 6-phosphate at an early step in glucose breakdown. Regulation of this enzyme controls whether the sugar will continue on in the glycolytic pathway. Considering this graph, under which condition is phosphofructokinase more active? Given what you know about glycolysis and regulation of metabolism by this enzyme, explain the mechanism by which phosphofructokinase activity differs depending on ATP concentration



2. Active mitochondria can be isolated from liver cells. If these mitochondria are then incubated in a buffer solution containing a substrate, such as succinate, dissolved oxygen will be used by the mitochondria. The concentration of dissolved oxygen in the buffer solution can be measured using an electrode. An experiment was carried out in which a suspension of active mitochondria was incubated in a buffer solution containing succinate, an intermediate of the Krebs cycle. The concentration of dissolved oxygen was measured every minute for five minutes. A solution containing sodium azide was then added to this preparation and the concentration of dissolved oxygen was measured for a further five minutes. Sodium azide combines with cytochromes and prevents electron transport. The results are shown in the graph below.



a) Explain why the concentration of oxygen decreased during the first five minutes.

b) Suggest what effect the addition of sodium azide will have on the production of ATP and give an explanation for your answer.

3. Coenzymes such as NAD are important in respiration.

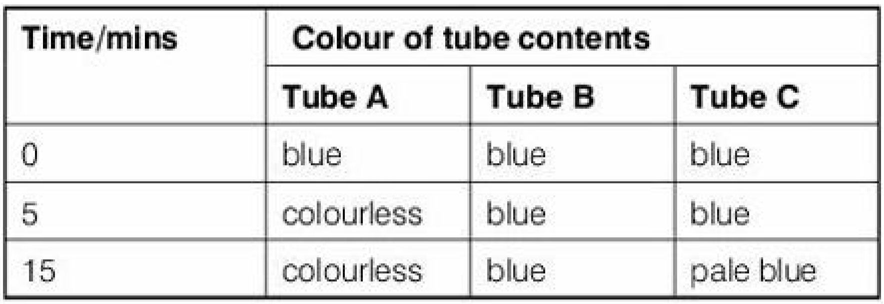
   They help enzymes to function by carrying hydrogen atoms from one molecule to another. Scientists can model the way coenzymes work in cells using a blue dye called DCPIP. It can accept hydrogen atoms and so become reduced. Reduced DCPIP is colorless.

   DCPIP + hydrogen → reduced DCPIP
   (blue color) → (colorless)

   In an investigation into respiration in yeast, three test tubes were set up as follows:

Tube A	Tube B	Tube C
2 cm^3 yeast suspension	2 cm^3 distilled water	2 cm^3 yeast suspension
2 cm^3 glucose solution	2 cm^3 glucose solution	2 cm^3 distilled water
1 cm^3 DCPIP	1 cm^3 DCPIP	1 cm^3 DCPIP

   All three tubes were incubated at a temperature of 30°C. The color of each tube was recorded at the start of the experiment and after 5 and 15 minutes. The results are shown in the table below:



Time/mins	Colour of tube contents		
	Tube A	Tube B	Tube C
0	blue	blue	blue
5	colourless	blue	blue
15	colourless	blue	pale blue

a) Tube B acts as a control. Explain why this control was necessary in this investigation.

b) Using your knowledge of respiration, suggest an explanation for the color change after 15 minutes in:

i) tube A

ii) tube C

c) How might the results in tube A after 15 minutes have been different if the experiment had been carried out at 60°C? Explain your answer.

d) After 20 minutes the contents of tube A were mixed with air by shaking it vigorously turning the DCPIP back to a blue color. Suggest a reason for this.

e) Suggest why conclusions made only on the basis of the results of this experiment may not be reliable.

THE END

DEAR STUDENTS,
Keep pushing forward with patience and persistence—every effort you make builds the foundation for your future success. Remember, even small steps count toward your goals, and one day, everything you've learned and practiced will truly matter. Stay confident and curious, because your dedication will lead to great discoveries and achievements.
E-SIGNED
MODEST TRUST AKATWIJUKA BSED (MUK)