

Respiration

1. Overview of Topic

Cellular respiration is defined as ‘the process by which chemical energy in organic molecules is released by oxidation’ i.e. it involves metabolic processes which allow organisms to obtain energy from organic molecules. Under this broad definition, there are 2 main energy-producing pathways:

- (1) **aerobic respiration** which occurs in the **presence of oxygen**.
- (2) **anaerobic respiration** which occurs in the **absence of oxygen**.

Respiration is an energy-releasing process. As ATP is the primary energy currency of the cell, main function of respiration is production of ATP.

Part of respiration occurs in **cytosol** and part of it in **mitochondria** of the cell.

2. Learning Outcomes

- a. outline the process of glycolysis, highlighting the location, raw materials used and products formed (knowledge of details of the intermediate compounds and isomerisation is not required)
- b. outline the processes of the link reaction and Krebs cycle, highlighting the location, raw materials used and products formed (in terms of dehydrogenation and decarboxylation)
- c. outline the process of oxidative phosphorylation including the role of oxygen and the electron transport chain in aerobic respiration (names of complexes in the ETC are not required)
- d. explain the production of a small yield of ATP from respiration in anaerobic conditions in yeast and in mammalian muscle tissue
- e. explain the significance of the formation of ethanol in yeast and lactate in mammals in the regeneration of NAD
- f. investigate the effect of factors such as substrate concentration, type of substrate and temperature on the rate of respiration
- g. outline chemiosmosis in photosynthesis and respiration (names of complexes in the ETC are not required). Use the knowledge gained in this section in new situations or to solve related problems.

3. References

Main references:

- Campbell, Reece *et al.* (2015) Biology, 10th edition. Benjamin-Cummings Publishing Co.
- Raven, Johnson, Losos, Mason and Singer (2008). Biology, 8th edition. McGraw-Hill.

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4. Respiration - Introduction

Notes to self

Cellular respiration is defined as 'the process by which chemical energy in organic molecules is released by oxidation' i.e. it involves metabolic processes which allow organisms to obtain energy from organic molecules.

Under this broad definition, there are 2 main energy-producing pathways:

- (3) **aerobic respiration** which occurs in the **presence of oxygen**.
- (4) **anaerobic respiration** which occurs in the **absence of oxygen**.

Functions of respiration:

Respiration is an energy-releasing process. As ATP is the primary energy currency of the cell, main function of respiration is production of ATP.

Some examples where ATP is required:

- (1) muscle contraction, beating of cilia (e.g. on cells lining trachea), beating of flagella (e.g. in sperm, bacteria)
- (2) active transport of substances into or out of cells (e.g. $\text{Na}^+\text{-K}^+$ pump in cell membranes)
- (3) synthesis of substances for growth and repair (e.g. translation)
- (4) electrical transmission of nerve impulses
- (5) maintenance of constant body temperature i.e. in homoeothermic/ warm-blooded animals
- (6) bioluminescence by fireflies, glow-worms and some deep sea animals

Locations of respiration:

Part of respiration occurs in **cytosol** and part of it in **mitochondria** of the cell.

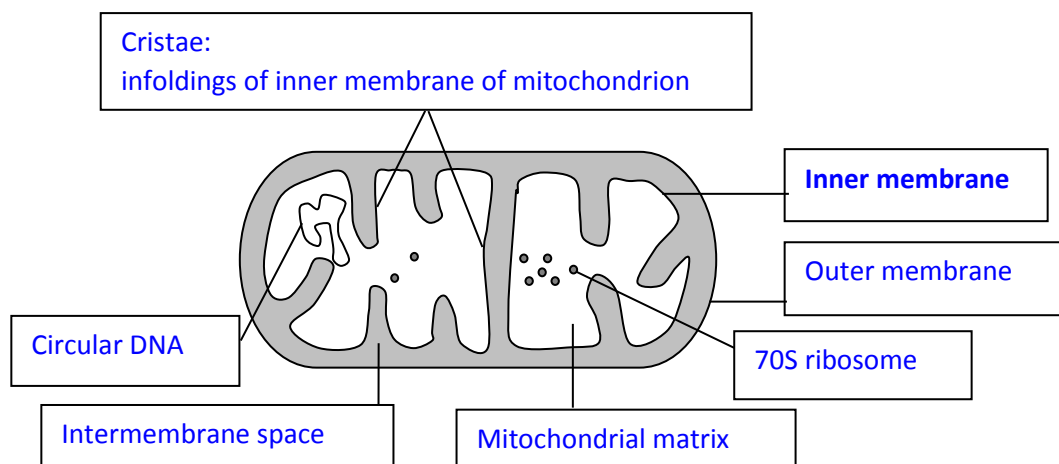


Figure 1. Diagram of a mitochondrion

5. Aerobic Respiration

- In a eukaryotic cell, aerobic respiration involves 4 main stages (see Fig. 2 for overview):
 - (1) **glycolysis** in cytosol
 - (2) **link reaction** in mitochondrial matrix
 - (3) **Krebs cycle** in mitochondrial matrix
 - (4) **oxidative phosphorylation** involving electron transport chain on cristae
- All 4 stages require many different **enzymes**.

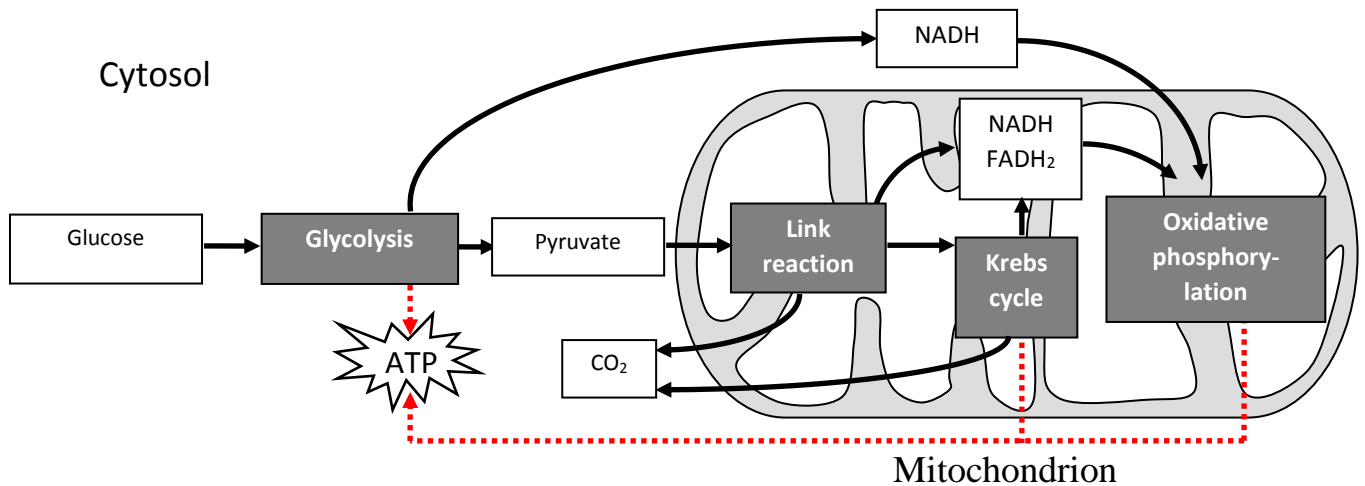
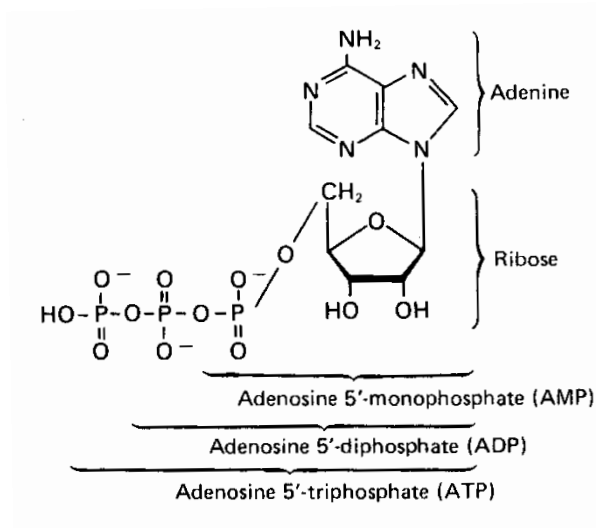


Figure 2. Respiration summary. Grey boxes indicate stages of aerobic respiration. White boxes indicate substrates and products.



Suitability of ATP as an energy source:

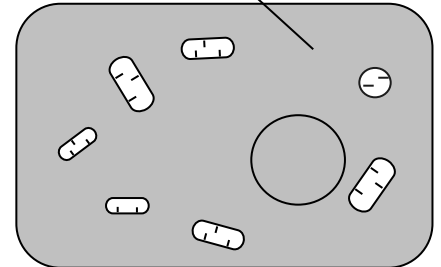
- Universally used – all cells and organisms use it as an energy source.
- Soluble, highly mobile and can be transported readily/ diffuses readily to point of need.
- Easy for terminal phosphate group to be lost
- Easy interconversion: $\text{ADP} + \text{P}_i$ forms ATP, and ATP can be hydrolysed to $\text{ADP} + \text{P}_i$, leading to energy release.

Figure 3. Structure of ATP. Loss of terminal phosphate group results in an ADP molecule, as occurs during the first stage of glycolysis. Loss of 2nd phosphate group will produce AMP.

5.1 Glycolysis

- The first stage of respiration involves glycolysis - oxidation of **glucose (6C) to 2 pyruvate (3C)**. In effect, a 6 carbon sugar is split into two 3-carbon sugars. (Glycolysis = splitting of sugar)
- It **does not require** O_2 (it occurs whether or not O_2 is present) and **does not release** CO_2 .
- It can be divided into 4 stages:

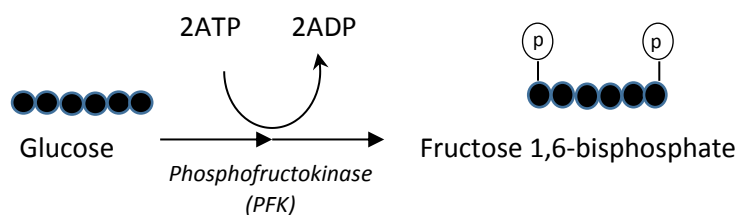
Glycolysis occurs in cytosol



(1) Phosphorylation of glucose

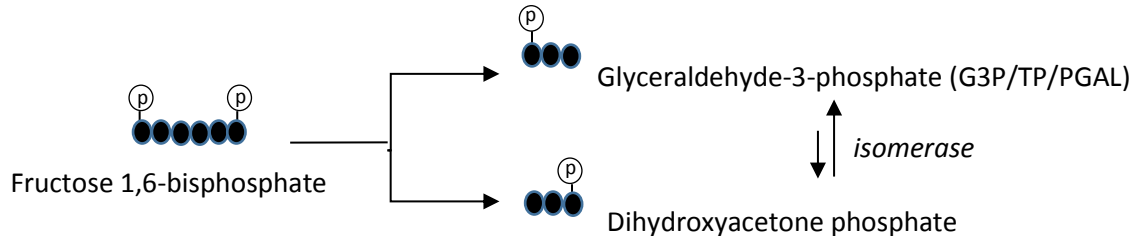
- ▶ First, 2 phosphate groups are added to glucose to produce **fructose 1,6-bisphosphate**.
- ▶ The 2 phosphate groups are donated to the sugar by 2 ATP molecules, which form 2 ADP molecules.
- ▶ This phosphorylation activates the sugar, making it more reactive and committing it to the glycolytic pathway. Phosphorylation also confers a negative charge to glucose, making it impermeable, cannot diffuse across cell membrane hence it is trapped within the cytosol.
- ▶ Therefore, phosphorylation of sugar involves **initial investment of 2 ATP molecules** - no ATP has been produced as yet; instead, 2 ATP molecules have been used up!
- ▶ **Phosphofructokinase (PFK)** catalyses addition of the 2nd phosphate group. This enzyme is **inhibited by excess ATP and/or citrate** in the cell. Since the ultimate goal of glycolysis is to produce ATP and too much of this end product (ATP) inhibits the enzyme, this is an example of **end product inhibition** (allosteric inhibition). Conversely, PFK is **stimulated by AMP and ADP (allosteric activators)**. Thus, rate of glycolysis is regulated according to the energy demands of the cells.

(Note: Hexokinase catalyses addition of the first phosphate)



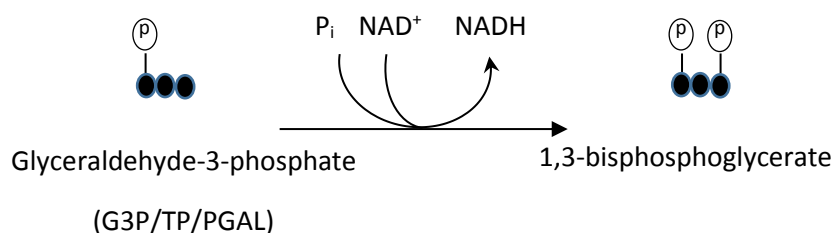
(2) Lysis

- ▶ Next, phosphorylated 6C sugar (fructose 1,6-bisphosphate) is **split** into two 3C sugar phosphates: **glyceraldehyde-3-phosphate (G3P)** and dihydroxyacetone phosphate. G3P is also known as triose phosphate (TP) and phosphoglyceraldehyde (PGAL).
- ▶ The 2 sugar phosphates (G3P and dihydroxyacetone) are isomers of each other, and can be converted from one form to the other through the action of an isomerase. The reaction favours formation of G3P, since it is constantly removed by the next step of the reaction.



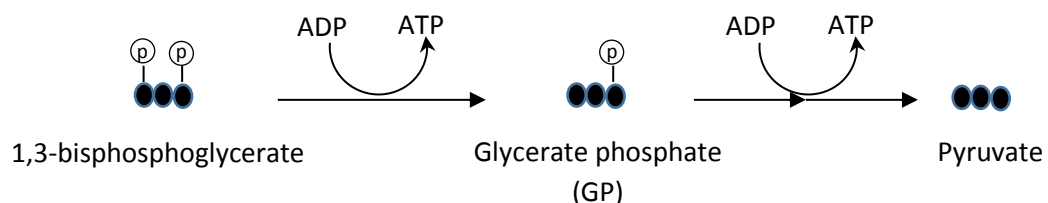
(3) Oxidation by dehydrogenation

- ▶ Oxidation can be defined in 3 ways:
 - (a) Addition of oxygen
 - (b) Removal of hydrogen (**dehydrogenation**)
 - (c) Removal of electrons
- ▶ During glycolysis, oxidation of respiratory substrate occurs by **dehydrogenation**.
- ▶ The substrate G3P is oxidised by dehydrogenation. At the same time, the **coenzyme** NAD^+ is reduced to NADH (remember: oxidation must always be coupled to a reduction). (*for details about NAD^+ , refer to pg 12*)
- ▶ As this redox reaction is highly exergonic, energy released is used to add a second phosphate group to G3P, forming 1,3-bisphosphoglycerate.



(4) Substrate-level phosphorylation

- ▶ Next, 1,3-bisphosphoglycerate is dephosphorylated to form the final product of glycolysis, **pyruvate**.
- ▶ The 2 phosphate groups on 1,3-bisphosphoglycerate are transferred by enzymes to 2 ADP molecules, forming 2 ATP.



- ▶ Since each G3P yields 2 ATP and 1 NADH, 2 G3P molecules will yield 4 ATP and 2 NADH.
- ▶ This process whereby an enzyme transfers a phosphate group directly from a substrate molecule (i.e. an organic molecule generated during the oxidation of glucose) to ADP is known as **substrate-level phosphorylation** (*as opposed to oxidative phosphorylation, refer to pg 12*).
- ▶ Considering the 2 ATP expended earlier as an initial investment, there is a **net gain of 2 ATP** and **2 NADH per glucose**.
- ▶ Overall equation for glycolysis would be:
Glucose + 2 ADP + 2 P_i + 2 NAD⁺ → 2 pyruvate + 2 ATP + 2 NADH

What happens to pyruvate at the end of glycolysis?

- (1) if oxygen is unavailable, pyruvate will be converted into ethanol or lactate (anaerobic respiration, refer to pg. 17).*
- (2) if oxygen is available, pyruvate enters mitochondrion into the next stage in aerobic respiration – **link reaction**.*

Video Link

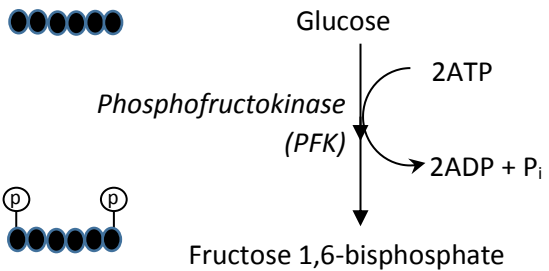
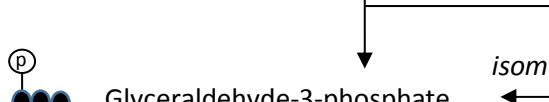
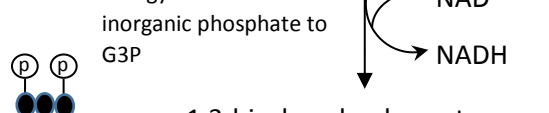
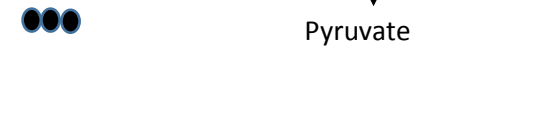
Glycolysis: <http://tinyurl.com/phprjl4>

http://highered.mheducation.com/sites/0072507470/student_view0/chapter25/animation_how_glycolysis_works.html

● - C atom

Ⓟ - phosphate group

Glycolysis Flowchart

PHOSPHORYLATION OF SUGAR - Initial ATP investment - Activation of glucose - Commit to glycolysis pathway	ΔE -2ATP		Feedback regulation of glycolysis PFK is an allosteric enzyme that is: - activated by ADP & AMP, - inhibited by citrate (from Krebs cycle) and ATP. Activity of PFK helps to control rate of glycolysis.
- Allosteric regulation by PFK			
LYSIS 6C → 2 (3C)			
OXIDATION BY DEHYDROGENATION - Reduction of NAD ⁺ to NADH - Inorganic phosphate group added to G3P in the process SUBSTRATE-LEVEL PHOSPHORYLATION - ATP produced by direct enzyme action on the substrate	Since 2 molecules of G3P: +NADH X 2		

Summary of Glycolysis

Energy is transferred from [glucose](#) to [pyruvate](#), [ATP](#) and [NADH](#).

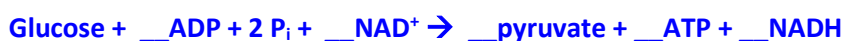
For **each glucose molecule**:

No. of ATP used up: _____

No. of ATP produced: _____

Net ATP produced: _____ No. of NADH produced: _____

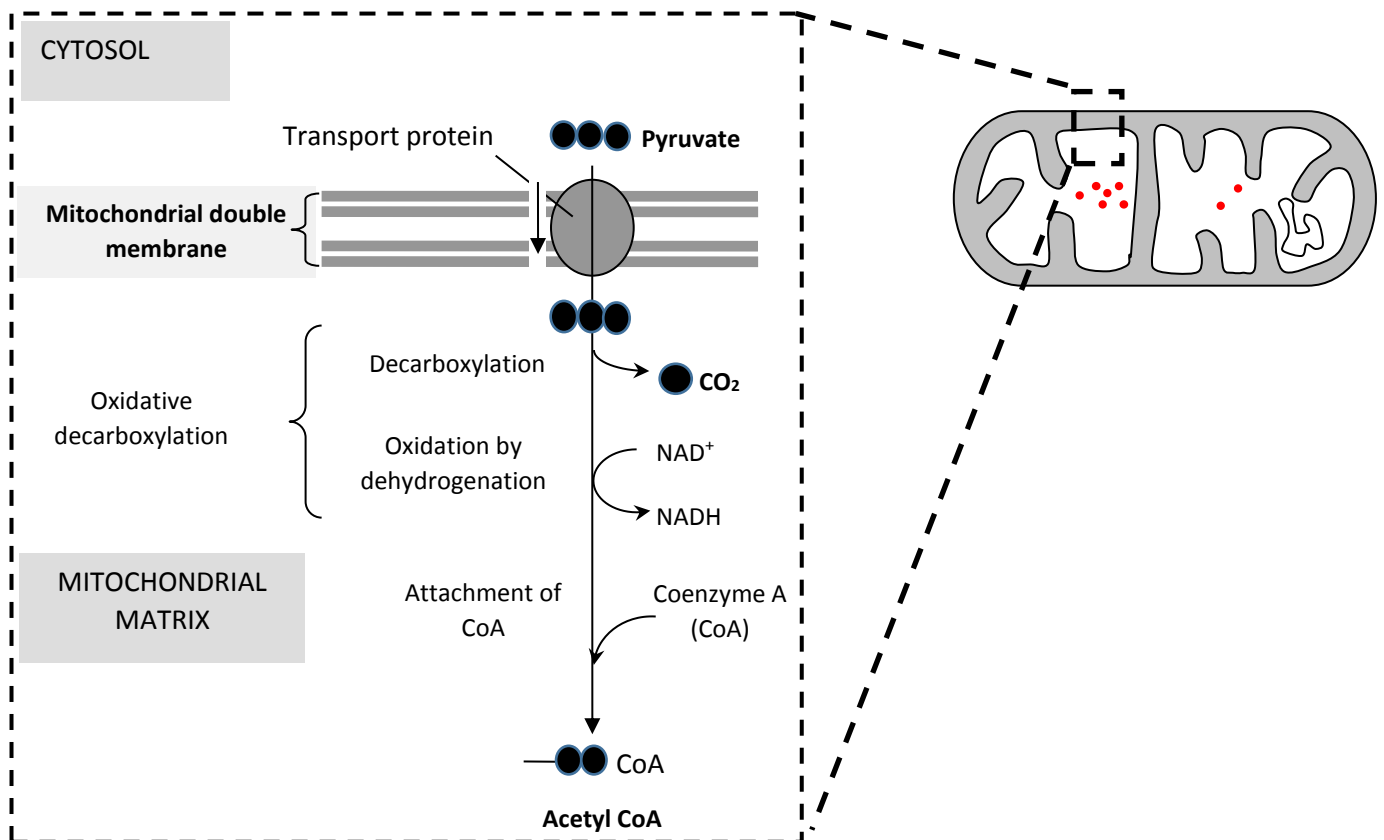
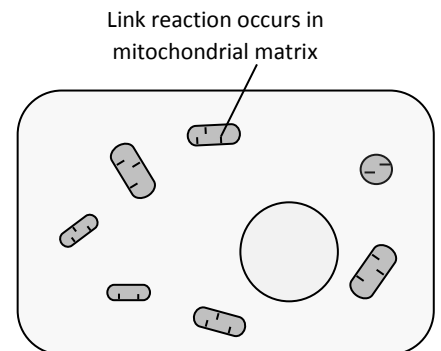
Overall equation:



5.2 Link Reaction / Oxidative Decarboxylation

A transport protein built into the mitochondrial membrane translocates pyruvate from cytosol into mitochondrion via active transport.

- ▶ Within matrix, each pyruvate (3C) is **decarboxylated**. This involves removal of C from pyruvate, in the form of CO_2 .
- ▶ **Oxidation by dehydrogenation** occurs, yielding NADH and acetyl coenzyme A (acetyl CoA), a 2C compound.
- ▶ Acetyl CoA moves on into Krebs cycle, which also takes place in mitochondrial matrix



Note: Fatty acids can also be used to produce acetyl CoA by a different pathway.

Figure 4. Link reaction. Each pyruvate is converted to acetyl CoA, with production of one molecule of CO_2 and NADH.

5.3 Krebs Cycle

- Krebs cycle involves 3 main stages:
 - (1) Acetyl CoA (2C) joins the cycle by combining with **oxaloacetate** (4C) to form **citrate** (6C).
 - (2) Citrate is decarboxylated and dehydrogenated to form **α -ketoglutarate** (5C) and NADH.

A decarboxylation step results in a loss of carbon in the form of CO_2 . This process involves oxidative decarboxylation.

- (3) **Oxaloacetate** (4C) is regenerated.

This involves 1 decarboxylation step and 3 dehydrogenation steps to yield 1 CO_2 , 2 NADH, 1 FADH_2 (reduced Flavin Adenine Dinucleotide, another coenzyme) and 1 ATP (by substrate-level phosphorylation).

Krebs cycle occurs in mitochondrial matrix

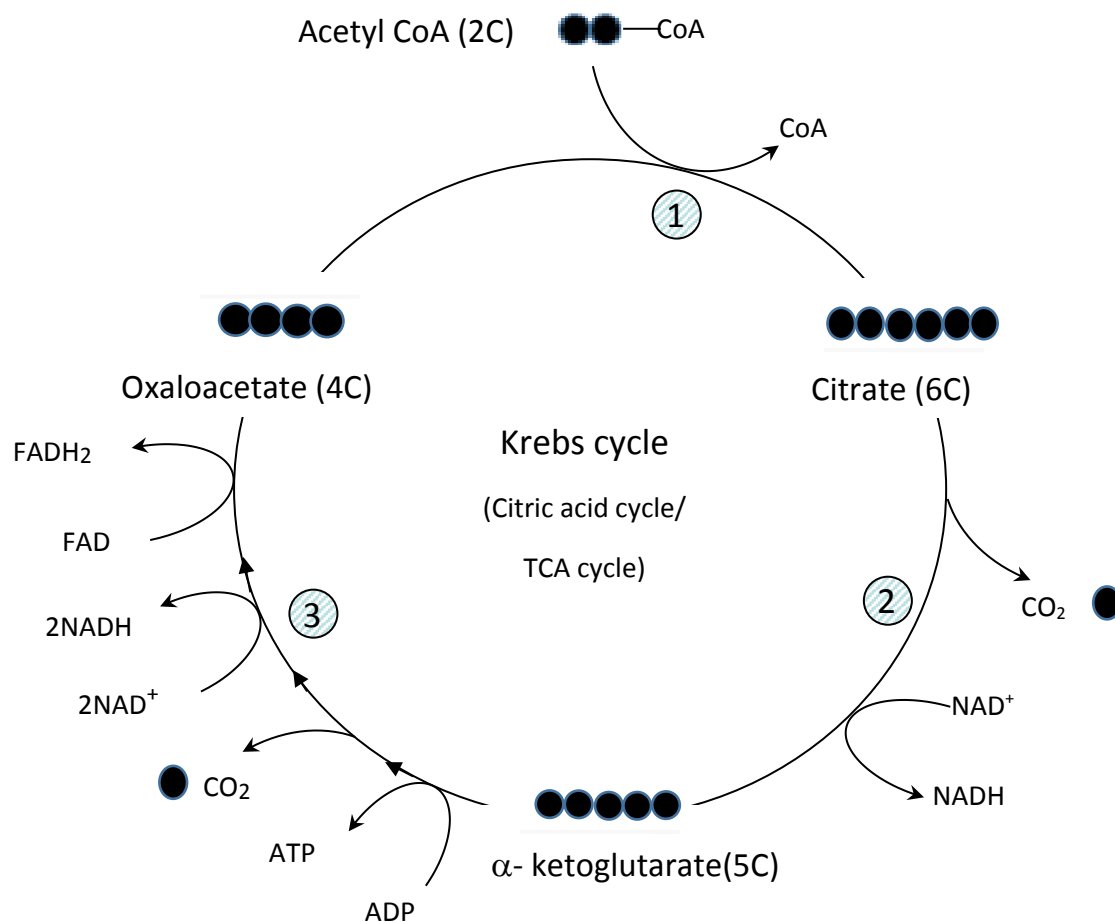
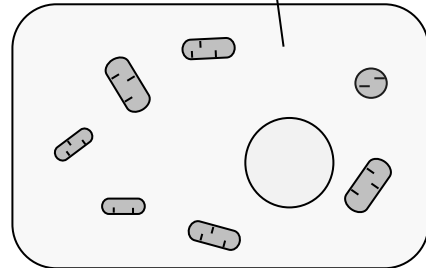


Figure 5. Krebs Cycle. It involves 3 main stages: (1) formation of citrate, (2) oxidation of the carbon substrate and (3) regeneration of oxaloacetate.

Note: Acids exist as salts in physiological systems and their names end with –ate. Citric acid is thus referred to as citrate.

- Krebs Cycle occurs in the **presence of oxygen**.
- Since for 1 glucose molecule, glycolysis yields 2 pyruvate and hence 2 acetyl CoA, **two rounds of Krebs cycle** are needed to completely oxidise one molecule of glucose.
- All the 6 carbons in glucose are lost as 6 CO₂. For each 6C glucose molecule, 4 CO₂ are released through Krebs cycle while 2 CO₂ are released in link reaction.

Summary of Krebs Cycle

Product	No. of molecules per acetyl CoA fed in	No. of molecules per glucose molecule
CO ₂		
NADH		
FADH ₂		
ATP		

Note: ATP produced in Krebs cycle is obtained from substrate-level phosphorylation.

Does Krebs cycle produce the bulk of the ATP from a glucose molecule?

- *Not directly. Most of the energy released in Krebs cycle is actually carried on the NADH and FADH₂ produced. The mobile electron carriers (NADH and FADH₂) with their reducing power will next be transported to electron transport chain, where the bulk of ATP is generated.*

Video Links

Krebs Cycle: https://www.youtube.com/watch?v=WWZ0_cHwhX8&t=1s

5.4 Oxidative Phosphorylation

- Location: inner mitochondrial membrane (cristae), which is highly folded to increase surface area for the accommodation of:

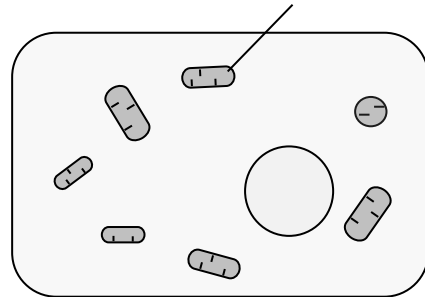
(1) Many **electron transport chains** (ETC, sometimes called respiratory chain) – this is a series of electron carriers (mainly proteins) with increasing electronegativity.

Each electron carrier has an energy level that is lower than the one preceding it.

The electron carriers alternate between reduced and oxidised states as they accept and donate electrons respectively.

(2) Many **ATP synthases** (previously: stalked particles) - enzyme used in ATP synthesis.

Oxidative phosphorylation occurs in inner mitochondrial membrane (cristae)



- Oxidative phosphorylation occurs in the **presence of oxygen**.
- NADH and FADH₂ generated in previous processes will now take part in oxidative phosphorylation (*refer to pg 12 for definition*).
- Function of NAD⁺ and FAD:
 - Through glycolysis, link reaction and Krebs cycle, organic food such as carbohydrates, fats and proteins are oxidised to yield high-energy electrons.
 - These electrons (together with protons) are transferred to NAD⁺ and FAD to form NADH (also called reduced NAD) and FADH₂ (also called reduced FAD).
 - NAD⁺ and FAD serve as **mobile electron carriers**, which transport the high-energy electrons from organic molecules to the electron transport chain in mitochondria.
 - As electrons pass down the electron transport chain, energy is released and coupled to the formation of ATP (*Oxidative Phosphorylation*).
 - By passing their electrons to the electron transport chain
 - NADH and FADH₂ are oxidised,
 - the coenzymes NAD⁺ and FAD are regenerated, allowing them to pick up more electrons (and protons) from glycolysis, link reaction and Krebs cycle.

What are the components of oxidative phosphorylation?

- flow of electrons down the **electron transport chain** releases energy which is used to pump H⁺ from mitochondrial matrix, across inner mitochondrial membrane, into intermembrane space.*
- production of ATP from ADP and P_i via **chemiosmosis** (refer to pg 13, 20 for definition).*

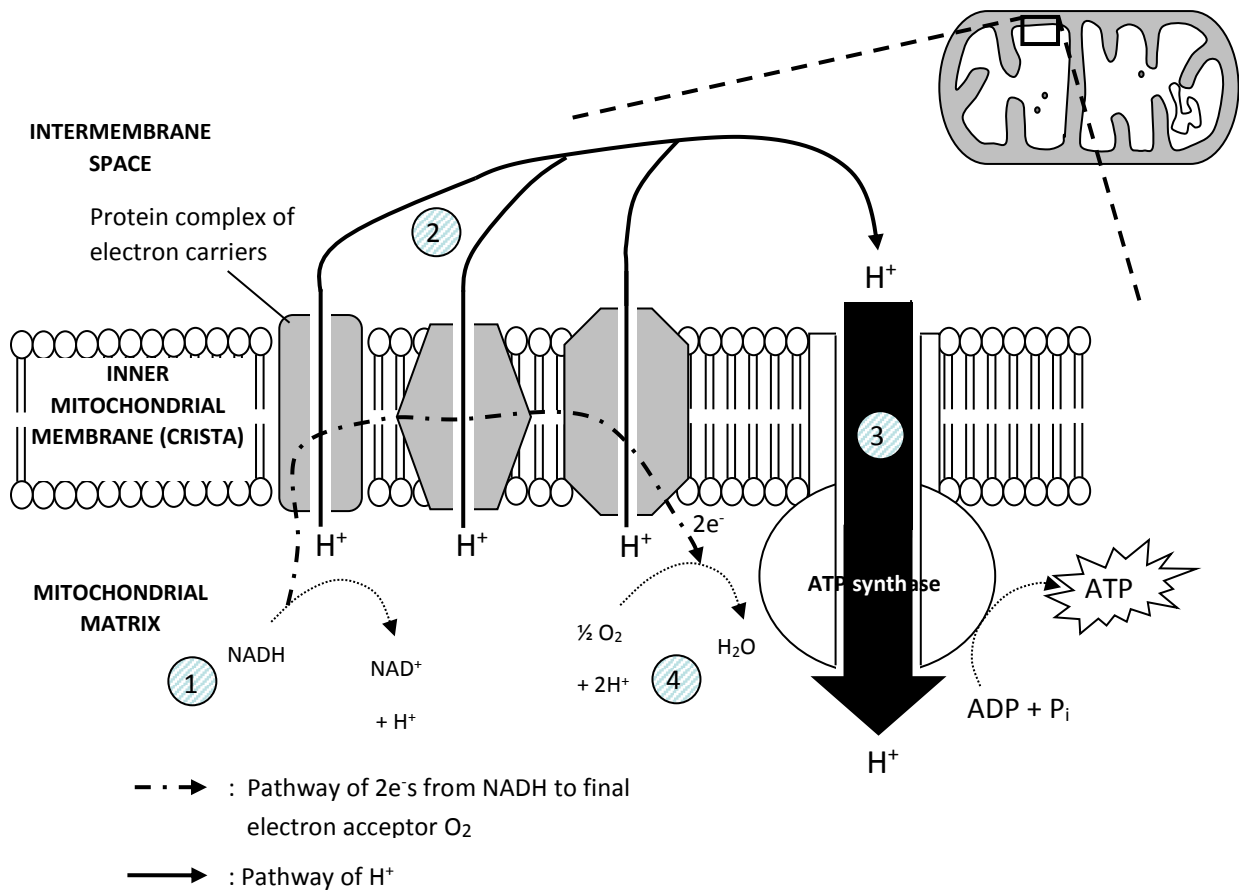
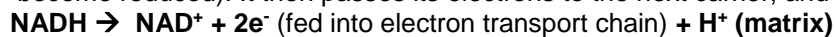


Figure 6. Oxidative phosphorylation involving electron transport chain

- Process of oxidative phosphorylation:

1 **NADH** molecules from glycolysis, link reaction and Krebs cycle donate electrons to the first electron carrier of electron transport chain (i.e. first electron carrier become reduced). It then passes its electrons to the next carrier, and so on.



2 As the high-energy electrons travel down the ETC, energy is **released** and it is coupled to the pumping of H⁺ (the term “pumping” means energy is required) from mitochondrial matrix into intermembrane space, via some of the electron carriers of ETC. This builds up a **proton-motive force** across cristae. Concentration of H⁺ is thus, always high in the intermembrane space.

Note: Proton-motive force is potential energy stored in the form of a proton chemical gradient, generated by pumping of H⁺ across a biological membrane during chemiosmosis.

3 As H⁺ flows down its concentration gradient/diffuses through **ATP synthase**, ADP is phosphorylated to form ATP. This process is called **chemiosmosis**, where energy stored in the form of a proton gradient across a membrane is used to drive cellular work (e.g. ATP synthesis).

4 **O₂** (molecular oxygen) acts as **final electron acceptor**, producing H₂O with electrons and H⁺.

Note: H_2O produced this way is called metabolic water, which is used by desert animals to supplement their water needs. This step is catalysed by cytochrome oxidase.

Although $\frac{1}{2} \text{O}_2$ is equivalent to a single O atom, the symbol O_2 is deliberately used to emphasise that it is molecular oxygen, not the O atom, which is reduced to H_2O .

Most of the electron carriers of the chain are grouped into 4 main protein complexes. But only 3 complexes are represented in the above diagram.

- Lipid bilayer of mitochondrial membranes, like any other membrane, is impermeable to ions like H^+ . Therefore, a proton gradient can be generated across the inner mitochondrial membrane. The only passage where H^+ can traverse the membrane is through ATP synthase.
- 90% of the ATP produced during aerobic respiration is produced via chemiosmosis.
- Importance of oxygen:
 - ▶ By acting as the final electron acceptor, O_2 (molecular oxygen) allows the electron carriers NADH and FADH_2 to continue donating their electrons to the chain, thereby generating ATP. **Overall, presence of O_2 allows oxidative phosphorylation to continue, to generate ATP.**
 - ▶ The coenzymes NAD^+ and FAD are regenerated when NADH and FADH_2 donate electrons to electron transport chain. This allows NAD^+ and FAD to pick up more electrons and protons from glycolysis, link reaction and Krebs cycle.
 - ▶ Reduction of oxygen to water removes H^+ from matrix, contributing to the generation of a proton gradient across inner mitochondrial membrane.
- Electron transport chain serves two important functions:
 - (1) generating a proton motive force to **produce ATP**
 - (2) **regeneration of coenzymes NAD^+ and FAD**. Without the regeneration of these coenzymes, glycolysis and the rest of the respiratory processes would not be able to continue efficiently.

Video Links

NAD: <https://www.youtube.com/watch?v=iwEK5U4zS2w&t=2s>

Oxidative Phosphorylation: Video: <http://tinyurl.com/nwsb628>

<http://www.youtube.com/watch?v=6W-7FG9KipA>

Proton Pump: Video: <http://tinyurl.com/kfjzmrI>

http://highered.mheducation.com/sites/007352543x/student_view0/chapter8/proton_pump.html

Overall Respiration: <https://www.youtube.com/watch?v=EYLr3pVNd7U&t=18s>

Summary of Oxidative Phosphorylation

In aerobic respiration,

Oxidative Phosphorylation

relates to

- ☐ reduced coenzyme molecules (i.e. NADH and FADH_2) being reoxidised to NAD^+ and FAD in the presence of O_2 and with energy released in the process.

relates to

- ☐ addition of a phosphate group to ADP to form ATP. This ATP synthesis is driven by the electrochemical proton gradient.

Thus, oxidative phosphorylation is the process by which the exergonic reoxidation of NADH and FADH_2 by oxygen is coupled to the formation of ATP, with an electrochemical proton gradient as an intermediate.

5.5 ATP produced per glucose molecule

- Each NADH entering electron transport chain can yield **3 ATP**.
- Each FADH₂ entering electron transport chain can yield **2 ATP**. This is because FADH₂ enters the chain at a lower energy potential i.e. it passes its electrons to a protein that is further down the chain. Hence, the electrons 'fall' down a smaller energy difference, and less energy is released to pump (less) H⁺ across the membrane

Summary on the number of various products per glucose molecule:

	CO ₂	ATP	NADH	FADH ₂
Glycolysis	-	2 (net)	2	-
Link reaction		-		-
Krebs cycle				
Sub-total	__CO ₂	__ATP	__ NADH	__FADH ₂
Oxidative phosphorylation	-	From NADH: __ x 3 ATP = From FADH: __ x 2 ATP =	-	-
Total ATP:		38		

Note: In reality, less than **38 ATP per glucose molecule** may be produced. This is because mitochondrial membrane is impermeable to the NADH generated by glycolysis. Electrons and protons of NADH are passed to either NAD⁺ or FAD inside mitochondrion via a shuttle system. If passed to FAD, then only 2 ATP will be produced instead of 3.

- For every glucose molecule:
 - 2 ATP in glycolysis + 2 ATP in Krebs cycle are formed through **substrate-level phosphorylation**.
 - 10 NADH and 2 FADH₂ enter electron transport chain to produce 34 ATP via **oxidative phosphorylation**.
 - In total, a potential 34 + 2 + 2 = 38 ATP are generated (i.e. 38 moles of ATP are generated from 1 mole of glucose).
- Oxidative phosphorylation thus, contributes to a whopping 90% of the total ATP generated.

6. Anaerobic Respiration

- What happens to the processes involved in aerobic respiration when oxygen is absent?
 - In the **absence of oxygen**, there is **no final electron acceptor** to accept electrons from the ETC. Electron carriers within the ETC remain reduced, and NADH and FADH₂ can no longer donate electrons to the ETC.

What happens if NADH and FADH₂ remain reduced?

NAD⁺ and FAD are not regenerated to pick up more electrons (and protons) from link reaction, Krebs cycle and oxidative phosphorylation. In turn, these three processes will come to a halt.

- How do some cells continue to produce ATP?
 - In the absence of oxygen, anaerobic respiration takes place.
 - Anaerobic respiration takes place in **cytosol** and it involves **glycolysis, followed by fermentation**.
 - Fermentation processes are pathways to regenerate NAD⁺ from NADH, thereby ensuring a steady supply of NAD⁺ for glycolysis to continue.
 - Two common fermentation pathways to regenerate NAD⁺ from NADH:
 - (1) alcohol fermentation
 - (2) lactic acid fermentation
 - Since oxygen is no longer present, **pyruvate** or its derivative **ethanal**, becomes the **final electron acceptor** to regenerate NAD⁺ via lactate and alcohol fermentation respectively.
- Functions of anaerobic respiration:
 - (1) **To produce a small yield of energy**
2 ATP are produced per glucose molecule, through glycolysis. It produces $2/38 = 1/19$ the amount of ATP generated in aerobic respiration
 - (2) **To regenerate NAD⁺ from NADH**
During glycolysis, oxidation of glucose to yield 2 ATP leads to reduction of NAD⁺ to form NADH. In order for glycolysis to continue, NAD⁺ needs to be regenerated. Alcohol and lactic acid fermentation include processes that recycle NAD⁺ concentrations in the cytosol.

Where does anaerobic respiration occur within the cell? Does it involve the mitochondria?

6.1 Alcohol Fermentation

- Following glycolysis, **pyruvate decarboxylase** converts **pyruvate** (3C) to **ethanal/acetaldehyde** (2C) through decarboxylation (CO_2 is released).
- NADH** produced during glycolysis has to be **recycled to NAD^+** so that glycolysis can continue, to produce 2 ATP each round.
- Alcohol dehydrogenase** reduces ethanal/ acetaldehyde (**final electron acceptor**) to **ethanol**, while removing H^+ from NADH to reform NAD^+ .
- Alcohol fermentation occurs in yeast and certain bacteria. It is used in wine and beer production, through anaerobic action of yeast.

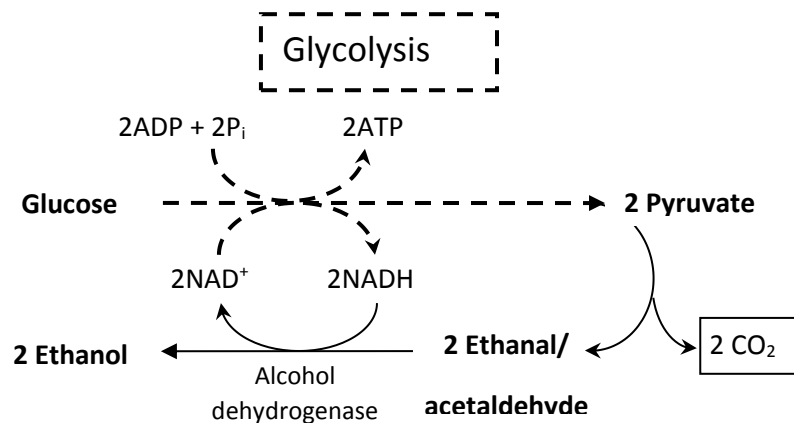


Figure 7. Alcohol fermentation. It involves glycolysis (top) to produce 2 ATP, and subsequent reduction of ethanal (bottom) to regenerate NAD^+ . NAD^+ is fed back into glycolysis so that ATP production in glycolysis can continue. Ethanol and CO_2 are the end products.

6.2 Lactic Acid Fermentation

- When a muscle contracts, the exceptionally high demand for ATP is met by a dramatic increase in rate of glycolysis. This rapidly depletes the limited supply of NAD^+ .
 - ▶ Oxidative phosphorylation, which normally replenishes NAD^+ supply, may not be able to replenish the NAD^+ quickly enough. Hence, muscle cells have to rely on an **additional** system to regenerate NAD^+ : anaerobic respiration (glycolysis followed by fermentation, a process that regenerates NAD^+).
 - ▶ Thus, anaerobic respiration can occur concurrently with aerobic respiration. The two pathways do not have to be mutually exclusive.
- Pyruvate** is the **final electron acceptor** and is reduced to become **lactic acid/lactate**. NAD^+ is regenerated in the process.
- Lactate dehydrogenase** catalyses the reaction.

- The end products are 2 ATP and 2 lactate per glucose molecule.
 - ▶ **No CO_2 is produced** since no decarboxylase is involved (unlike in alcohol fermentation).

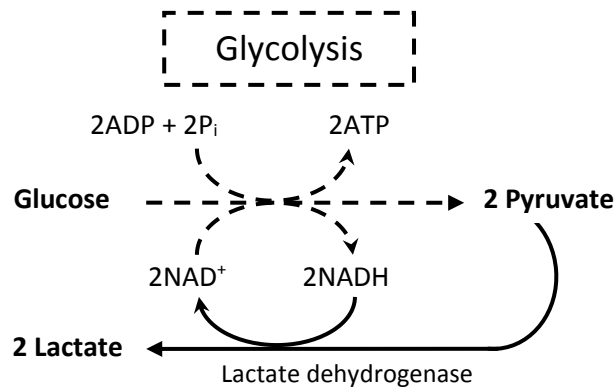


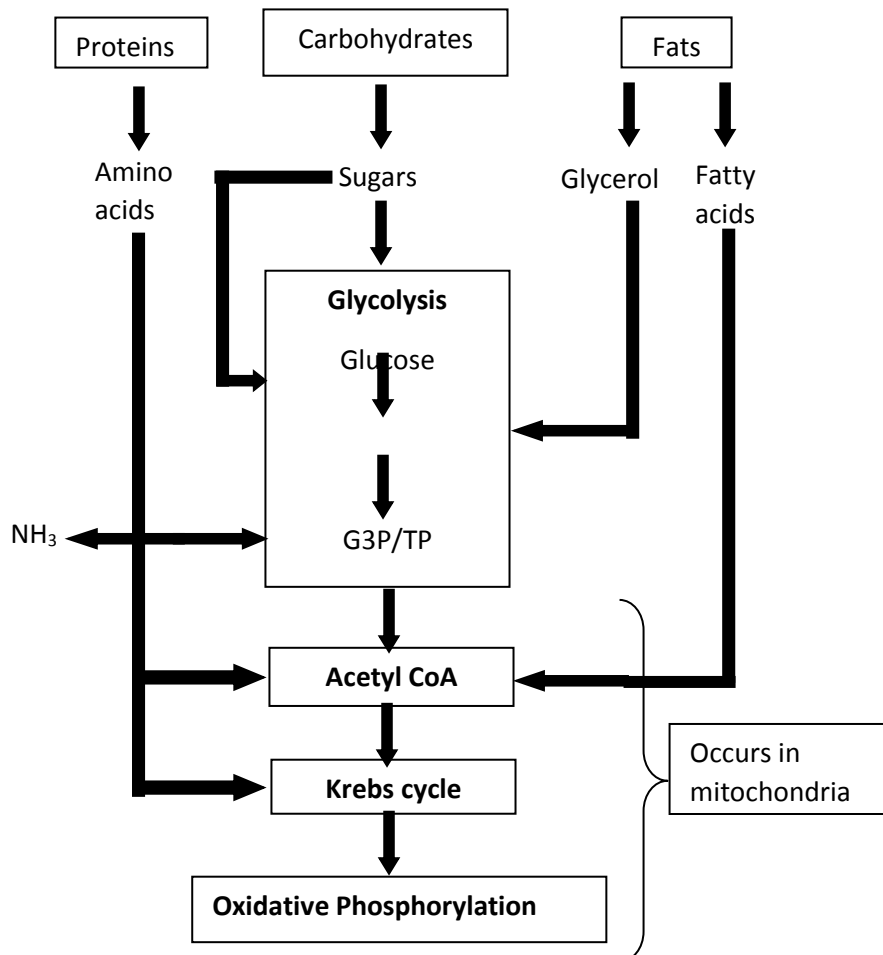
Figure 8. Lactic acid fermentation. This involves both glycolysis (top) followed by lactic acid fermentation (bottom)

Note: Only 2 ATP per glucose are produced during anaerobic respiration, compared to 38 ATP produced during aerobic respiration!

- During strenuous exercise, lactic acid accumulates in the muscle faster than it can be removed.
 - ▶ As excessive lactic acid accumulates, muscle fatigue eventually sets in.
- As with ethanol, lactate still contains a large part of the energy originally contained in glucose.
 - ▶ Lactate is eventually carried from muscle cells via blood to liver, where it can be converted back into pyruvate by liver cells. This pyruvate can then enter link reaction and Krebs cycle during aerobic respiration to produce more ATP.
- Lactic acid fermentation is used in cheese and yoghurt production, through anaerobic action of certain bacteria and fungi.

7. Other Substrates Used in Respiration

Apart from glucose, other sugars, proteins and fats can also be used as respiratory substrates. These enter the respiratory cycle at various points. Note that amino acids are first deaminated (amino group is removed) before the remaining acid enters the cycle:



SUMMARY OF IMPORTANT TERMS

1. **Chemiosmosis** – mechanism by which energy stored in the proton gradient drives ATP synthesis.
2. **Oxidative phosphorylation** – mechanism by which the exergonic re-oxidation of reduced coenzyme molecules (NAD^+ and FAD) by O_2 is coupled to the formation of ATP, with an electrochemical proton gradient as an intermediate.
3. **Proton motive force** – potential energy stored in the form of a proton gradient, generated by pumping of H^+ across a membrane.
4. **Substrate-level phosphorylation** – synthesis of ATP by direct enzyme action. An enzyme transfers a phosphate group directly from a substrate molecule to ADP to form ATP.

KEYWORDS include

Processes	Molecules	Organelles
chemiosmosis	ATP	cristae
electron transport chain	ATP synthase	cytosol
glycolysis	carbon dioxide	matrix
Krebs cycle	electrons (and protons)	mitochondria
link reaction	final electron acceptor	
lysis	NAD ⁺ / FAD	
oxidation by dehydrogenation	NADH / FADH ₂	
oxidative phosphorylation	oxygen / molecular oxygen	
phosphorylation	water	
proton motive force	lactate	
proton gradient	lactate dehydrogenase	
regenerate NAD ⁺ and FAD		

TRUE OR FALSE?

- ☐ Glycolysis produces 4 ATP.
- ☐ The mitochondrion is the organelle where all respiratory processes take place.
- ☐ During respiration, O₂ is reduced to form CO₂.
- ☐ Through respiration, chemical energy in organic food is converted to heat energy + energy stored in the form of ATP
- ☐ Water formed during respiration is called metabolic water.
- ☐ Microorganisms such as yeast can carry out anaerobic respiration; large mammals such as humans cannot.
- ☐ Proteins and fats can also be used to produce energy through respiration. However, they first need to be converted to glucose, as glucose is the primary respiratory substrate.
- ☐ Oxygen is a double-edged sword – while we need it to respire and produce ATP, it is also a cause of ageing in our cells.

