Respiration

1. Exchange of Gases:

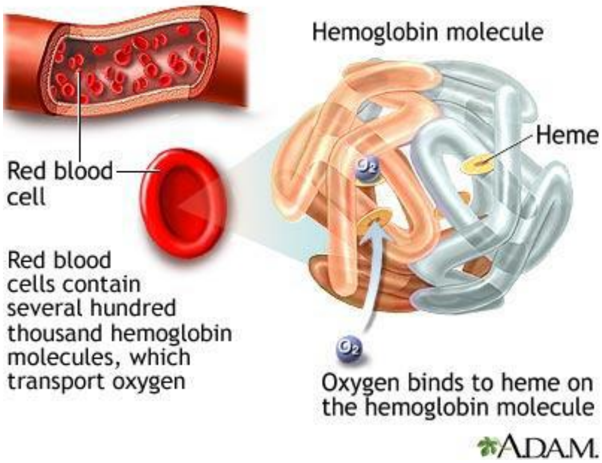
Almost all the living organisms require oxygen (O_2) to break down various food substances like carbohydrates, fats and proteins to derive energy for performing various functions. During this oxidation of nutrients, a harmful gas carbon dioxide (CO_2) is also released. Therefore, an adequate supply of O_2 must be continuously provided to the cells and CO_2 produced by the cells must be eliminated out. This process of exchange of O_2 from the atmosphere with CO_2 produced by the cells is called breathing.

In general, overall respiration involves the following steps:

1) Breathing or gaseous exchange by which atmospheric air (O_2) is drawn in and CO_2 rich alveolar air is released out.
2) Diffusion of gases (O_2 and CO_2) across alveolar membrane.
3) Transport of gases by the blood.
4) Diffusion of O_2 and CO_2 between blood and tissues.
5) Cellular respiration that utilizes O_2 for the breakdown of glucose to oxidize it to CO_2 and H_2O, and produces energy for daily life functioning

2. Oxygen Transport through blood:

Oxygen once reached to the lung through breathing, it diffuses across the alveolar membrane and is further transported via blood to the different cells of the body where it is consumed. Approximately 1.5% of the oxygen transported by the blood is dissolved directly in the blood plasma. However, most of the oxygen (~ 98.5) is transported from the lungs to the tissues by binding with a protein called haemoglobin (Hb).



Haemoglobin is a globular protein molecule and its primary function is to transport oxygen from lung to tissues and to carry CO_2 from tissues to the lung. Haemoglobin is found in red blood cells (RBC) and is made up of four protein chains (globin): two α-subunits (141 amino acids) and two β-subunits (146 amino acids). Each polypeptide chain is attached to a prosthetic group "heme", which is an iron (Fe^{2+})-porphyrin compound that binds to the one oxygen molecule. Therefore, each haemoglobin molecule can carry maximum four oxygen molecules.

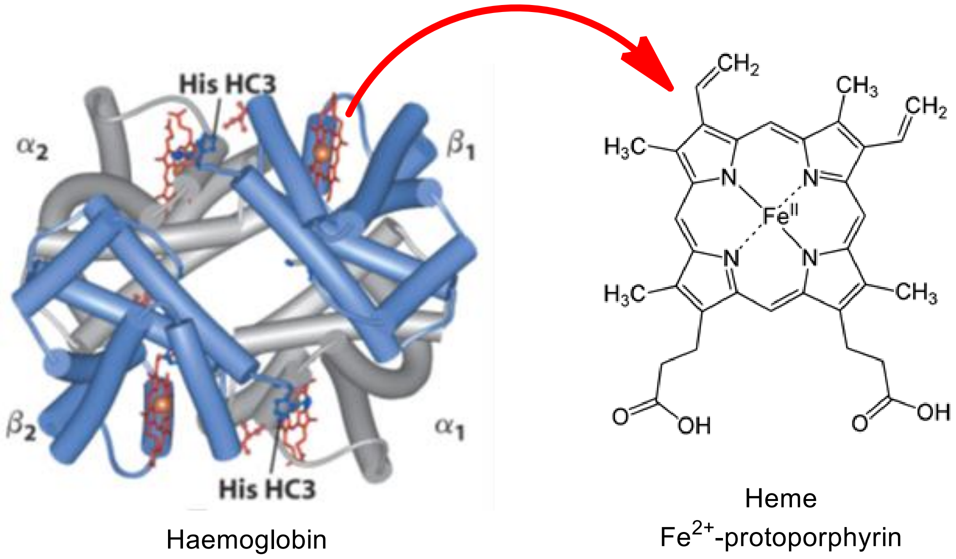


Fig. Structure of Haemoglobin

The binding of oxygen and its dissociation from Haemoglobin is principally governed by the partial pressure of oxygen. Pressure contributed by an individual gas in a mixture of gases is called partial pressure and is represented as PO_2 for oxygen and PCO_2 for carbon dioxide. The higher the PO_2 greater is the binding.

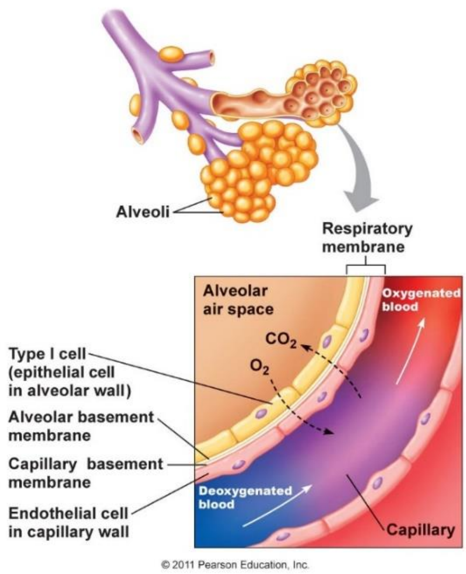


Fig. Gaseous exchange in lung

The oxygen rich air when reaches the alveoli, it has PO_2 ~100 mm Hg and that of PCO_2 is 40 mm Hg. Therefore, oxygen moves down the pressure gradient and diffuses across the membrane from the alveoli to the blood capillary. Inside capillaries, it enters the red blood cells and binds with haemoglobin to form oxyhaemoglobin (Hb–O_2). Oxyhaemoglobin is a bright red-colored molecule that gives oxygenated blood a bright red color. Oxygen binds reversibly to the haemoglobin, as a result; it can readily dissociate from the heme to give deoxygenated haemoglobin, which is dark red in color.

$$\mathbf{Hb + O_2 \leftrightarrow Hb{-}O_2}$$

The tissues have a lower partial pressure of oxygen (PCO_2 ~40 mm Hg**)** because of oxygen utilization and a higher carbon dioxide concentration because of carbon dioxide production. Oxygenated blood when reaches to the tissues, oxygen dissociates from Hb to diffuse out to the tissues, whereas CO_2 gas binds to Hb.

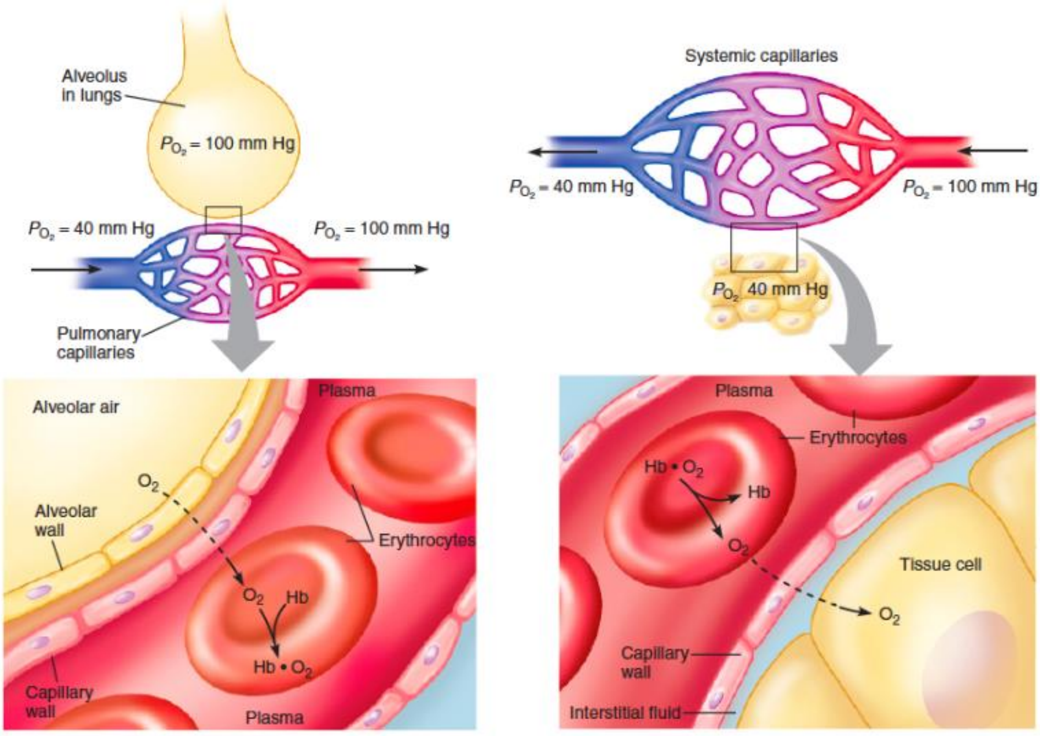


Fig. Transport of oxygen by binding with haemoglobin

2.1 The mechanism of oxygen binding to Haemoglobin:

Haemoglobin binds with oxygen in a cooperative manner to form oxyhaemoglobin i.e. binding of one molecule of oxygen to one heme increases the oxygen binding affinity within the remaining heme groups of Hb. When one molecule of oxygen binds to heme group, the shape of globin chain is altered, leading to overall change in the quaternary structure of Hb. This structural transition of Hb protein, further facilitates the binding of successive oxygen molecules until all four heme groups are occupied. Cooperative behaviour is also observed in dissociation: as the first oxygen molecule dissociates and is released at the tissues, the next oxygen molecule dissociates more readily. When all four heme sites are occupied, the haemoglobin is said to be saturated.

In fully deoxygenated haemoglobin, the molecule's quaternary structure is described as the 'T' or 'tense' form in which the crevices are small, making it difficult for oxygen to gain access to the heme. As each successive oxygen binds to the molecule, the structural changes described above result in the molecule relaxing, enlarging the crevice on adjacent globin chains and increasing their oxygen affinity. When fully oxygenated with four oxygen molecules, the haemoglobin achieves its 'R' or 'relaxed' quaternary structure.

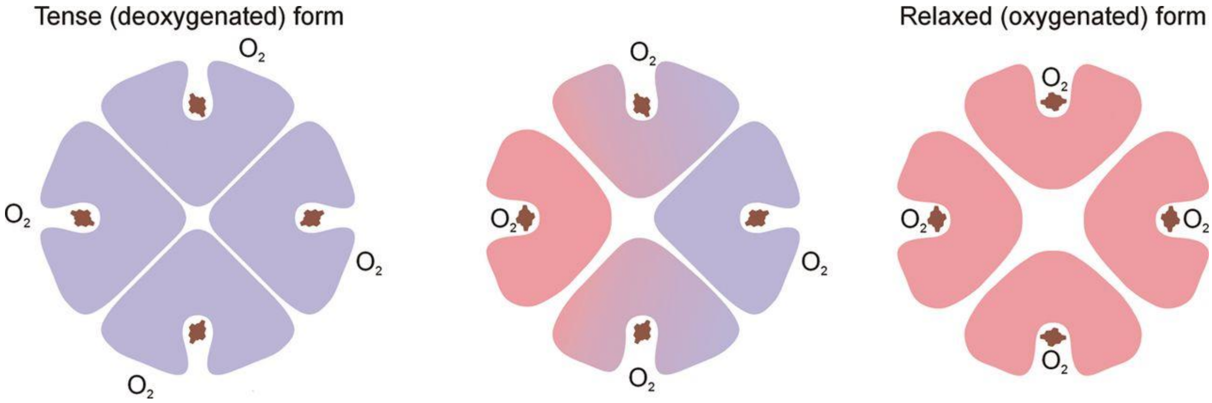


Fig. Cooperative binding of oxygen to haemoglobin

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2.2 Oxygen-haemoglobin Dissociation curve:

An oxygen–haemoglobin dissociation curve is a graph that describes the relationship of partial pressure to the binding of oxygen to heme and its subsequent dissociation from heme. This graph of percent saturation of haemoglobin as a function of PO_2 is sigmoid-shaped, which is due to cooperative binding of oxygen to the haemoglobin. At very low partial pressure when most of the haemoglobin is in deoxyhaemoglobin state (tense form), the affinity for oxygen is the lowest. This results in a small increase in percent saturation. With increasing PO_2 most of the haemoglobin acquires at least one oxygen molecule. This causes haemoglobin to undergo conformational changes such that, each subsequent oxygen molecule binds to haemoglobin more easily. Hence, cooperativity leads to steep rise in curve gradient (PO_2 from ~15 to 70 mm Hg). With further increase in PO_2 (Above 70 mm Hg), O_2 binds to haemoglobin and only fewer binding sites become available so the curve starts to levels off again. 100 percent O_2 saturation of haemoglobin means that every heme unit in all RBCs of body is bound to oxygen. In a healthy individual, at 100 mm Hg the haemoglobin saturation generally ranges from 95 percent to 98 percent.

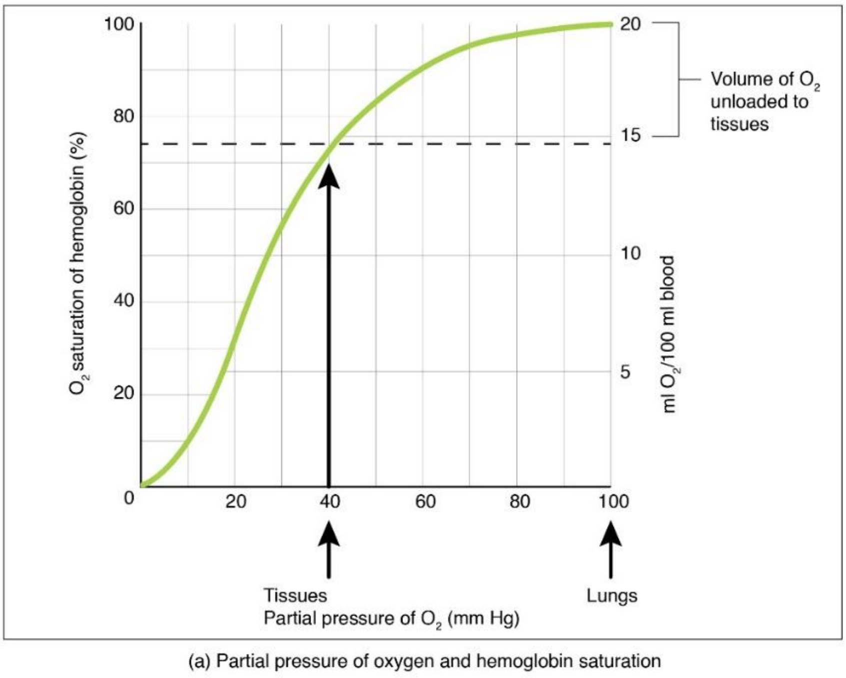

Fig. Oxygen-haemoglobin Dissociation curve

Image credit: https://opentextbc.ca/anatomyandphysiology/chapter/22-5-transport-of-gases/

3. Myoglobin:

Like haemoglobin, myoglobin is also a globular protein which is composed of single α-helical protein chain that is attached to a prosthetic group heme moiety. Due to presence of only one binding site (heme group), myoglobin can carry just one oxygen molecule. Heme consists of a protoporphyrin ring co-ordinated to central iron ion in Fe^{2+} state.

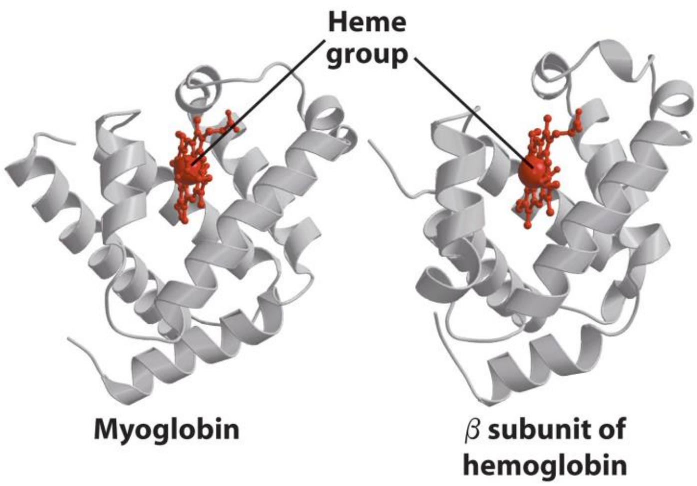

Fig. Structure of myoglobin

Myoglobin is the oxygen storage protein of the muscle, which serves as a reserve supply of oxygen for muscle functioning. Myoglobin grabs oxygen from haemoglobin in tissues, where oxygen PO_2 is low and releases it in the muscle cells. In comparison to haemoglobin, myoglobin absorbs or releases an oxygen molecule at a much lower partial pressure. The muscles of aquatic mammals, such as whales and dolphins, are particularly rich in myoglobin, which allows them to be submerged for long periods of time.

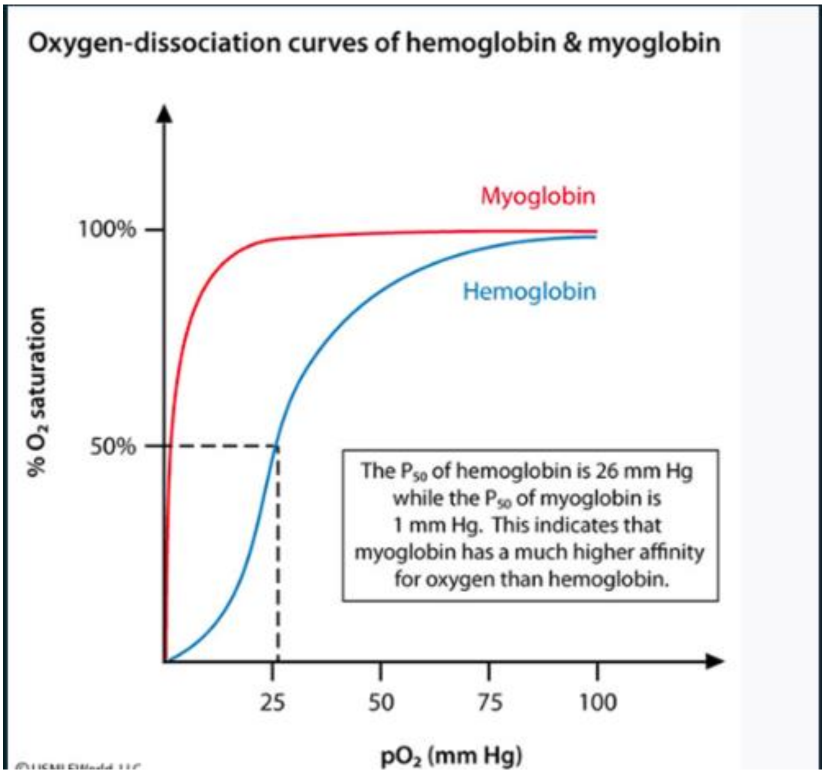

Fig. Oxygen Dissociation curve for haemoglobin and myoglobin

In contrast to haemoglobin, the oxygen-dissociation curve for myoglobin is hyperbolic that rises sharply then levels off as it reaches the maximum saturation. The half-saturation, the point at which half of the myoglobin is bound to oxygen, is 1 mm Hg for myoglobin whereas it is ~26 mm Hg for haemoglobin. This shows that myoglobin has a strong affinity for oxygen. Therefore, it can accept oxygen from haemoglobin at the tissues where PO_2 is 40 mm Hg. The hyperbolic curve also reflects that since myoglobin's oxygen binding affinity is quite high it will release an oxygen molecule only when PO_2 falls below 5 mm Hg. Thus, myoglobin delivers oxygen to muscles only during emergency situation when oxygen level depletes completely.

Overall, myoglobin is less efficient oxygen carrier than haemoglobin, because Hb loses its affinity for oxygen as the pressure goes down and releases the oxygen into the tissues, while myoglobin's strong affinity for oxygen keeps the oxygen bound to it instead of releasing it into the tissues.

3.1 Comparison of Haemoglobin and Myoglobin:

	HAEMOGLOBIN	MYOGLOBIN
1.	Haemoglobin = Heme: Blood Globular protein found in blood (water soluble)	Myoglobin = Myo: Muscle Globular protein exists in muscle cells (water soluble).
2.	Binds to the oxygen in lungs and releases to the tissues (including muscles).	Binds and releases oxygen to the muscle cells.
3.	Haemoglobin has 4 polypeptide chains of two different types- 2 alpha and 2 beta	It contains single polypeptide chain.
4.	It consists of 4 heme units each of which can bind to one oxygen molecule. Therefore, one molecule of Hb can carry up to 4 oxygen molecules.	It comprises of one polypeptide chain attached to single heme group. One molecule of myoglobin carries one oxygen molecule.
5.	Quaternary protein structure	Quaternary protein structure
6.	Haemoglobin has lower oxygen binding affinity towards oxygen than myoglobin.	Myoglobin binds to O2, tightly and firmly. (grabs oxygen from Hb in tissues and releases to the muscle cells).
7.	Oxygen dissociation curve is Sigmoid	Oxygen dissociation curve is hyperbolic
8.	It requires more pressure of oxygen to get saturated.	It becomes saturated at higher partial pressure.
9.	It is a transport protein which supplies the oxygen in whole body	Myoglobin is a storage protein which supplies oxygen to the muscles only during starving time of oxygen.

4. Cellular Respiration:

Our body is composed of several types of cells that are organized into tissues and organs that perform specific functions. Living cells require a constant source of energy in the form of ATP (adenosine triphosphate) for the life processes. Cellular respiration is the process by which cells regenerate the energy (ATP) by the oxidation of foods (eg. glucose). This process occurs in three stages: glycolysis, the Krebs cycle, and electron transport chain. The latter two stages i.e. krebs cycle and electron transport demands oxygen.

However, cellular respiration can occur both in presence of oxygen (aerobically), or without oxygen (anaerobically).

4.1 Aerobic Respiration:

- Occurs in the presence of oxygen in most of the eukaryotes and prokaryotes.
- Takes place in specialized organelle mitochondria of the cell.
- During aerobic cellular respiration glucose is completely oxidised to liberate energy (in the form of ATP). CO_2 and H_2O are formed as byproducts.
- Oxidation of 1 glucose molecule produces 38 ATP.
- Involves three steps –

1. Glycolysis	Glucose is converted into 2 molecules of pyruvic acid (Takes place in the cytoplasm)
2. Krebs cycle 3. Electron tansport chain	Aerobic oxidation of pyruvic acid into CO_2 and H_2O (Takes place in the mitochondria)

- Overall Reaction: –

$$\underset{\text{Glucose}}{C_6H_{12}O_6} + 6O_2 \longrightarrow 6CO_2 + 6H_2O + \text{Energy (38 ATP)}$$

4.2 Anaerobic Respiration:

Some organisms have potential to generate energy even in the absence of oxygen, which is also known as fermentation. During the process glucose undergoes glycolysis, followed by further anaerobic process of fermentation to yield 2 molecules of ATP. This can be of two types:

4.2.1 Alcoholic Fermentation: This occurs in yeasts and some bacteria. Partial oxidation of glucose in absence of oxygen produces ethyl alcohol and 2 ATP molecules. This process finds its commercial application in baking and brewing industry. Alcoholic fermentation in yeasts releases CO_2 gas that makes dough rise to give bread its holes.

$$\underset{\text{Glucose}}{C_6H_{12}O_6} \longrightarrow \underset{\text{Ethyl alcohol}}{2C_2H_5OH} + 2CO_2 + 2\ \text{ATP}$$

4.2.2 Lactic acid Fermentation: This occurs in muscle cells, when due to rigorous exercising body cannot supply enough oxygen to the muscles. Under anaerobic conditions muscle can continue to produce ATP by partial oxidation of glucose. Lactic acid is produced in muscle that causes the burning sensation, pain and fatigue.

$$\underset{\text{Glucose}}{C_6H_{12}O_6} \longrightarrow \underset{\text{Lactic acid}}{2\,H_3C-CH(OH)-COOH} + 2\,ATP$$

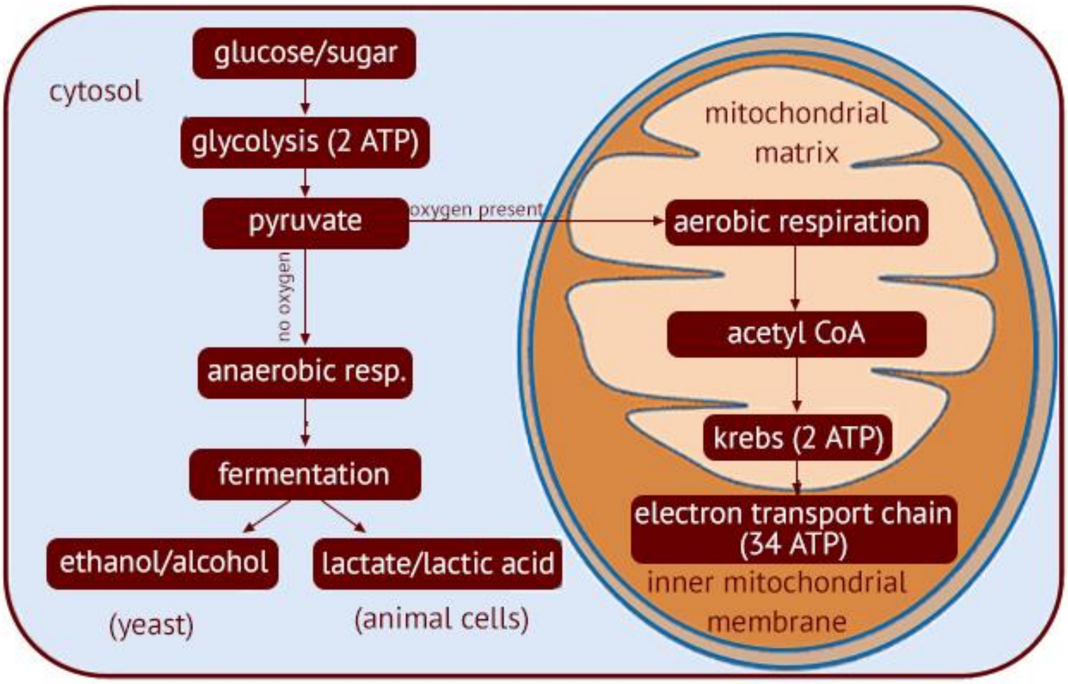

Fig. Schematic representation of Cellular Respiration

Image credit: https://www.philpoteducation.com/mod/book/view.php?id=782&chapterid=1130#/

5. Respiratory Quotient:

Respiratory quotient, also known as the respiratory ratio (R.Q.), is defined as the volume of carbon dioxide released over the volume of oxygen absorbed during respiration. The volume of carbon dioxide released, and the volume of oxygen consumed by the cell during respiration depends upon the kind of respiratory substrate utilized. Therefore, RQ is a measure of efficiency of combustion of food substrate in the process of respiration to release energy.

$$\text{R.Q.} = \frac{\text{Volume of } CO_2 \text{ released}}{\text{Volume of } O_2 \text{ absorbed}}$$

It is calculated for a particular substrate i.e., carbohydrates, organic acid, fat, and protein. Carbohydrates are oxidized through aerobic respiration resulting in an equal ratio of CO_2 release and O_2 consumption. Therefore, for carbohydrates RQ is always 1. Subsequently, the R.Q. for fat and protein is 0.7 and 0.8, respectively. In anaerobic respiration, since oxygen is not involved, hence R.Q. is infinity.

For Carbohydrate:

$$\underset{\text{Glucose}}{C_6H_{12}O_6} + 6O_2 \longrightarrow 6CO_2 + 6H_2O + 36\ \text{ATP}$$

$$\text{R.Q.} = \frac{\text{Volume of } CO_2 \text{ released}}{\text{Volume of } O_2 \text{ absorbed}} = \frac{6\ CO_2}{6\ O_2} = 1$$

For Fat:

$$\underset{\text{Tripalmitin}}{C_{51}H_{98}O_6} + 145\ O_2 \longrightarrow 102\ CO_2 + 98\ H_2O$$

$$\text{R.Q.} = \frac{102\ CO_2}{145\ O_2} = 0.7$$

The cells of the body consume an average 250 ml of oxygen per minute and produce about 200 ml of carbon dioxide per minute. Hence, the average human respiratory quotient is 0.8.