Bioenergetics

Bioenergetics, or biochemical thermodynamics, is the study of the energy changes accompanying biochemical reactions. Biologic systems are essentially isothermic and use chemical energy to power living processes. In addition death from starvation occurs when available energy reserves are depleted, and certain forms of malnutrition are associated with energy imbalance.Metabolic reactions involved in energy generation break down ingested or stored fuels such as carbohydrate, lipid, or protein termed as catabolic pathways. These reactions result in the conversion of large complex molecules to smaller molecules(ultimately CO_2 and H_2O), with production of storable or conservable energy, and often require the consumption of oxygen during this process. Such reactions are accelerate during periods of fuel deprivation or stress to an organism.

Free energy is the useful energy in system

Gibbs change in free energy (ΔG) is that portion of the total energy change in a system that is available for doing work, also known as the chemical potential. Biologic Systems Conform to the General Laws of Thermodynamics. On the other hand, if ΔG is positive, the reaction proceeds only if free energy can be gained; it is endothermal , and when ΔG is negative, the reaction proceeds only if free energy can be accepted; it is exothermal. If ΔG is zero, the system is at equilibrium and no net change of energy.

1-First law of thermodynamics:

The total energy of a system, including its surroundings, remains constant. It implies that within the total system, energy is neither lost nor gained during any change , chemical energy may be transformed into heat or into electrical, radiant, or mechanical energy:

For example, chemical energy available in a metabolic fuel such as glucose can be converted in the process of glycolysis to another form of chemical energy (ATP). In skeletal muscle chemical energy involved in the energy rich phosphate bonds of ATP may be converted to mechanical energy during the process of muscle contraction.

The energy involved in electropotential of protons across the mitochondrial membrane may be converted to chemical energy using the proton gradient to drive ATP synthesis:

$$\Delta U = Q - W$$

ΔU: change internal energy
Q: quantities of heat supply
W: work done

2-second law of thermodynamics states:
The total entropy (S) of a system must increase if a process is spontaneously. Entropy is the extent of disorder or randomness of the system:

$$\Delta S = \frac{q}{T}$$

ΔS: change in Entropy
q: transfer of heat
T: temperature

Equilibrium in a system will result when the randomness or disorder (entropy) is at a maximum. quantity termed free energy is employed.

$$\Delta G = \Delta H - T\Delta S$$

ΔG: change in Free energy
ΔH: change in Enthalpy

It can be deduced from this relationship that at equilibrium G=0. Furthermore, any process that exhibits a negative free energy change is called as exothermic reaction and when as negative free energy change is called as endothermic reaction .

Biologic oxidation

Oxidation, which occurs in living systems is called biological oxidation. Biological oxidations are exothermic. During biological oxidations, the reacting chemical systems move from a higher energy level to a lower one and therefore there is liberation of energy. The energy released as heat is converted to chemical energy by formation of energy rich compound ATP. The formation of ATP from ADP and Pi is termed phosphorylation, as biological oxidative phosphorylation. Biological oxidation is that oxidation which occurs in biological systems to produce energy. Oxidation can occur by:

1. Addition of oxygen
2. Removal of hydrogen
3. Removal of electrons

Electrons are not stable in the free state, so their removal form a substance (oxidation) must be accompanied by their acceptance by another substance (reduction) hence the reaction is called oxidation-reduction reaction or redox reaction and the involved enzymes are called oxido-reductases. These enzymes catalyze oxidation- reduction reactions. They are classified into five groups:

1. oxidases
2. aerobic dehydrogenises
3. anaerobic dehydrogenises.
4. hydroperoxidases and 5-oxygenases.

The coenzyme include:

1. FMN (Flavin adenine mononucleotide) as in L-amino acid oxidase.
2. FAD (Flavin adenine dinucleotide) as in D-amino acid oxidase, xanthine oxidase, aldehyde dehydrogenase and glucose oxidase.

Electron transport chain

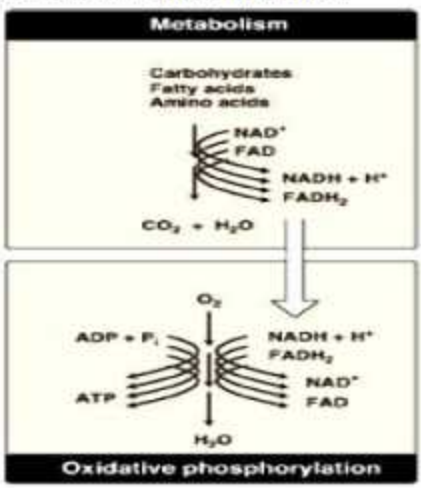
Energy-rich molecules, such as glucose, are metabolized by a series of oxidation reactions ultimately yielding CO2 and water . The metabolic intermediates of these reactions donate electrons to specific coenzymes, nicotinamide adenine dinucleotide (NAD+) and flavin adenine dinucleotide (FAD), to form the energy-rich reduced forms, NADH and FADH2. These reduced coenzymes can, in turn, each donate a pair of electrons to a specialized set of electron carriers, collectively called the electron transport chain (ETC).. As electrons are passed down the ETC,

they lose much of their free energy. This energy is used to move protons across the inner mitochondrial membrane, creating a proton gradient that drives the production of ATP from ADP and inorganic phosphate (Pi),. The coupling of electron transport with ATP synthesis is called oxidative phosphorylation.

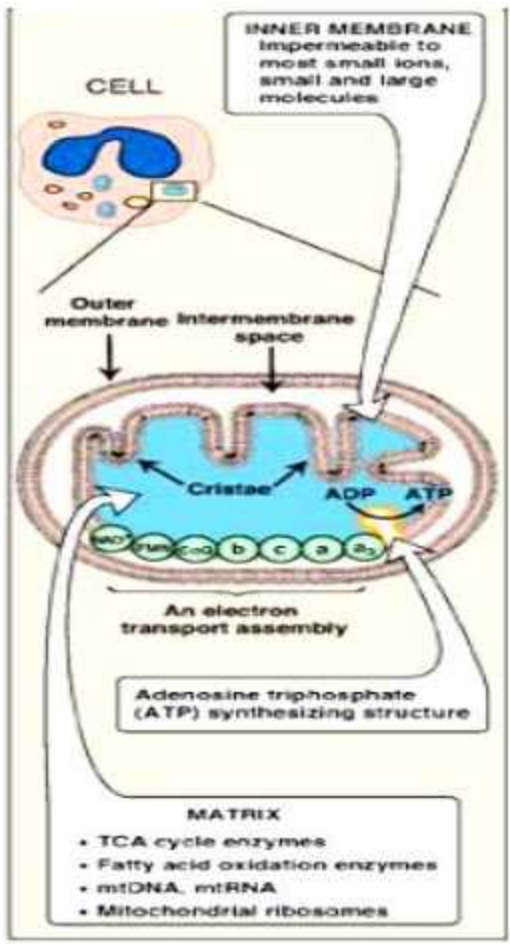
A-The electron transport chain of the mitochondrion

The ETC (except for cytochrome c) is located in the inner mitochondrial membrane and is the final common pathway by which electrons derived from different fuels of the body flow to oxygen (O2).

1. Membranes of the mitochondrion: The mitochondrion contains an outer and an inner membrane separated by the intermembrane space. Although the outer membrane contains special channels (formed by the protein porin), making it freely permeable to most ions and small molecules, the inner membrane is a specialized structure that is impermeable to most small ions, including protons and small molecules such as ATP, ADP, pyruvate, and other metabolites important to mitochondrial function. Specialized carriers or transport systems are required to move ions or molecules across this membrane. The inner mitochondrial membrane is unusually rich in protein, over half of which is directly involved in oxidative phosphorylation.



2-**Matrix of the mitochondrion:** This gel-like solution in the interior of mitochondria is also rich in protein. Also molecules include the enzymes responsible for the oxidation of pyruvate, amino acids, and fatty acids (by β-oxidation) as well as those of the tricarboxylic acid (TCA) cycle. The synthesis of glucose, urea, and heme occurs partially in the matrix of mitochondria. In addition, the matrix contains NAD+ and FAD (the oxidized forms of the two coenzymes that are required as hydrogen acceptors), and ADP and Pi, which are used to produce ATP. The matrix also contains mitochondrial DNA (mtDNA) and RNA (mtRNA) and ribosomes.



B. Organization of the electron transport chain

The inner mitochondrial membrane contains five separate protein complexes, called Complexes I, II, III, IV, and V. Complexes .These complexes accept or donate electrons to the relatively mobile electron carriers, coenzyme Q and cytochrome c. Each carrier in the ETC can receive electrons from an electron donor and can subsequently donate electrons to the next acceptor in the chain. The electrons ultimately combine with O2 and protons to form water.

C. Reactions of the electron transport chain

With the exception of coenzyme Q, which is a lipid-soluble quinone, all members of this chain are proteins. These are:

1. Formation of NADH: Both electrons but only one proton (that is, a hydride ion [:H–]) are transferred to the NAD+, forming NADH plus a free proton. NAD+ is reduced to NADH by dehydrogenases that remove two hydrogen atoms from their substrate. The final steps in the overall oxidation of food stuffs (carbohydrate, fat and amino acids) result in formation of NADH. The electron transport chain (ETC) oxidizes NADH by transferring electrons (reducing equivalents) by a series of oxidation reduction reactions to O_2, the terminal electron acceptor.

2. NADH dehydrogenase: The free proton plus the hydride ion carried by NADH are transferred to NADH dehydrogenase, a protein complex (Complex I) embedded in the inner mitochondrial membrane. At Complex I, electrons move from NADH to FMN to the iron of the iron-sulfur centers and then to coenzyme Q. As electrons flow, they lose energy. This energy is used to pump protons across the inner mitochondrial membrane, from the matrix to the intermembrane space. The coenzymes of dehydrogenases may be either:

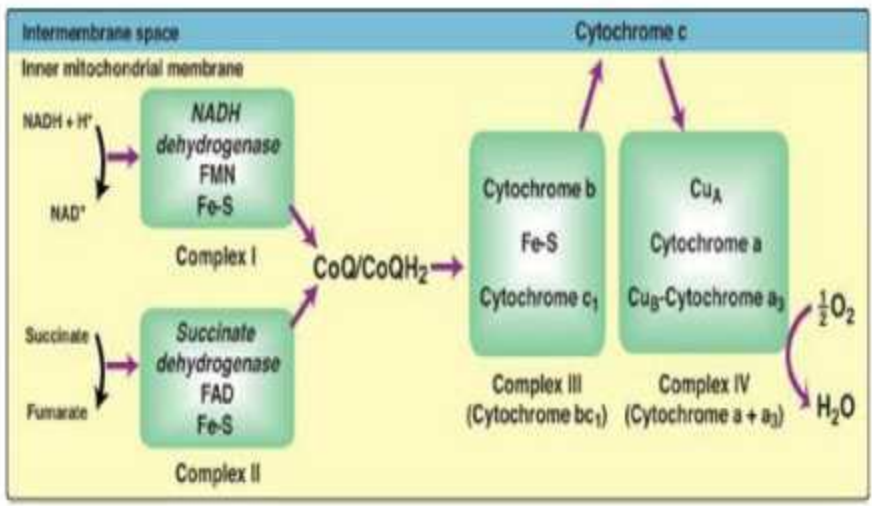
– Nicotinamide coenzymes (NAD+ or NADP+)

– Flavin coenzymes (FMN or FAD).

3. Succinate dehydrogenase: At Complex II, electrons from the Succinate dehydrogenase catalyzed oxidation of succinate to fumarate move from the coenzyme, FAD to an iron-sulfur protein, and then to coenzyme Q.

4. Coenzyme Q: Coenzyme Q (CoQ) transfers electrons to (cytochrome).
5. Cytochromes(Complex III): the cytochrome iron is reversibly converted from its ferric (Fe3+) to its ferrous (Fe2+) form as a normal part of its function as an acceptor and donor of electrons. Electrons are passed along the chain from cytochrome bc1 (Complex III), to cytochrome c, and then to cytochromes Complex IV. As electrons flow, protons are pumped across the inner mitochondrial membrane at Complexes III and IV.

6. Cytochrome (Complex IV): is the only electron carrier in which the heme iron has an available coordination site that can react directly with O2 and so also is called cytochrome oxidase. At Complex IV, the transported electrons, O2, and free protons are brought together, and O 2 is reduced to water .



7. Site-specific inhibitors: These compounds prevent the passage of electrons by binding to a component of the chain.

Oxidative phosphorylation

Aerobic organisms are able to capture available free energy of respiratory substrates than anaerobic organisms. Oxidative phosphorylation is the metabolic pathway in which the mitochondria in cells use their structure, enzymes, and energy released by the oxidation of nutrients to reform ATP. Most of this takes place inside mitochondria, which have been termed the "powerhouses" of the cell. Respiration is coupled to the generation of the high-energy intermediate ATP by oxidative phosphorylation offers insight into how this is accomplished. A number of drugs (eg, amobarbital) and poisons (eg,cyanide, carbon monoxide) inhibit oxidative phosphorylation, usually with fatal consequences.

Mitochondria have an outer membrane that is permeable to most metabolites, an inner membrane that is selectively permeable. Most of the energy liberated during the oxidation of carbohydrate, fatty acids, and amino acids is made available within mitochondria .

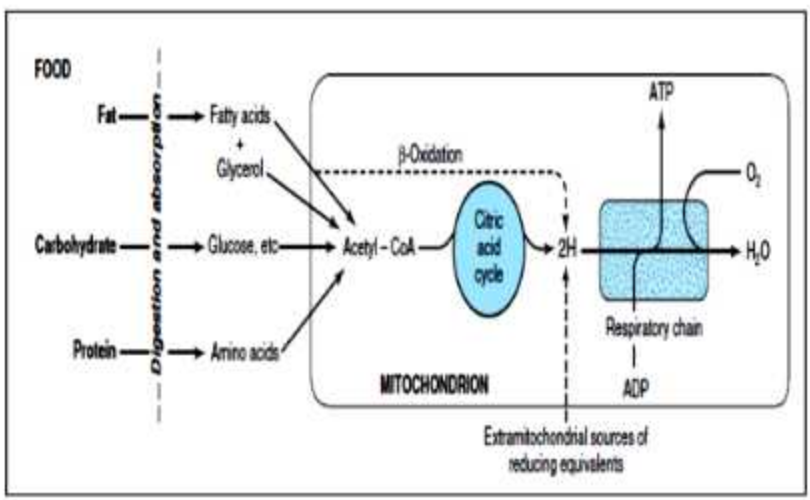


Figure: Role of the respiratory chain of mitochondria in the conversion of food energy to ATP

During oxidative phosphorylation, electrons are transferred from electron donors to electron acceptors such as oxygen, in redox reactions. These redox reactions release energy, which is used to form ATP. These linked sets of proteins are called electron transport chains.

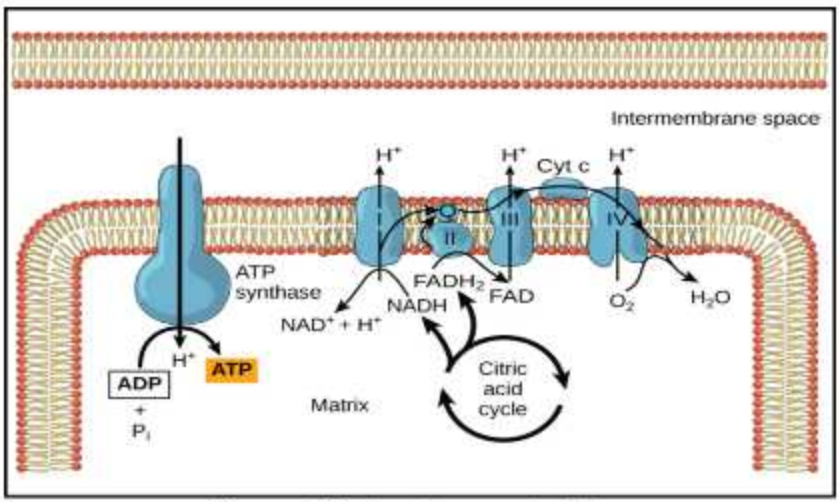


Figure: Electron transport chains

NAD^+ and NADP+ coenzymes:

Nicotinamide adenine dinucleotide (NAD) is a coenzyme found in all living cells. The compound is a dinucleotide, because it consists of two nucleotides joined through their phosphate groups. One nucleotide contains an adenine base and the other nicotinamide. Nicotinamide adenine dinucleotide exists in two forms, an oxidized and reduced form abbreviated as NAD^+ and NADH respectively. NADPH is the reduced form of $NADP^+$. $NADP^+$ differs from NAD^+ in the presence of an additional phosphate group:

$$MH_2 + NAD^+ / NADP^+ \rightarrow M + NADH + H^+ / NADPH + H^+$$

Role of NADPH

-NADPH is required for the biosynthesis of fatty acids, cholesterol, steroid hormones and neurotransmitters.

– It is required for oxidation-reduction reactions involved in detoxification, e.g.for detoxification of drugs by microsomal cytochrome P450 mono-oxygenase and for reduction of oxidized glutathione.

– In RBC, NADPH is required to maintain the level of reduced glutathione. The reduced glutathione protects the RBC membrane from toxic effect of H_2O_2 by reducing H_2O_2 to H_2O

– NADPH also keeps iron of hemoglobin in reduced ferrous (Fe2+) state and prevents the formation of methemoglobin that carry (Fe3+).

– NADPH is necessary for phagocytosis carried out by white blood cell

Role of Flavin-coenzyme (FMN or FAD) linked dehydrogenases

Flavin mononucleotide (FMN) and flavin adenide dinucleotide (FAD) are derived from vitamin riboflavin. Unlike NAD+, both hydrogen atoms from substrate are accepted by FMN or FAD. The general reaction can be written as:

$$MH2 + FAD/FMN \rightarrow M + FADH2/FMNH2$$

Most of the FMN linked dehydrogenases are concerned with mitochondrial electron transport chain, e.g. NADH-dehydrogenase.