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Energy of Life – at the level of cells and molecules

The production of energy, its storage, and its use are central to the economy of the cell.

Cells require energy to do all their work.

Energy – ability to do work

Based on:
Molecular Cell Biology, Lodish et al.
Essencial Cell Biology, Alberts et al.
Principles of Biochemistry, Freeman & Company Lehninger
Cell Energy and Cell Functions, *Nature Education*

Biochemical Energetics

In cell, the energy is associated with chemical bonds and chemical reactions.

Living Systems Use Various Forms of Energy, Which Are Interconvertible

Kinetic Energy

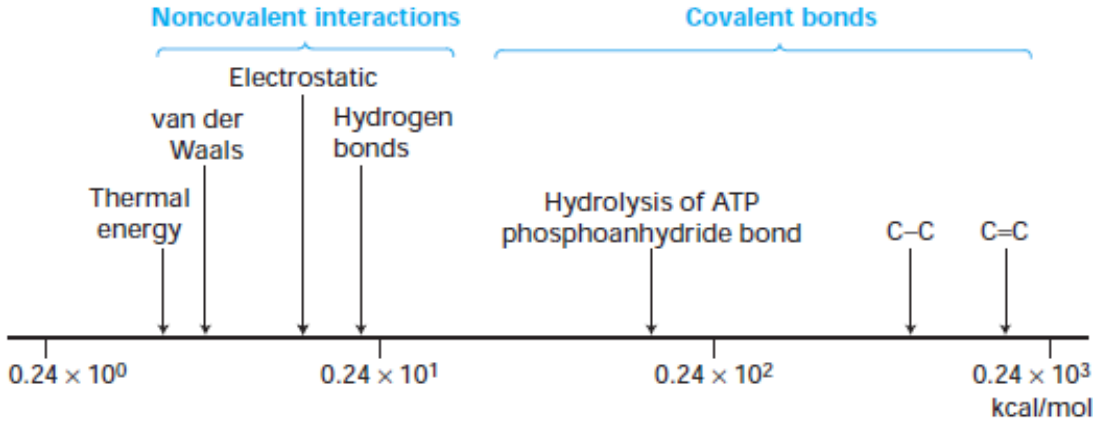
1) Heat, or ***thermal energy*** - the energy of the motion of molecules

2) ***Radiant energy*** - the kinetic energy of photons, or waves of light

3) ***Electric energy*** - the energy of moving electrons or other charged particles.

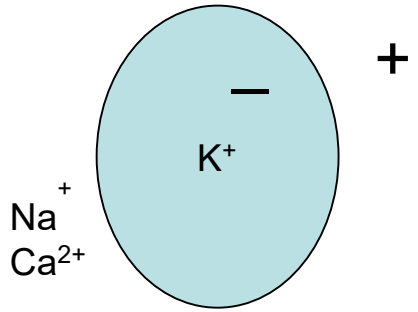
Potential Energy or Stored Energy

1) The potential energy ***stored in the bonds*** connecting atoms in molecules. Most of the biochemical reactions involve the making or breaking of at least one covalent chemical bond.



2) The energy in a ***concentration gradient***

3) An ***electric potential***
- the energy of charge separation.



Because all forms of energy are interconvertible, they can be expressed in the same units of measurement, such as the calorie or kilocalorie.

Interconvertibility of All Forms of Energy

According to **the first law of thermodynamics**, energy is neither created nor destroyed, but can be converted from one form to another.

Examples:

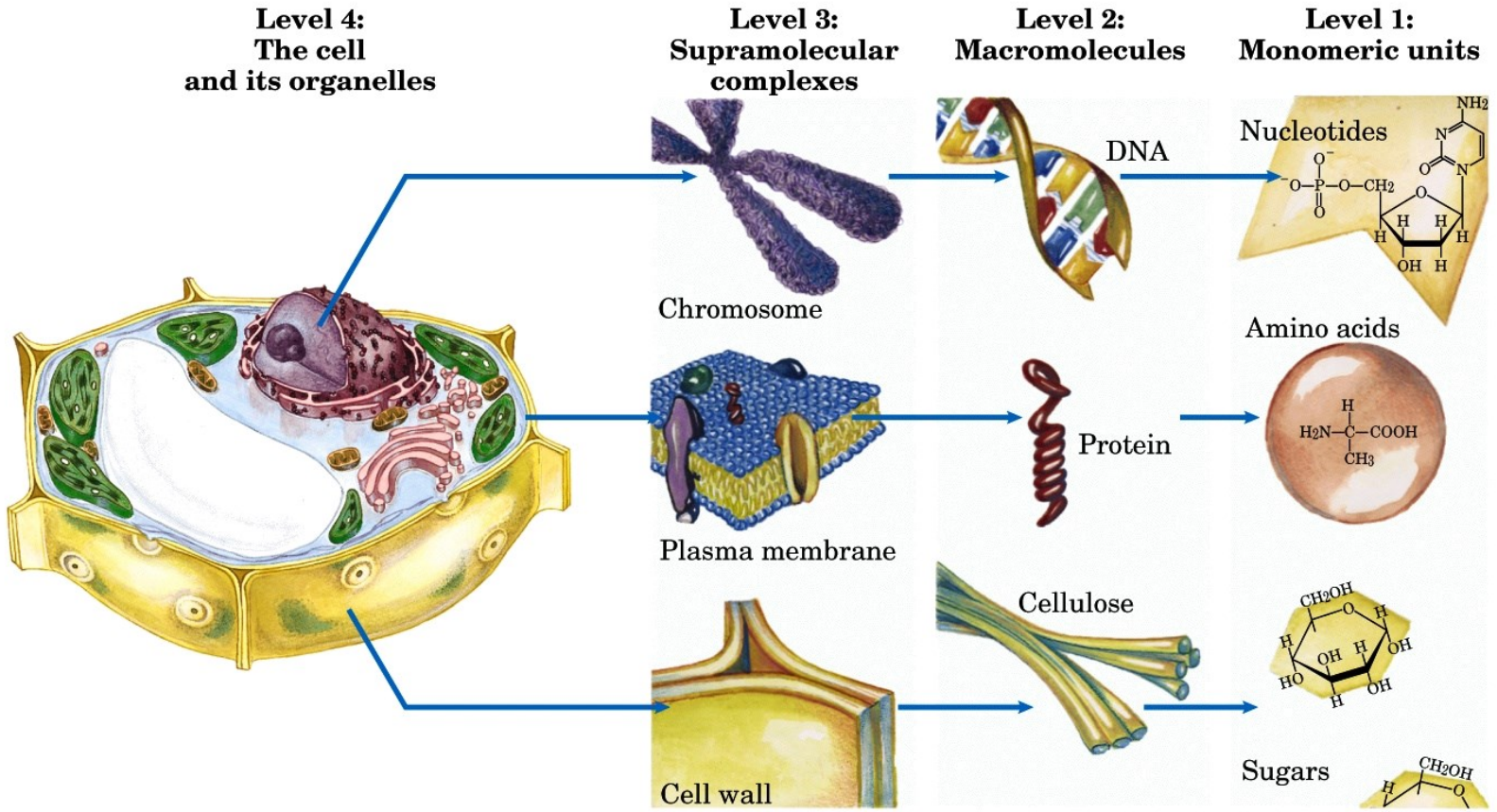
- In photosynthesis, the radiant energy of light is transformed into the chemical potential energy of the covalent bonds between the atoms in a sucrose or starch molecule.

- In muscles and nerves, chemical potential energy stored in covalent bonds is transformed, respectively, into kinetic and electric energy.

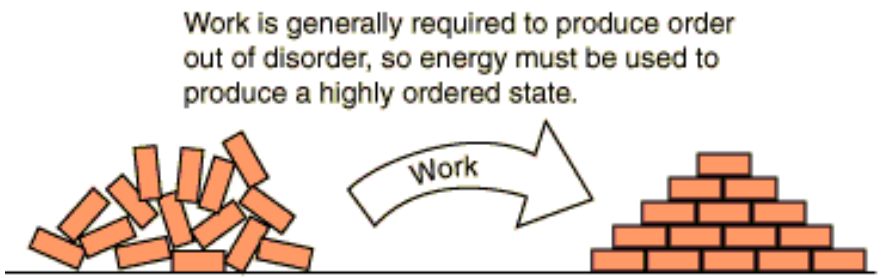
- In all cells, chemical potential energy, released by breakage of chemical bonds, is used to generate potential energy in the form of concentration and electric potential gradients.

- In all cells, energy stored in chemical concentration gradients or electric potential gradients is used to synthesize chemical bonds, or to transport other molecules “uphill” against a concentration gradient (transport of nutrients and many waste products).

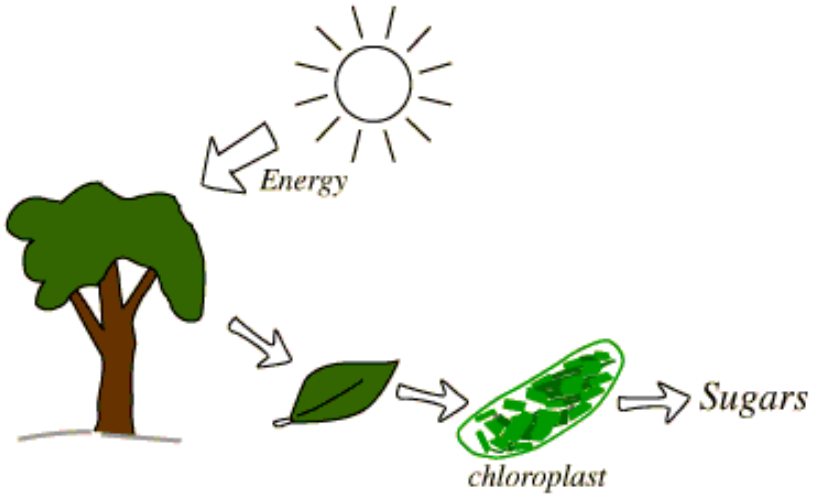
The second law of thermodynamics assumes that systems naturally progress from order to disorder, i.e., to a higher entropy.



Entropy is a measure of the degree of randomness or disorder of a system. Entropy increases as a system becomes more structured (but more disordered in surrounding) and decreases as it becomes more disordered (more structured in surrounding.



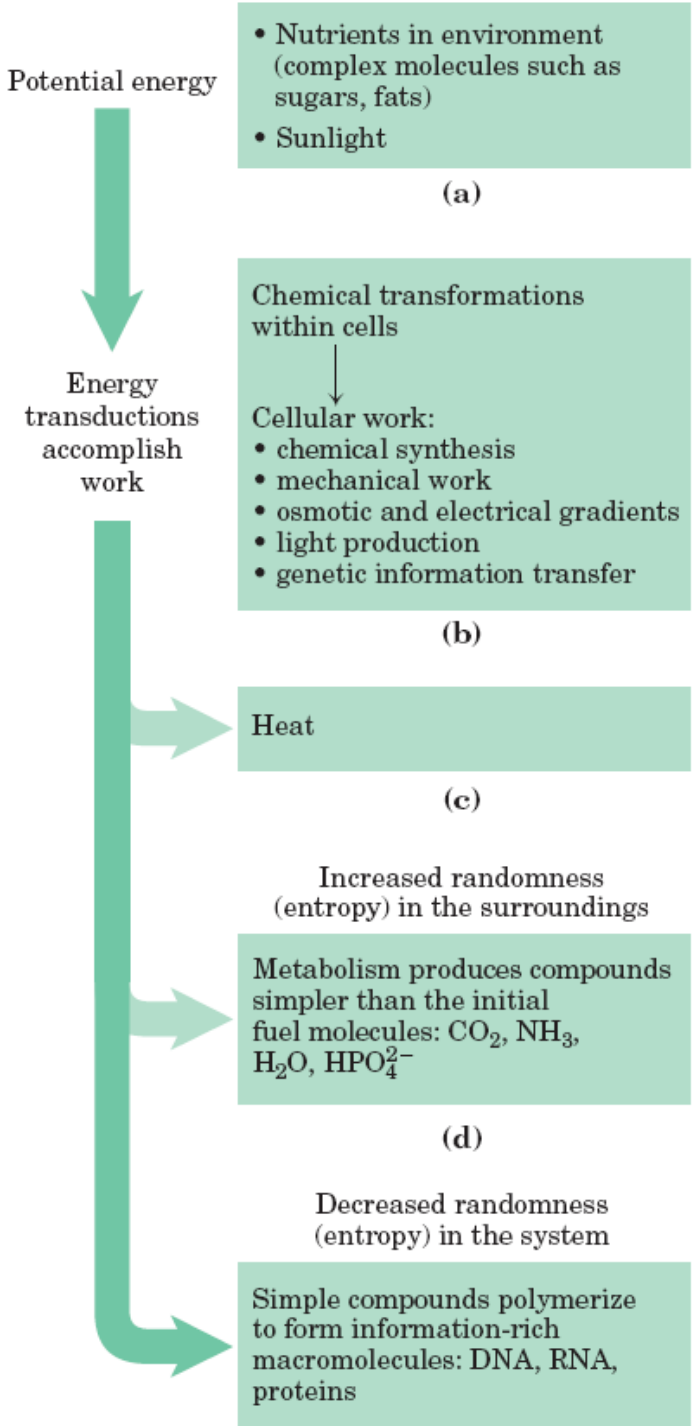
Order can be produced with an expenditure of energy. As a side effect, heat is produced (the most disordered form of energy) leading to a higher entropy in the surrounding.



Plants (autotrophic organisms) use energy from the sun in chloroplasts. Using chlorophyll in photosynthesis, they convert the sun's energy into storable form in ordered sugar molecules. In this way, carbon and water in a more disordered state are combined to form the more ordered sugar molecules.

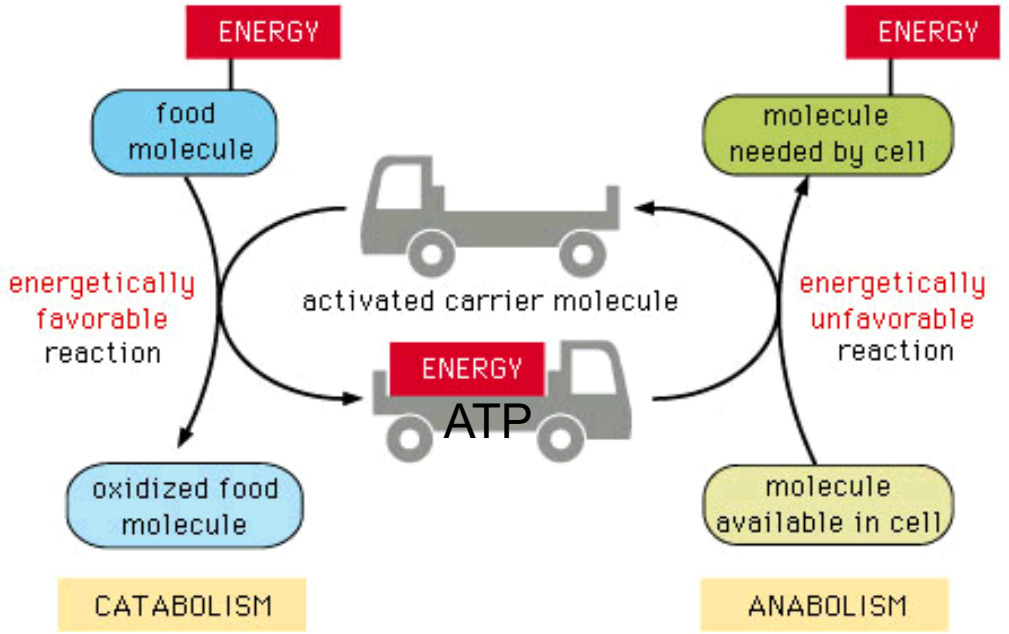
In animals (heterotrophic organisms), mitochondria use the energy stored in sugar molecules from food to form more highly ordered structures.

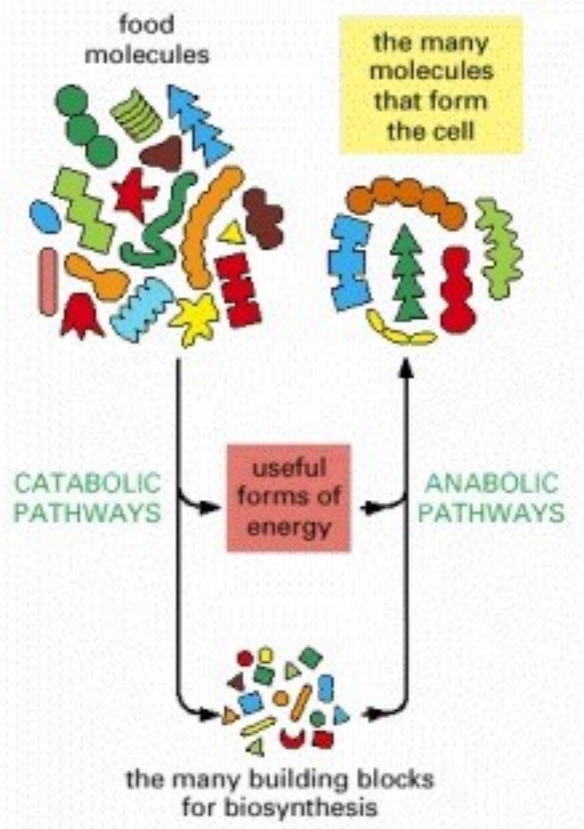
Interconvertibility of All Forms of Energy
Energy Pyramid



Some energy interconversion in living organisms. During metabolic energy transductions, the randomness of the system plus surroundings (expressed quantitatively as entropy) increases as the potential energy of complex nutrient molecules decreases. **(a)** Living organisms extract energy from their surroundings; **(b)** convert some of it into useful forms of energy to produce work; **(c)** return some energy to the surroundings as heat; and **(d)** release end-product molecules that are less well organized than the starting fuel, increasing the entropy of the universe. One effect of all these transformations is **(e)** increased order (decreased randomness) in the system in the form of complex macromolecules. \

Anabolism is powered by catabolism





Catabolism is the set of metabolic pathways that break down molecules into smaller units and release energy.

Anabolism is the set of metabolic pathways that construct (synthetize) molecules from smaller units and require energy.

Many anabolic processes are powered by ATP that is supplied by catabolism.

Since a major portion of the energy stored in the chemical bonds of food molecules is dissipated as heat, **the mass of food** required by any organism that derives all of its energy from catabolism **is much greater than the mass of the molecules** that can be produced by anabolism.

The Change in Free Energy (ΔG) – a measure of potential energy – Determines the Direction of a Chemical Reaction

ΔG is a difference between the G values after and before the change:

$$\Delta G = G_{products} - G_{reactants}$$

In mathematical terms,
Gibbs's law states that **systems change to minimize free energy**

1) If **Δ*G* is negative,** the reaction **occurs spontaneously with the release of energy (the exergonic reaction)**.

Reaction 2: $\text{ATP} \longrightarrow \text{ADP} + \text{P}_\text{i}$
(exergonic; ΔG_2 is negative)

2) If **Δ*G* is positive**, the reaction **is not spontaneous**, requires absorbtion of energy (**the endergonic reaction**).

Reaction 1: $\text{Glucose} + \text{P}_\text{i} \longrightarrow \text{glucose 6-phosphate}$
(endergonic; ΔG_1 is positive)

3) If **Δ*G* is zero**, both forward and reverse reactions occur at equal rates; **the reaction is at equilibrium**.

Reaction 3: $\text{Glucose} + \text{ATP} \longrightarrow \text{glucose 6-phosphate} + \text{ADP}$

ΔG :

- depends on the difference in free energy of products and reactants (or final state and initial state)
- is independent of the path of the transformation and is unaffected by the mechanism of a reaction
- cannot tell us anything about the rate of a reaction

The ΔG of a reaction depends on the change in enthalpy ΔH (sum of bond energies), the change in entropy ΔS (the randomness of molecular motion), and the temperature *T:*

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

Where:

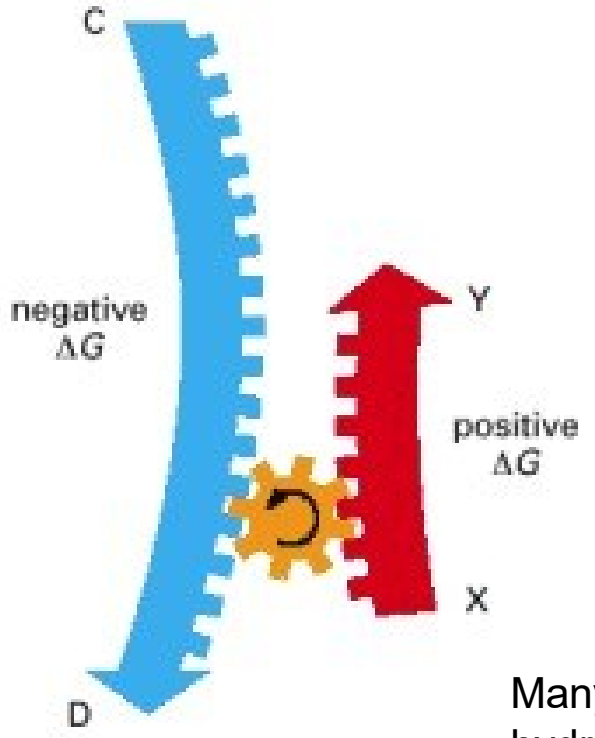
H - is the bond energy, or enthalpy, of the system;

T - is its temperature in degrees Kelvin (K);

S - is a measure of randomness (entropy)

An Unfavorable Chemical Reaction Can Proceed If It Is Coupled with an Energetically Favorable Reaction

A chemical reaction having a positive ΔG can proceed if it is coupled with a reaction having a negative ΔG of larger magnitude.



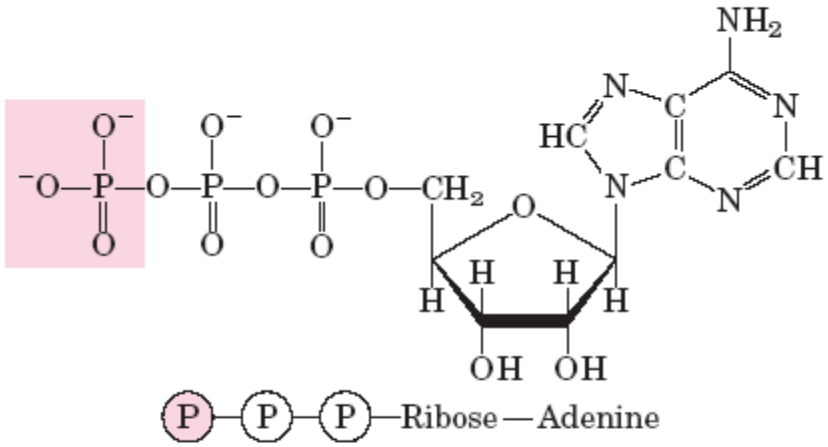
The energetically unfavorable reaction X → Y is driven by the energetically favorable reaction C → D, because the free-energy change for the pair of coupled reactions is less than zero.

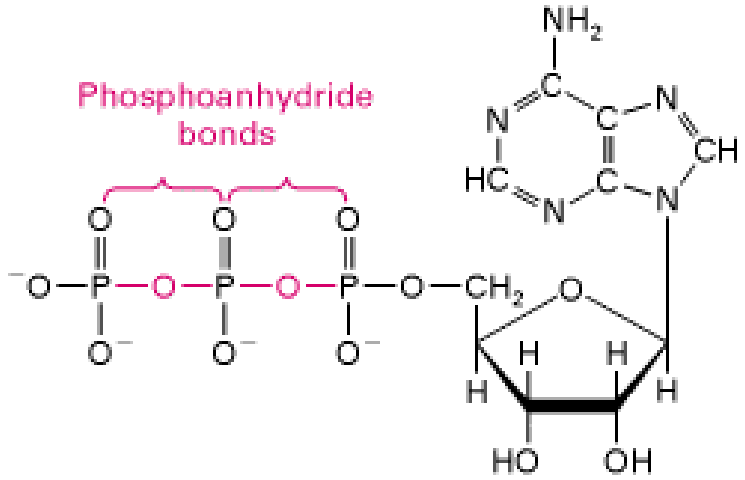
$A \rightleftharpoons B + X$		$\Delta G^{\circ\prime} = +5$ kcal/mol
$X \rightleftharpoons Y + Z$		$\Delta G^{\circ\prime} = -10$ kcal/mol
Sum:	$A \rightleftharpoons B + Y + Z$	$\Delta G^{\circ\prime} = -5$ kcal/mol

Many energetically unfavorable cellular reactions are fueled by hydrolysis of one or both of the two phosphoanhydride bonds in ATP.

Hydrolysis of Phosphoanhydride Bonds in ATP Releases Substantial Free Energy

The most important molecule for capturing and transferring free energy is adenosine triphosphate, **ATP**.





Adenosine triphosphate (ATP)

FIGURE 1–25 **Adenosine triphosphate (ATP).** The removal of the terminal phosphoryl group (shaded pink) of ATP, by breakage of a phosphoanhydride bond, is highly exergonic, and this reaction is coupled to many endergonic reactions in the cell

ATP serves as an energy carrier in cells

Hydrolysis of a phosphoanhydride bond ("high-energy" bond) in the following reactions has a highly negative $\Delta G^{\circ\prime}$ of app. - 7.3 kcal/mol:

$$\underset{\textbf{(ATP)}}{Ap{\sim}p{\sim}p} + H_2O \longrightarrow \underset{\textbf{(ADP)}}{Ap{\sim}p} + P_i + H^+$$

$$\underset{\textbf{(ATP)}}{Ap{\sim}p{\sim}p} + H_2O \longrightarrow \underset{\textbf{(AMP)}}{Ap} + PP_i + H^+$$

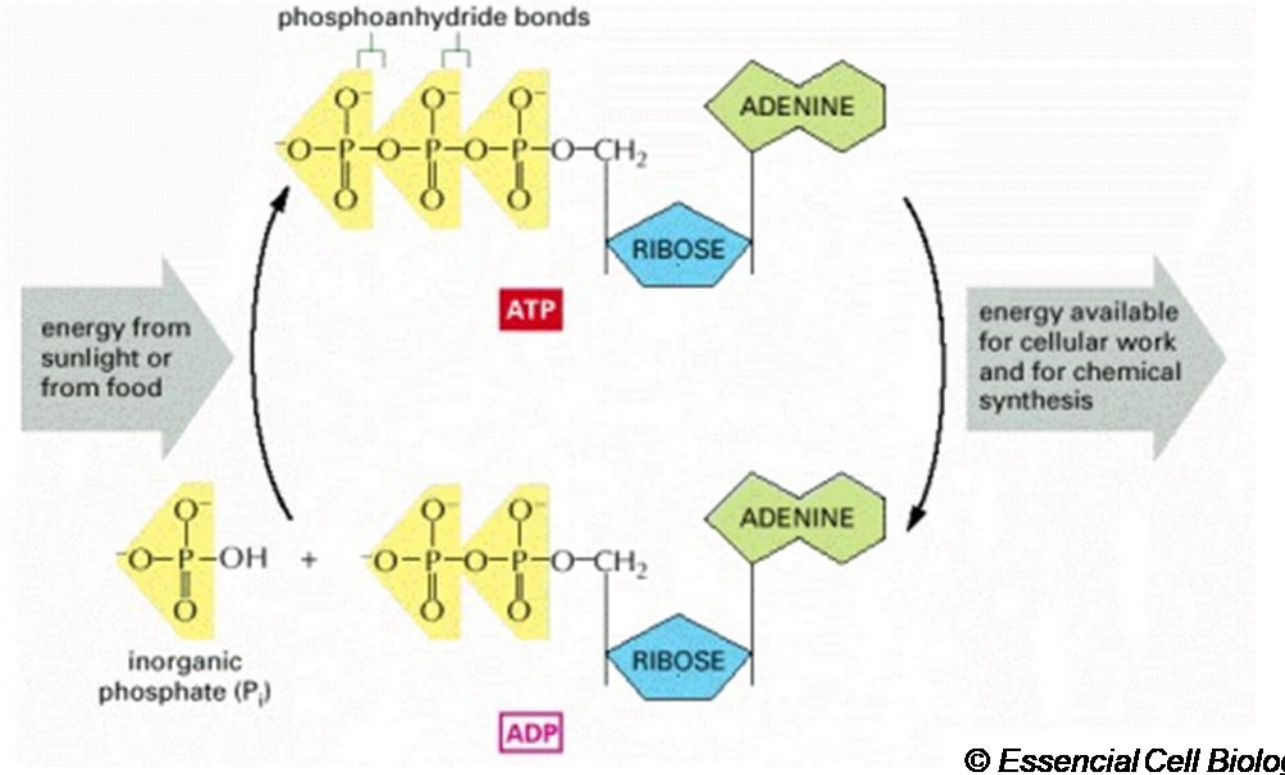
$$\underset{\textbf{(ADP)}}{Ap{\sim}p} + H_2O \longrightarrow \underset{\textbf{(AMP)}}{Ap} + P_i + H^+$$

$$P_i^{2-} + H^+ + ADP^{3-} \longrightarrow ATP^{4-} + H_2O$$

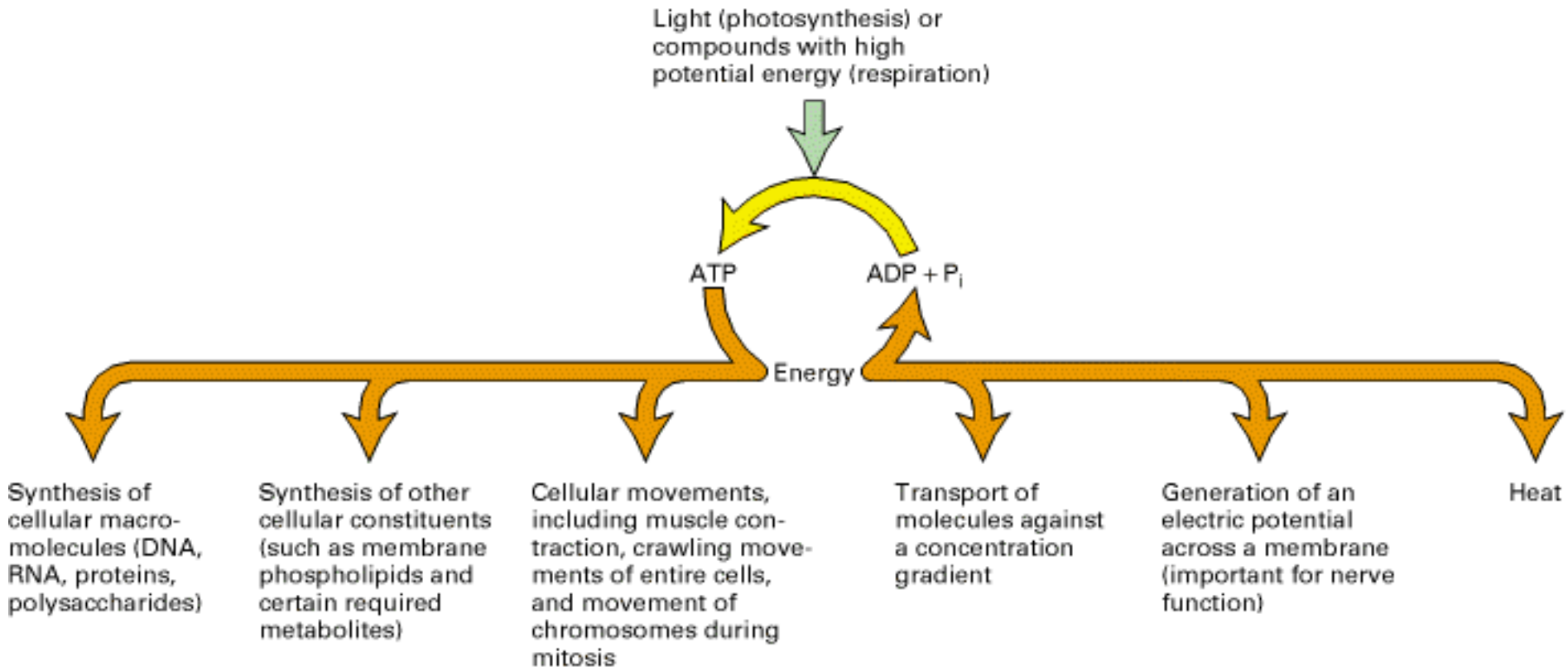
The energy to drive ATP synthesis is produced primarily by two main processes

1) **aerobic oxidation**, which occurs in nearly all cells, and

2) **photosynthesis**, which occurs only in leaf cells of plants, bacteria and certain unicellular organisms.



ATP Is Used to Fuel Many Cellular Processes : ATP cycle



ATP is formed by photosynthesis in plants and by the catabolism of energy-rich compounds in most cells (cellular respiration).

The hydrolysis of ATP is linked to many key cellular functions; the free energy released by the breaking of the phosphoanhydride bond is trapped as usable energy.

TABLE 15.2 Some activated carriers in metabolism

Carrier molecule in activated form	Group carried	Vitamin precursor
ATP	Phosphoryl	
NADH and NADPH	Electrons	Nicotinate (niacin)
$FADH_2$	Electrons	Riboflavin (vitamin B_2)
$FMNH_2$	Electrons	Riboflavin (vitamin B_2)
Coenzyme A	Acyl	Pantothenate
Lipoamide	Acyl	
Thiamine pyrophosphate	Aldehyde	Thiamine (vitamin B_1)
Biotin	CO_2	Biotin
Tetrahydrofolate	One-carbon units	Folate
S-Adenosylmethionine	Methyl	
Uridine diphosphate glucose	Glucose	
Cytidine diphosphate diacylglycerol	Phosphatidate	
Nucleoside triphosphates	Nucleotides	

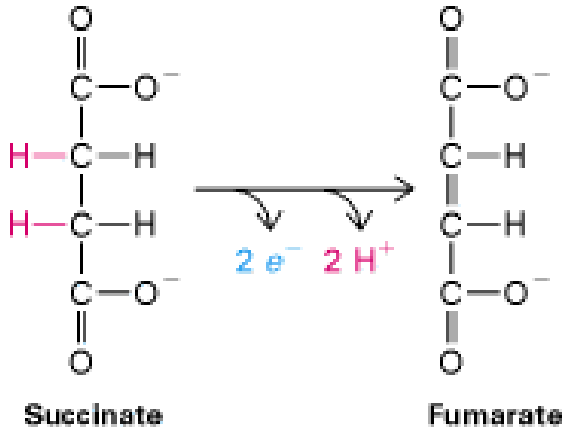
NOTE: Many of the activated carriers are coenzymes that are derived from water-soluble vitamins.

Table 15-2
Biochemistry, Sixth Edition

The activated energy carriers usually arise from ATP coupled reactions.
Thus, the energy of the carrier transferred groups used in biosynthetic reactions originates from the catabolic reactions that form ATP.

Many Cellular Processes Involve Oxidation-Reduction Reactions

The tendency of an atom or molecule to gain electrons is its **reduction potential *E*** (in volts). The tendency to lose electrons is the **oxidation potential**.

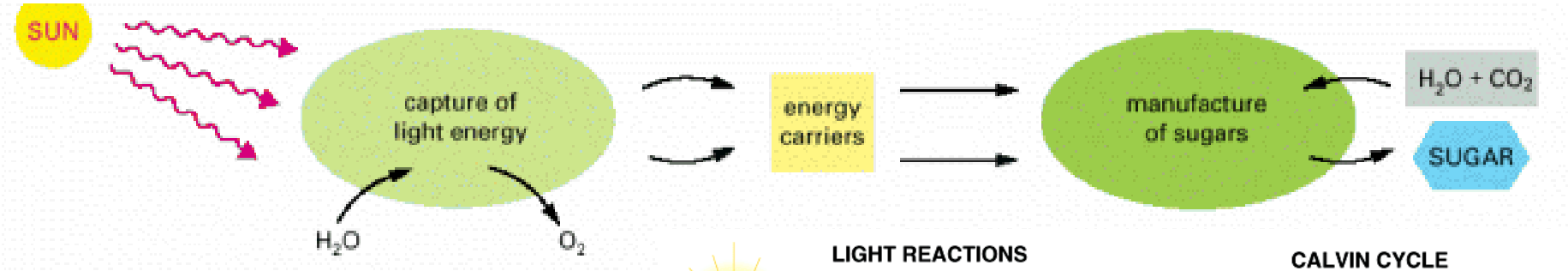


Succinate is converted to fumarate by the loss of two electrons and two protons. This oxidation reaction, which occurs in mitochondria as part of the citric acid cycle, is coupled to reduction of FAD to $FADH_2$.

Oxidation and reduction reactions always occur in pairs. The ΔE for an oxidation-reduction reaction is the sum of the oxidation potential and the reduction potential of the two partial reactions.

Oxidation-reduction reactions with a positive ΔE ($\Delta E > 0$) have a negative ΔG ($\Delta G < 0$) and thus tend to proceed spontaneously.

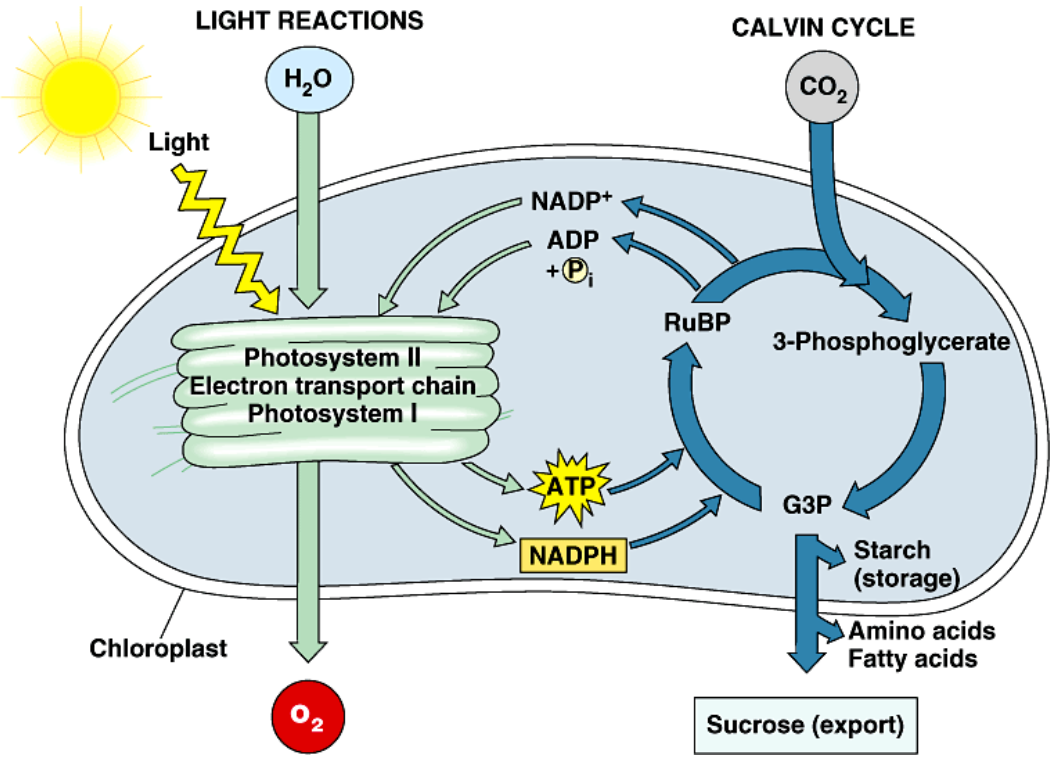
Light energy captured by photosynthesis in plants and photosynthetic bacteria is the source of chemical energy for almost all cells



Photosynthesis

$$6CO_2 + 6H_2O \xrightarrow{\text{light}} C_6H_{12}O_6 + 6O_2$$

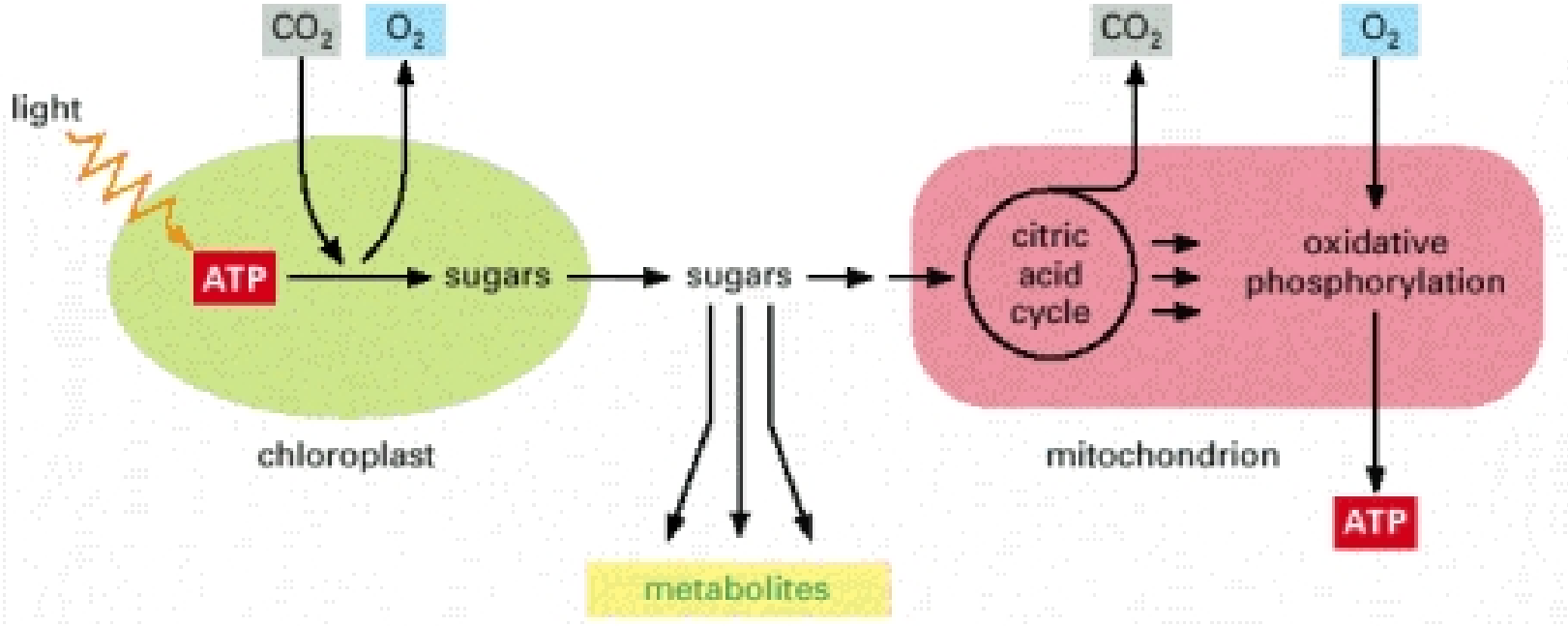
(light-driven reduction of CO_2)

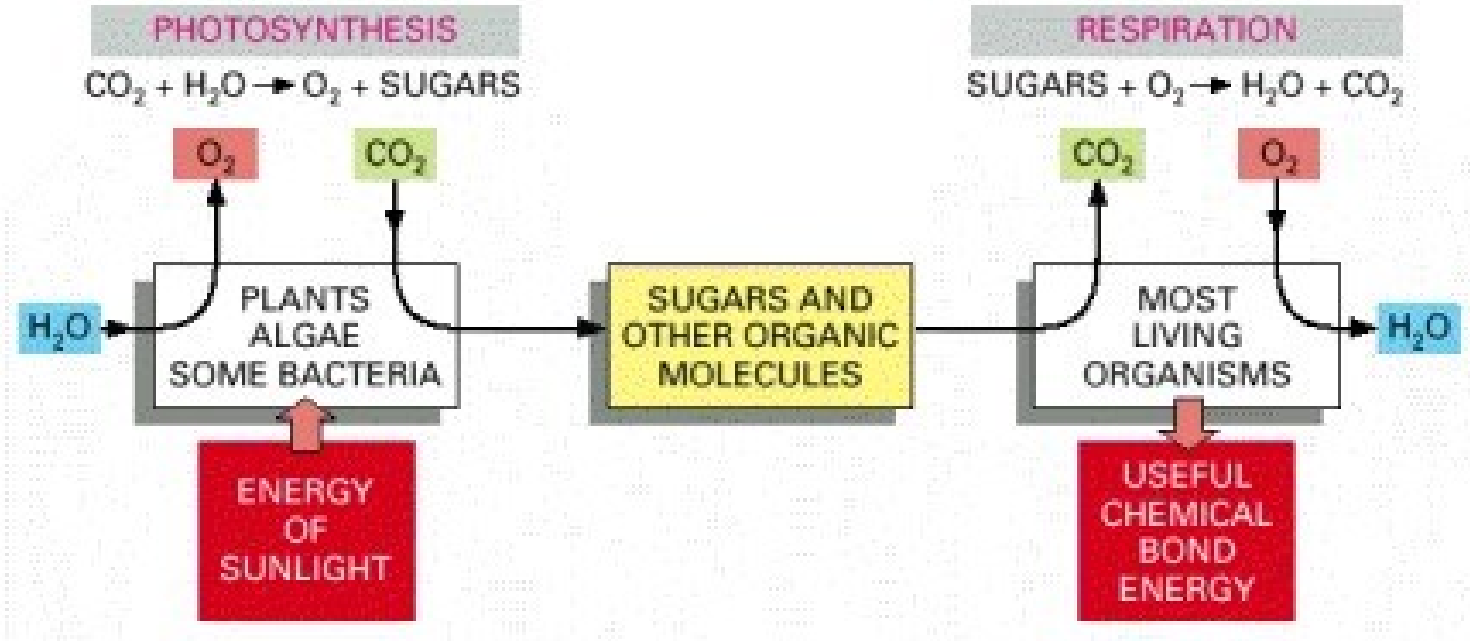


The principle of photosynthesis:

In **light stage**, sunlight is converted to chemical energy in the form of ATP (free energy containing molecule) and NADPH (high energy electron carrying molecule). Chlorophyll absorbs light energy and starts reactions that result in the production of ATP, NADPH, and oxygen (through the splitting of water). Oxygen is released. Both ATP and NADPH are used in the dark reactions (the **dark stage**) to produce sugar (and other organic compounds) from CO_2.

In plants, the chloroplasts and mitochondria collaborate to supply cells with metabolites and ATP





Photosynthesis and respiration as complementary processes in the living world

Photosynthesis uses the energy of sunlight to produce sugars and other organic molecules. These molecules in turn serve as food for other organisms.

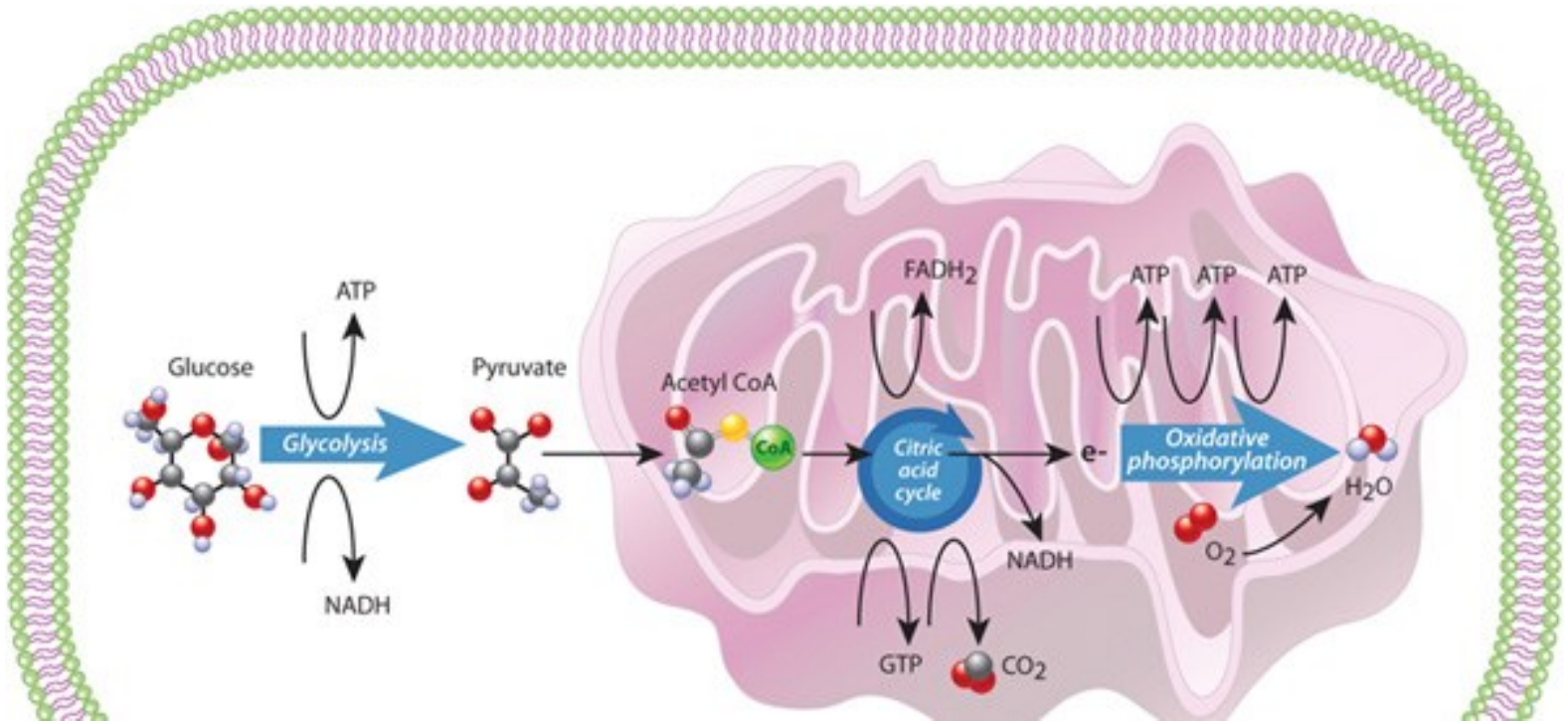
Photosynthesis must have preceded respiration on the Earth.

In animals, the free energy in sugars and other molecules derived from food is released in **the process of respiration**.

All synthesis of ATP in animal cells and in nonphotosynthetic microorganisms results from the chemical transformation of energy-rich dietary or storage molecules.

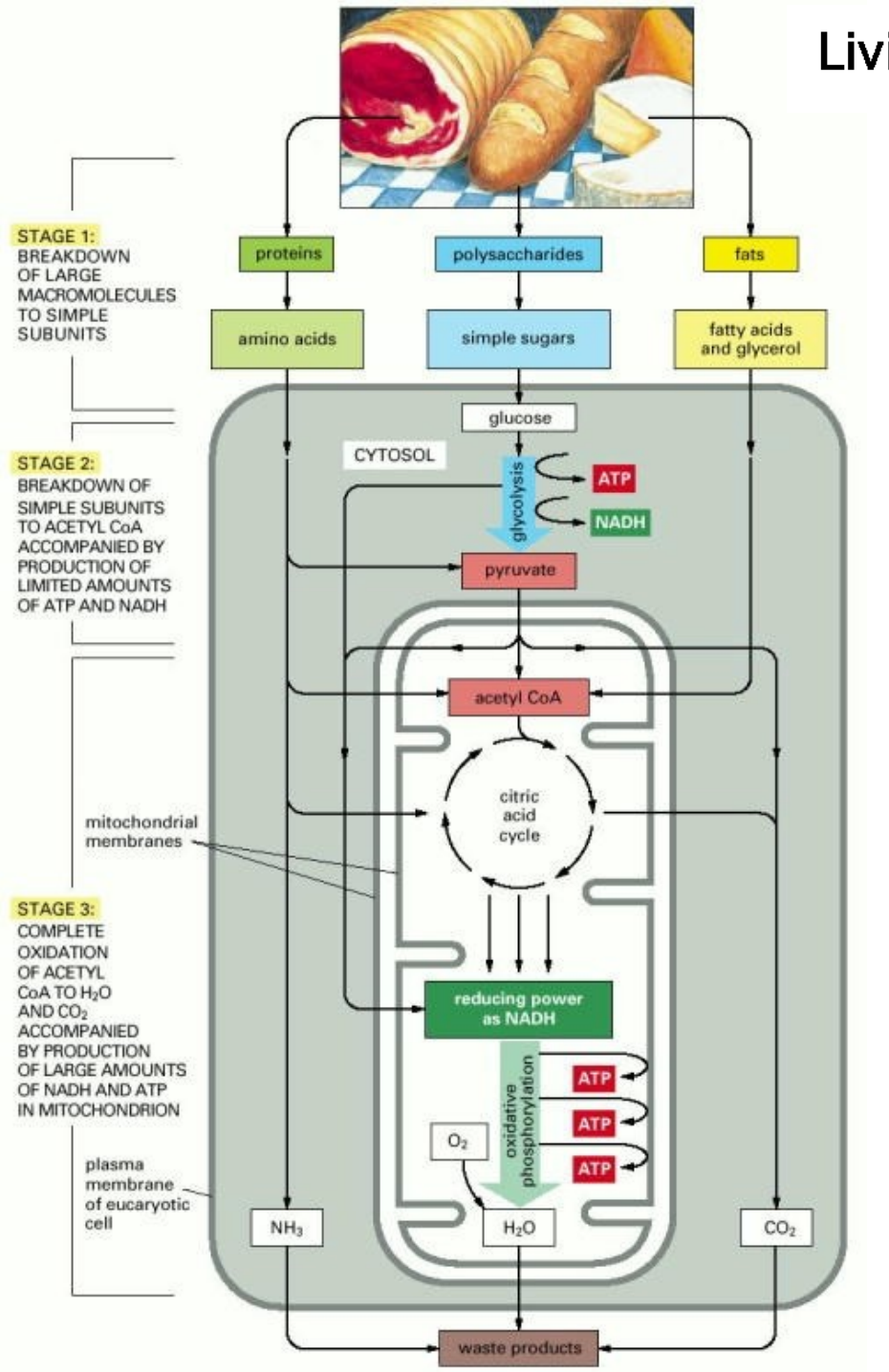
$$C_6H_{12}O_6 + O_2 \longrightarrow 6CO_2 + 6H_2O + \text{energy}$$

(energy-yielding oxidation of glucose)



Steps of Cellular Respiration. Glycolysis (**I**) takes place in the cytoplasm. Within the mitochondrion, the citric acid cycle (**II**) occurs in the mitochondrial matrix, and oxidative phosphorylation (**III**) occurs at the inner mitochondrial membrane.

Living organisms extract energy from food

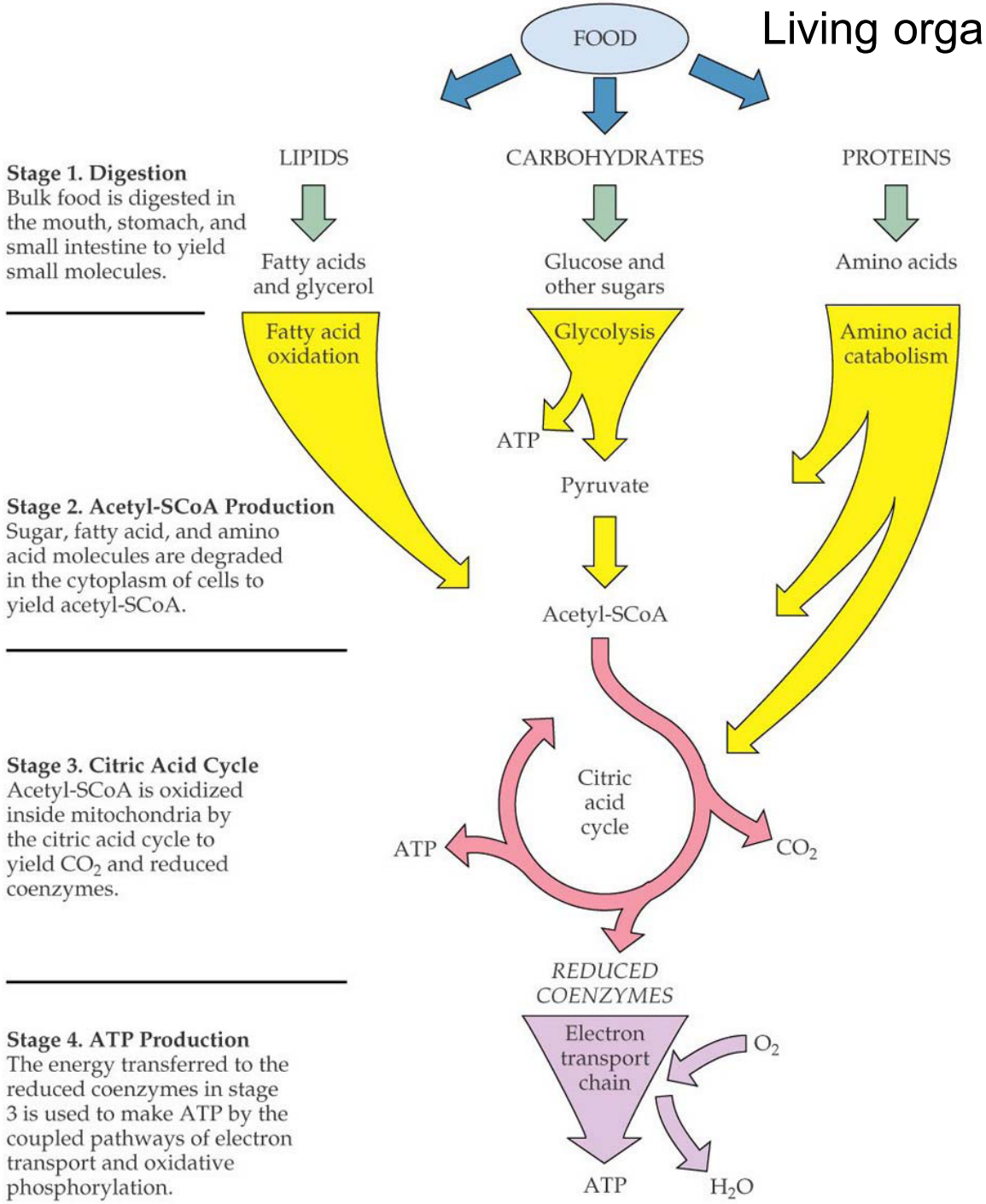


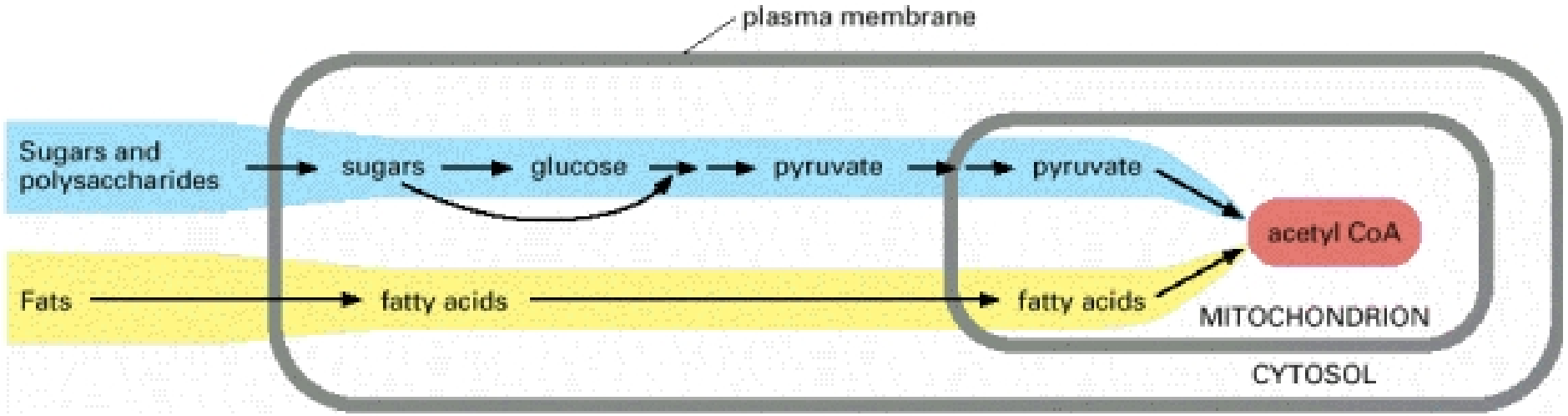
This series of reactions produces ATP, which is then used to drive biosynthetic reactions and other energy-requiring processes in the cell.

Stage 1 occurs outside cells.
Stage 2 occurs mainly in the cytosol, except for the final step of conversion of pyruvate to acetyl groups on acetyl CoA, which occurs in mitochondrial matrix.
Stage 3 occurs in mitochondria:

- the citric acid cycle – in matrix
- oxidative phosphorylation – in inner mitochondrial membrane

Living organisms extract energy from food

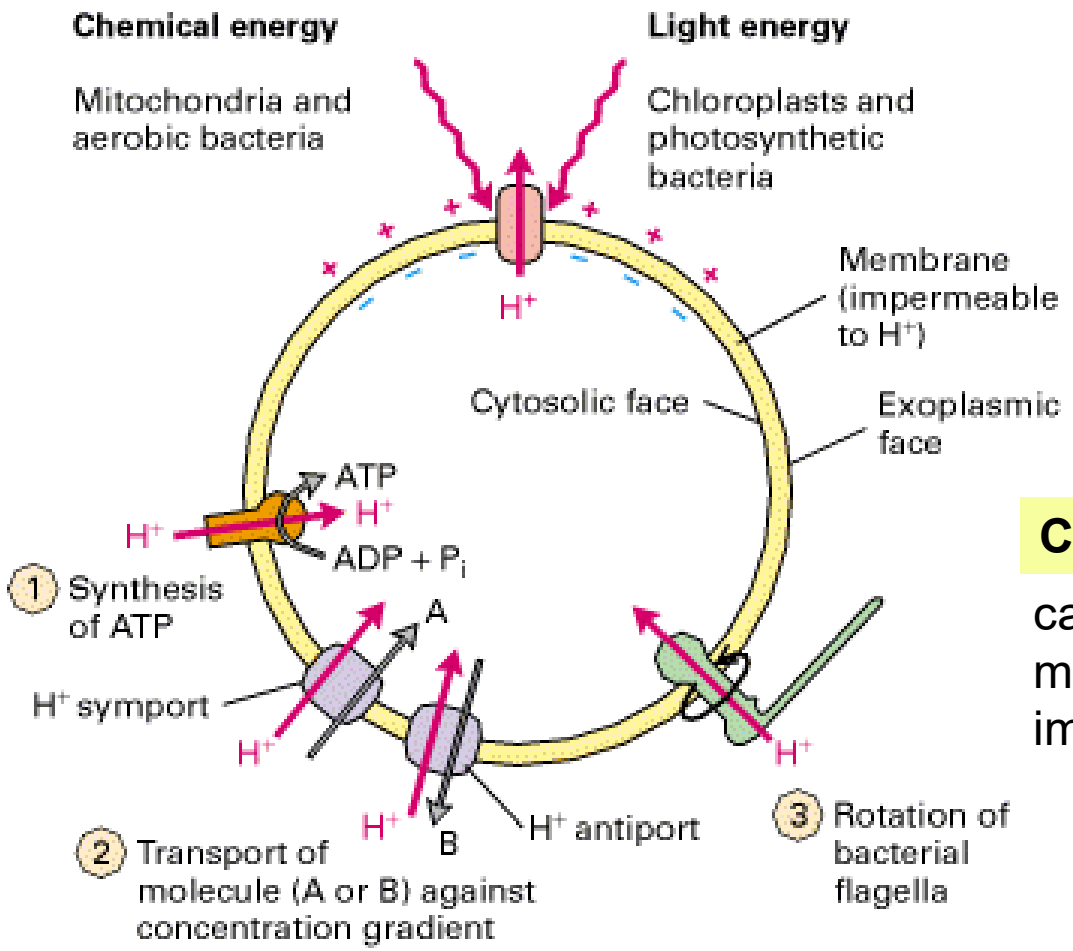




Pathways for the production of acetyl CoA from sugars and fats

The mitochondrion in eucaryotic cells is the place where acetyl CoA is produced from both types of major food molecules.

Therefore, most of the cell's oxidation reactions occur in mitochondria and most of ATP is made in mitochondria.



Chemiosmotic coupling

can occur only in sealed, closed, membrane-limited compartments that are impermeable to H^+.

In photosynthesis, energy absorbed from light is used to move protons across the membrane, generating a transmembrane proton concentration gradient and a voltage gradient, collectively called the *proton-motive force (pmf)*.

In mitochondria and aerobic bacteria, energy liberated by the oxidation of carbon compounds is used to move protons across the membrane, again generating *pmf*.

The generated ***pmf*** **can be used** to power ATP synthesis (**1**) , transport of metabolites across the membrane against their concentration gradient (**2**), and rotation of bacterial flagella (**3**).

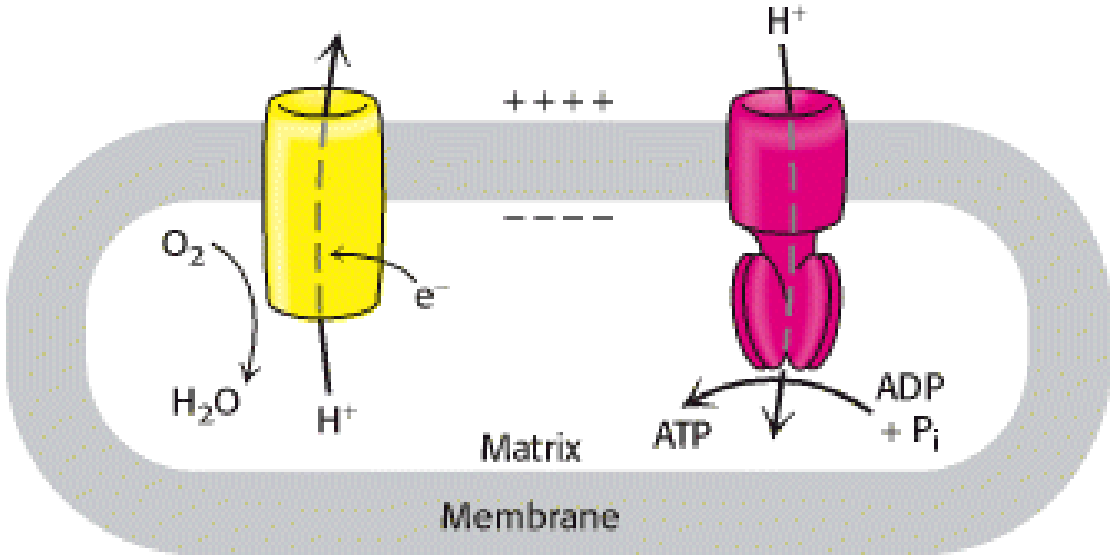
$$pmf = \Delta\Psi + \Delta pH \text{ (mV)}$$

The proton-motive force (pmf, proton electrochemical gradient), a combination of a proton concentration (pH) gradient (**ΔpH**) (exoplasmic face > cytosolic face) and an electric potential (negative cytosolic face) (**ΔΨ**), can be generated across the inner mitochondrial membrane, chloroplast thylakoid membrane, and bacterial plasma membrane.

It is the energy source for ATP synthesis by the F_OF_1 complexes (ATP syntases) located in these energy-transducing membranes.

Chemiosmotic coulping

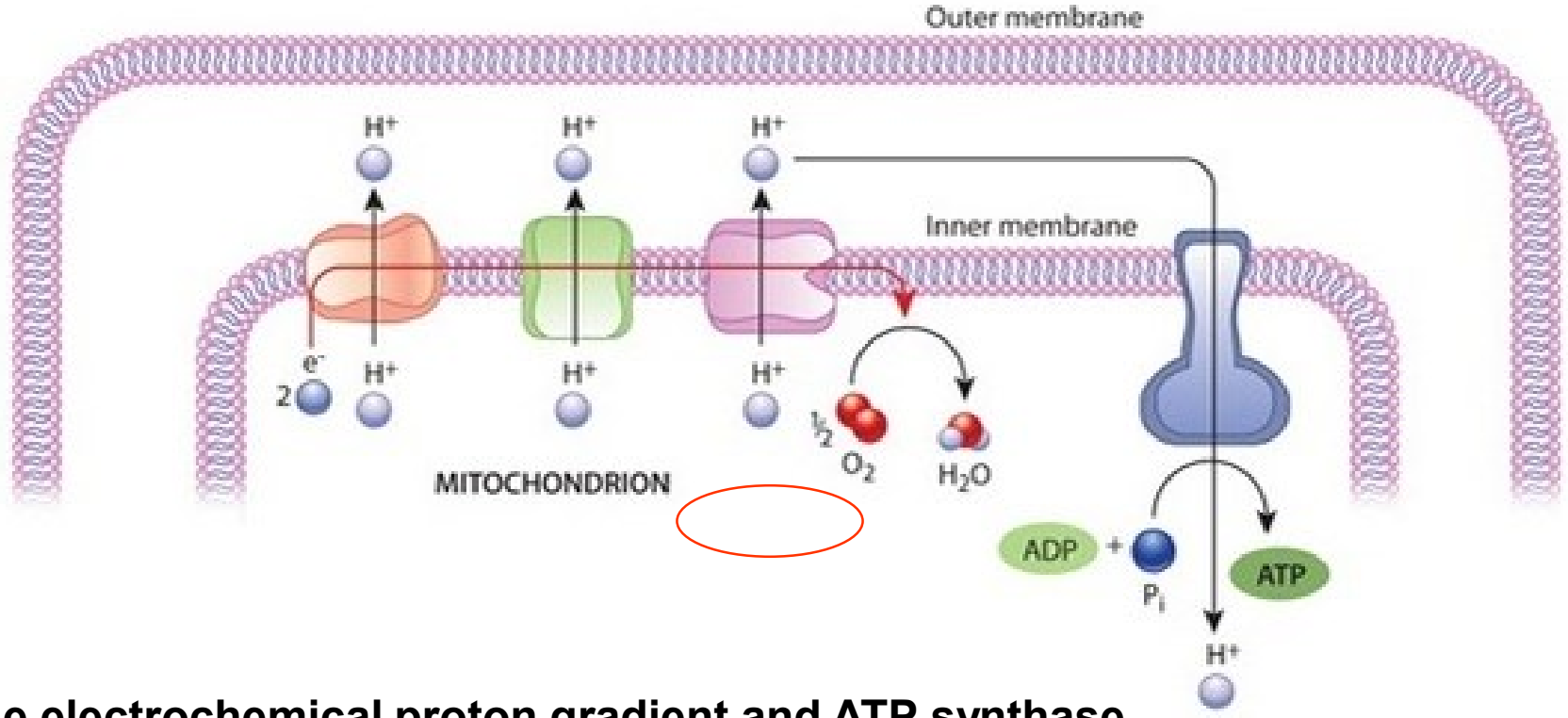
In the mitochondrion, the flow of electrons from NADH and $FADH_2$ to O_2 is coupled to the uphill transport of H+ from the matrix across the inner membrane to the intermembrane space, generating the proton-motive force (*pmf*). The *pmf* in mitochondria is due mainly to a voltage gradient across the inner membrane.



$$pmf = \Delta p = \Delta\Psi + \Delta pH \text{ (mV)}$$

The movement of protons back across the inner membrane, driven by *pmf*, is coupled to the synthesis of ATP from ADP and P_i by the F_OF_1 complex of ATP synthase – **OXIDATIVE PHOSPHORYLATION**.

OXIDATIVE PHOSPHORYLATION

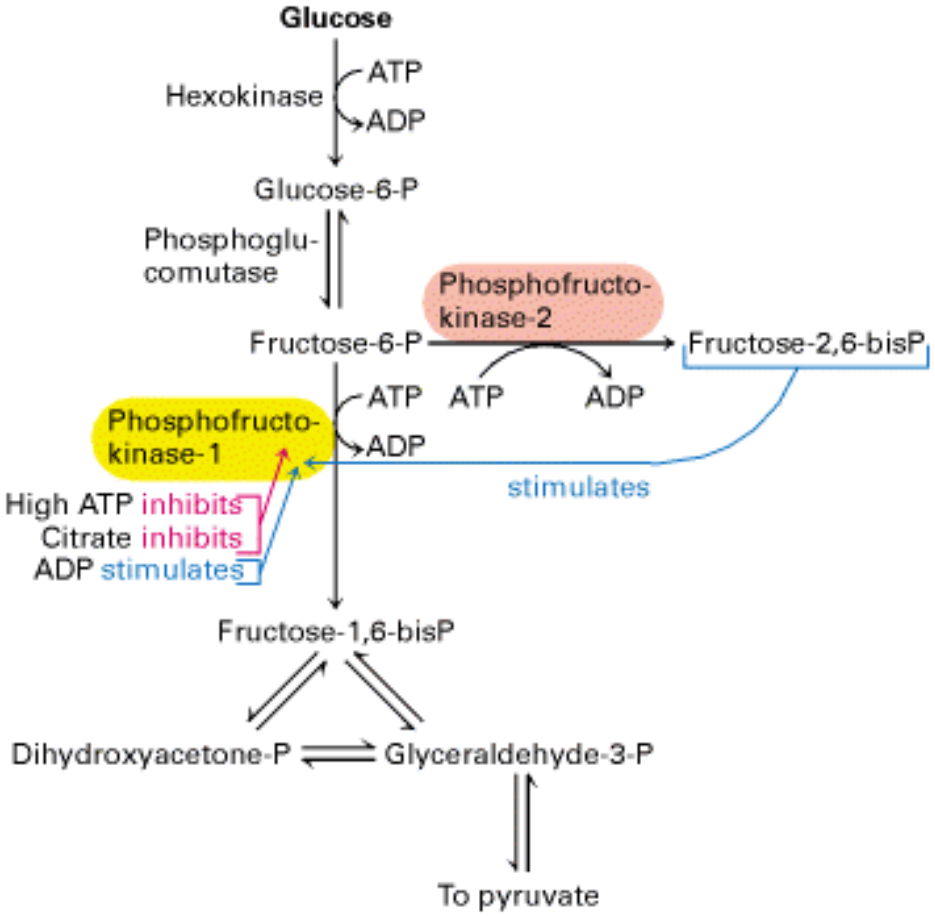


The electrochemical proton gradient and ATP synthase

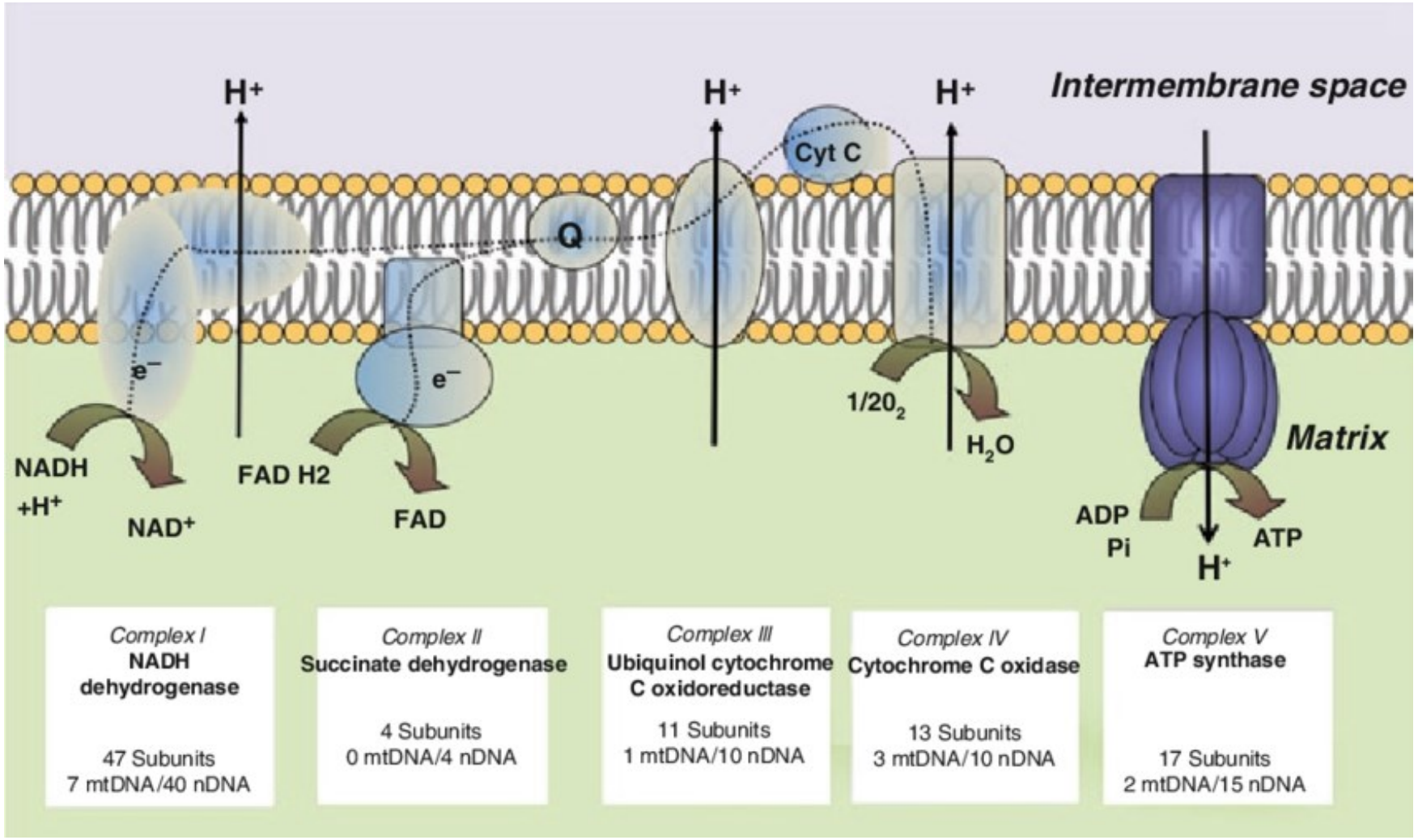
At the inner mitochondrial membrane, a high energy electron is passed along an electron transport chain. The energy released pumps H+ out of the matrix space. The gradient created by this drives H+ back through the membrane, through ATP synthase that results in ATP synthesis.

The Rate of Glucose Oxidation Is Adjusted to Meet the Cell's Need for ATP

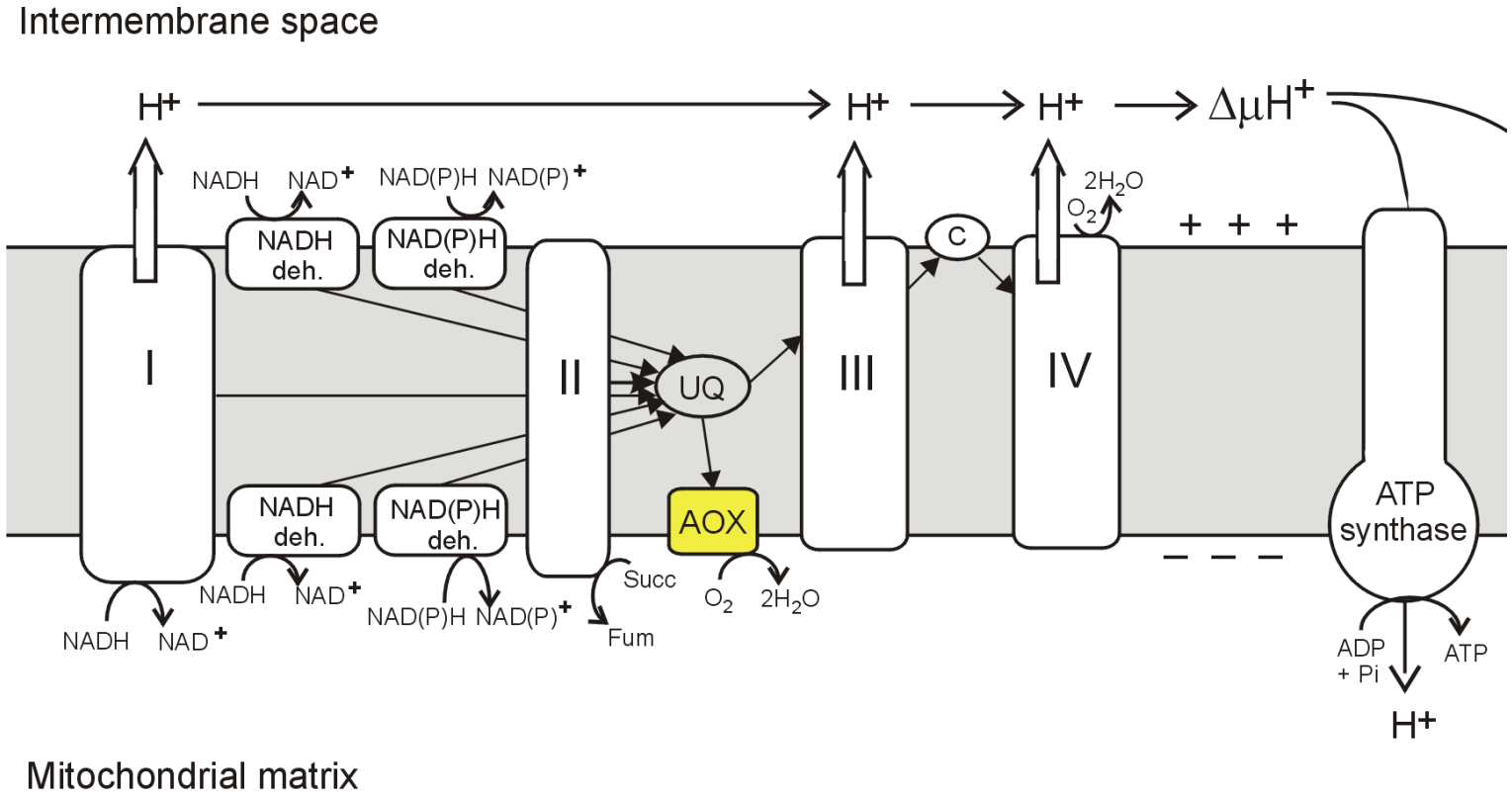
The rate of glycolysis and Krebs cycle, which depends on the cell's need for ATP, is controlled by the inhibition and stimulation of several enzymes.



Phosphofructokinase-1 is the main control point in the regulation of the glycolytic pathway. It is allosterically inhibited by ATP and citrate, and stimulated by ADP and fructose 2,6-bisphosphate


H+
H+
H+
Intermembrane space
Cyt C
Q
e−
e−
NADH
+H+
NAD+
FAD H2
FAD
1/20₂
H₂O
Matrix
ADP
Pi
ATP
H+
Complex I
NADH dehydrogenase
47 Subunits
7 mtDNA/40 nDNA
Complex II
Succinate dehydrogenase
4 Subunits
0 mtDNA/4 nDNA
Complex III
Ubiquinol cytochrome C oxidoreductase
11 Subunits
1 mtDNA/10 nDNA
Complex IV
Cytochrome C oxidase
13 Subunits
3 mtDNA/10 nDNA
Complex V
ATP synthase
17 Subunits
2 mtDNA/15 nDNA

Plant-type mitochondrial respiratory chain

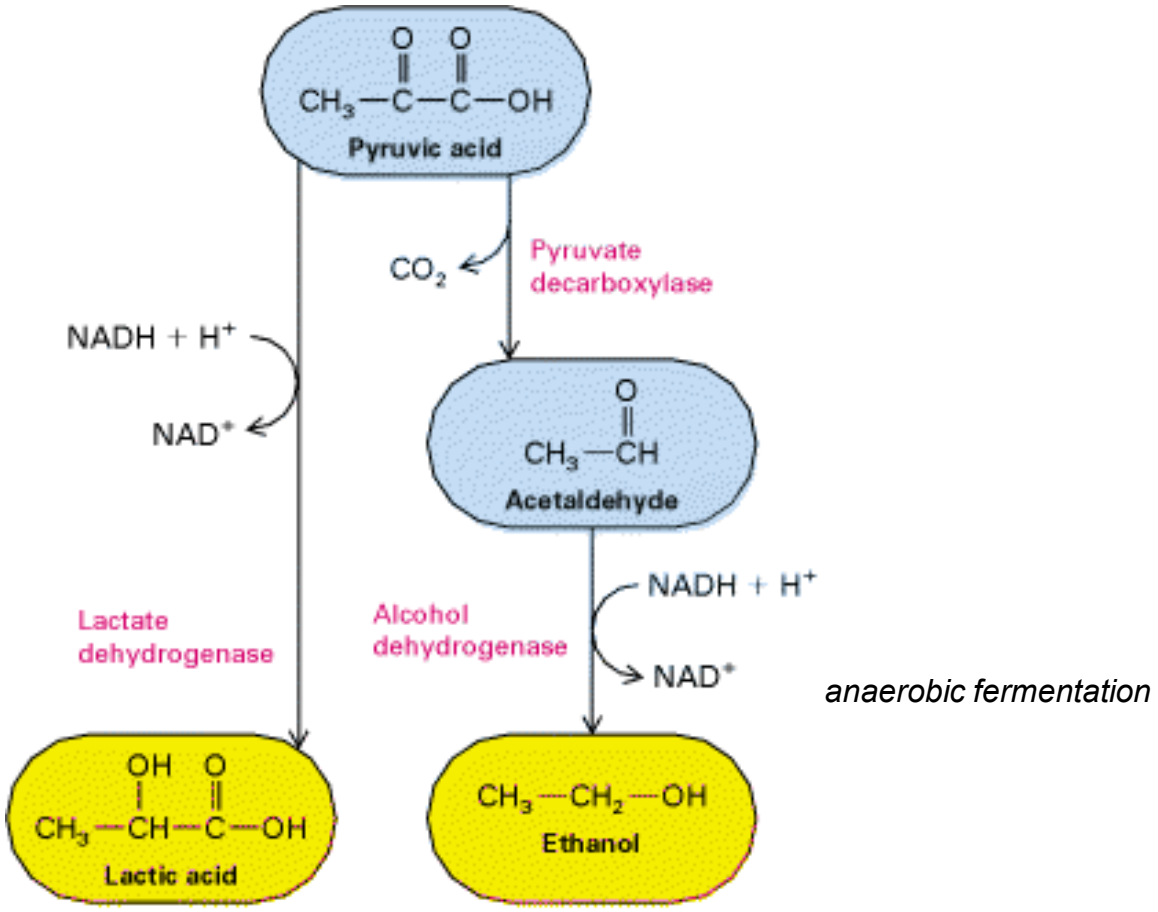


Additional electron carriers:

- External NAD(P)H dehydrogenases
- Internal NAD(P)H dehydrogenases
- Alternative oxidase

The anaerobic metabolism of glucose.

In anaerobic cells, pyruvate can be metabolized further to lactate or to ethanol plus CO_2, with the reoxidation of NADH. Anaerobic metabolism of each glucose molecule yields only two ATP molecules.



anaerobic fermentation

Overall reactions of anaerobic metabolism:

Glucose + 2 ADP + 2 P_i ⟶ 2 lactate + 2 ATP

Glucose + 2 ADP + 2 P_i ⟶ 2 ethanol + 2 CO_2 + 2 ATP

Mitochondrial aerobic oxidation

Mitochondrial oxidation reactions generate 34 of the 36 ATP molecules produced from the conversion of glucose to CO_2

Oxidation of pyruvate and fatty acids to CO_2 and H_2O and the coupled synthesis of ATP involve three groups of reactions:

1. Oxidation of pyruvate and fatty acids to CO_2, coupled to the reduction of the coenzymes NAD^+ and FAD to NADH and $FADH_2$, respectively. These reactions (**Citric acid cycle**) occur in the matrix.

2. Electron transfer from NADH and $FADH_2$ to O_2. These reactions occur in the inner membrane and are coupled to the generation of a proton-motive force across it.

Electrons from NADH and $FADH_2$ move via a series of membrane-bound electron carriers of **respiratory chain** in the inner mitochondrial membrane to O_2, regenerating NAD^+ and FAD. This stepwise movement of electrons is coupled to pumping of protons across the inner membrane. The resulting proton-motive force powers ATP synthesis and generates most of the ATP resulting from aerobic oxidation of glucose.

3. Harnessing of the energy stored in the electrochemical proton gradient for ATP synthesis by the F_OF_1 complex in the inner membrane (**OXIDATIVE PHOSPHORYLATION**).

Mitochondrial Oxidation of Fatty Acids Is Coupled to ATP Formation

Oxidation of fatty acids in mitochondria yields acetyl CoA, which enters the citric acid cycle, and yields the reduced coenzymes NADH and $FADH_2$. Subsequent oxidation of acetyl CoA and the reduced coenzymes is coupled to the formation of a proton-motive force that powers ATP formation.

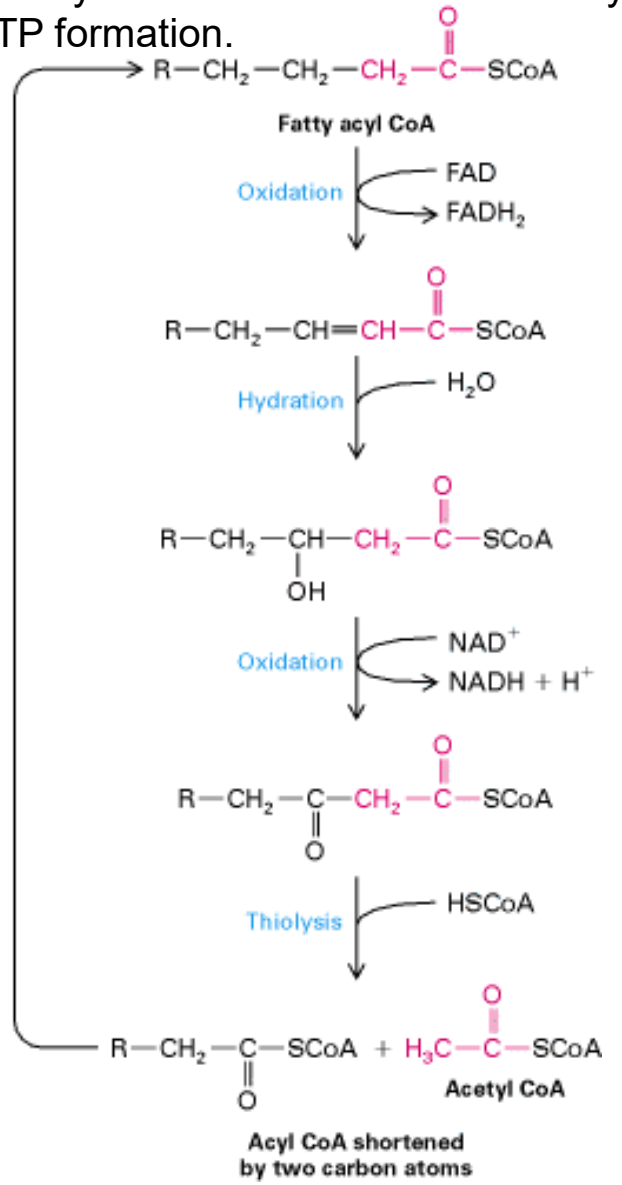


Fig. Four enzyme-catalyzed reactions convert a fatty acyl CoA molecule to acetyl CoA and a fatty acyl CoA shortened by two carbon atoms. Concomitantly, 1 NAD+ molecule is reduced to NADH and 1 FAD molecule is reduced to FADH2. The cycle is repeated on the shortened acyl CoA until fatty acids are completely converted to acetyl CoA.

Oxidation of Fatty Acids in Peroxisomes Generates No ATP

In most eukaryotic cells, oxidation of fatty acids, especially very long chain fatty acids, occurs mainly in peroxisomes and is not linked to ATP production; the released energy is converted to heat. The electrons released during peroxisomal oxidation of fatty acids are used to form H_2O_2, which is decomposed to H_2O and O_2 by catalase.

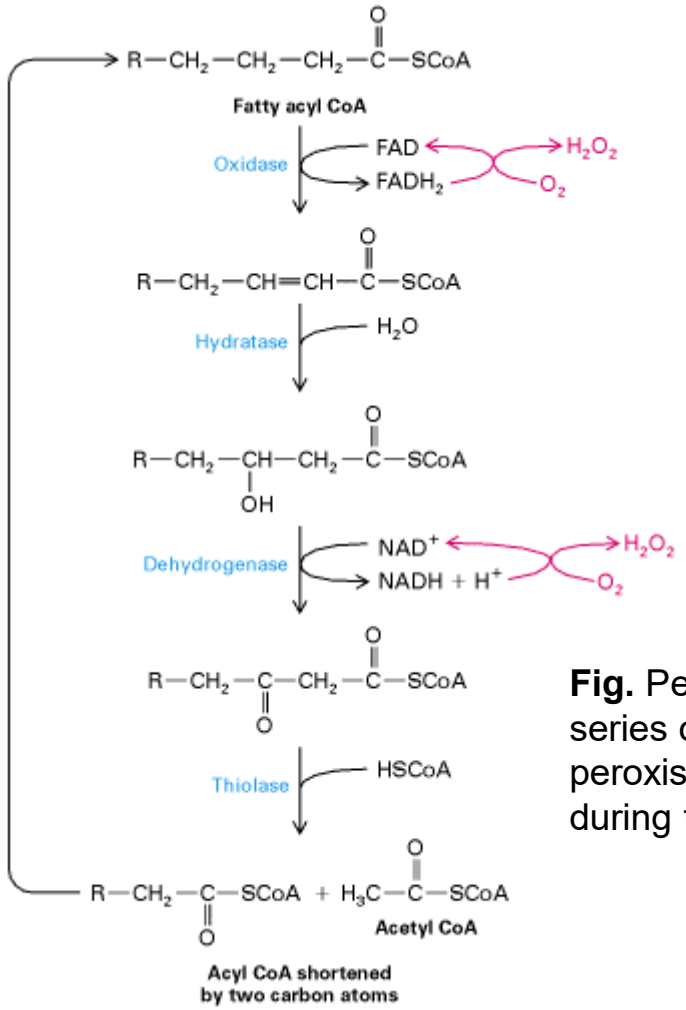


Fig. Peroxisomes degrade fatty acids with more than 12 carbon atoms by a series of reactions similar to those used by liver mitochondria. In peroxisomes, the electrons and protons transferred to FAD and NAD+ during the oxidation reactions are then transferred to oxygen, forming H2O2.