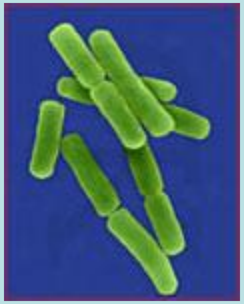


METABOLISMO: PRINCIPI GENERALI

BASIC ENERGY CONCEPTS

- **Cells**

open, non-equilibrium systems

- **First law of thermodynamics**

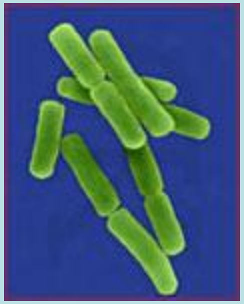
conservation of energy - energy can neither be created nor destroyed in the universe

- **Second law of thermodynamics**

energy spontaneously disperses (if it is not hindered from doing so)

predicts the probability of the dispersal

entropy change measures how much or how widely energy is spread out in a process



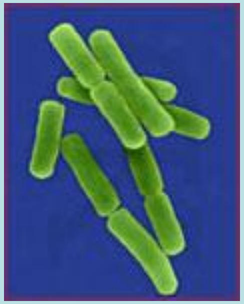

SECOND LAW OF THERMODYNAMICS

• Greatest good - because of the second law, life is possible

life can take in concentrated energy and use some of that energy to synthesize "uphill" complex biochemicals and to run highly regulated interdependent processes, including millions of non-spontaneous reactions

• Biggest bad - because of the second law, life is always threatened

non-spontaneous metabolic reactions are metastable; life cannot function unless a multitude of "molecular machines" and biochemical cycles operate synchronically in using energy to oppose second law predictions

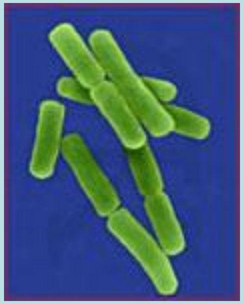


EXAMPLE: PHOTOSYNTHESIS

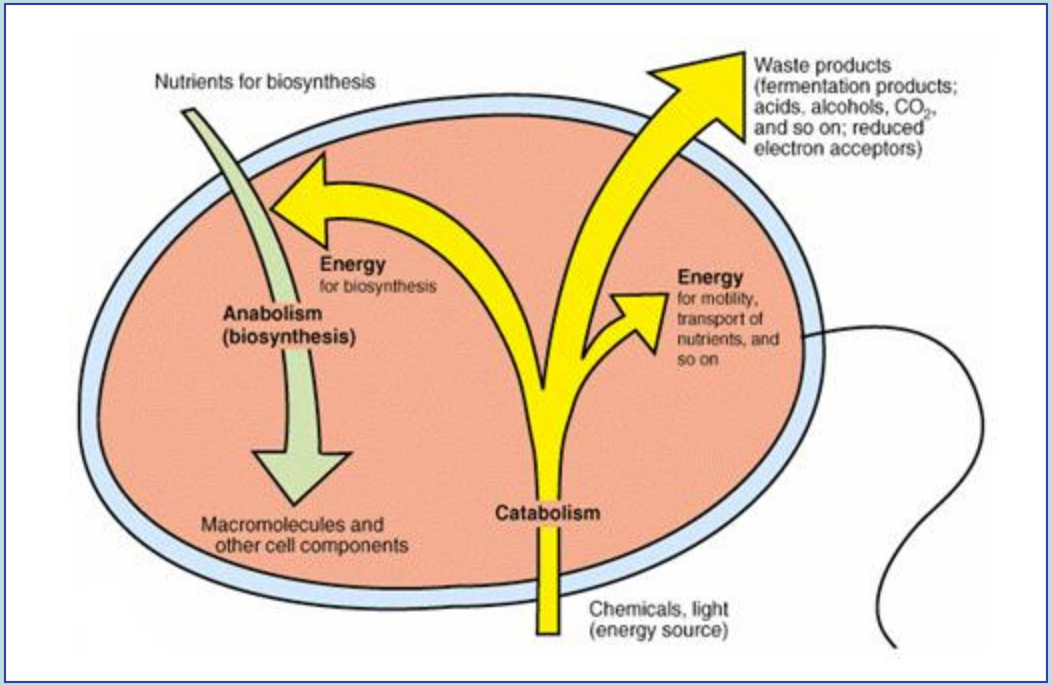
• Energy dispersal and diversion of part of the energy flow

Photosynthesizing organisms take certain wavelengths of the sun's dispersing energy, plus carbon dioxide and water, and make new chemical compounds that are more complex and more energy-containing

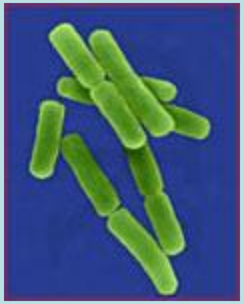
Photosynthesis is in the 30% range; 70% of the sun's energy is dispersed to the environment (net entropy increase)



METABOLISMO: PRINCIPI GENERALI



Nutrizione e metabolismo




METABOLISMO: PRINCIPI GENERALI

METABOLISM

• Metabolism

sum total of all reactions that occur in a cell

• Catabolic reactions

break down of complex molecules into smaller, simpler molecules with the release of energy and reducing power (electrons)

• Anabolic reactions

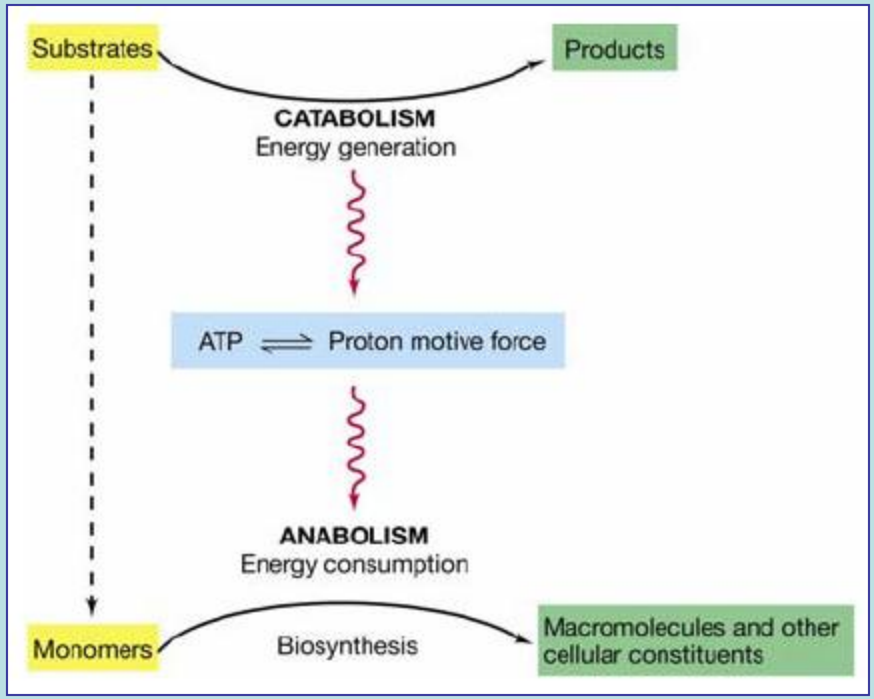
synthesis of complex molecules from simpler ones

requires energy and reducing power (electrons) to form cell structures

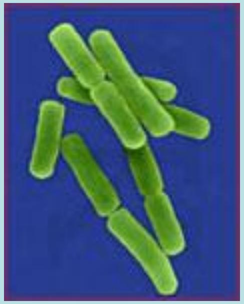
• Catabolic and anabolic reactions

coupled, highly regulated, interdependent, and simultaneous

METABOLISMO: PRINCIPI GENERALI



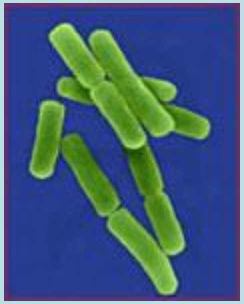
Nutrizione e metabolismo

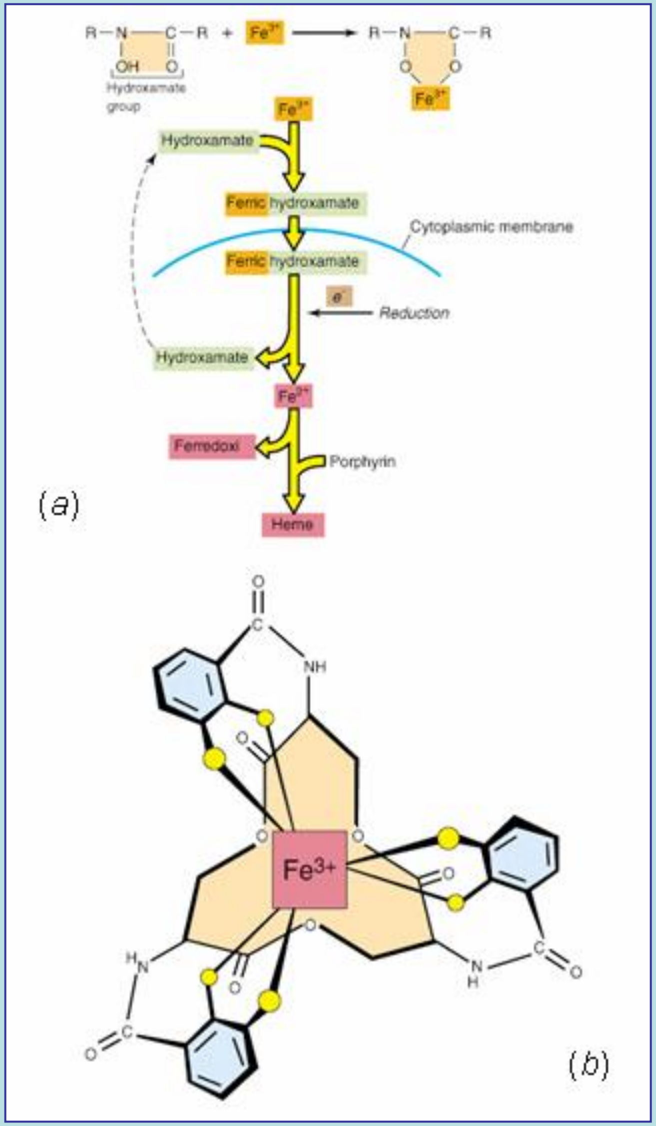



LA NUTRIZIONE MICROBICA

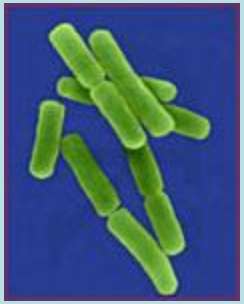
Elements Required by Microorganisms

Element	Proportion of Prokaryotic Cells' Dry Weight	Function
Carbon	50%	Basic structural component of organic compounds
Oxygen	20%	Component of many organic and inorganic compounds; O_2 is the final electron acceptor in aerobic respiration
Nitrogen	14%	Constituent of amino acids and nucleotides
Hydrogen	8%	Constituent of organic compounds; electrons of hydrogen atoms are used in redox reactions
Phosphorus	3%	As phosphate (PO_4^{2-}), constituent of nucleic acids, phospholipids, some coenzymes, and ATP
Sodium	1%	Cation used to maintain electrical balance of cells
Sulfur	1%	Constituent of the amino acids cysteine and methionine; disulfide bonds are important for tertiary structure of proteins
Potassium	1%	Inorganic cation involved in maintaining electrical balance inside cells; cofactor for some enzymes, including some involved in protein synthesis
Chlorine	0.5%	Principal inorganic anion involved in maintaining electrical balance of cells
Magnesium	0.5%	Component of chlorophyll; cofactor for some enzymes
Calcium	0.5%	Responsible in part for the resistance of bacterial endospores; cofactor for some enzymes; constituent of some algal cell walls and protozoan shells
Iron	0.25%	Constituent of cytochromes in electron transport chains; cofactor for some enzymes
Trace elements (cobalt, copper, manganese, molybdenum, nickel, selenium, silicon, tungsten, vanadium, and zinc)	0.25%	Cofactors of some enzymes, silicon is a constituent of some algal cell walls



Esempi di agenti chelanti prodotti dai micoorganismi per il trasporto del ferro: (a) idrossimato; (b) enterobactina. Il ferro è legato, in entrambi i casi, come Fe^{3+}.



CATALISI ENZIMATICA

HOW CAN LIFE EXIST?

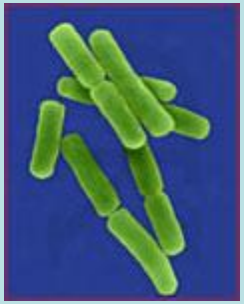
• Activation energy is the innate obstacle to the second law of thermodynamics in chemical reactions

• Role of biological catalysts

• Metastable patterns among biological structures and processes are highly regulated by a vast variety of feedback systems

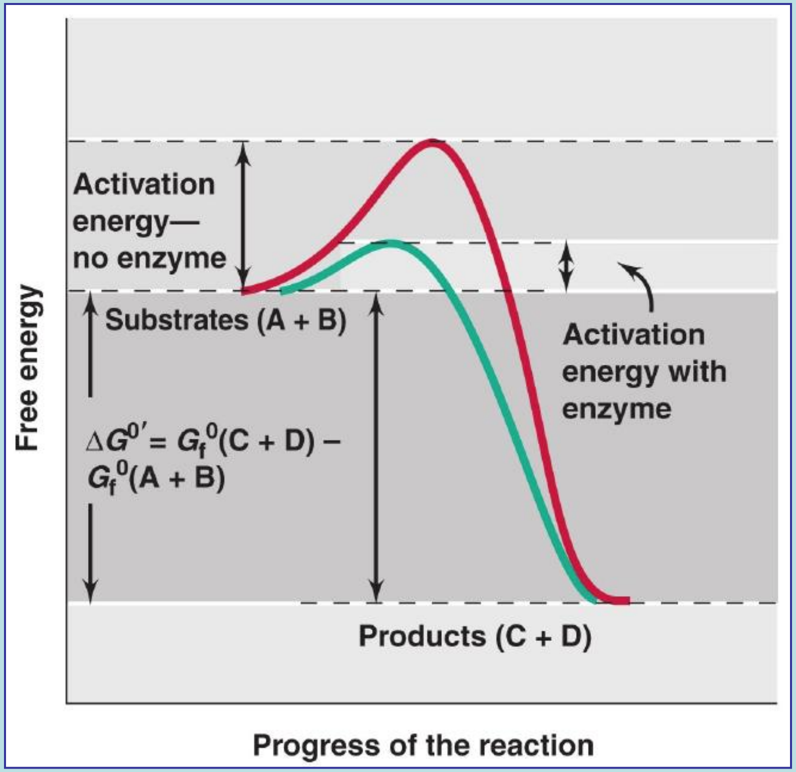
• Example:

storage of energy in ATP is contrary to the predictions of the second law. Energy within the bonds of the ATP molecule is kept from being dispersed by activation energy barriers until life needs it for a reaction

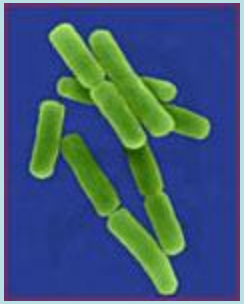


CATALISI ENZIMATICA

Progress of a hypothetical reaction: A + B → C + D and the concept of activation energy



Nutrizione e metabolismo




CATALISI ENZIMATICA

ENZYMES

• What is an enzyme?

• Functional enzyme

• Mechanism of enzymatic reaction

“generic” version

one enzyme - many substrates

many enzymes - one substrate

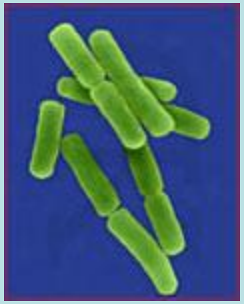
classes of enzymes

• Regulation of enzymes

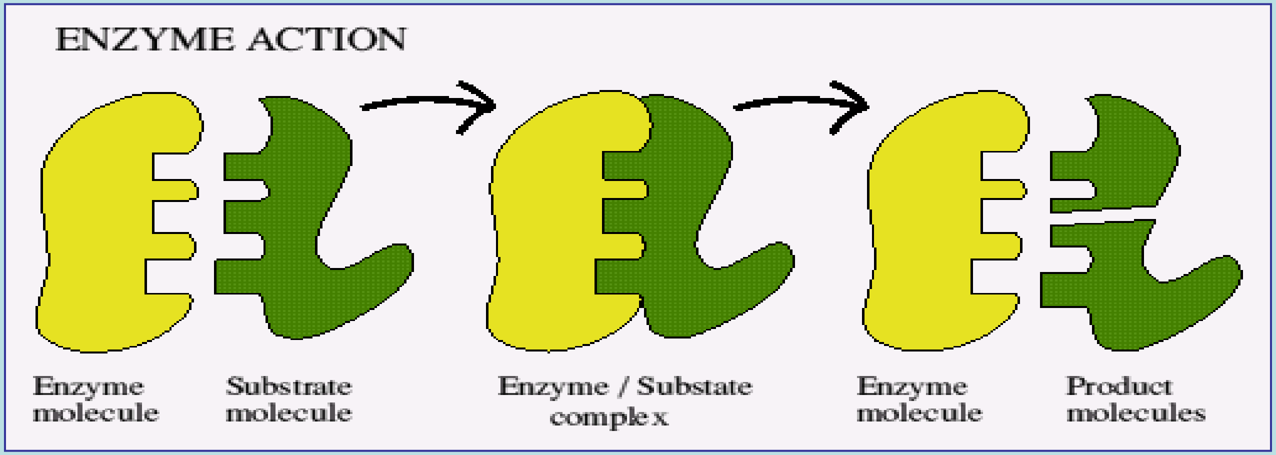
via synthesis

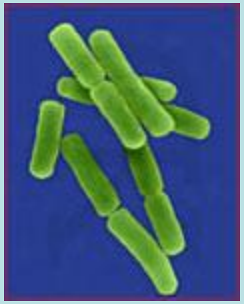
via activity

Nutrizione e metabolismo



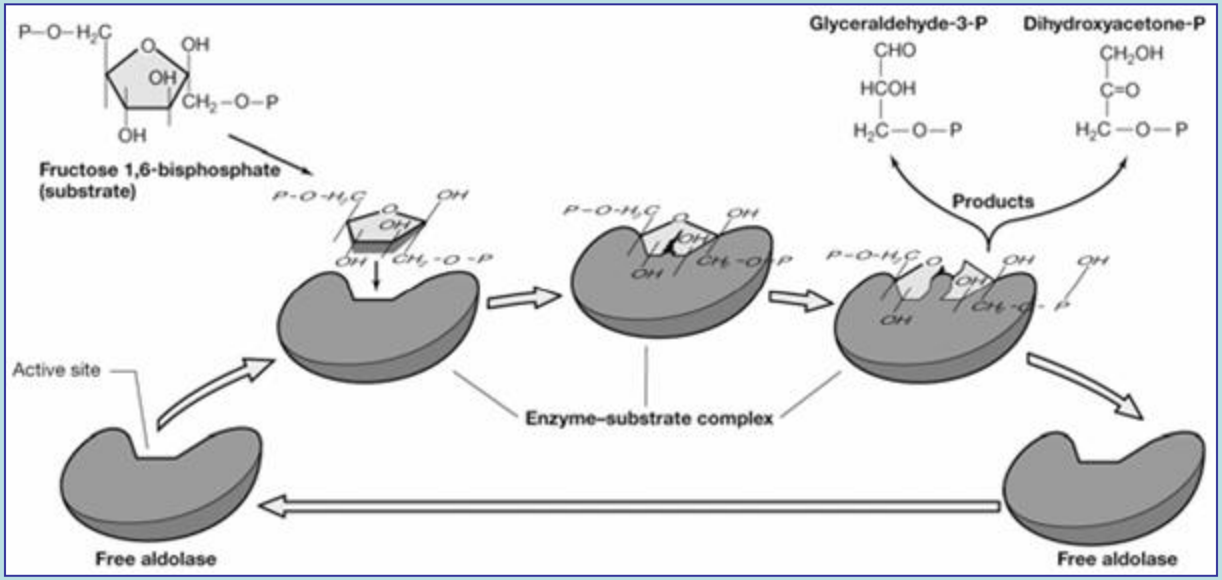

CATALISI ENZIMATICA



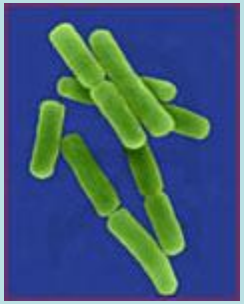


CATALISI ENZIMATICA

Ciclo catalitico della fruttosio-difosfato-aldolasi

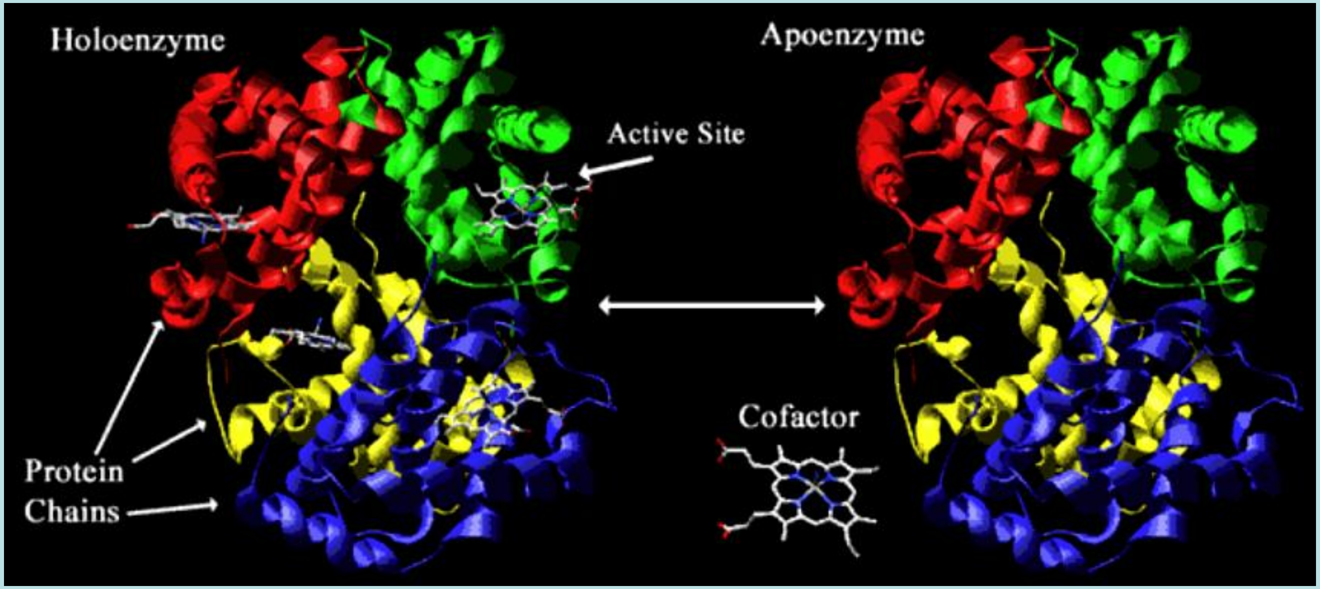


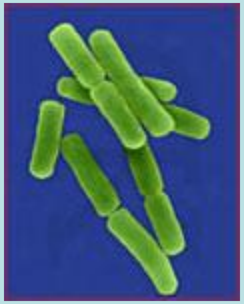
Nutrizione e metabolismo



CATALISI ENZIMATICA

ENZYME/CO-ENZYME SYSTEMS

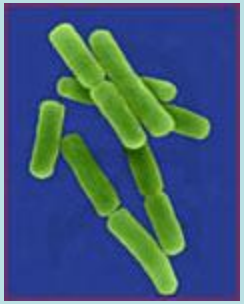





CONSERVAZIONE DELL'ENERGIA

ENERGY PRODUCTION

- **Redox reaction**
  - – oxidation: loss of electrons
  - – reduction: gain of electrons
- **Each molecule has the potential to donate and accept electrons from another molecule**



CONSERVAZIONE DELL'ENERGIA

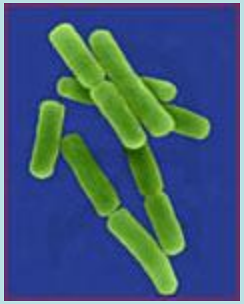
Reduction and Oxidation (A)

An atom becomes more reduced when it undergoes a chemical reaction in which it

1) gains electrons

2) by bonding to a less electronegative atom

3) … and often this occurs when the atom becomes bonded to a hydrogen



CONSERVAZIONE DELL'ENERGIA

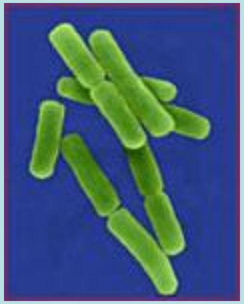
Reduction and Oxidation (B)

An atom becomes more oxidized when it undergoes a chemical reaction in which it

1) loses electrons

2) by bonding to a more electronegative atom

3) … and often this occurs when the atom becomes bonded to an oxygen



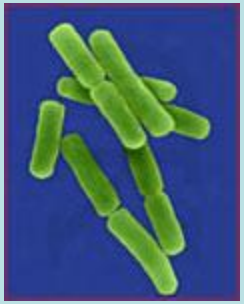
CONSERVAZIONE DELL'ENERGIA

Reduction and Oxidation (C)

i) In metabolic pathways, we are often concerned with the oxidation or reduction of carbon

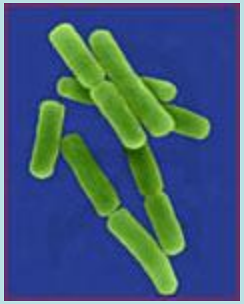
ii) Reduced forms of carbon (*e.g.* hydrocarbons, methane, fats, carbohydrates, alcohols) carry a great deal of potential chemical energy stored in their bonds

iii) Oxidized forms of carbon (e.g. ketones, aldehydes, carboxylic acids, carbon dioxide) carry very little potential chemical energy in their bonds

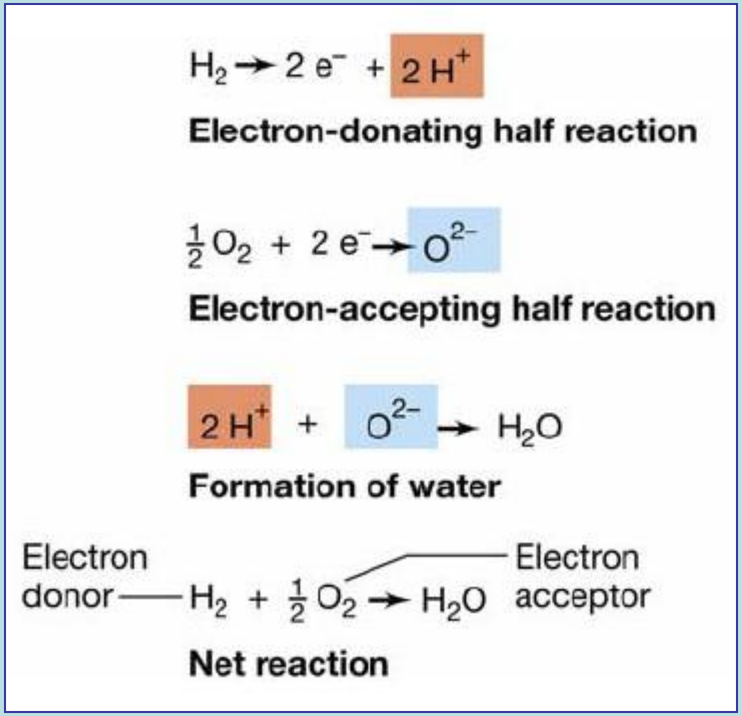


Reduction and Oxidation (D)

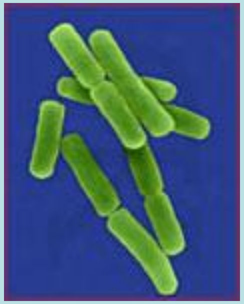
Reduction and oxidation always occur together. In a reduction-oxidation reaction (redox reaction), one substance gets reduced, and another substance gets oxidized. The thing that gets oxidized is called the electron donor, and the thing that gets reduced is called the electron acceptor.



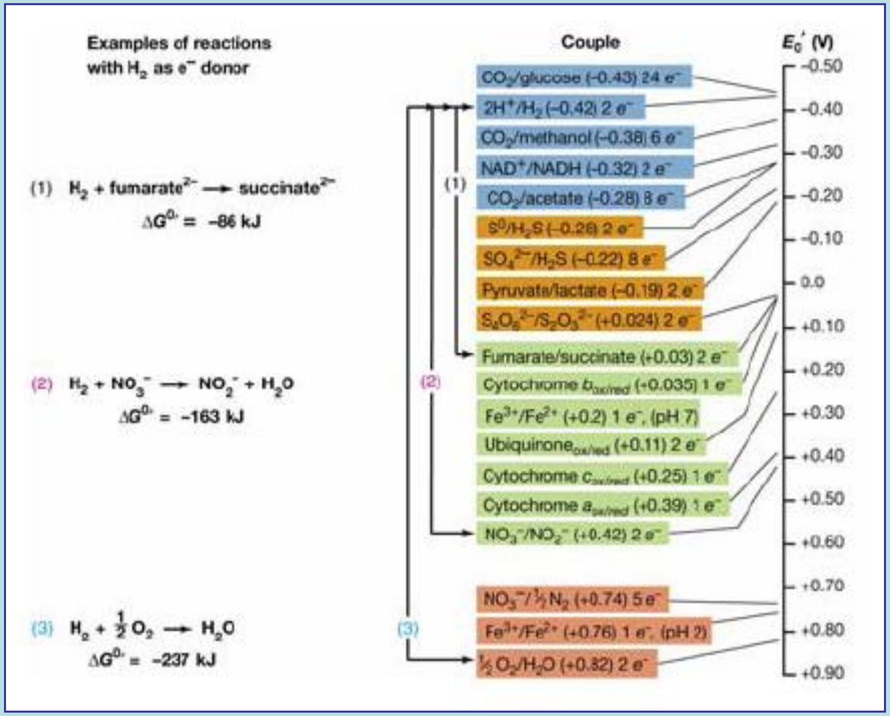
CONSERVAZIONE DELL'ENERGIA



Esempio di reazione di ossido-riduzione

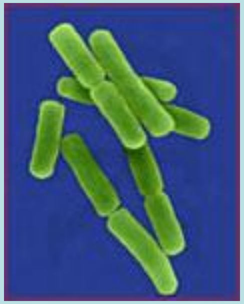


CONSERVAZIONE DELL'ENERGIA



La torre dei potenziali delle più importanti coppie redox, ricorrenti in ambito metabolico

Nutrizione e metabolismo

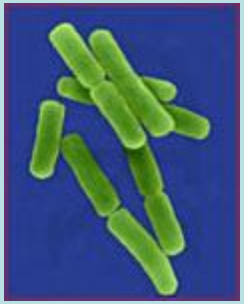



CONSERVAZIONE DELL'ENERGIA

Cofactors for Redox Reactions

(***a***) Enzymes that catalyze redox reactions typically require a cofactor to "shuttle" electrons from one part of the metabolic pathway to another part.

(***b***) There are two main redox cofactors: NAD and FAD. These are (relatively) small organic molecules in which part of the structure can either be reduced (*e.g.*, accept a pair of electrons) or oxidized (*e.g.*, donate a pair of electrons).



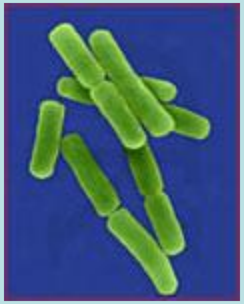
CONSERVAZIONE DELL'ENERGIA

Cofactors for Redox Reactions

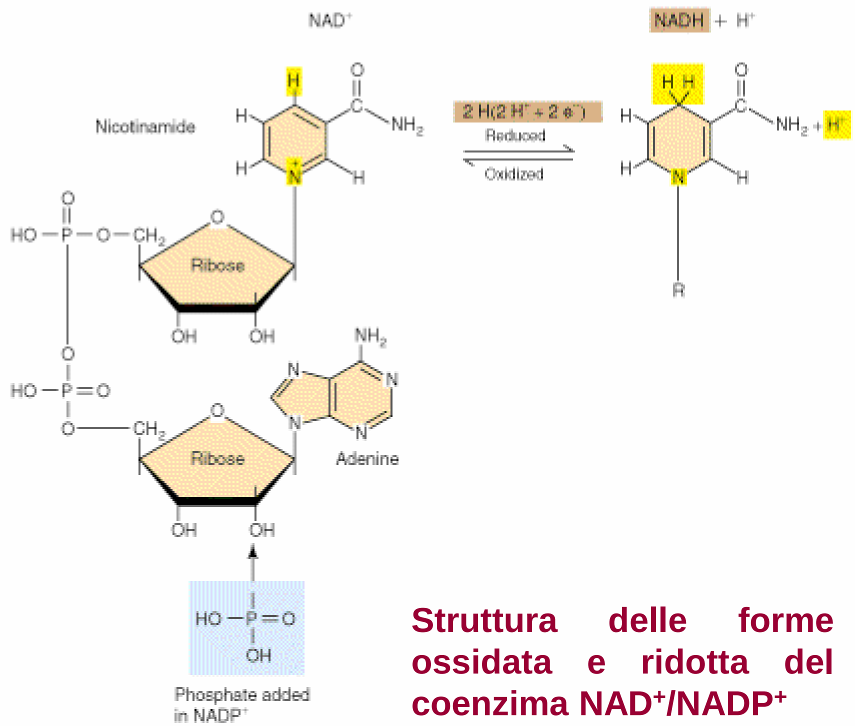
$$NAD_{(oxidized)} + H^+ + \text{Pair of electrons} \rightarrow NADH_{(reduced)}$$

$$FAD_{(oxidized)} + H^+ + \text{Pair of electrons} \rightarrow FADH_{(reduced)}$$

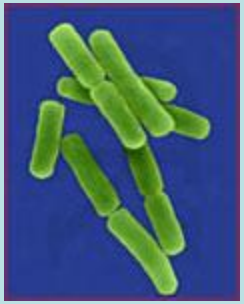
NAD and FAD are present only in small (catalytic) amounts – they cannot serve as the final electron acceptor, but must be regenerated (reoxidized) in order for metabolism to continue



Nicotinammide-adenin-dinucleotide

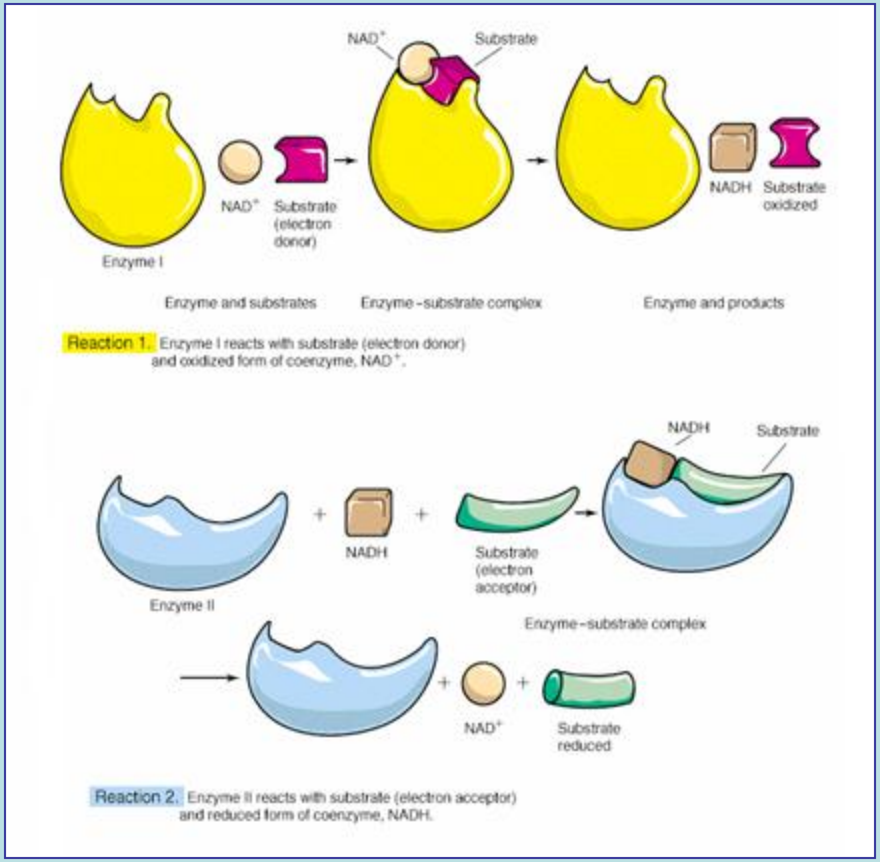


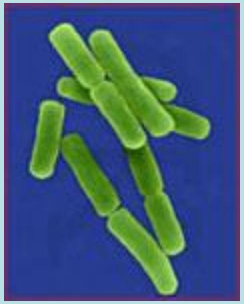
Struttura delle forme ossidata e ridotta del coenzima NAD^+/$NADP^+$



CONSERVAZIONE DELL'ENERGIA

Rappresentazione schematica di ossido-riduzione mediata da NAD^+ e NADH





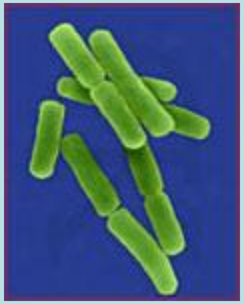
CONSERVAZIONE DELL'ENERGIA

ATP

ATP hydrolysis is used as an energy source in many biological reactions that require energy – for example, active transport in the sodium-potassium pump. During catabolism, energy released from the oxidation of carbon is captured and used to synthesize ATP from ADP and phosphate.

$$C_6H_{12}O_6 + 6\ O_2 \rightarrow 6\ CO_2 + 6\ H_2O + \text{Energy}$$

$$\text{ADP} + \text{Phosphate} + \text{Energy} \rightarrow \text{ATP} + H_2O$$



ATP: A "currency of energy" for many cellular reactions

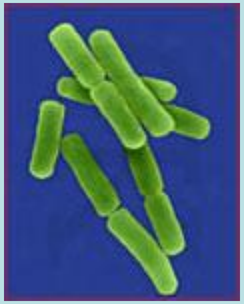
ATP stands for adenosine triphosphate. It is a nucleotide with three phosphate groups linked in a small chain.

The last phosphate in the chain can be removed by hydrolysis (the ATP becomes ADP, or adenosine diphosphate).

This reaction is energetically favorable: it has a $\Delta G^{0'}$ of about – 7.5 kcal/mol

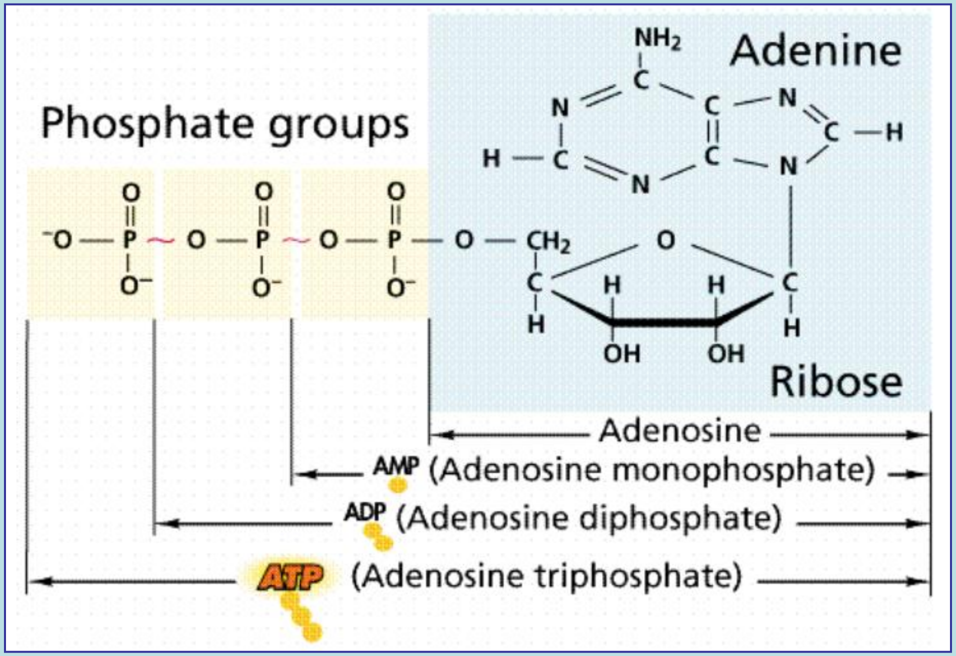
ATP + H_2O $\rightarrow$ ADP + Phosphate + Energy (7.5 kcal/mol)

.

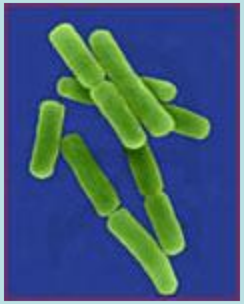



CONSERVAZIONE DELL'ENERGIA

ATP

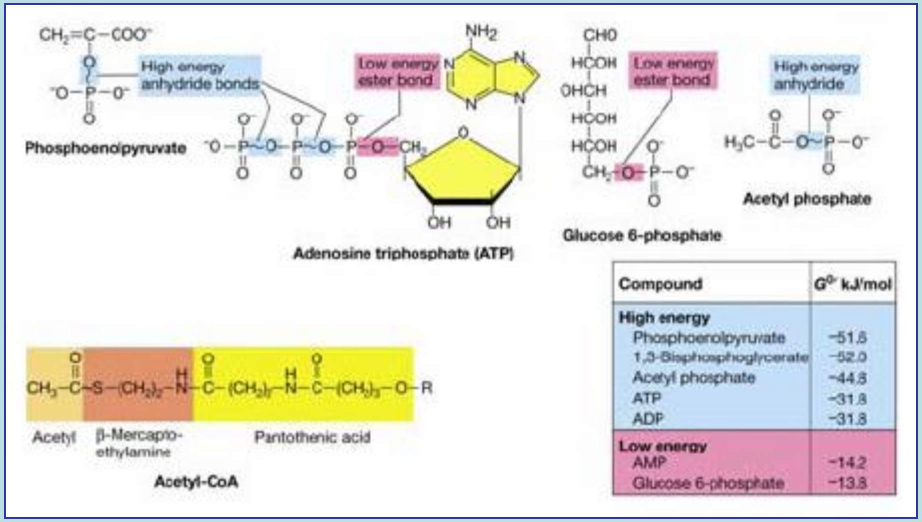


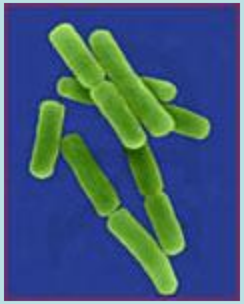
Nutrizione e metabolismo



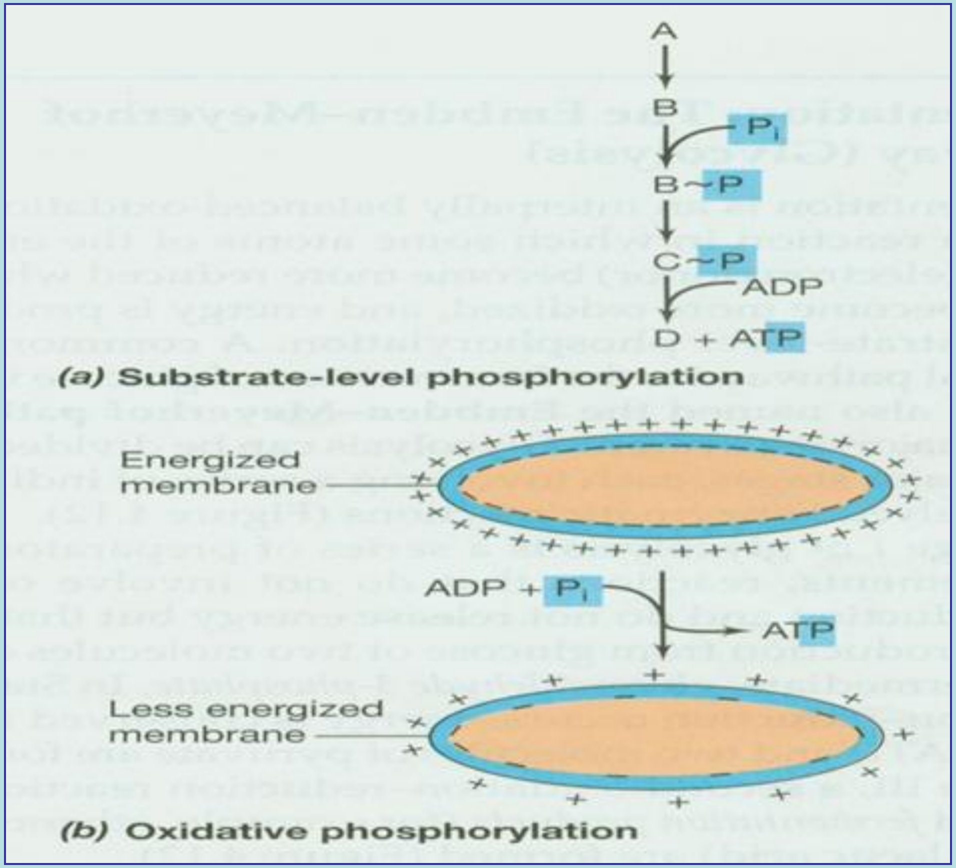

CONSERVAZIONE DELL'ENERGIA

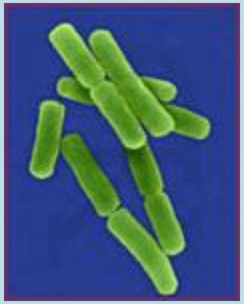
Composti importanti nelle reazioni di trasformazione dell'energia all'interno della cellula microbica



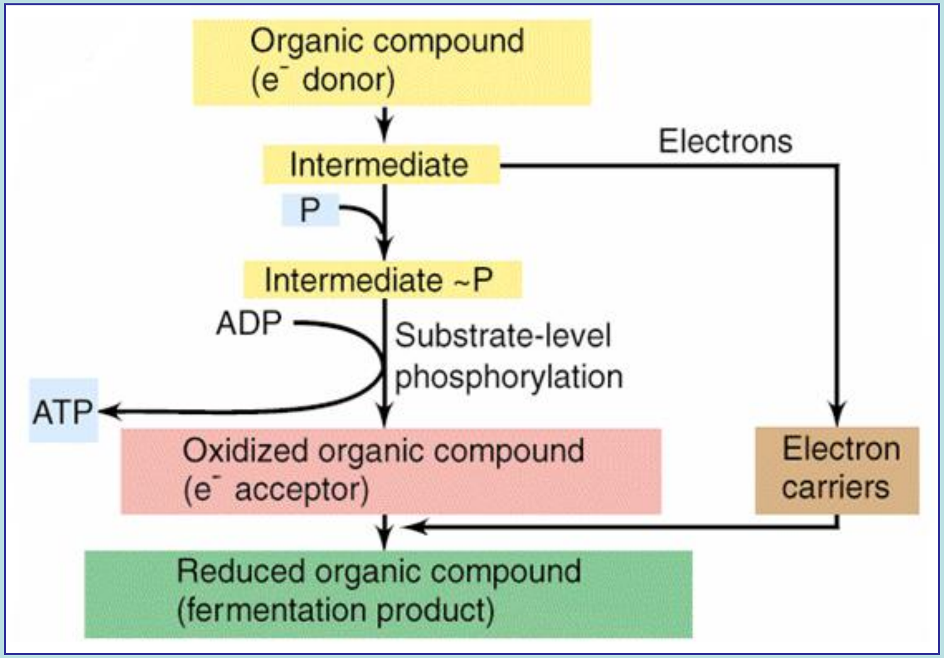



Conservazione dell'energia nella fermentazione e nella respirazione

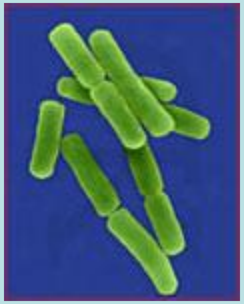





LA NUTRIZIONE MICROBICA



Nutrizione e metabolismo



ALTERNATIVE CATABOLICHE

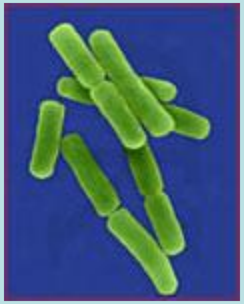
4 major glycolytic pathways found in different bacteria:

1) **Embden-Meyerhof-Parnas pathway**
“Classic” glycolysis
Found in almost all organisms

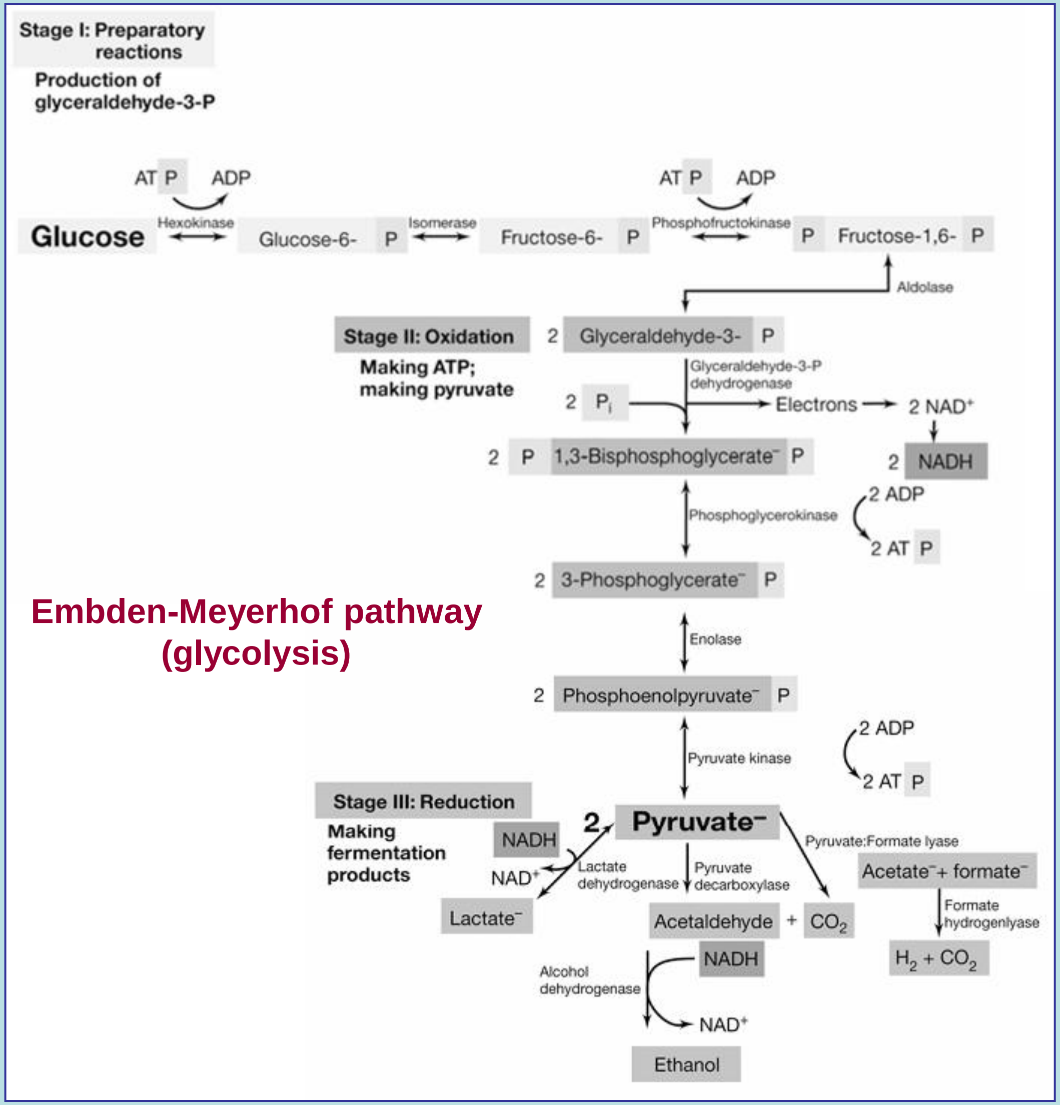
2) **Hexose monophosphate pathway**
Also found in most organisms
Responsible for synthesis of pentose sugars used in nucleotide synthesis

3) **Entner-Doudoroff pathway**
Found in *Pseudomonas* and related genera

4) **Phosphoketolase pathway**
Found in *Bifidobacterium* and *Leuconostoc*

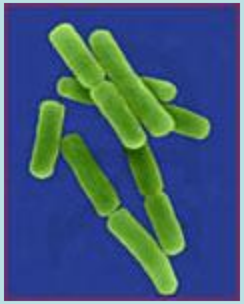



ALTERNATIVE CATABOLICHE



Embden-Meyerhof pathway (glycolysis)

Nutrizione e metabolismo



ALTERNATIVE CATABOLICHE

Features of glycolytic pathways

a) Partial oxidation of glucose to form pyruvic acid

b) A small amount of ATP is made

c) A small amount of NAD is reduced to NADH

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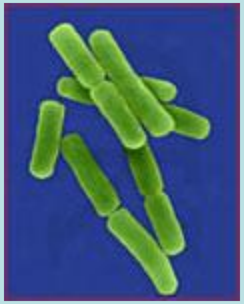
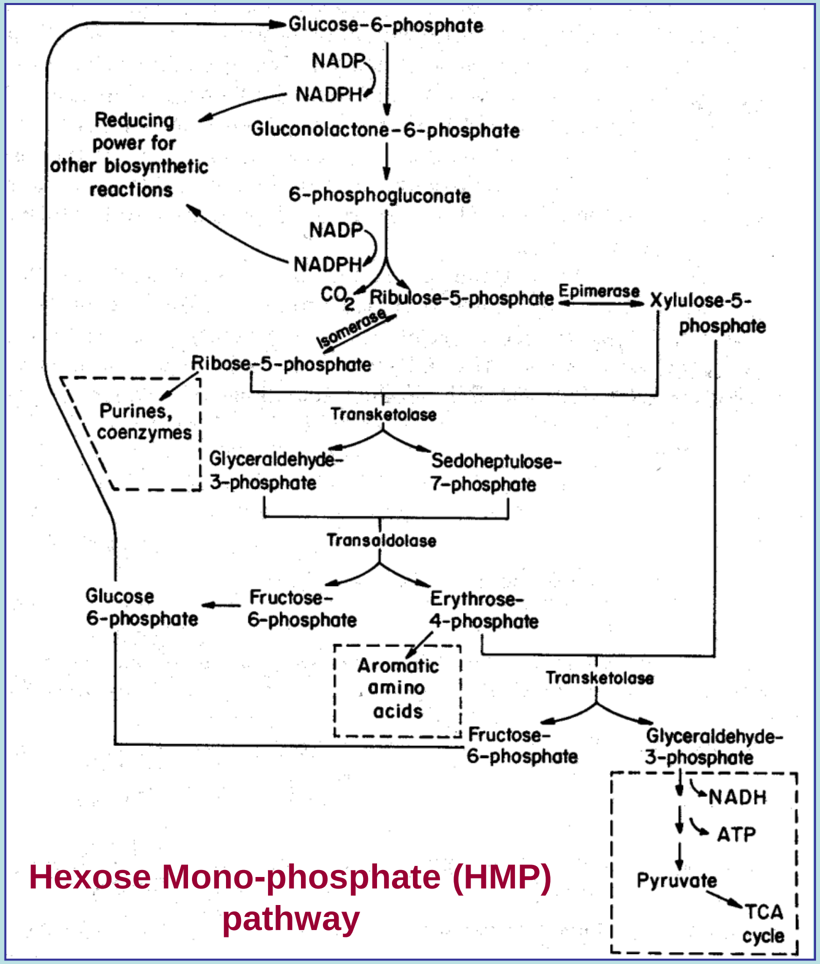
Nutrizione e metabolismo

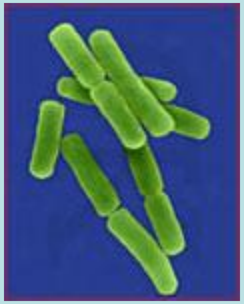



ALTERNATIVE CATABOLICHE



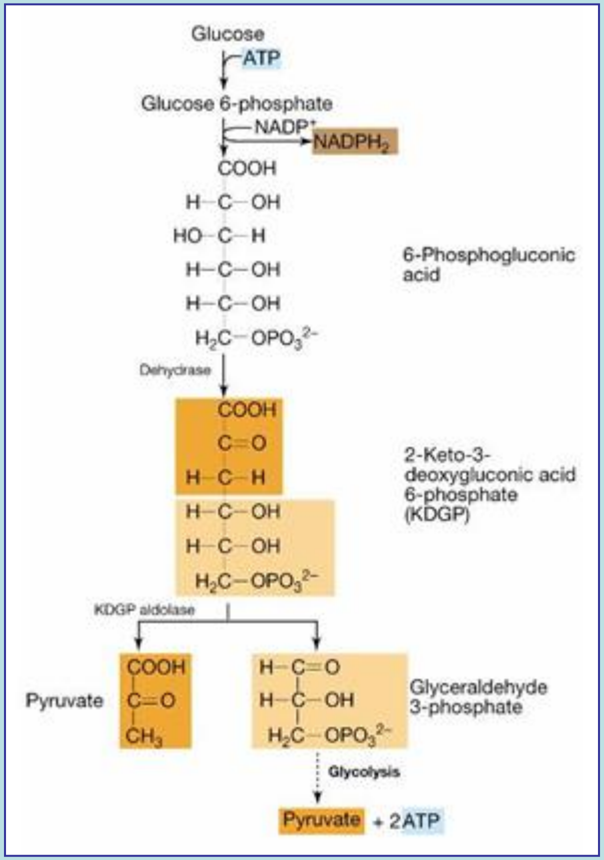
Hexose Mono-phosphate (HMP) pathway

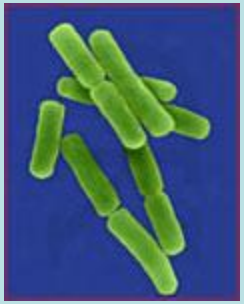
Nutrizione e metabolismo



ALTERNATIVE CATABOLICHE

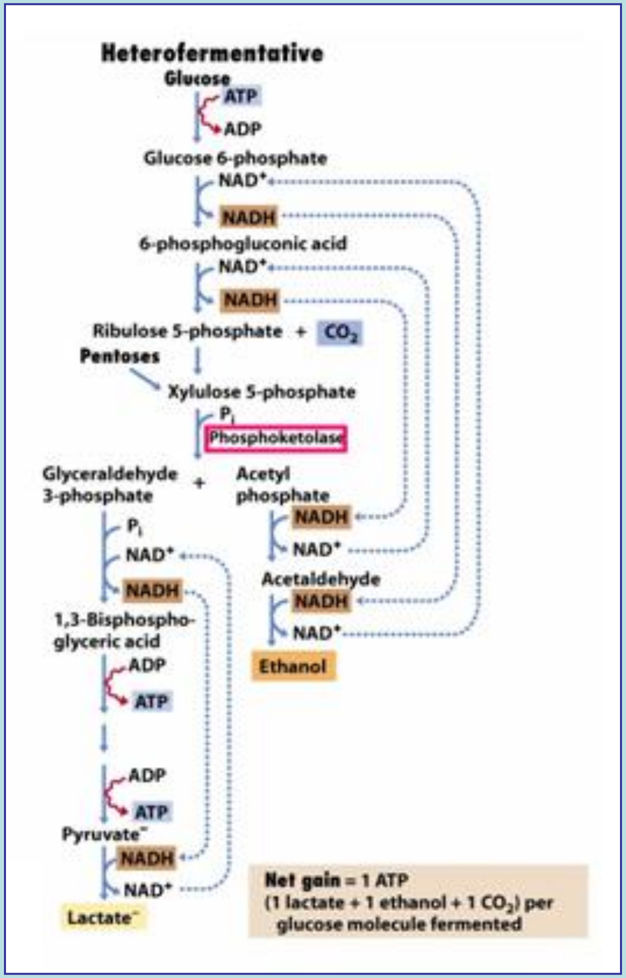
The Entner-Doudoroff pathway of glucose catabolism in pseudomonads

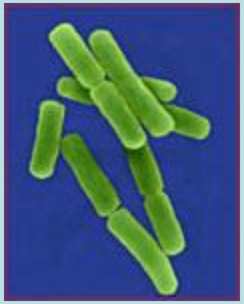





ALTERNATIVE CATABOLICHE

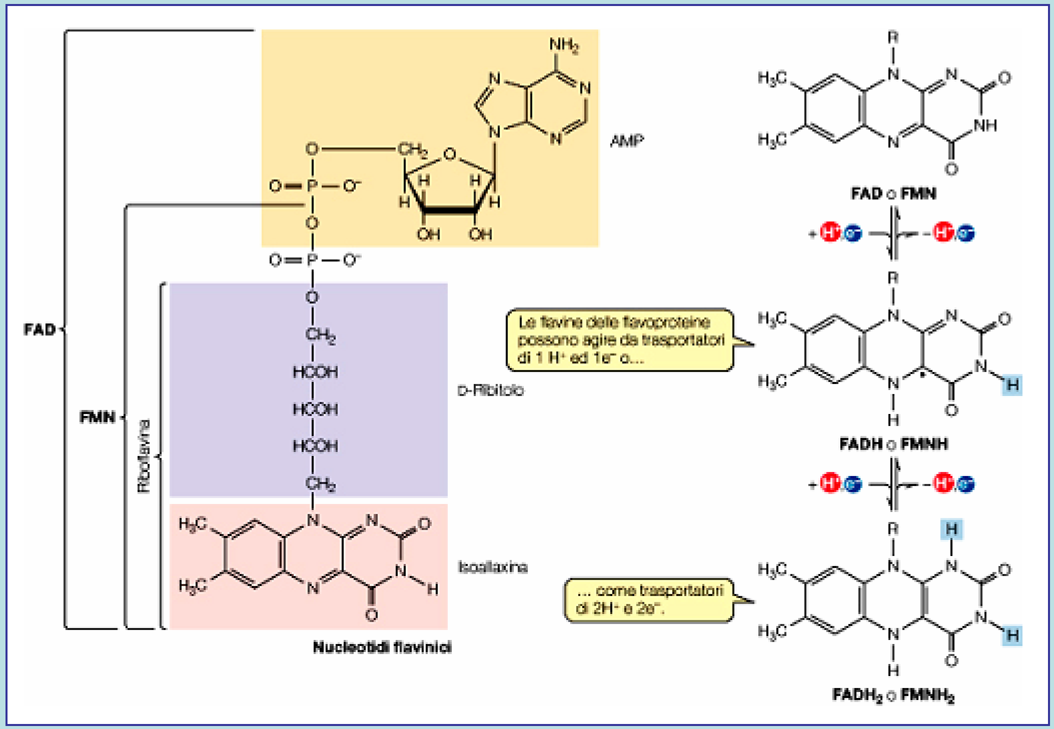
The phosphoketolase pathway

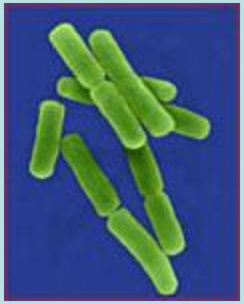




TRASPORTATORI DI MEMBRANA

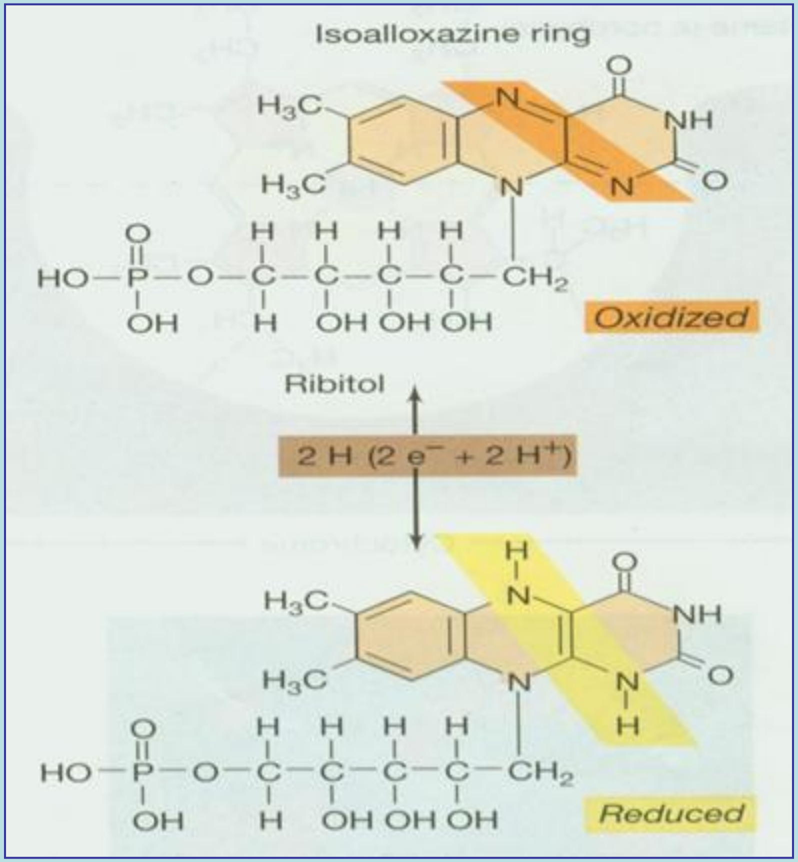
NUCLEOTIDI FLAVINICI

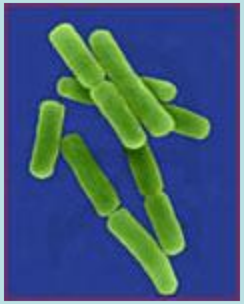




TRASPORTATORI DI MEMBRANA

Il trasportatore di idrogeno flavin-mononucleotide (FMN)



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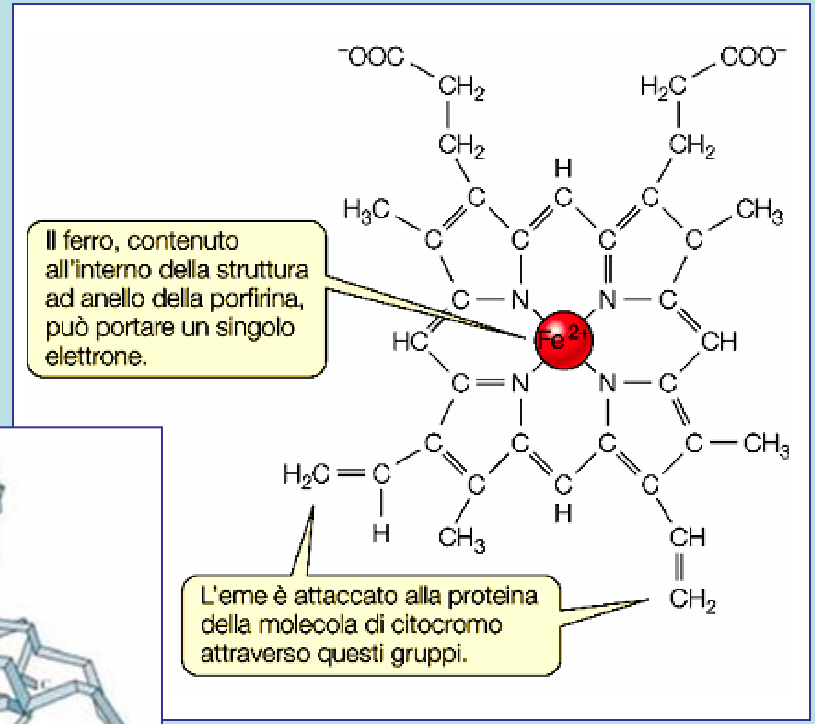
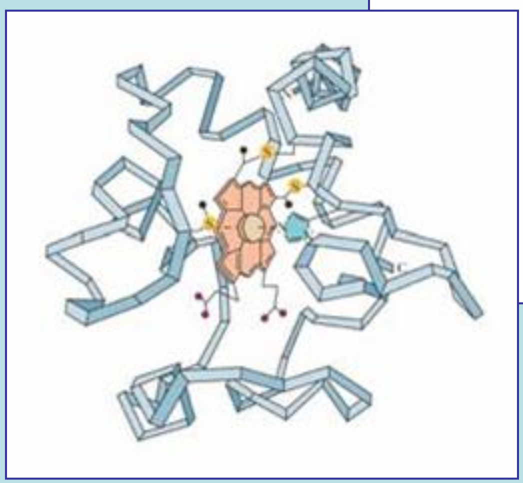
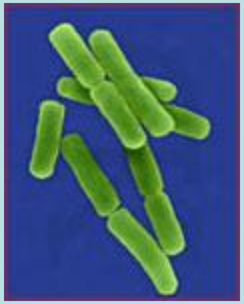


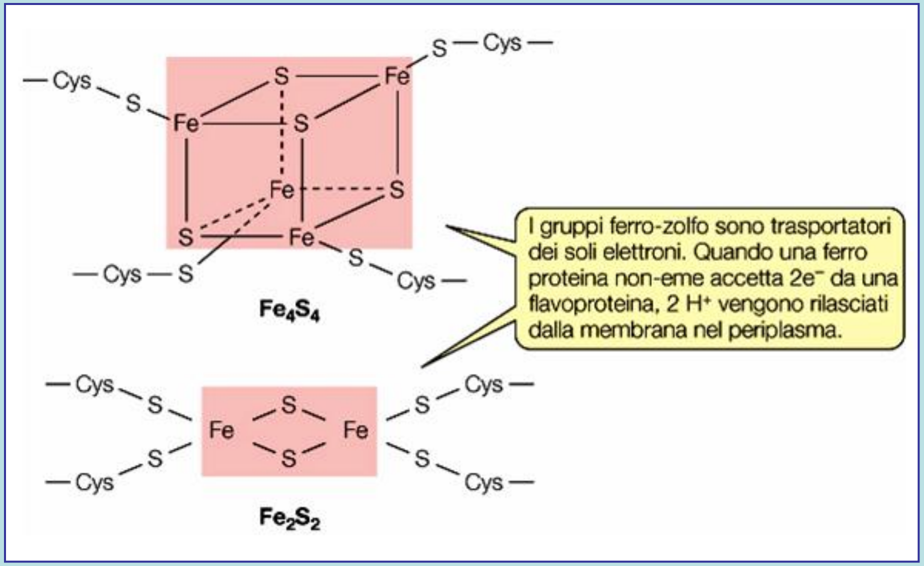


Struttura dei citocromi

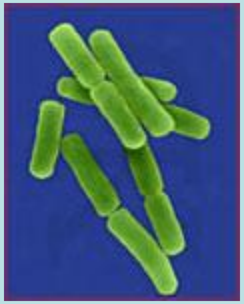


TRASPORTATORI DI MEMBRANA

Ferro-Zolfo proteine non-eme

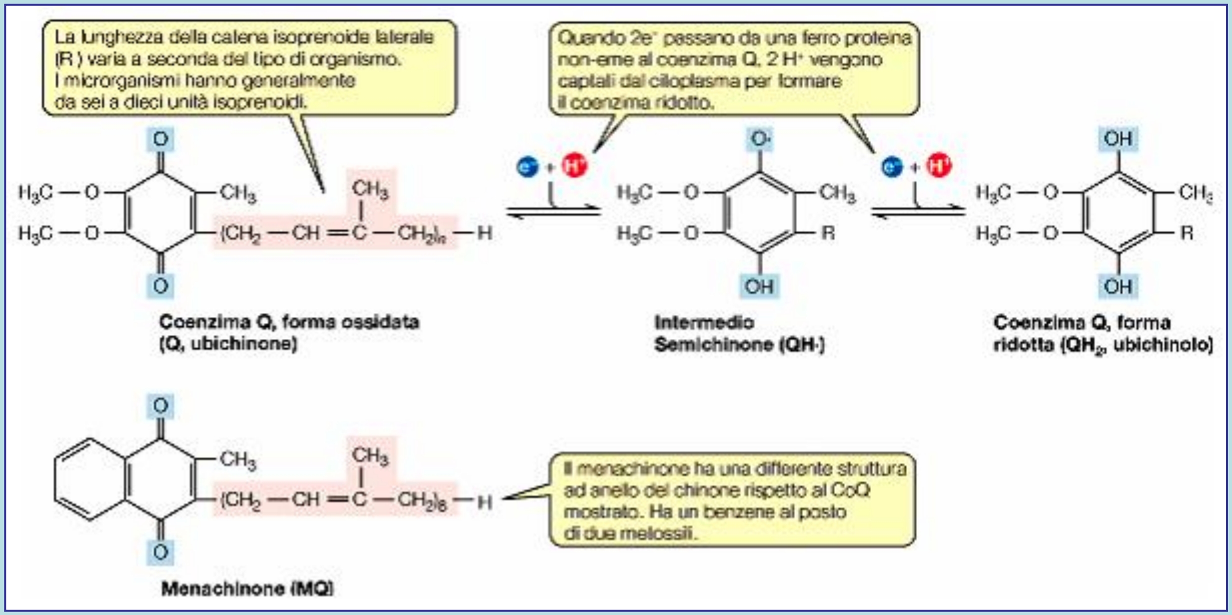


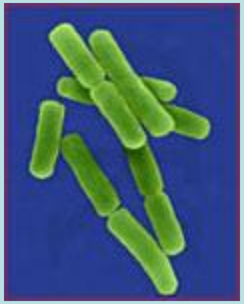
Nutrizione e metabolismo



TRASPORTATORI DI MEMBRANA

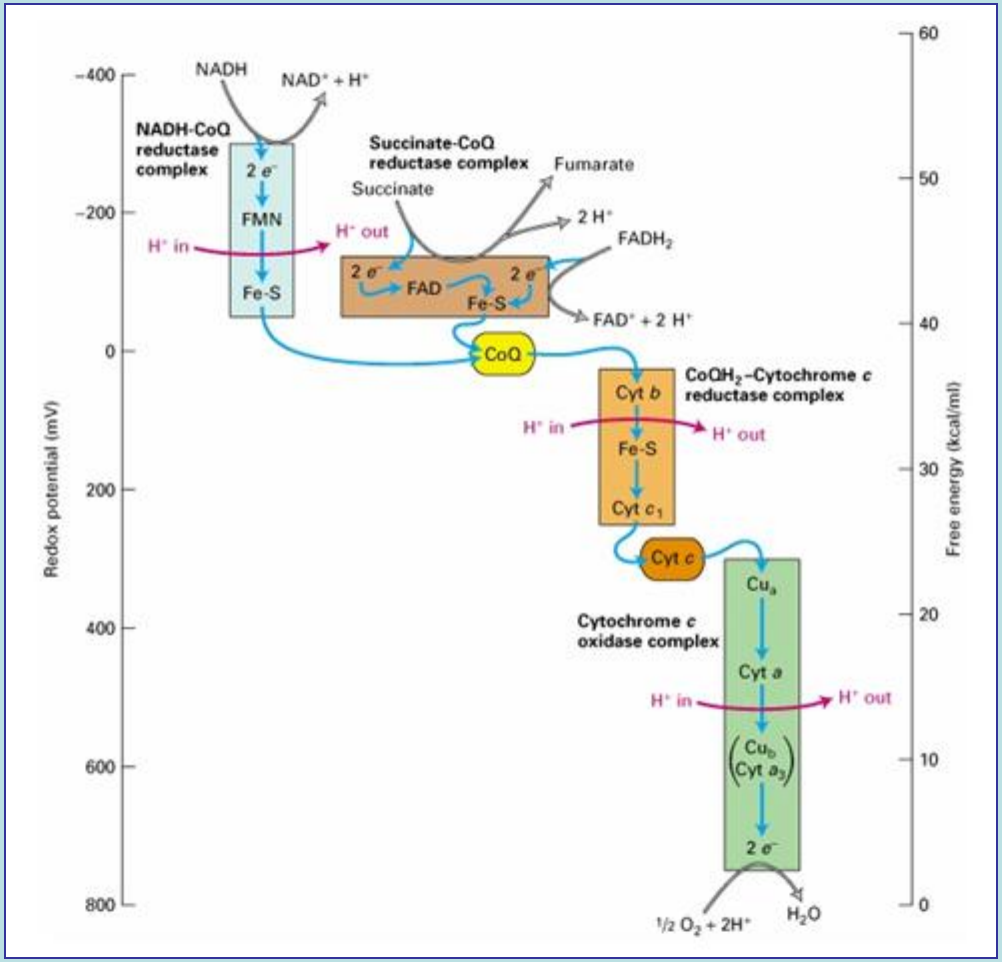
Struttura delle forme ossidata e ridotta del coenzima Q



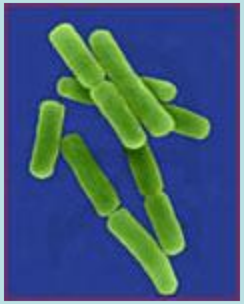


TRASPORTATORI DI MEMBRANA

Catene di trasporto degli elettroni e rispettiva relazione con l'E_0'

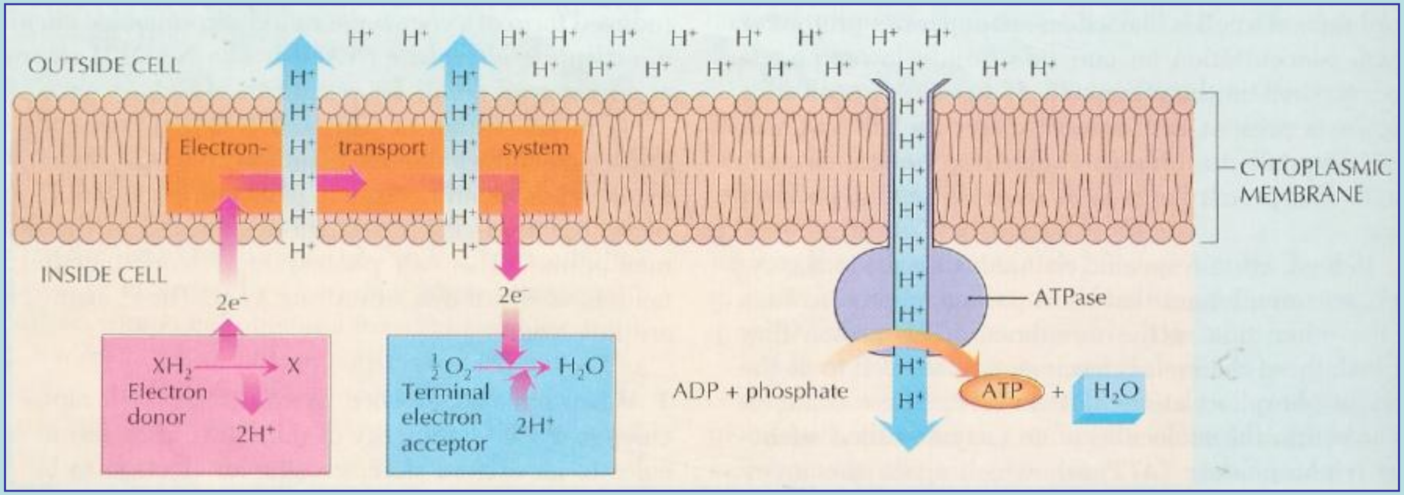


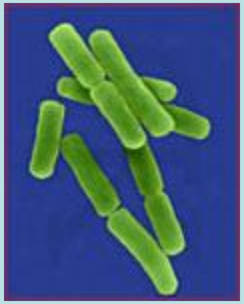
Nutrizione e metabolismo



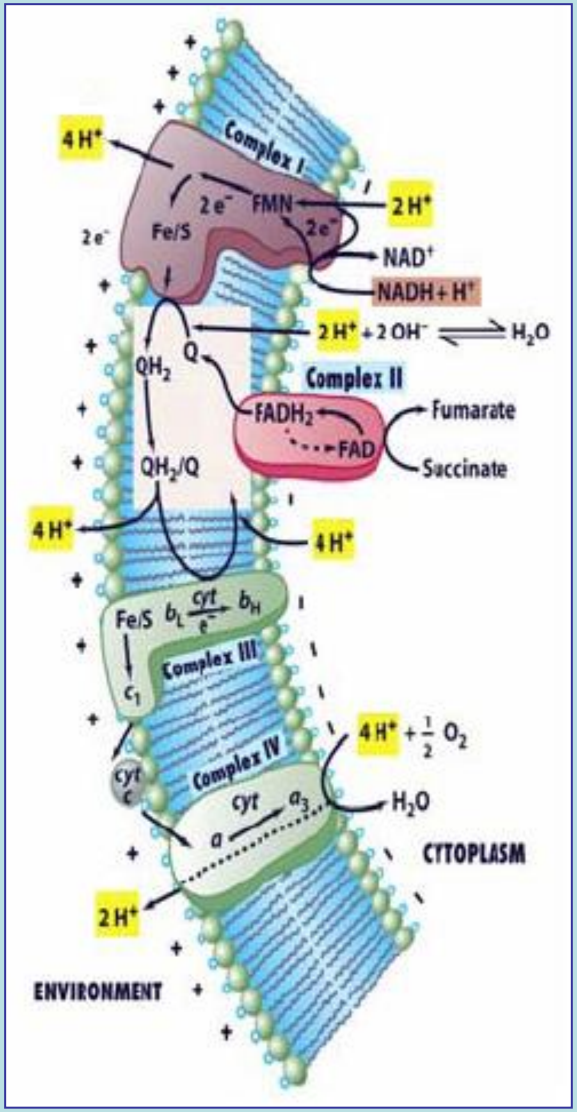
FORZA MOTRICE PROTONICA

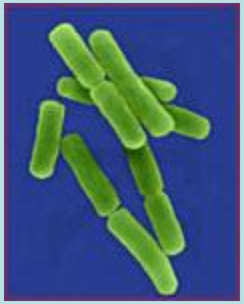
Formazione della Proton Motive Force





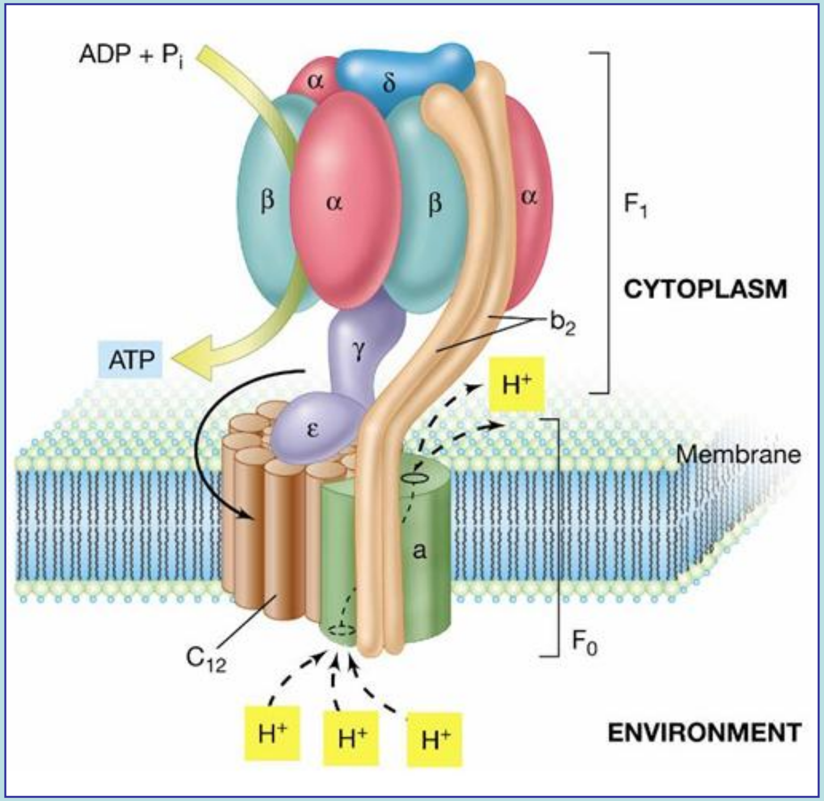
Generazione della forza motrice protonica durante la respirazione aerobica

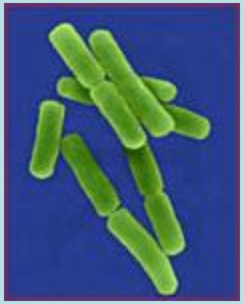





FORZA MOTRICE PROTONICA

Struttura e funzione dell'ATPasi batterica



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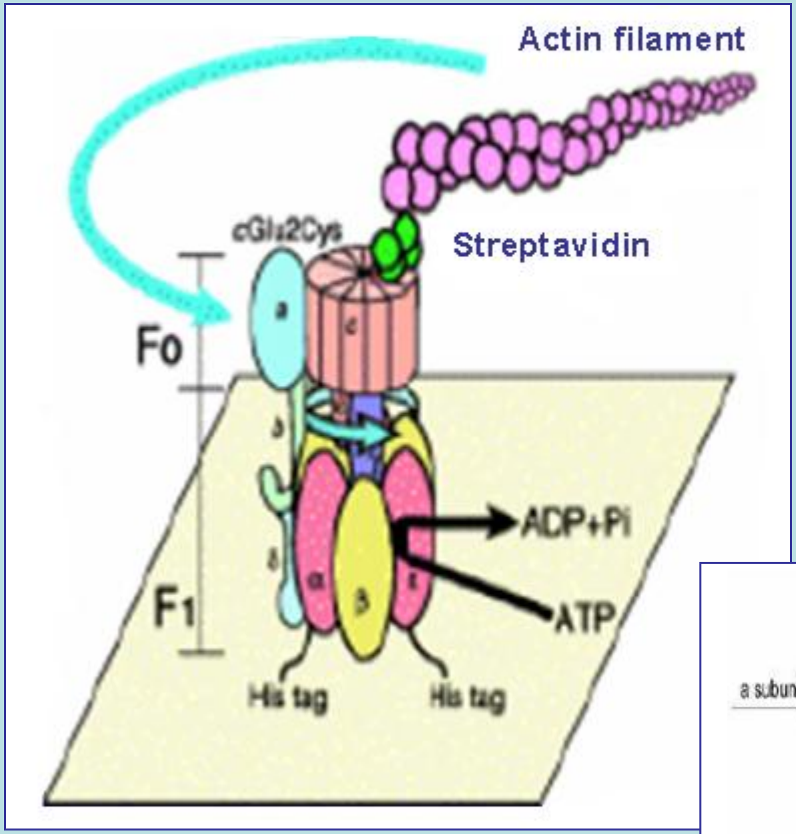
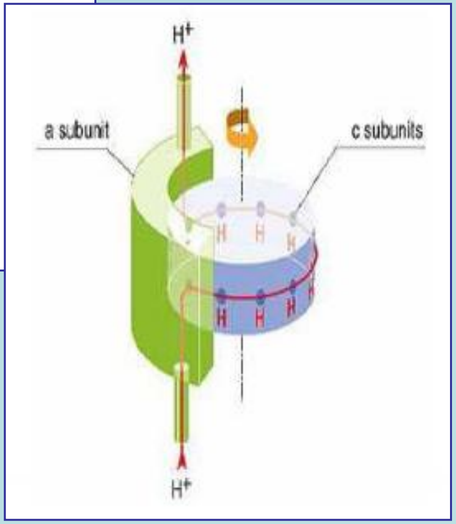
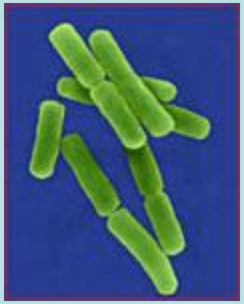


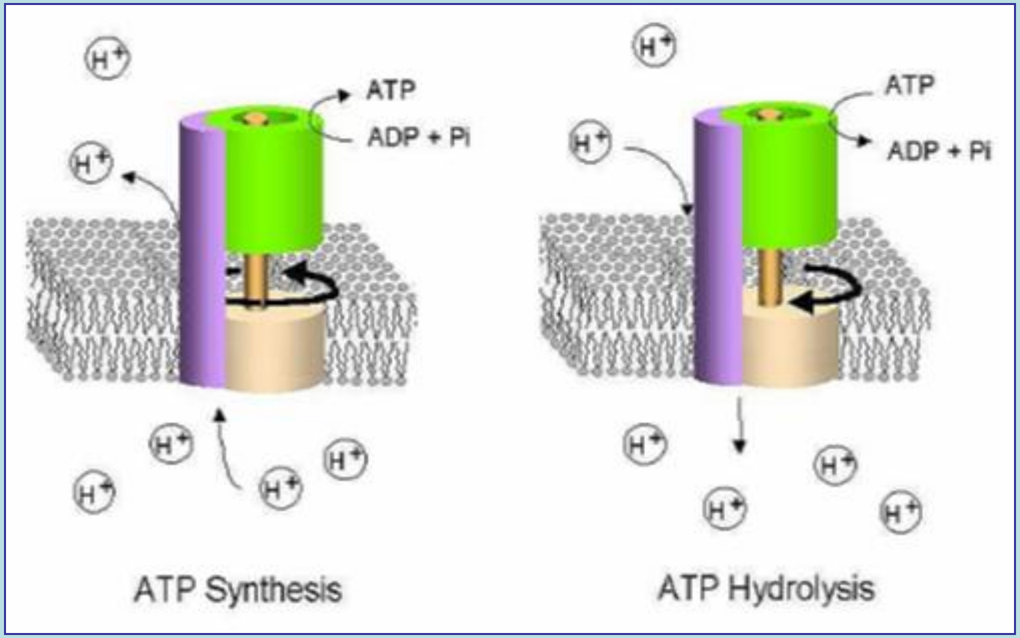
L'ATPasi F_1F_0 in realtà ruota

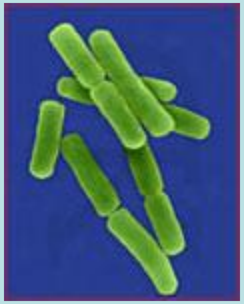




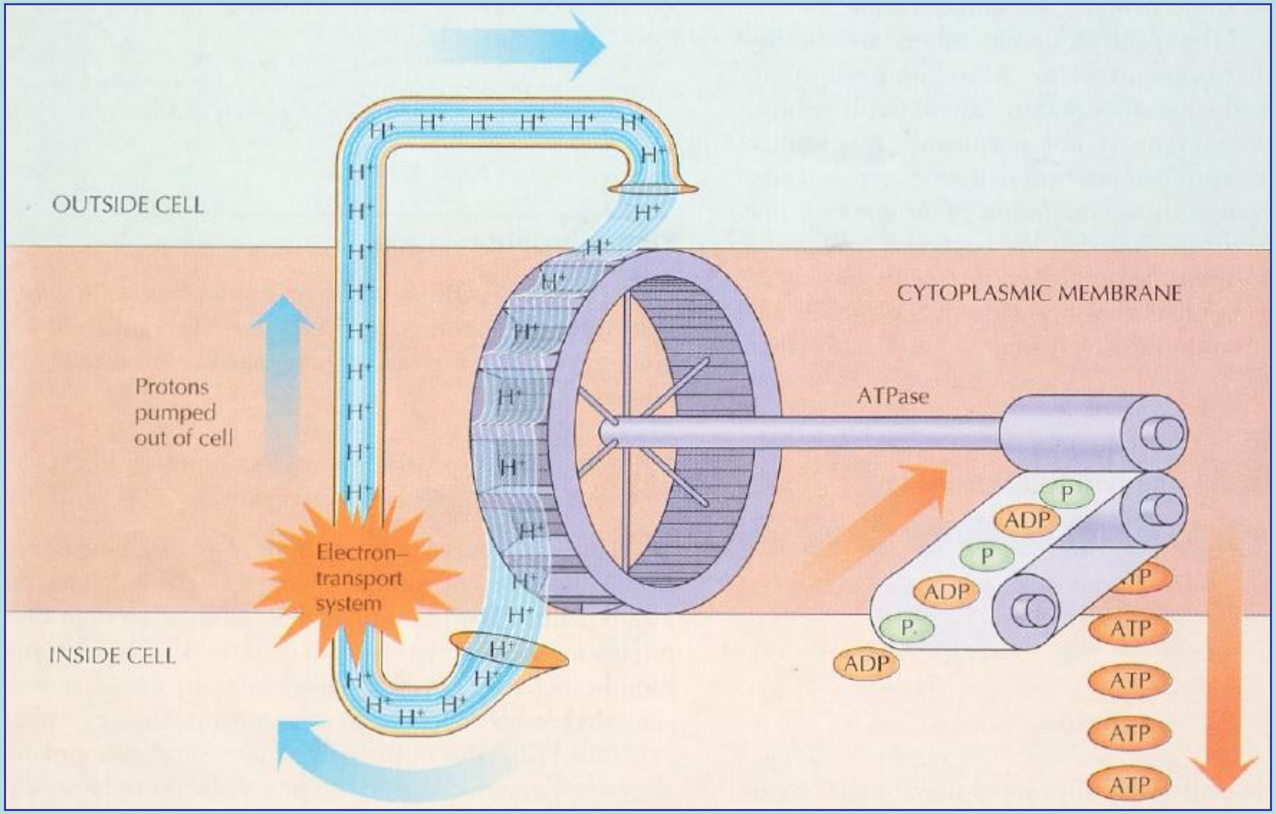

FORZA MOTRICE PROTONICA

La sintesi di ATP è il frutto di un'attività ATPasica in senso inverso



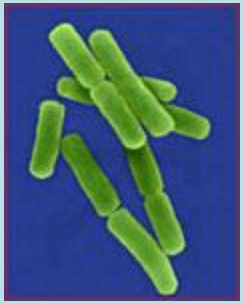


Sintesi di ATP via Proton Motive Force



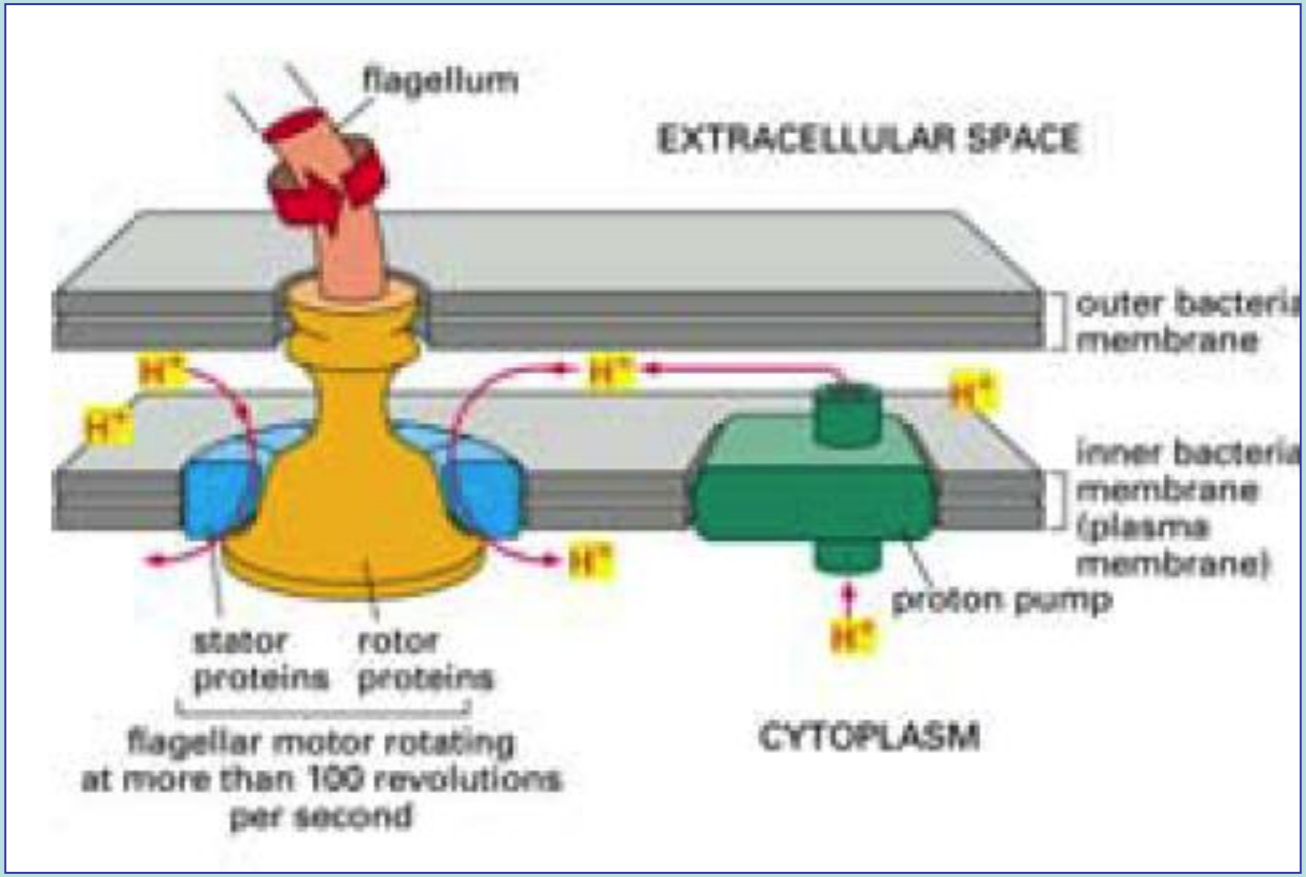
FORZA MOTRICE PROTONICA

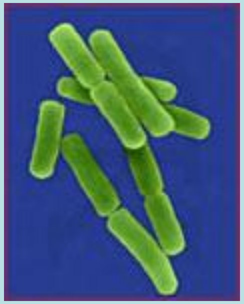
Nutrizione e metabolismo




FORZA MOTRICE PROTONICA

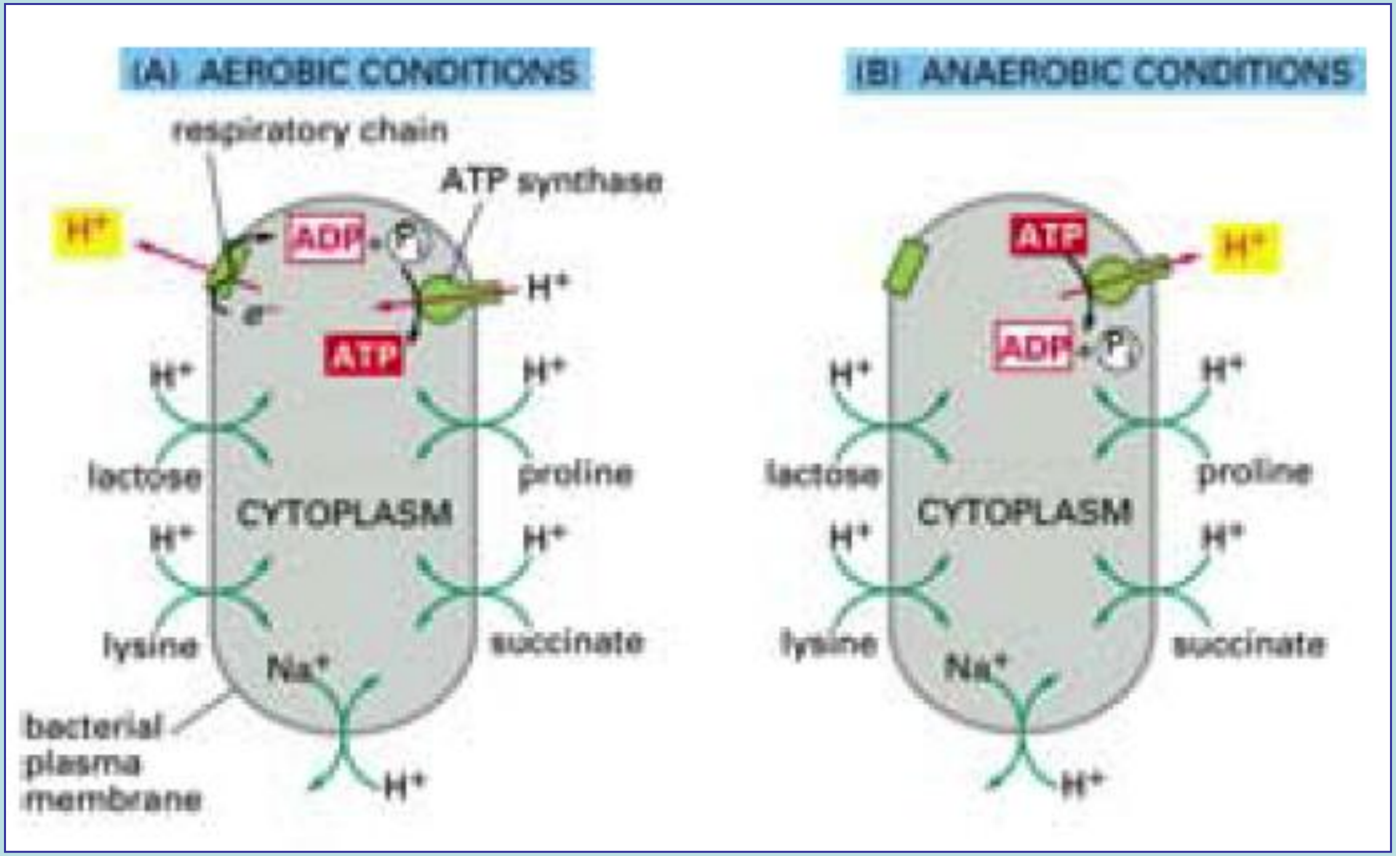
Movimento dei flagelli spinto dalla Proton Motive Force

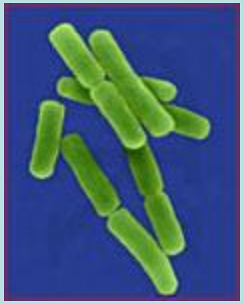




FORZA MOTRICE PROTONICA

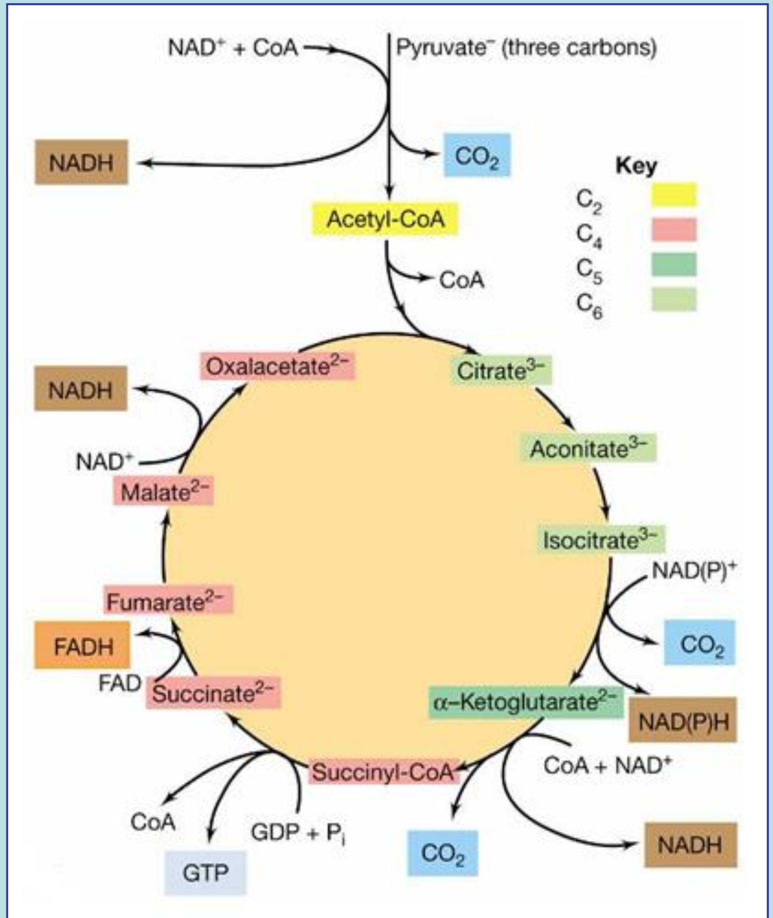
Trasporto transmembrana spinto dalla Proton Motive Force

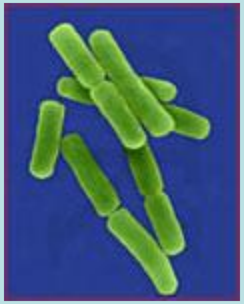




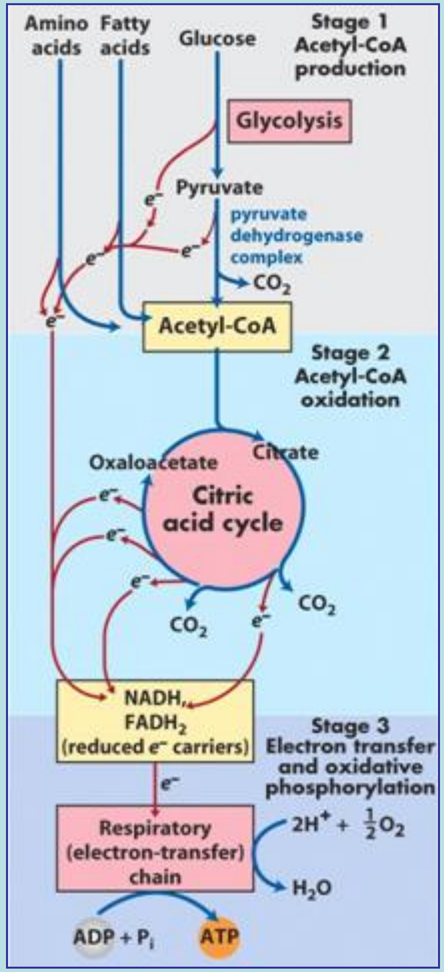
RESPIRAZIONE AEROBICA

IL CICLO DEGLI ACIDI TRICARBOSSILICI






BILANCIO ENERGETICO DELLA RESPIRAZIONE AEROBICA

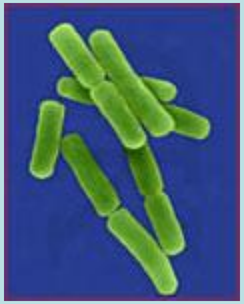


Glycolysis:

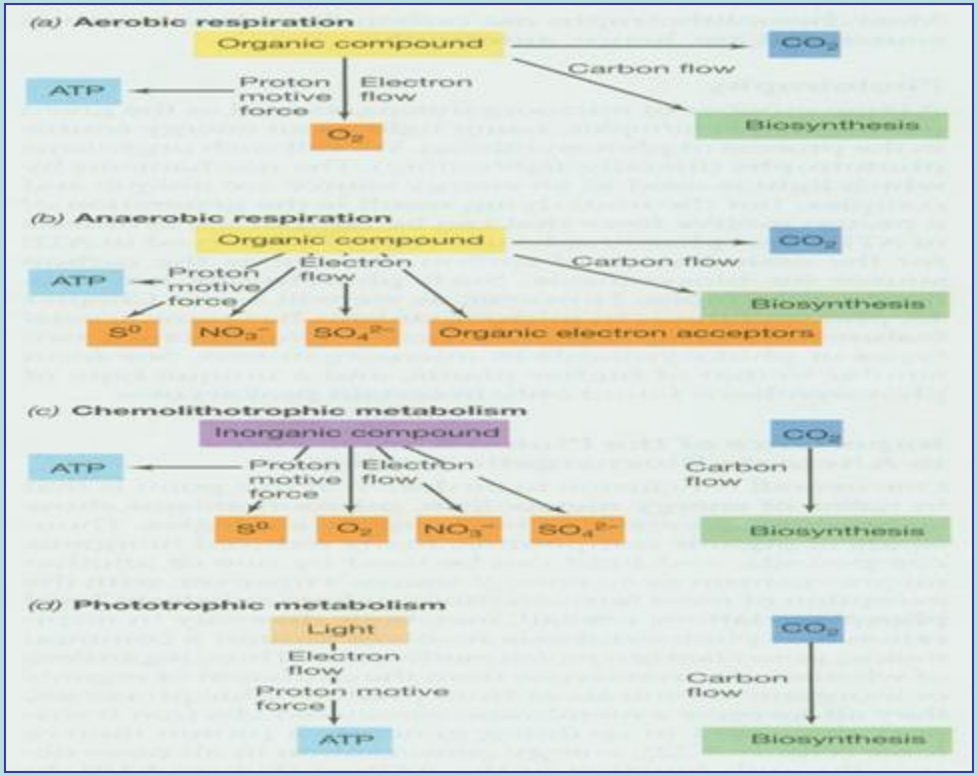
4	ATP	by substrate-level phosphorylation
-2	ATP	used to initiate glycolysis
2	ATP	net gain to cell

The Electron Transport System and TCA Cycle:

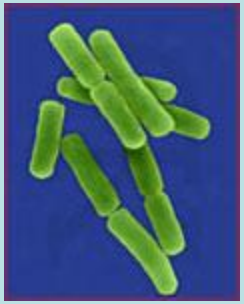
4	ATP	from NADH produced in glycolysis
24	ATP	from NADH generated in TCA cycle
4	ATP	from $FADH_2$ generated in TCA cycle
2	ATP	via GTP produced by substrate-level phosphorylation
36	ATP	net gain to cell from aerobic catabolism of one glucose molecule



ALTRI ASSETTI METABOLICI



Nutrizione e metabolismo



ALTRI ASSETTI METABOLICI

ALL MICROBIAL METABOLISM CAN BE ARRANGED ACCORDING TO THREE PRINCIPLES:

1. how the organism obtains carbon for synthesising cell mass:

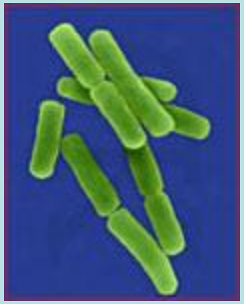
Autotrophic	carbon is obtained from carbon dioxide (CO_2)
Heterotrophic	carbon is obtained from organic compounds
Mixotrophic	carbon is obtained from both organic compounds and by fixing carbon dioxide

2. how the organism obtains reducing equivalents used either in energy conservation or in biosynthetic reactions:

Lithotrophic	reducing equivalents are obtained from inorganic compounds
Organotrophic	reducing equivalents are obtained from organic compounds

3. how the organism obtains energy for living and growing:

Chemotrophic	energy is obtained from external chemical compounds
Phototrophic	energy is obtained from light



ALTRI ASSETTI METABOLICI

In practice, these terms are almost freely combined. Typical examples are as follows:

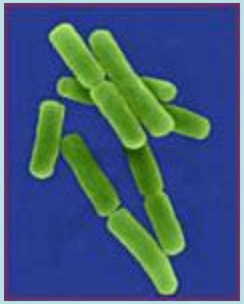
1.chemolithoautotrophs obtain energy from the oxidation of inorganic compounds and carbon from the fixation of carbon dioxide. Examples: Nitrifying bacteria, Sulfur-oxidising bacteria, Iron-oxidising bacteria, Knallgas-bacteria (e.g. *Hydrogenobacter*).

2.photolithoautotrophs obtain energy from light and carbon from the fixation of carbon dioxide, using reducing equivalents from inorganic compounds. Examples: Cyanobacteria (water as reducing equivalent donor), *Chlorobiaceae*, *Chromaticaceae* (hydrogen sulfide as reducing equivalent donor), *Chloroflexus* (hydrogen as reducing equivalent donor).

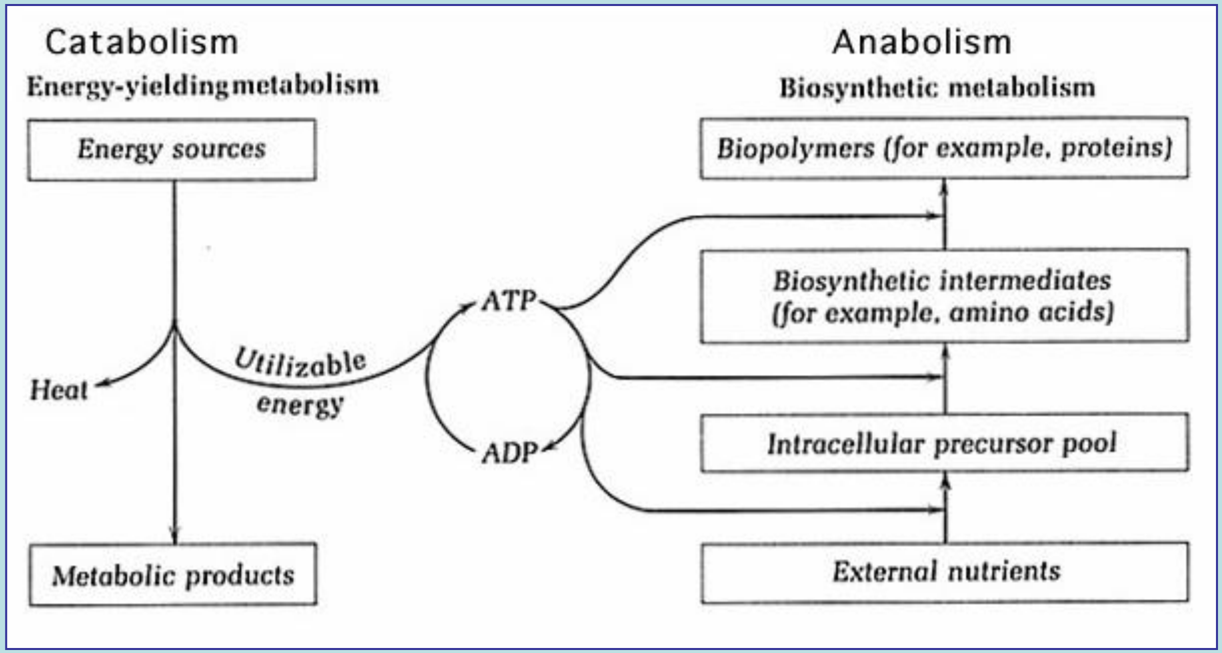
3.chemolithoheterotrophs obtain energy from the oxidation of inorganic compounds, but can not fix carbon dioxide. Examples: some *Nitrobacter* sp., *Wolinella* (with H_2 as reducing equivalent donor), some Knallgas-bacteria.

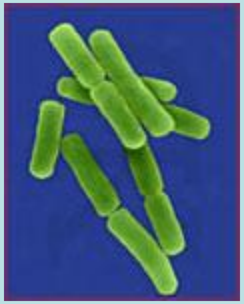
4.chemoorganoheterotrophs obtain energy, carbon and reducing equivalents for biosynthetic reactions from organic compounds. Examples: most bacteria (e.g. *Escherichia coli*, *Bacillus* sp., *Actinobacteria*).

5.photoorganotrophs obtain energy from light, carbon and reducing equivalents for biosynthetic reactions from organic compounds. Some species are strictly heterotrophic, many others can also fix carbon dioxide and are mixotrophic. Examples: *Rhodobacter*, *Rhodopseudomonas*, *Rhodospirillum*, *Rhodomicrobium*, *Heliobacterium*, *Chloroflexus* (alternatively to photolithoautotrophy with hydrogen).



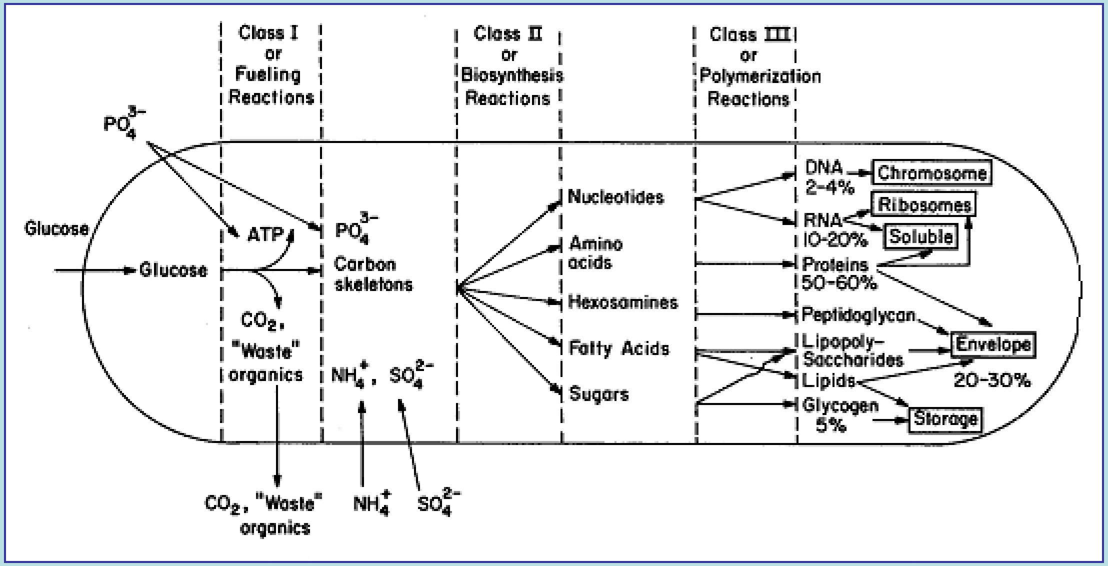

CATABOLISMO/ANABOLISMO

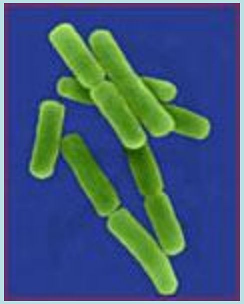




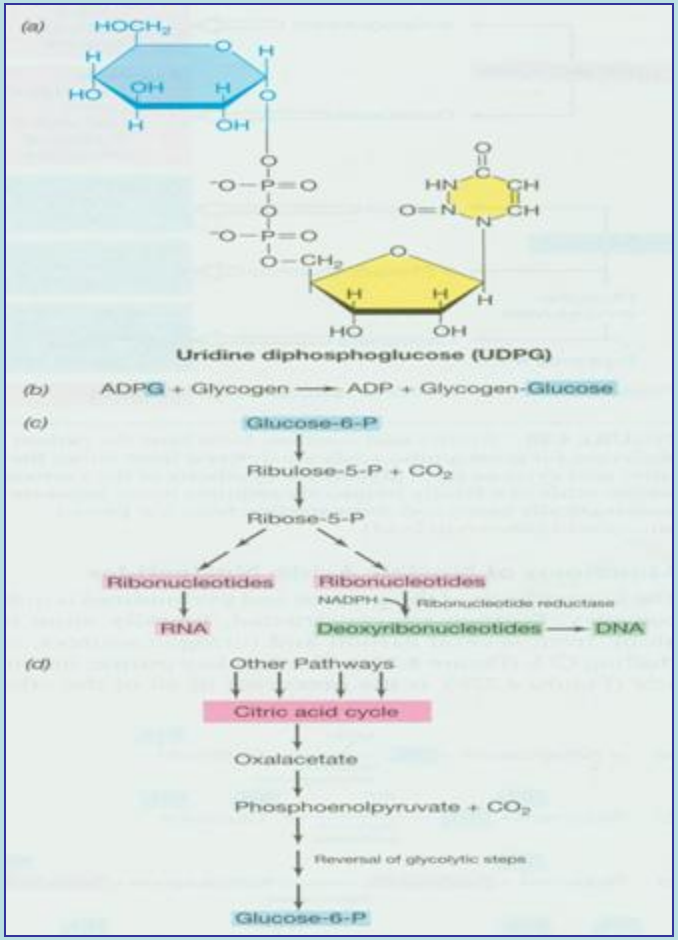
CATABOLISMO/ANABOLISMO

Rappresentazione schematica delle reazioni all'interno di una cellula batterica



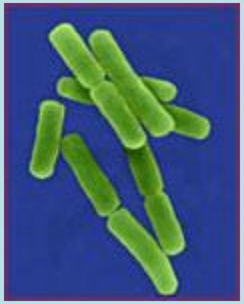


BIOSINTESI

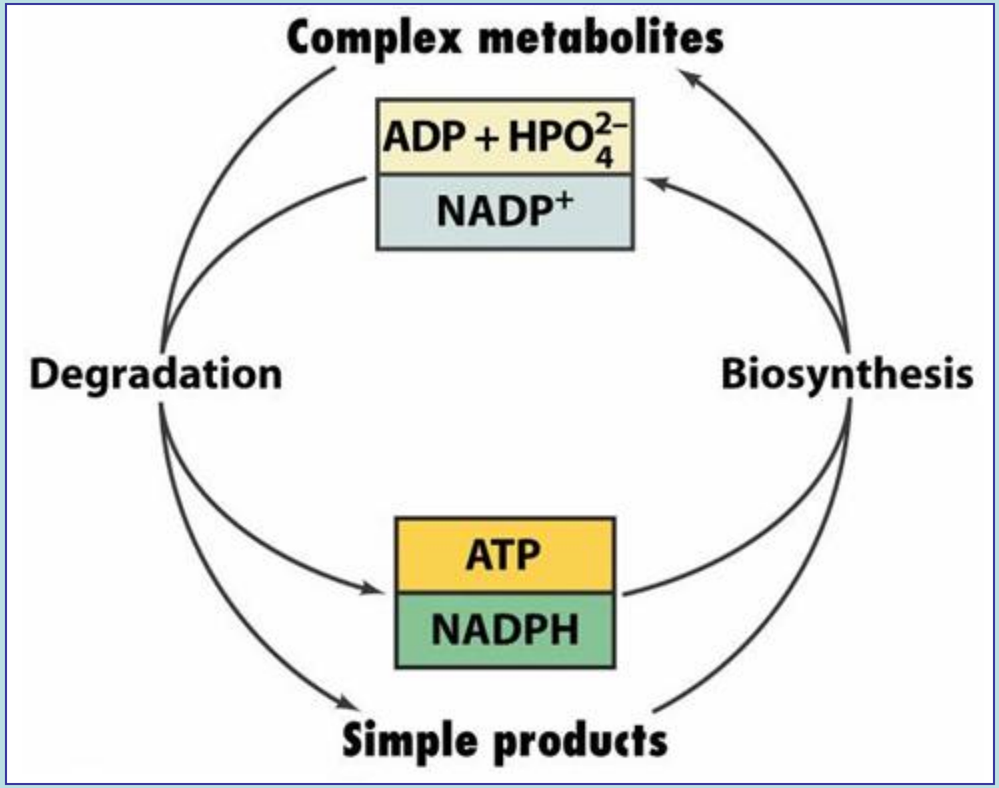


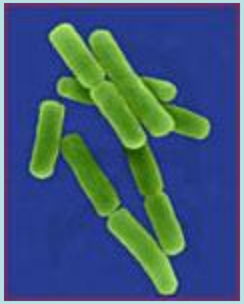
Biosintesi degli zuccheri

Nutrizione e metabolismo



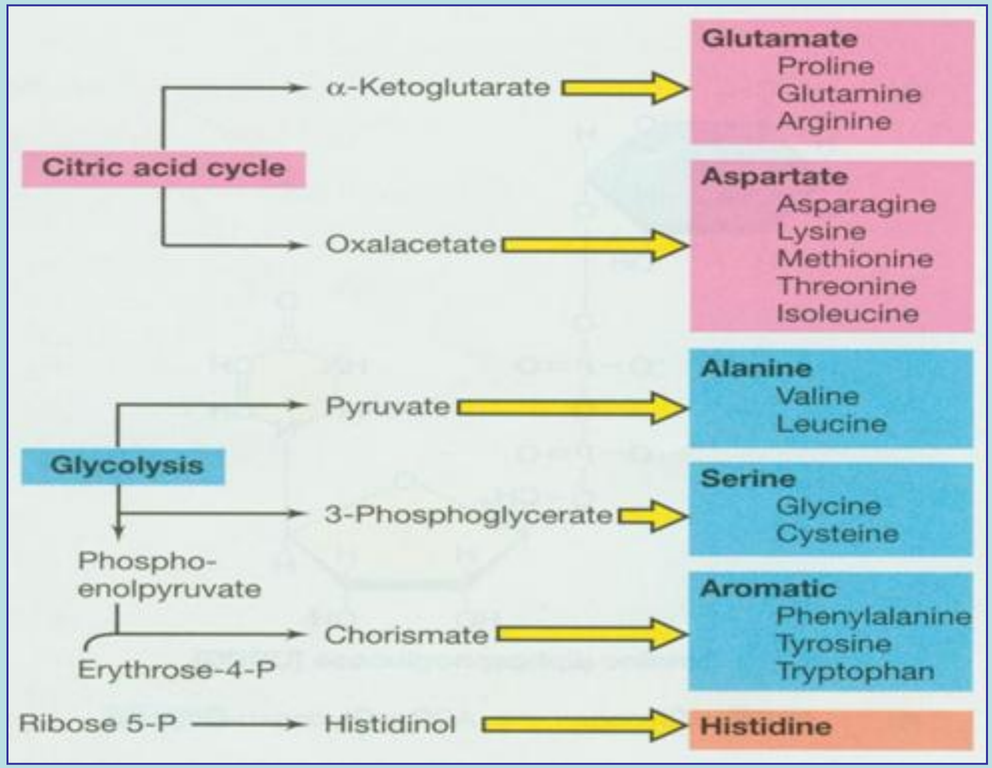

BIOSINTESI

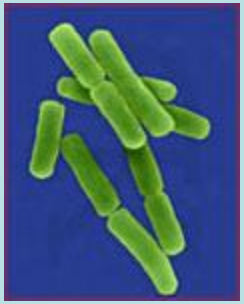

Complex metabolites
ADP + HPO$_4^{2-}$
NADP$^+$
Degradation
Biosynthesis
ATP
NADPH
Simple products



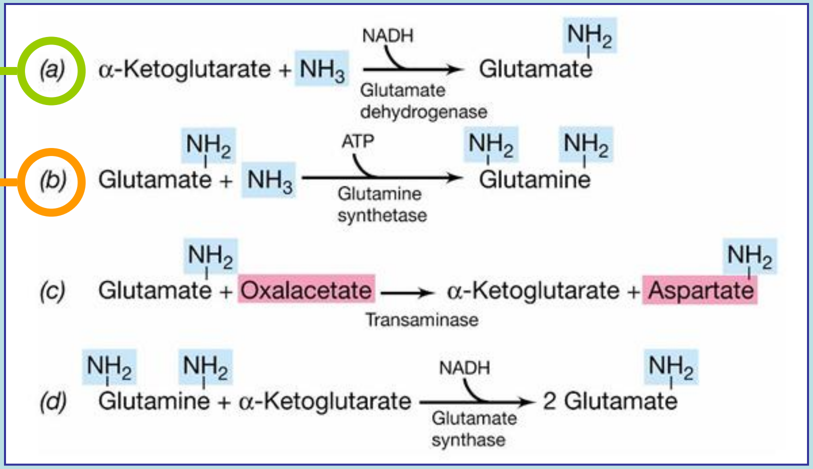

BIOSINTESI

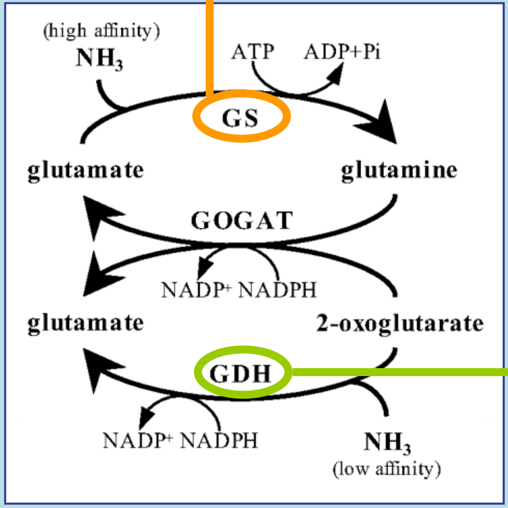
Origine biosintetica degli aminoacidi





BIOSINTESI

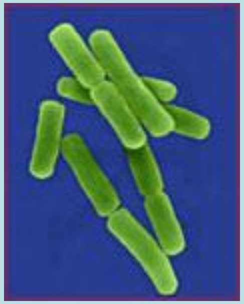




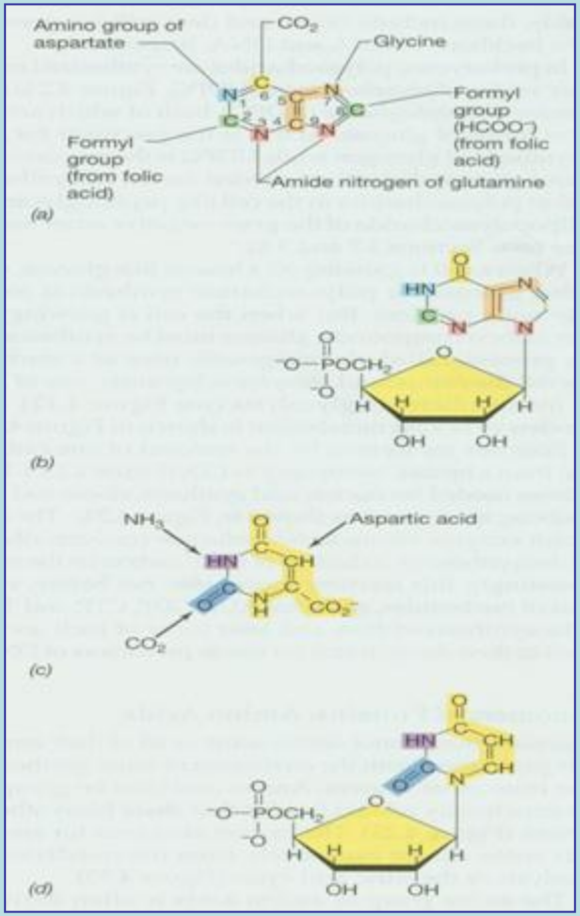
GS = glutamine synthase
GOGAT = glutamate synthase
GDH = glutamate deydrogenase

Incorporazione dell'ammonio nei batteri

Nutrizione e metabolismo

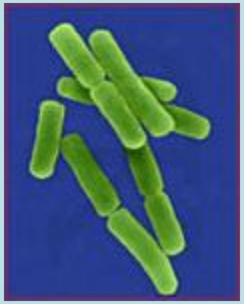



Biosintesi delle purine e delle pirimidine

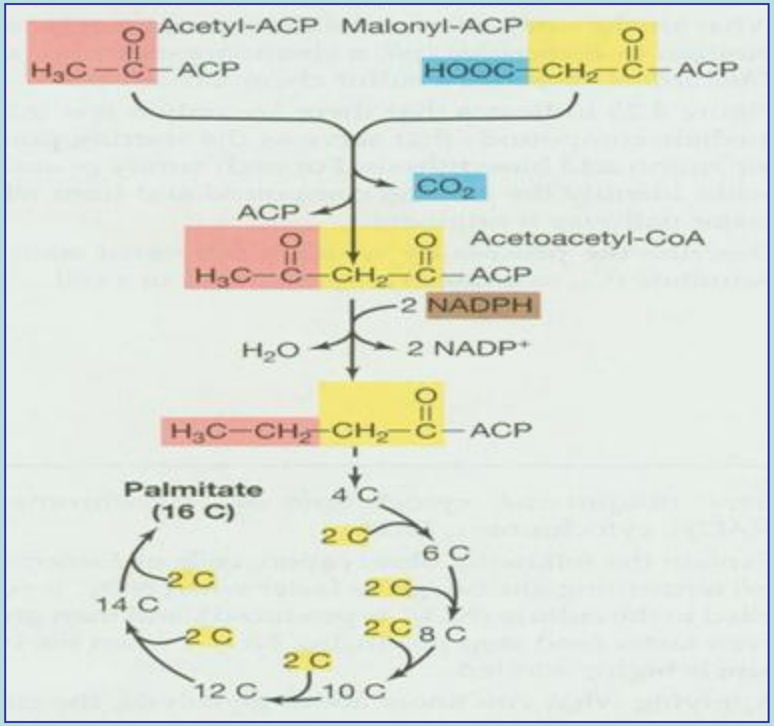


BIOSINTESI

Nutrizione e metabolismo



Biosintesi degli acidi grassi



BIOSINTESI

Nutrizione e metabolismo