Biochemistry For Pharmacy College Students

Metabolism

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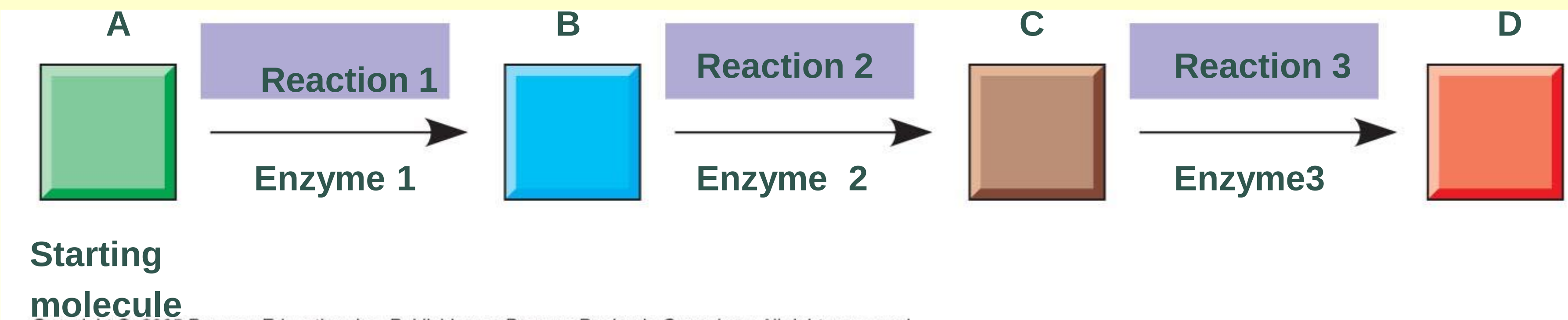
I. Introduction to Metabolism

- In a pathway, the product of one reaction serves as the substrate of the subsequent reaction. Different pathways can also intersect, forming an integrated and purposeful network of chemical reactions. These are collectively called Metabolism.



Introduction to Metabolism

- Metabolism: is the sum of all the chemical changes
- occurring in a cell, a tissue, or the body.

Most pathways can be classified as either anabolic (synthetic) or catabolic (degradative).

Anabolic pathways form complex end products from simple precursors, for example, the synthesis of the polysaccharide, glycogen, from glucose, Proteins from amino acids and Lipids from fatty acids and glycerol.

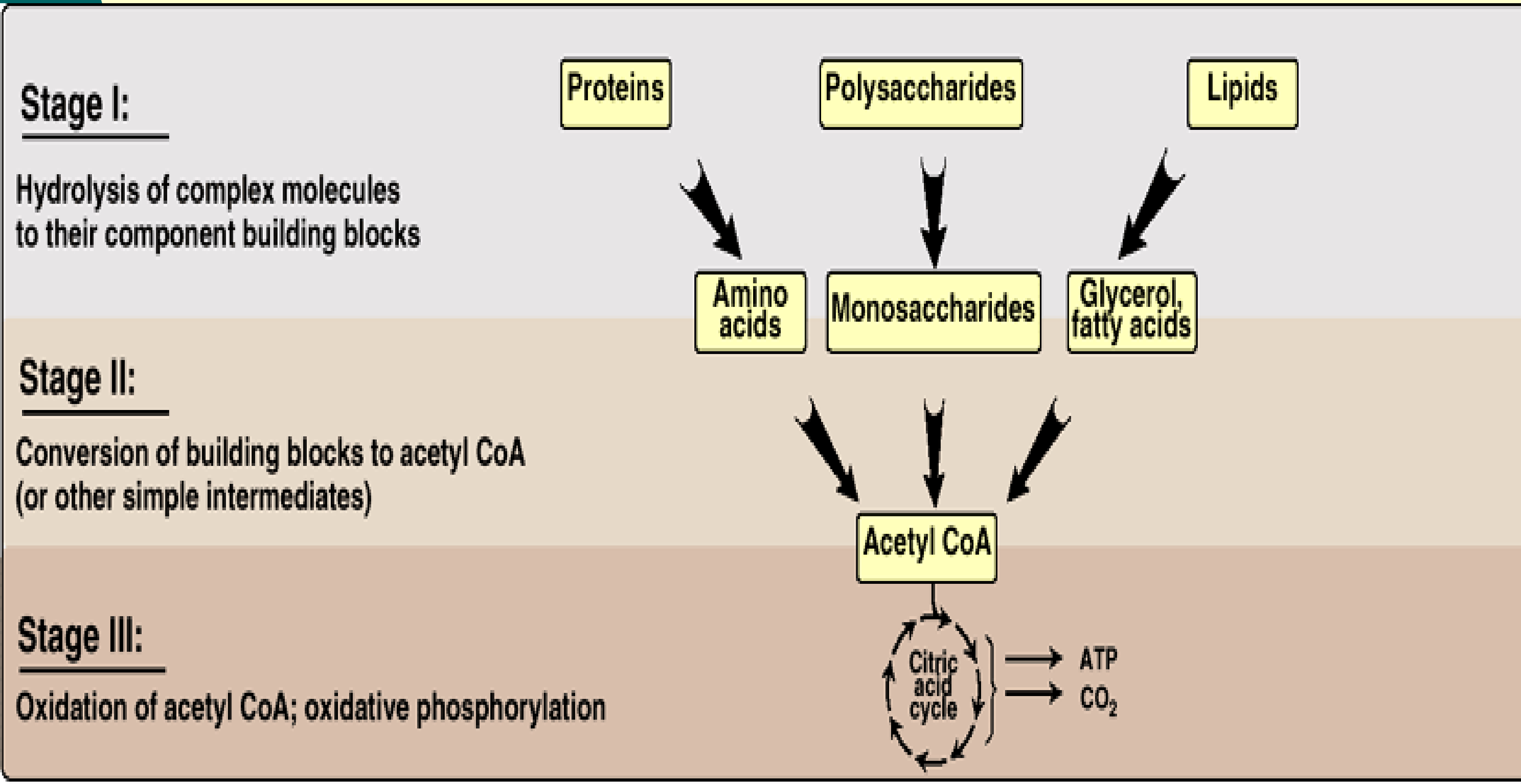
Catabolic reactions break down complex molecules, such as proteins, polysaccharides, and lipids, to a few simple molecules, for example, CO_2, NH_3 (ammonia), and water. supply chemical energy in the form of ATP from the degradation of energy-rich fuel molecules.

Catabolic Pathways :

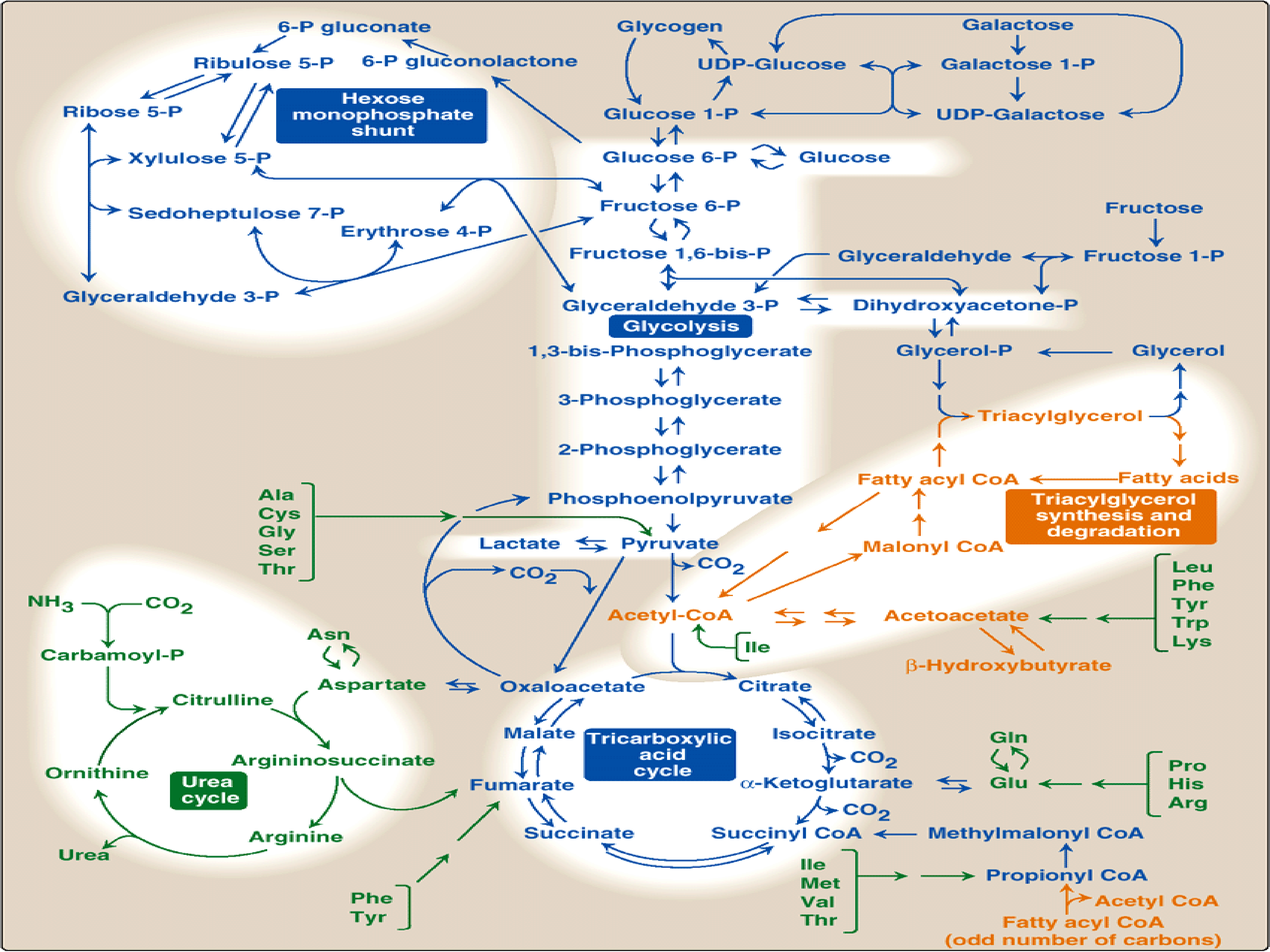
- Catabolism also allows molecules in the diet (or nutrient molecules stored in cells) to be converted into building blocks needed for the synthesis of complex molecules.

- Energy generation by degradation of complex molecules occurs in three stages.

Catabolic Pathways :



Note: Pathways that regenerate a component are called cycles



6-P gluconate
Ribulose 5-P
6-P gluconolactone
Ribose 5-P
Hexose monophosphate shunt
Xylulose 5-P
Sedoheptulose 7-P
Erythrose 4-P
Glyceraldehyde 3-P
Glycogen
UDP-Glucose
Galactose
Galactose 1-P
Glucose 1-P
UDP-Galactose
Glucose 6-P
Glucose
Fructose 6-P
Fructose 1,6-bis-P
Fructose
Glyceraldehyde
Fructose 1-P
Glyceraldehyde 3-P
Dihydroxyacetone-P
Glycolysis
1,3-bis-Phosphoglycerate
Glycerol-P
Glycerol
3-Phosphoglycerate
Triacylglycerol
2-Phosphoglycerate
Fatty acyl CoA
Fatty acids
Triacylglycerol synthesis and degradation
Ala
Cys
Gly
Ser
Thr
Phosphoenolpyruvate
Lactate
Pyruvate
Malonyl CoA
CO_2
CO_2
Leu
Phe
Tyr
Trp
Lys
NH_3
CO_2
Acetyl-CoA
Acetoacetate
Carbamoyl-P
Asn
Ile
β-Hydroxybutyrate
Aspartate
Oxaloacetate
Citrate
Citrulline
Malate
Tricarboxylic acid cycle
Isocitrate
Gln
Argininosuccinate
CO_2
Pro
Ornithine
Urea cycle
Fumarate
α-Ketoglutarate
Glu
His
Arg
CO_2
Arginine
Succinate
Succinyl CoA
Methylmalonyl CoA
Urea
Ile
Met
Val
Thr
Propionyl CoA
Phe
Tyr
Acetyl CoA
Fatty acyl CoA (odd number of carbons)

Bioenergetics

Bioenergetics is the subject of a field of biochemistry that concerns energy flow through living systems. Includes the study of thousands of different cellular processes such as cellular respiration and many other metabolic processes that can lead to production and utilization of energy in forms such as ATP molecules, involved in making and breaking of chemical bonds in the molecules found in biological organisms.

Living organisms obtain energy from organic and inorganic materials, the amount of energy obtained by the organism from food is less than the amount present in the food due to its loss by Digestion, Metabolism and thermogensis (Processes of heat production).

Biological Oxidation

Biological Oxidation involves transfer of electrons.

Oxidation is the loss of electrons by a molecule, atom, or ion.

Reduction is the gain of electrons by a molecule, atom, or ion.

Redox reactions, or oxidation-reduction reactions, have a number of similarities to acid–base reactions. Like acid–base reactions, redox reactions are a matched set, that is, there cannot be an oxidation reaction without a reduction reaction happening simultaneously.

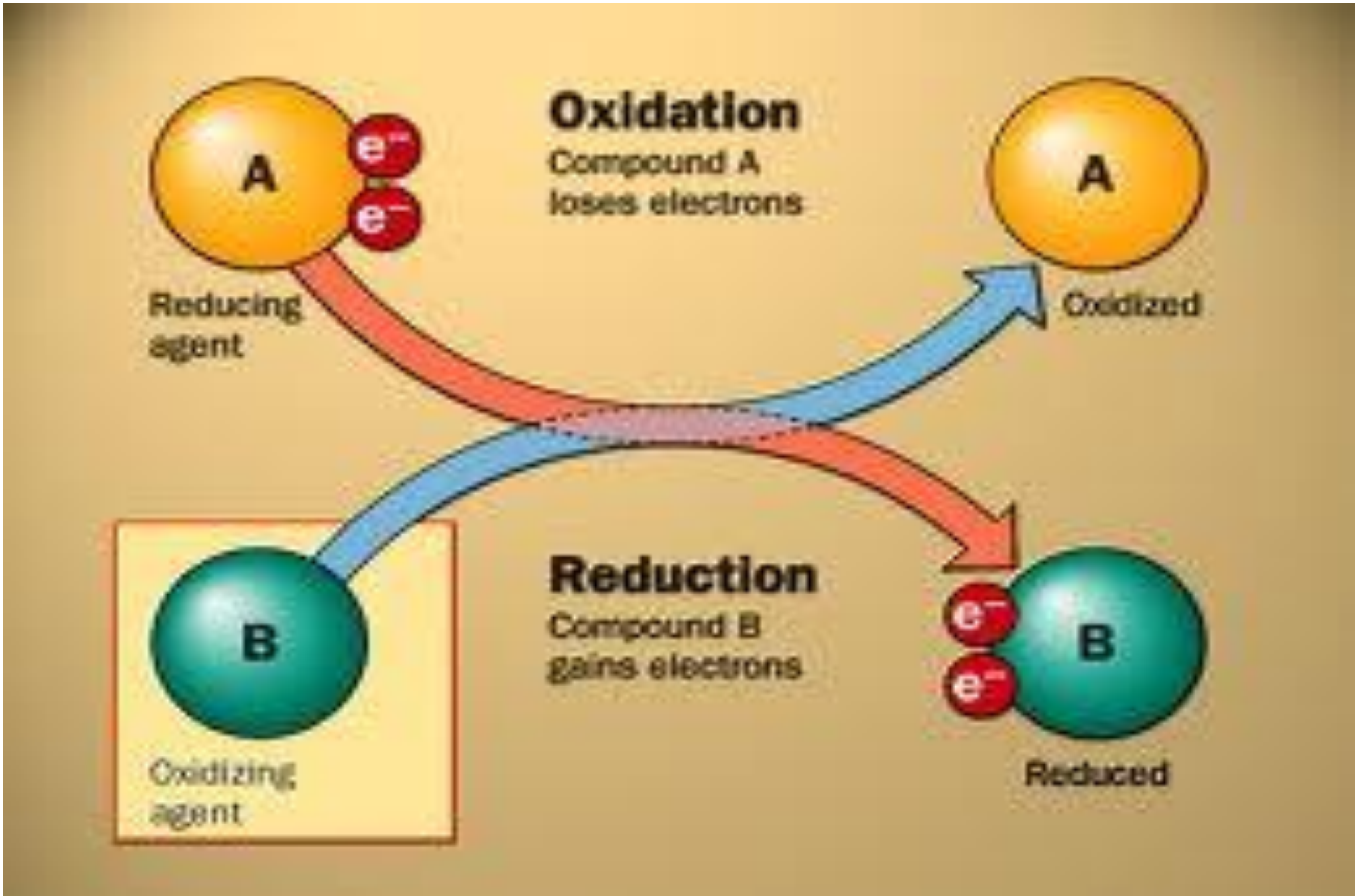
Types of reactions: **Aerobic** (bind with O_2) & **Anaerobic**.

Exergonic reaction is a spontaneous reaction that releases energy (liberating energy). The reactants are usually complex molecules that are broken into simpler products. The entire reaction is usually catabolic. The release of energy, also called free energy is negative and equal to - ΔG because energy is lost from the bonds formed by the products.

Endergonic reaction is an anabolic reaction that consumes energy (requiring energy). and is nonspontaneous

It has a positive ΔG because energy is required to break bonds.

Oxidation-Reduction reactions



B. ΔG of the forward and back reactions

C. ΔG depends on the concentration of reactants and products

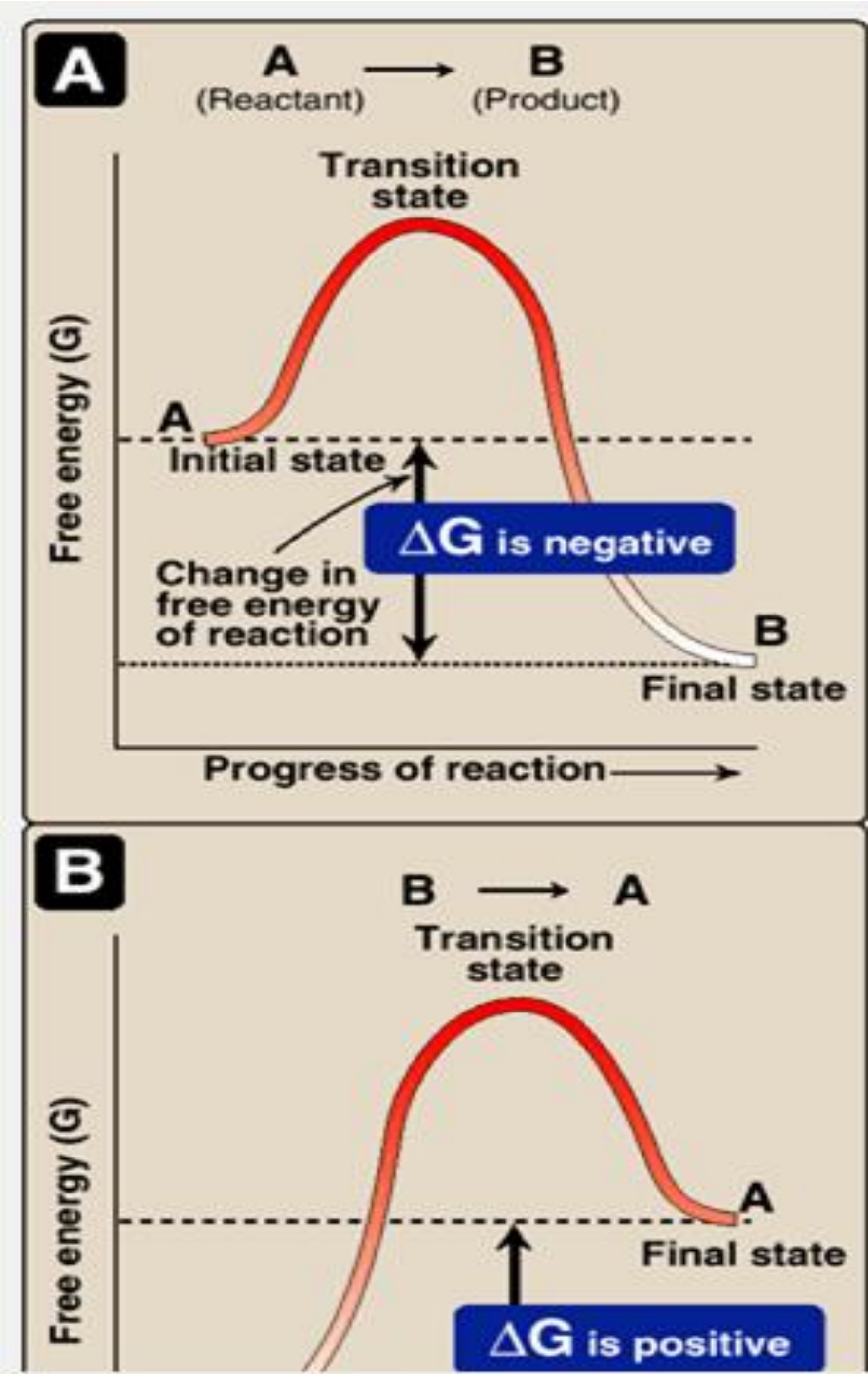
D. Standard free energy change, ΔG°

$$\Delta G = \Delta G^0 + RT \ln \frac{[B]}{[A]}$$

1-ΔG° is predictive only under standard conditions:

2-Relationship between ΔG° and K_{eq}

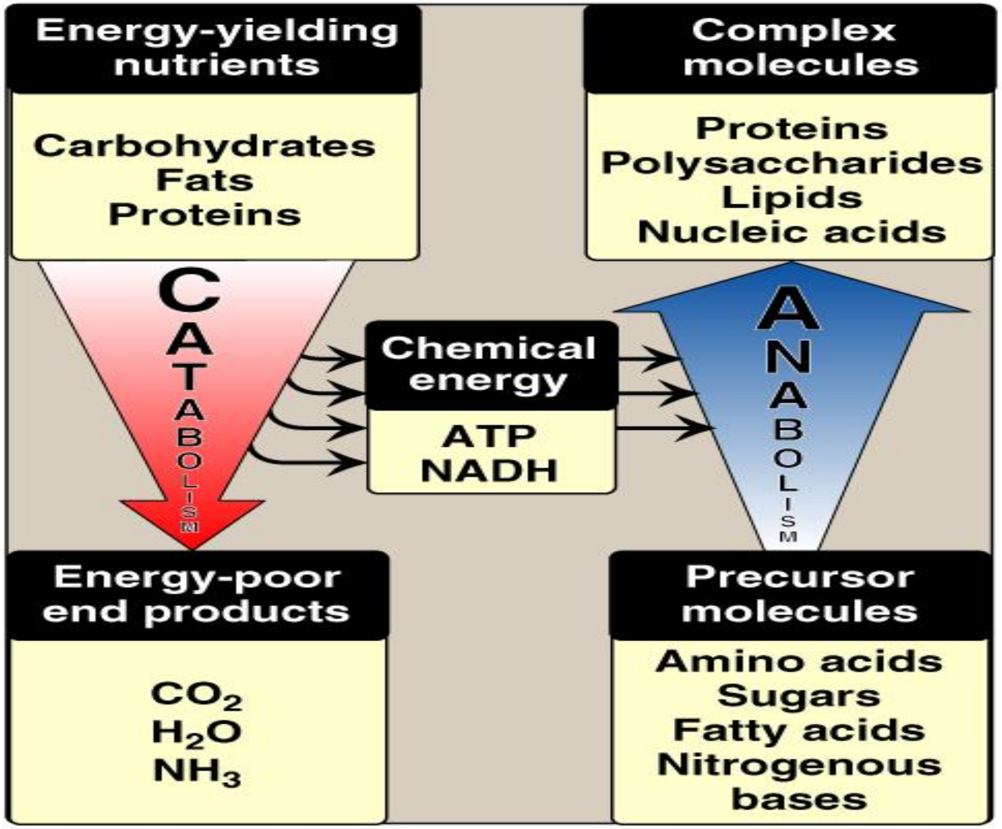
$$\Delta G = 0 = \Delta G^0 + RT \ln \frac{[B]_{eq}}{[A]_{eq}}$$



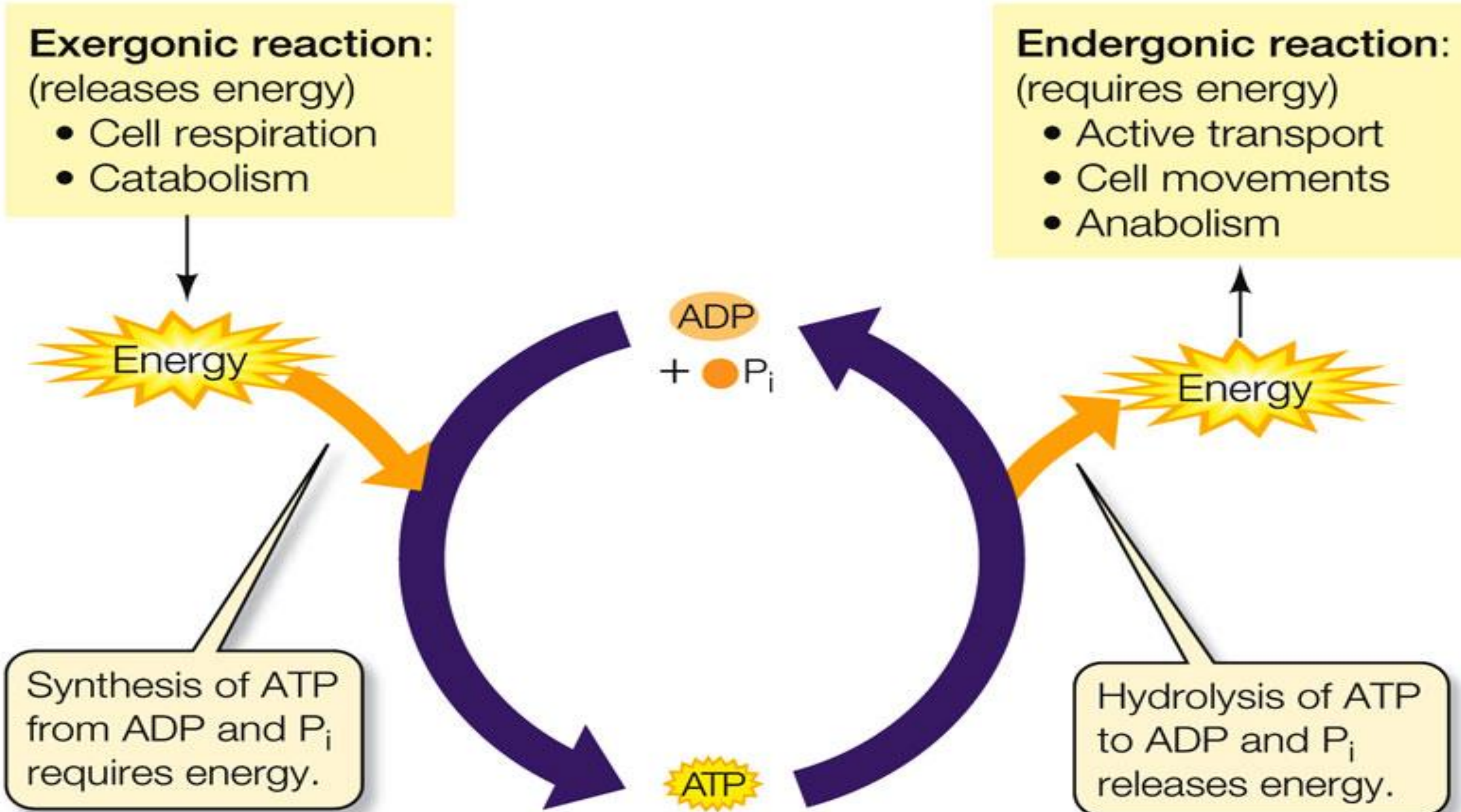
Catabolism Vs Anabolism

Note that catabolism is a convergent process-that is, a wide variety of molecules are transformed into a few common end products. .

By contrast, anabolism is a divergent process in which a few biosynthetic precursors form a wide variety of polymeric or complex products.



Biological Oxidation and The Regeneration of ATP



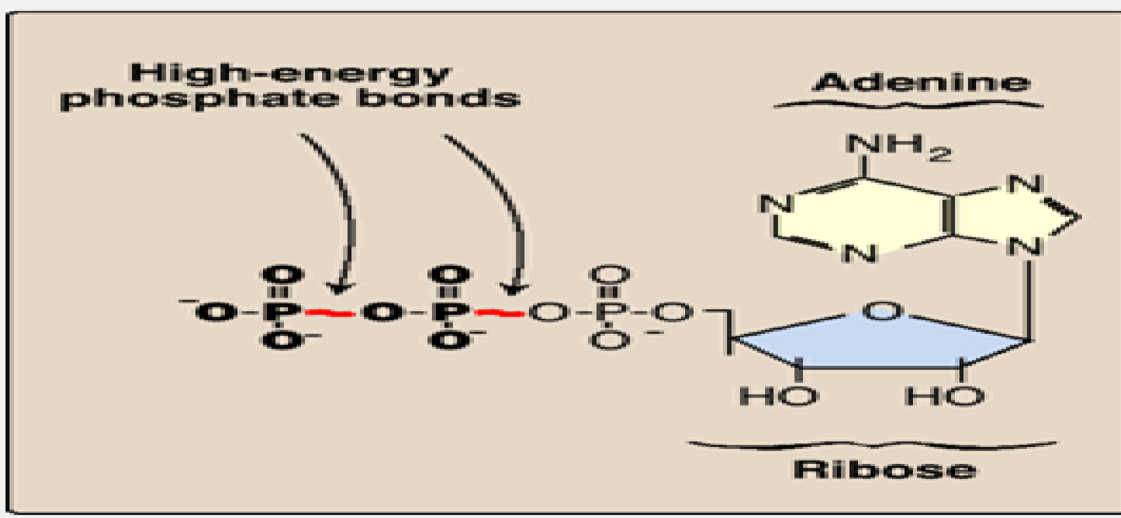
LIFE 8e, Figure 6.6

ATP as An Energy Carrier

Reactions are coupled through common intermediates

$A + B \rightarrow C + D$
$D + X \rightarrow Y + Z$

D is the common intermediate and can serve as a carrier of chemical energy between the two reactions. Many coupled reactions use ATP to generate a common intermediate. These reactions may involve ATP cleavage—that is, the transfer of a phosphate group from ATP to another molecule. Other reactions lead to ATP synthesis by transfer of phosphate from an energy-rich intermediate to adenosine diphosphate (ADP), forming ATP.



Biological Oxidation

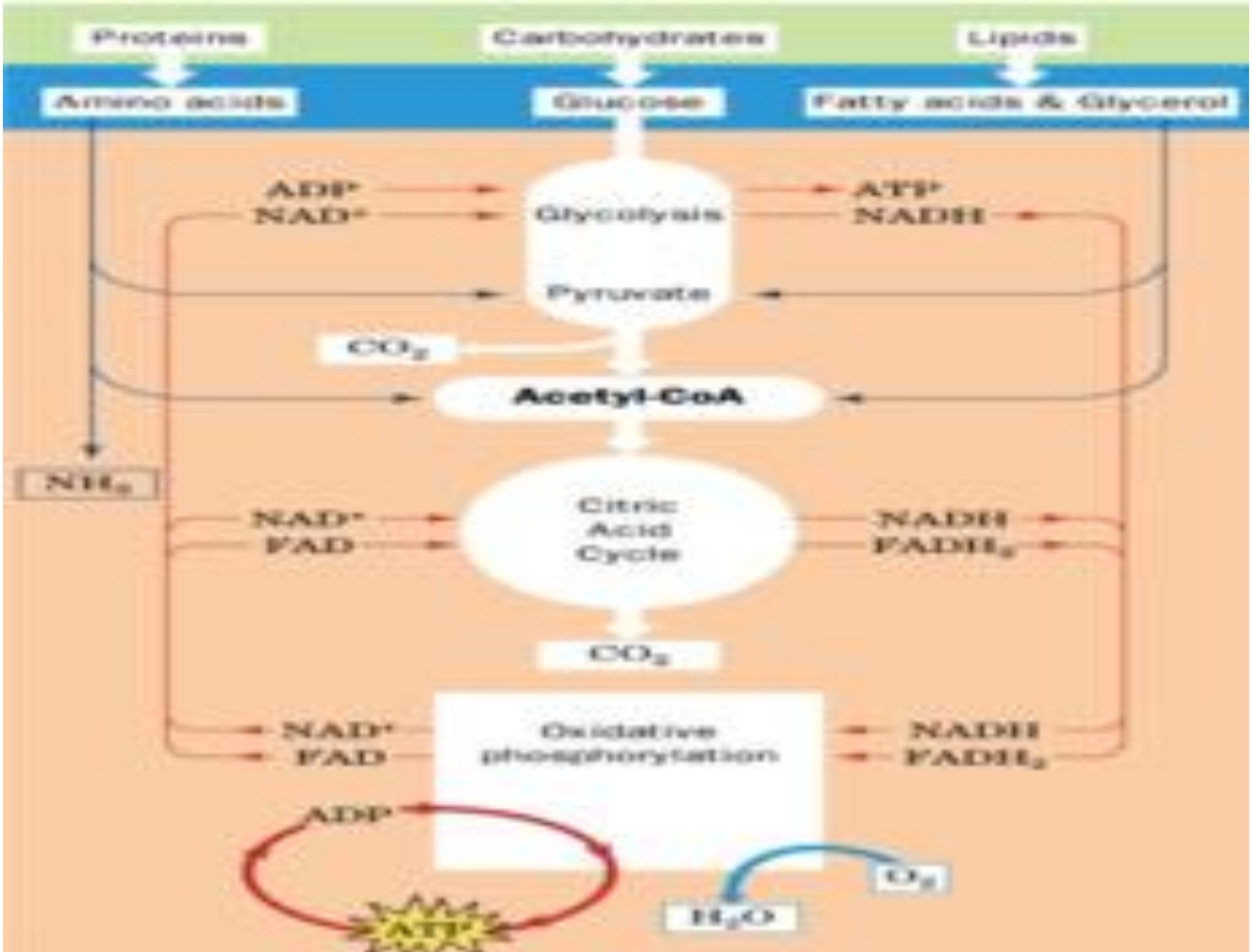
Major nutrients are:

- Carbohydrates (4 Kcal/ g) partially reduced break to Glucose.
- Protiens (4 Kcal/ g) partially reduced break to A.A.
- Fat (9 Kcal/ g) highly reduced break to Glycerol & F.A.

Human needs 30-40 Kcal/ Kg per one day.

When nutrient oxidized in the body, ATP synthesized and Heat is generated.

Living organisms produce ATP from energy sources via oxidative phosphorylation. The terminal P bonds of ATP are weak compared with the stronger bonds formed when ATP is broken down to AMP and P. This hydrolysis of ATP is used as a battery to store energy in cells.



Proteins
Carbohydrates
Lipids
Amino acids
Glucose
Fatty acids & Glycerol
ADP
NAD+
Glycolysis
ATP
NADH
Pyruvate
CO2
Acetyl-CoA
NH3
NAD+
FAD
Citric
Acid
Cycle
NADH
FADH2
CO2
NAD+
FAD
Oxidative
phosphorylation
NADH
FADH2
ADP
ATP
O2
H2O

Glycolysis

Is the metabolic pathway that converts glucose $C_6H_{12}O_6$, into pyruvate, $CH_3COCOO^- + H^+$.The free energy released in this process is used to form a high-energy compounds ATP (Adenosine Triphosphate) & NADH (reduced nicotinamide adenine dinucleotide).

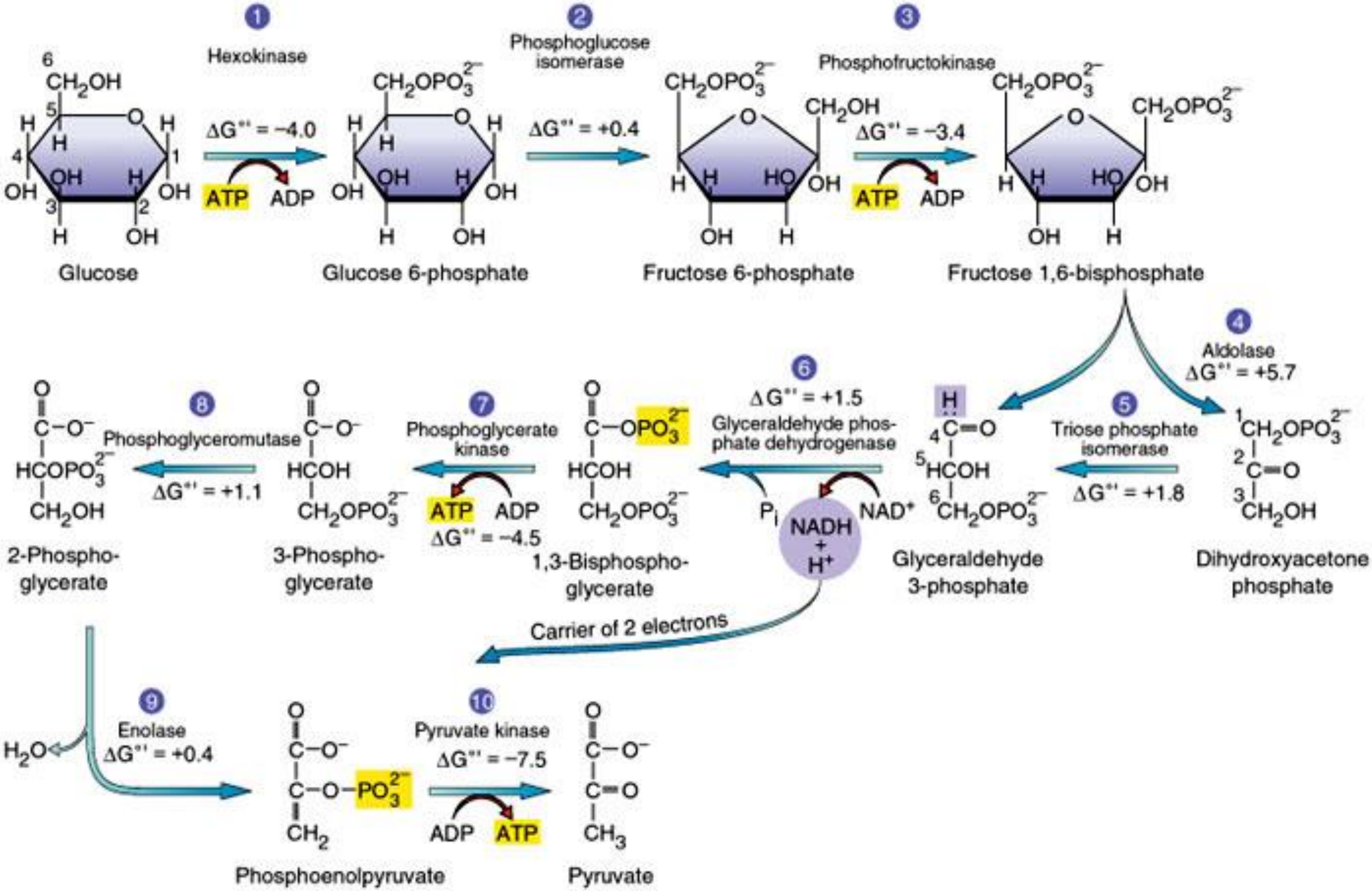
Glycolysis is of ten reactions involving ten intermediate compounds (one of the steps involves two intermediates).

most monosaccharides, such as fructose, glucose, and galactose, can be converted to one of these intermediates

It occurs, with variations, in nearly all organisms, both Aerobic and anaerobic. It occurs in the cytosol of the cell.

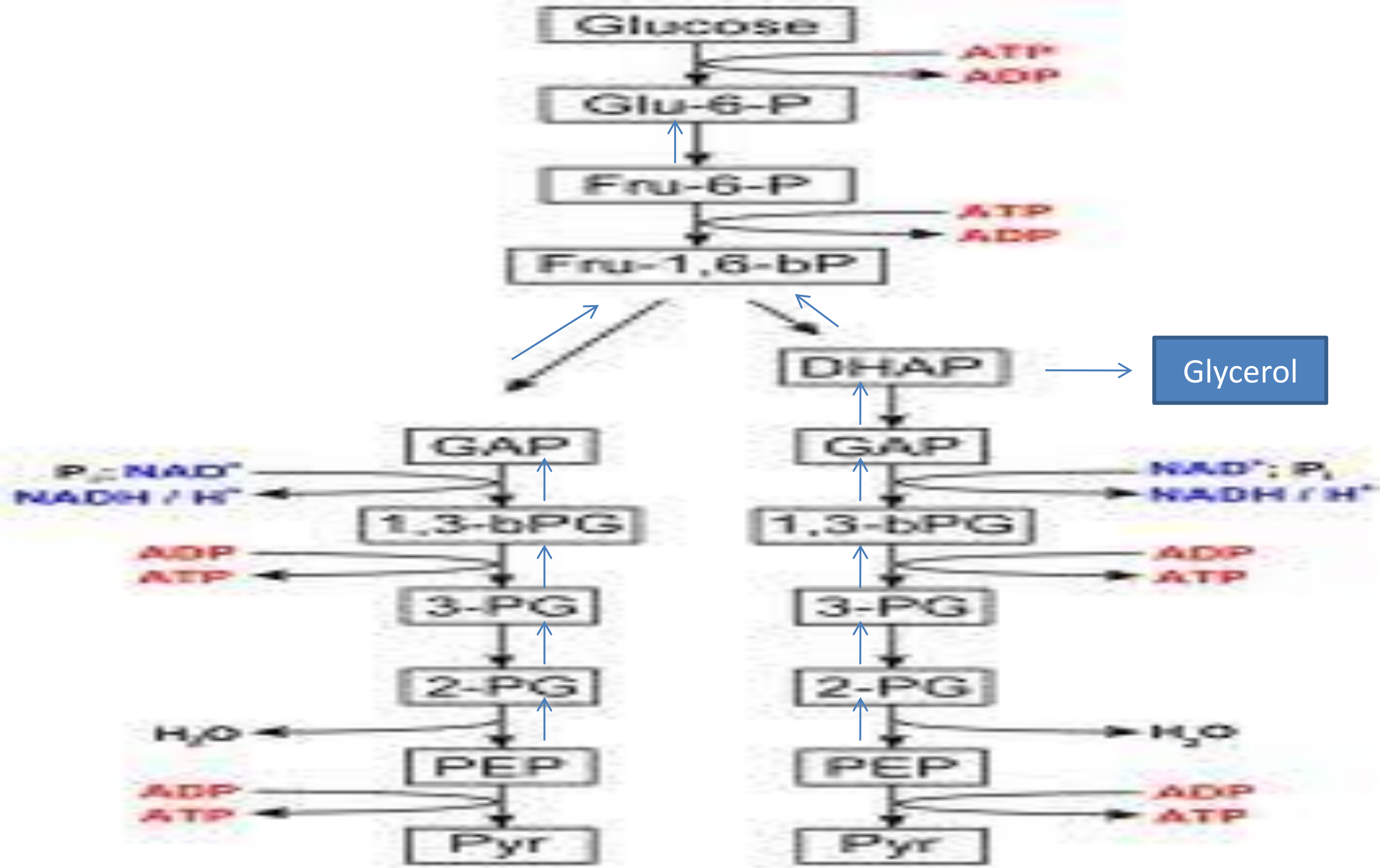
Since glucose leads to 2 triose sugars in the preparatory phase, This yields 2 NADH and 4 ATP molecules, leading to a net gain of 2 NADH and 2 ATP molecules from the glycolytic pathway per glucose

Glycolysis



1
Hexokinase
ΔG°' = −4.0
ATP
ADP
Glucose
Glucose 6-phosphate
2
Phosphoglucose isomerase
ΔG°' = +0.4
Fructose 6-phosphate
3
Phosphofructokinase
ΔG°' = −3.4
ATP
ADP
Fructose 1,6-bisphosphate
4
Aldolase
ΔG°' = +5.7
Dihydroxyacetone phosphate
5
Triose phosphate isomerase
ΔG°' = +1.8
Glyceraldehyde 3-phosphate
6
ΔG°' = +1.5
Glyceraldehyde phosphate dehydrogenase
P_i
NAD+
NADH + H+
1,3-Bisphosphoglycerate
7
Phosphoglycerate kinase
ATP
ADP
ΔG°' = −4.5
3-Phosphoglycerate
8
Phosphoglyceromutase
ΔG°' = +1.1
2-Phosphoglycerate
Carrier of 2 electrons
9
Enolase
ΔG°' = +0.4
H2O
Phosphoenolpyruvate
10
Pyruvate kinase
ΔG°' = −7.5
ADP
ATP
Pyruvate

Glycolysis



Glucose
ATP
ADP
Glu-6-P
Fru-6-P
ATP
ADP
Fru-1,6-bP
DHAP
Glycerol
GAP
GAP
P_i; NAD⁺
NADH / H⁺
NAD⁺; P_i
NADH / H⁺
1,3-bPG
1,3-bPG
ADP
ATP
ADP
ATP
3-PG
3-PG
2-PG
2-PG
H₂O
H₂O
PEP
PEP
ADP
ATP
ADP
ATP
Pyr
Pyr

Glycolysis Regulation

The flux through the glycolytic pathway is adjusted in response to conditions both inside and outside the cell.

The rate in liver is regulated to meet major cellular needs: (1) the production of ATP, (2) the provision of building blocks for biosynthetic reactions, and (3) to lower blood glucose, one of the major functions of the liver. When blood sugar falls, glycolysis is stopped in the liver to allow the reverse process, gluconeogenesis. In glycolysis, the reactions catalyzed by hexokinase, phosphofructokinase, and pyruvate kinase are effectively irreversible in most organisms. In metabolic pathways, such enzymes are potential sites of control, and all three enzymes serve this purpose in glycolysis.