Introduction to metabolism

objectives

By the end of this lecture the First Year students will be able to:

- Understand the concept of metabolic pathways
- Identify types and characteristics of metabolic pathways (anabolic and catabolic)
- Identify ATP as the energy source for cells

Metabolism

- All the chemical reactions taking place inside a cell are collectively known as **METABOLISM**
- Metabolism consists of:
  - Energy consuming (anabolic) pathways
  - Energy producing (catabolic) pathways

Pathway *vs* Chemical Reaction

Metabolic Pathway

- A multi-step sequence of chemical reactions
- Product of first reaction becomes a substrate for second reaction
- Integrated pathways: Metabolism

Glycolysis is a metabolic pathway

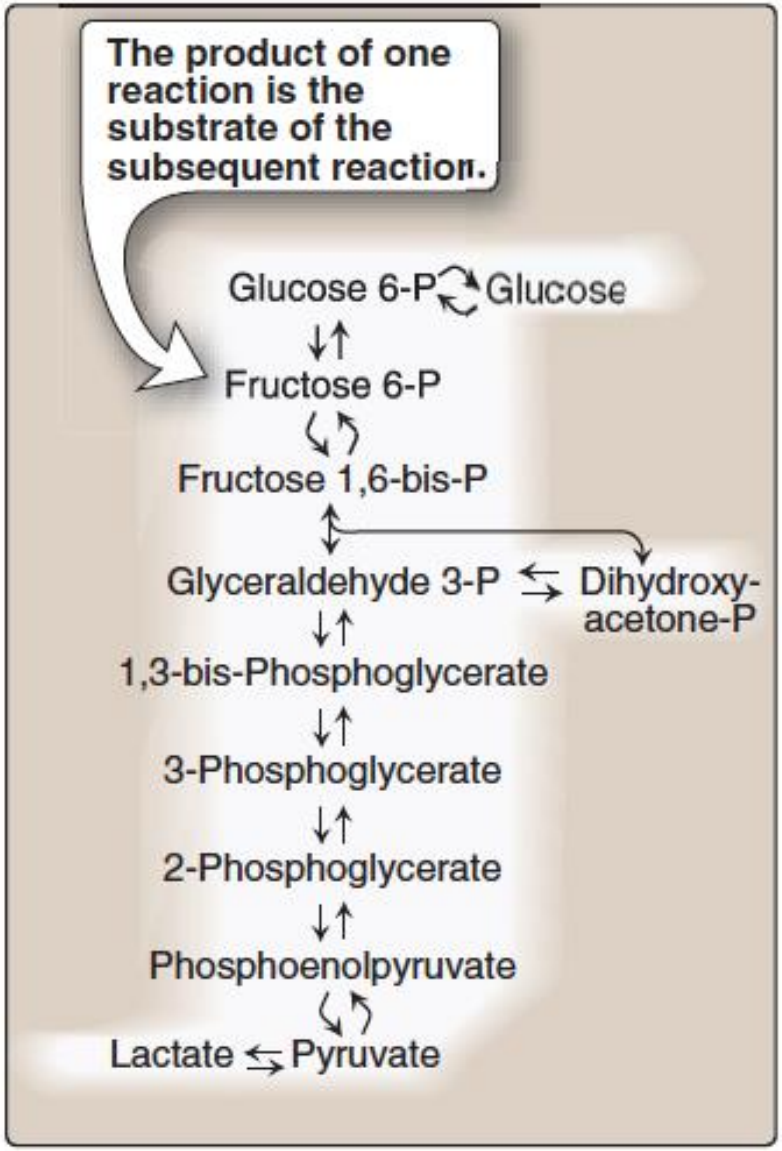
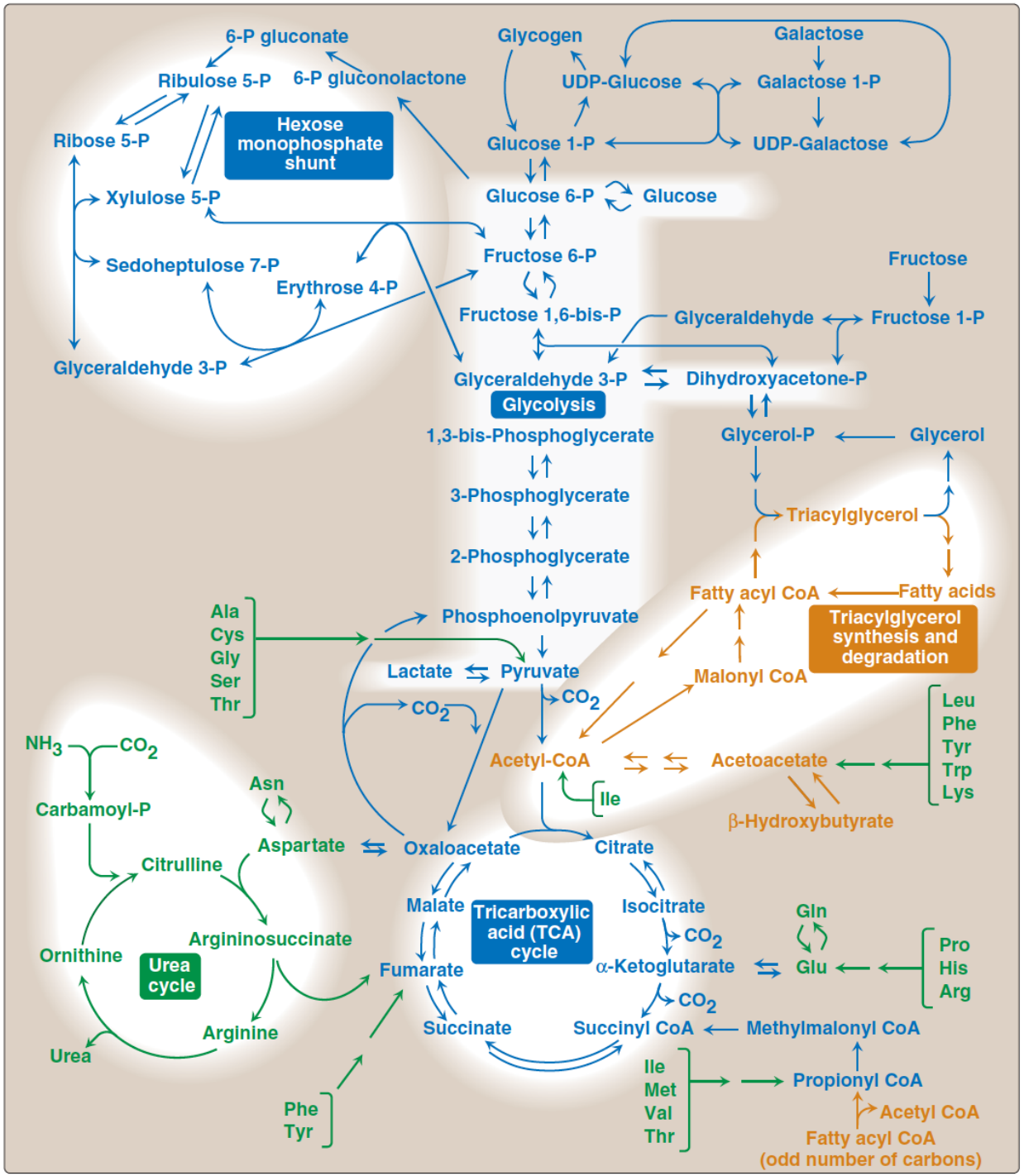


Figure 8.1
Glycolysis, an example of a metabolic pathway.

Metabolic Map

- Different pathways can intersect to form an integrated and purposeful network of chemical reactions called ”The Metabolic Map”


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
Galactose
UDP-Glucose
Galactose 1-P
Glucose 1-P
UDP-Galactose
Glucose 6-P
Glucose
Fructose 6-P
Fructose
Fructose 1,6-bis-P
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
CO2
Leu
Phe
Tyr
Trp
Lys
NH3
CO2
Acetyl-CoA
Acetoacetate
Ile
β-Hydroxybutyrate
Carbamoyl-P
Asn
Aspartate
Oxaloacetate
Citrate
Citrulline
Malate
Tricarboxylic acid (TCA) cycle
Isocitrate
Gln
Argininosuccinate
Ornithine
Urea cycle
Fumarate
α-Ketoglutarate
Glu
Pro
His
Arg
Arginine
Urea
Succinate
Succinyl CoA
Methylmalonyl CoA
Phe
Tyr
Ile
Met
Val
Thr
Propionyl CoA
Acetyl CoA
Fatty acyl CoA
(odd number of carbons)

Classification

- Most pathways can be classified as:
  - Catabolic
  - Anabolic
- Pathways that regenerate a component are called cycles

Catabolic Pathways

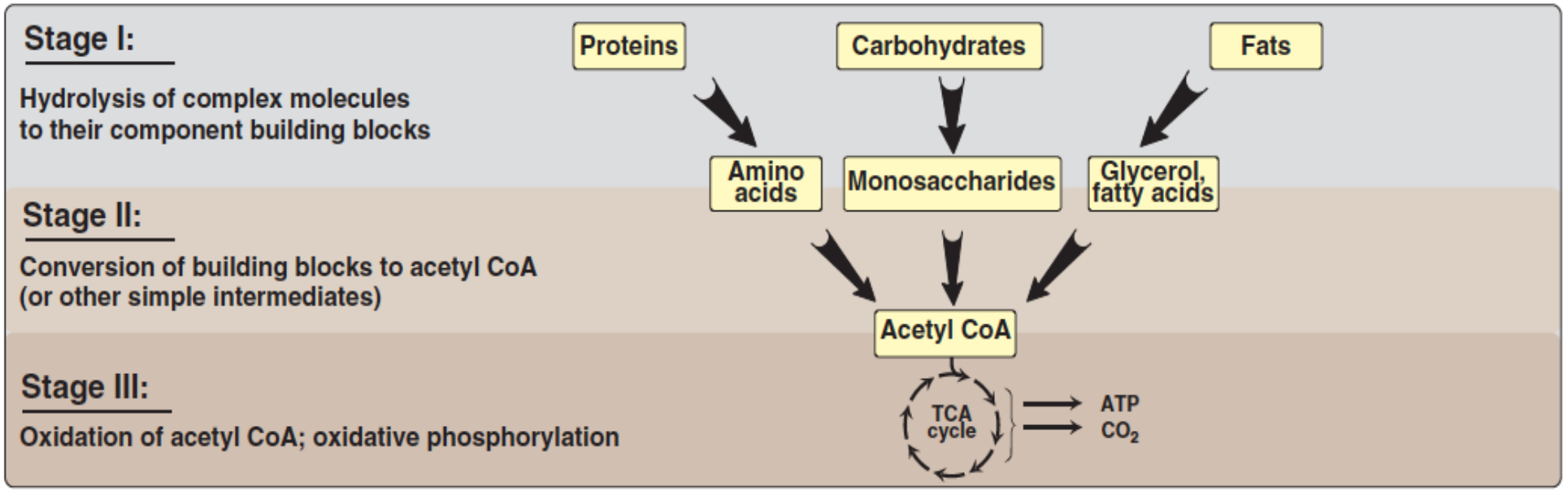


Figure 8.3
Three stages of catabolism.

Anabolic Pathways

- Formation of precursor molecules into complex molecules
- Endergonic reactions (require ATP)
- A divergent process (few precursors form more complex products)

Catabolism *Vs* Anabolism

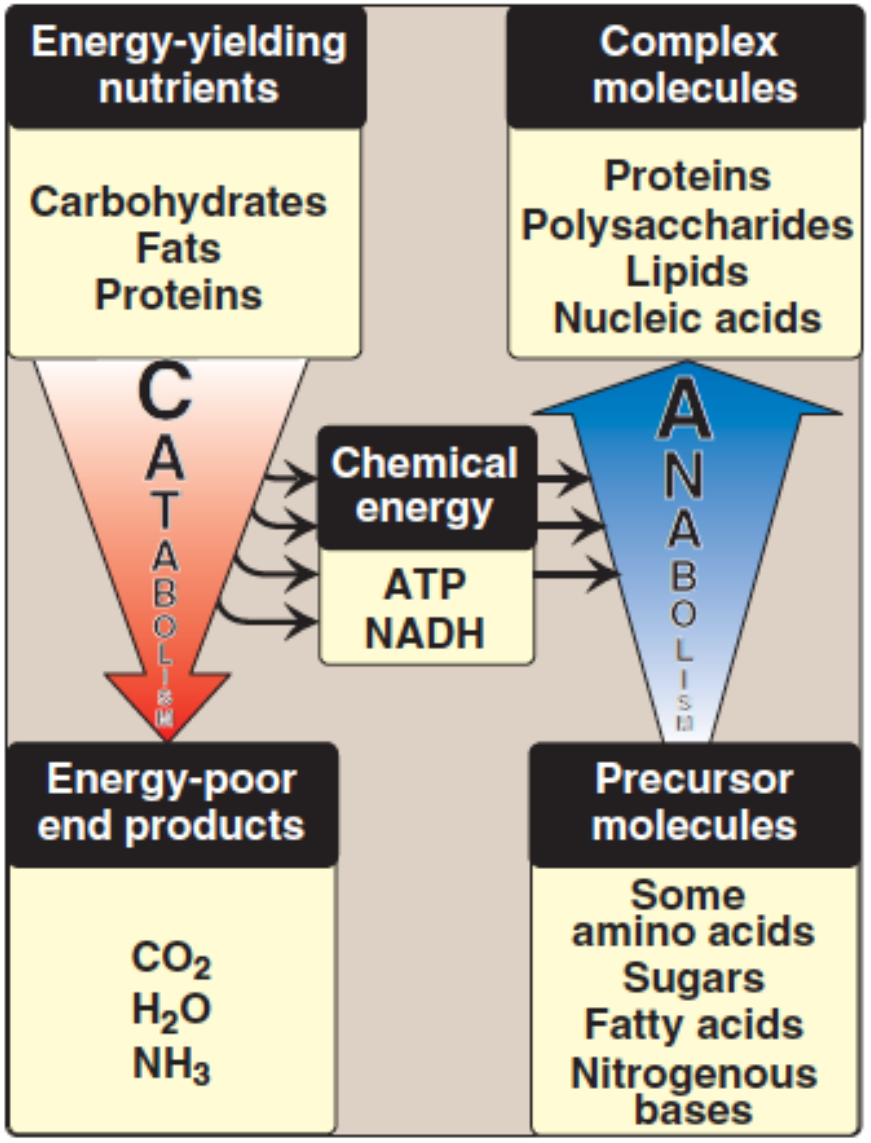


Figure 8.4
Comparison of catabolic and anabolic pathways.

Comparison of catabolic and anabolic pathways

Catabolic

- Complex to simple molecules
- Exergonic
- Involves oxidation
- Require NAD^+
- Convergent process

Anabolic

- Simple to complex molecules
- Endergonic
- Involves reduction
- Require NADPH
- Divergent process

Amphibolic Pathways

- Amphi means dual
- Amphibolic: Both catabolic and anabolic

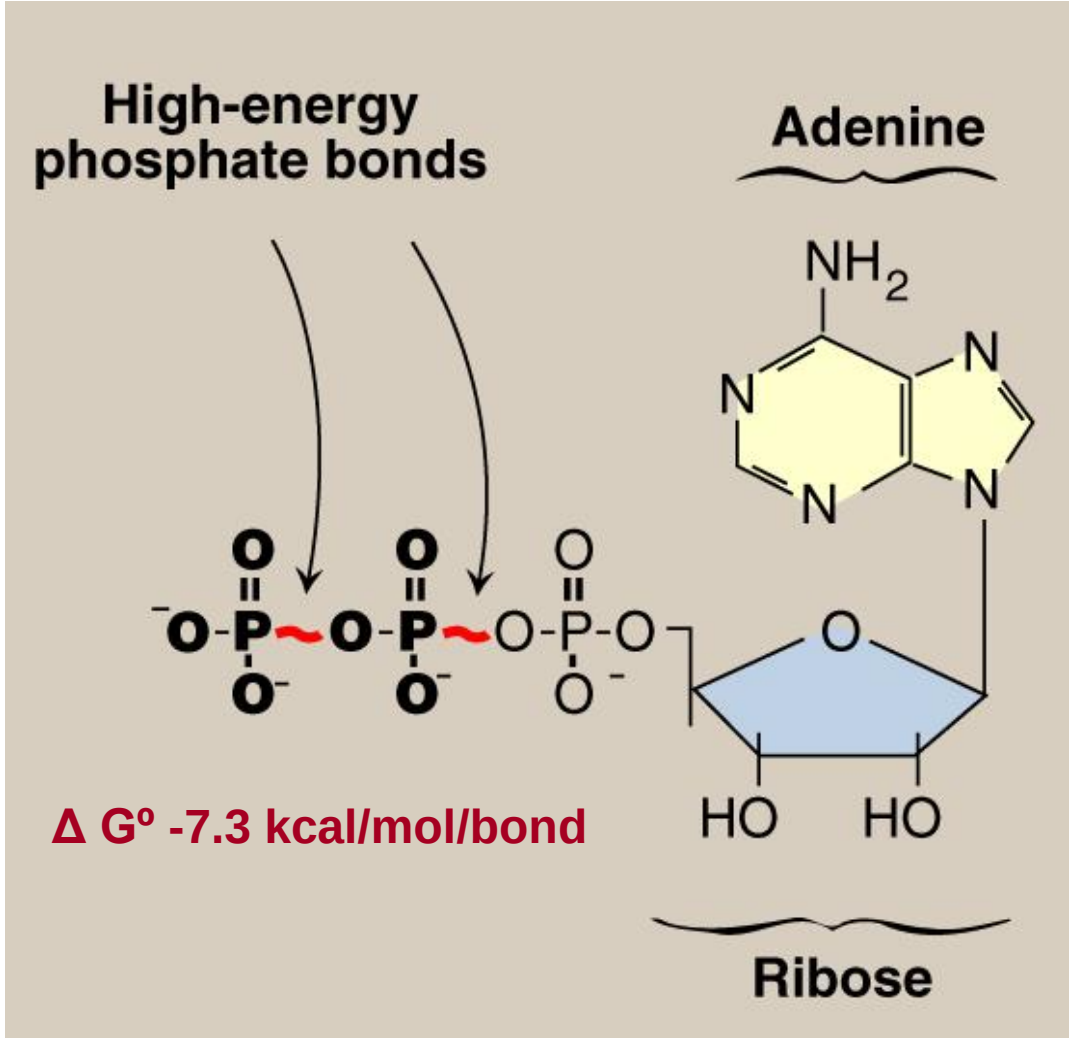
Example:

- Krebs cycle is mainly a catabolic cycle but with some anabolic features
- Krebs cycle is used for the synthesis of glucose from amino acids
- It is amphibolic

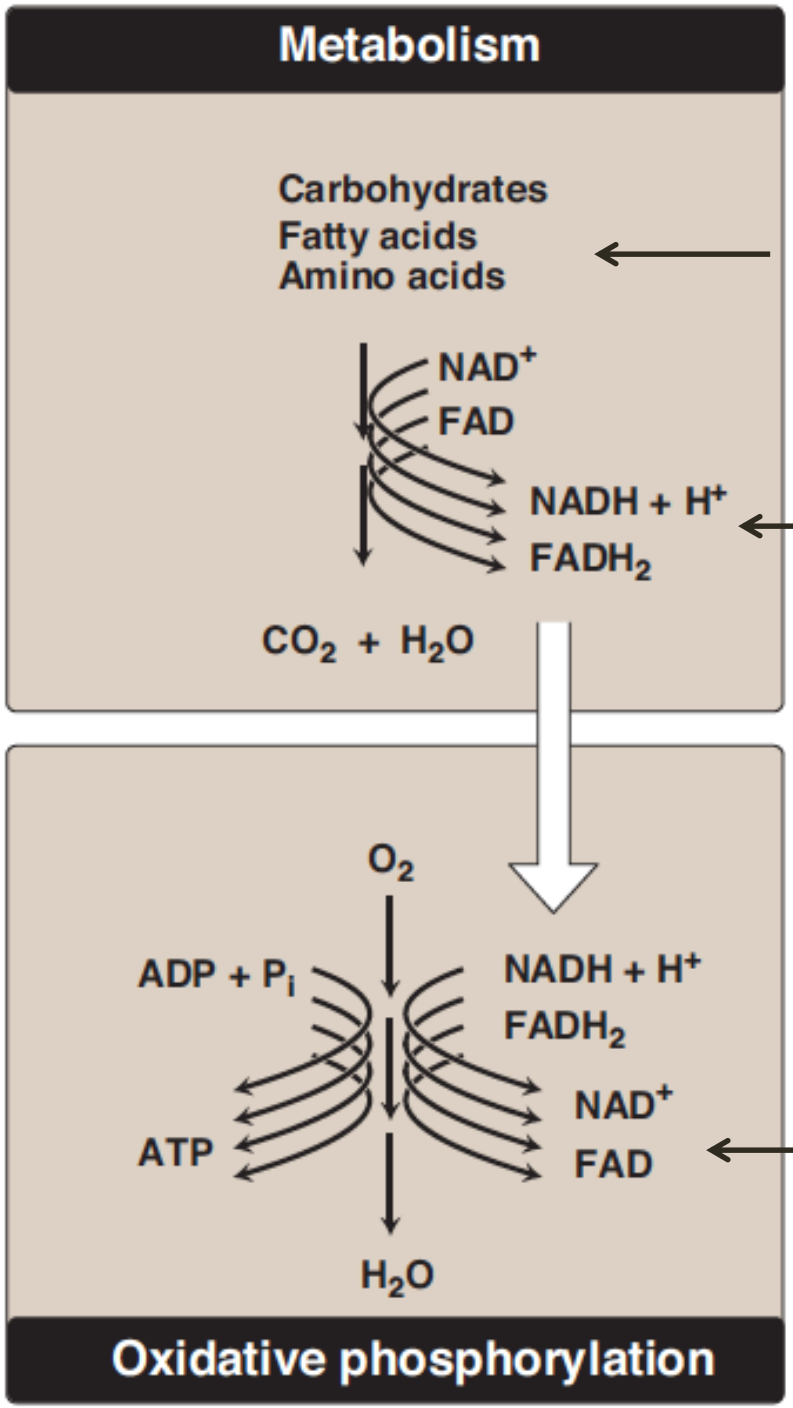
Energy Currency: ATP

- The free energy liberated by the hydrolysis of ATP is used to drive the endergonic reactions
- ATP is formed from ADP and P_i when fuel molecules are oxidized
- This ATP-ADP cycle is the fundamental mode of energy exchange in biological systems

Adenosine Triphosphate (ATP)



Oxidation-Reduction in Metabolism



Energy rich compounds

Transfer of electrons

Energy-rich Reduced coenzymes

Oxidized coenzymes

Oxidation / Reduction

Oxidation:

Loss of hydrogen

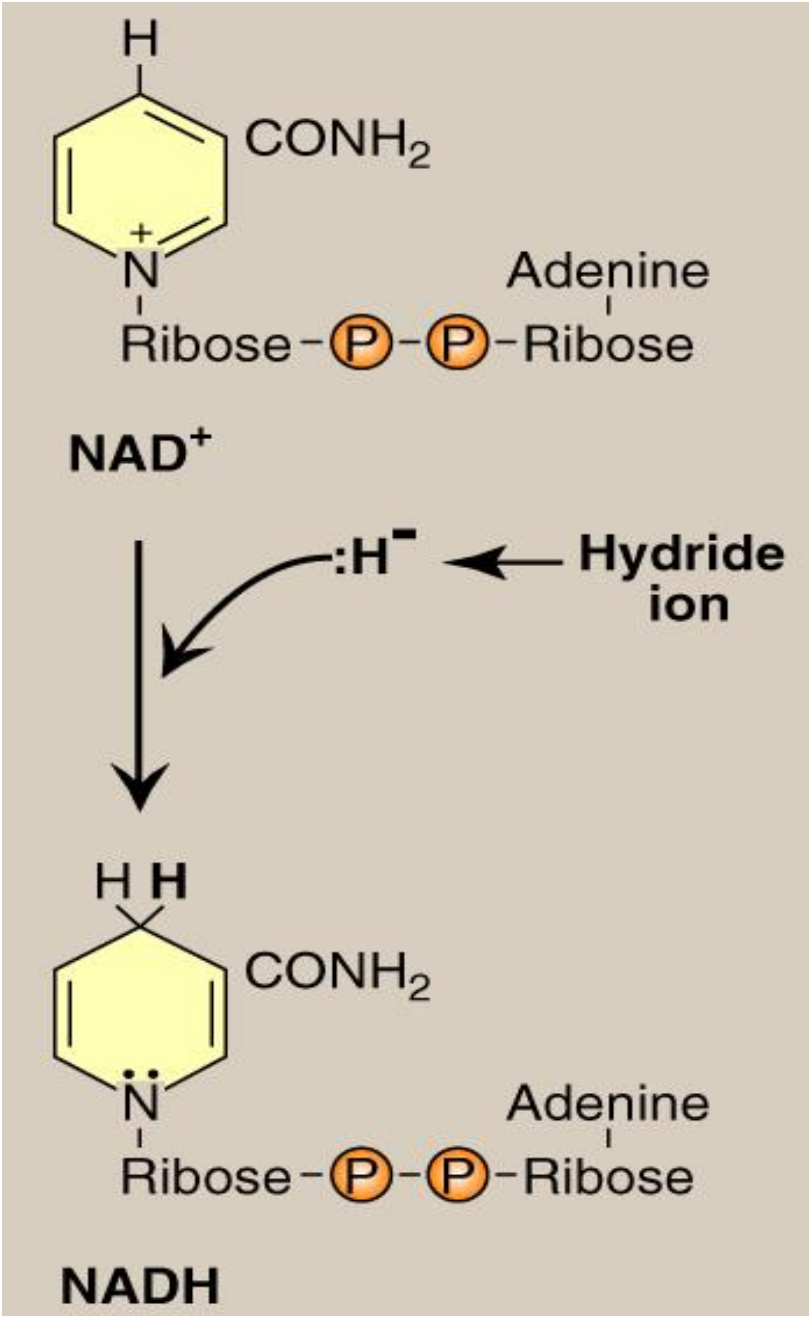
Loss of electrons

Reduction:

Gain of hydrogen

Gain of electrons

NAD^+ / NADH


H
CONH2
+
N
Adenine
Ribose – P – P – Ribose
NAD+
:H−
Hydride ion
H H
CONH2
N
Adenine
Ribose – P – P – Ribose
NADH

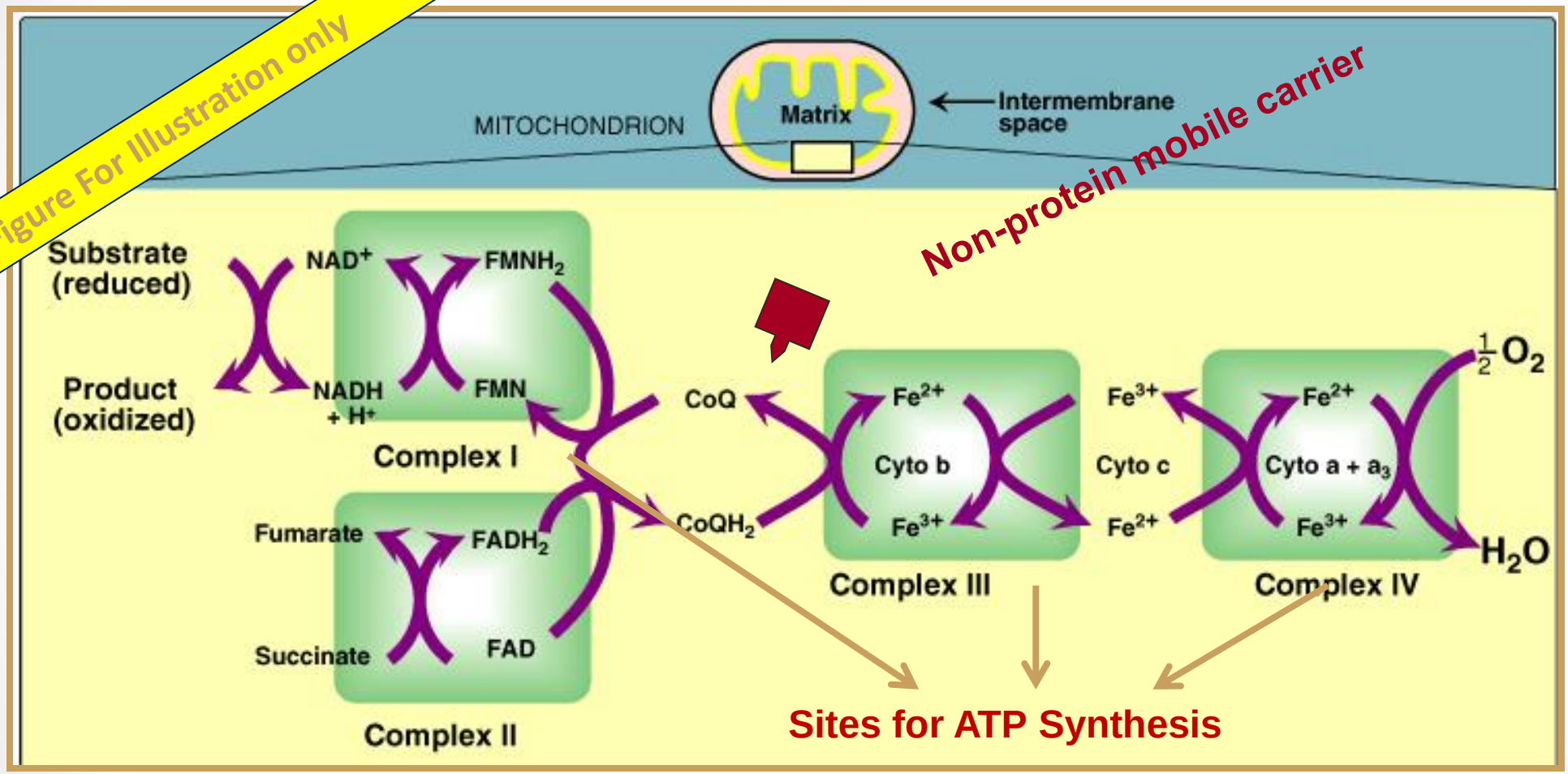
Regulation of Metabolism

- Intracellular signals:
  - Substrate availability
  - Product inhibition
  - Allosteric activators or inhibitors
- Intercellular communications:
  - Chemical signaling (hormones):
    Second messenger
    - cAMP, cGMP
    - Ca^{++}/phosphatidylinositol

Metabolic Fuel

- Carbohydrates and lipids (mainly) and proteins (little extent) are used for energy production
- Glucose and fatty acids are a major source of energy
- Amino acids are a minor source of energy
- Glucose is the major metabolic fuel of most tissues

Electron Transport Chain (ETC)



Electron transport and ATP synthesis are tightly coupled processes

Take home message

- Metabolism is the sum of all biochemical pathways that occur inside the cells
- A metabolic pathway is a multistep sequences of enzyme-catalyzed reactions
- Catabolism is a convergent process that provides energy to cells in the form of ATP
- Anabolism is a divergent process that consumes energy for the synthesis of complex molecules
- Metabolic pathways are tightly regulated and highly integrated
- ATP is the energy currency of the cells

references

- Lippincott's Illustrated Reviews, Biochemistry, 5th edition, Denise R. Ferrier, Lippincott Williams & Wilkins, USA, pp 91-94.