**Metabolism:** A complex series of inter-related, enzymatically controlled chemical reactions responsible for the production of biological energy and the synthesis of biomolecules.

i) **Catabolism:** The oxidative degradation of fuel molecules (polysaccharides, fats, proteins) to produce ATP, and reducing power (electron donor molecules) in the form of NADH, FADH$_2$ and NADPH. Generates precursors for synthesis of nucleotides.

ii) **Anabolism:** The biosynthesis of molecules such as amino acids, nucleosides, glycogen, triacylglycerides, etc., usually via reduction of precursors.

Production of biological energy in the form of ATP.

\[
\Delta G = \Delta H^0 + \Delta U - TAS = \Delta U - TAS
\]

$\Delta G < 0$ spontaneous reaction, $\Delta G > 0$ endothermic, energy input required

$\Delta G$ is path independent (G is a state variable)

$\Delta G$ contains no information on reaction rates

$\Delta G^+$ controls reaction rate. Catalysis lowers $\Delta G^+$
\[ A + B \xrightleftharpoons[k_2]{k_1} C + D \quad k_1, k_2 \text{ are rate constants} \]

Law of Mass Action (1884)
\[
\frac{d[A]}{dt} = \frac{d[B]}{dt} = k_2 [C][D] - k_1 [A][B]
\]
\[
-\frac{d[C]}{dt} = -\frac{d[D]}{dt}
\]

@ equilibrium
\[
\frac{d[A]}{dt} = \frac{d[C]}{dt} = \ldots \text{ etc.} = 0
\]

\Rightarrow k_1 [A][B] = k_2 [C][D]

Equilibrium constant (rate independent)
\[ K_{eq} = \frac{k_1}{k_2} = \frac{[C][D]}{[A][B]} \]

Relative to free energy
\[ G = U + PV - TS \]

@ constant P, T
\[
DG = DG^0 + RT \ln \frac{[B][D]}{[A][B]}
\]

\[ DG < 0 \quad \text{exothermic, spontaneous} \]
\[ DG = 0 \quad \text{equilibrium} \]
\[ DG > 0 \quad \text{endothermic} \]

@ equilibrium
\[
DG = 0 \quad \Rightarrow \quad DG^0 = -RT \ln K_{eq}
\]
\[ K_{eq} = e^{-\frac{DG^0}{RT}} \]

Note:
For multiple reaction
\[ aA + bB \xrightleftharpoons{} cC + dD \quad K_{eq} = \frac{[C]^c[D]^d}{[A]^a[B]^b} \]
\[ A \rightarrow B \quad \Delta G^\circ = -7.8 \text{ kcal/mole} \]
\[ \text{RT} = 0.58 \text{ kcal/M} \]

\[ \text{AMP} + \text{H}_2\text{O} \rightarrow \text{ADP} + \text{P}_i + \text{H}^+ \quad \Delta G^\circ = -3.3 \text{ kcal/mole} \]

**Coupled reaction**

\[ A + \text{AMP} + \text{H}_2\text{O} \rightarrow \text{B} + \text{ADP} + \text{P}_i + \text{H}^+ \quad \Delta G^\circ = -3.3 \text{ kcal/mole} \]

\[ \Delta G^\circ = \frac{-RT}{e} \cdot \ln(\frac{[B]}{[A]}) \]

\[ \text{no ATP coupling} \quad K_{eq} = \frac{e^{-\Delta G^\circ/RT}}{e^{-\Delta G^\circ/RT}} = 10.1 \times 10^{-3} = \frac{[B]}{[A]} \]

\[ \text{with ATP} \quad K_{eq} = \frac{[B][\text{ADP}][\text{P}_i]}{[A][\text{AMP}]} \]

\[ k_{eq} = e^{-3.3/0.06} = 2.96 \]

\[ \frac{[B][\text{ADP}][\text{P}_i]}{[A][\text{AMP}]} = 2.96 \]

\[ k_{eq} = 2.96 \times 5000 = 14,800 \]

So, the enhancement is

\[ \frac{n \times \text{AMP}}{\text{AMP}} = \frac{14,800}{10^{-3}} \approx 10^8 \]

**Energy Charge**

\[ \text{Energy charge} = \frac{[\text{AMP}] + \frac{1}{2}[\text{ADP}] + \frac{1}{2}[\text{ATP}]}{[\text{AMP}] + [\text{ADP}][\text{AMP}]} \cdot \frac{[\text{AMP}]}{[\text{AMP} + [\text{ADP}][\text{AMP}]}} \]
Redox reactions: Transfer of electrons from one chemical species (the one being oxidized) to another species (the one being reduced).

\( \text{e.g.:} \quad \text{Zn}^{++} + 2e^- \rightarrow \text{Zn} \quad \text{(oxidation)} \quad 0.76 \text{V} \)

\( \text{Cu}^{++} + 2e^- = \text{Cu} \quad \text{reduction} \quad 0.34 \text{V} \)

\( \text{Cu}^{++} + \text{Zn} = \text{Zn}^{++} + \text{Cu} \)

\( \Delta \varepsilon_0 = 1.10 \text{V} \)

Voltage diff. for 1 M of \( \text{Zn}^{++} \) and \( \text{Cu}^{++} \) in each side:

\( aA + bB \rightarrow cC + dD \)

Nernst equation:

\( \Delta \varepsilon = \Delta \varepsilon_0 - \frac{0.059}{n} \log \frac{[C]^{c}[D]^{d}}{[A]^{a}[B]^{b}} \)

\( n = \# \text{ of electrons transferred} \) e.g. \( n = 2 \) for \( \text{Zn}^{++} + \text{Cu} \rightarrow \text{Zn} + \text{Cu}^{++} \)

\( \Delta G = n \cdot \frac{\Delta \varepsilon}{n} \)

\( \Delta G = \frac{\text{charge (C)}}{\text{mole}} = \frac{(1.6 \times 10^{-19})(6.022)}{0.36} \approx 9.6 \times 10^5 \frac{\text{C}}{\text{mole}} \)
Principle Catabolic Pathways

1) Glycolysis prepares starches and sugars for final, complete oxidation (occurs in the cell's cytosol)

\[
\text{Glycogen} \xrightarrow{\text{enzymes}} \text{Glucose} \xrightarrow{\text{ATP}} \text{Pyruvate} \\
\text{starch} \quad 2 \text{ADP} \rightarrow 2 \text{ATP} \\
\text{NAD}^+ \rightarrow \text{NADH} \\
\text{Acetyl-CoA} \rightarrow \text{citric acid cycle}
\]

2) The Citric Acid Cycle is the final common pathway for oxidation of fuel molecules.
   i) builds up reducing power in the form of NADH and FADH$_2$
   ii) produces carbon skeletons for biosynthesis
   iii) takes place in the mitochondrion

3) Oxidative phosphorylation used reducing power of NADH and FADH$_2$
   from the citric acid cycle to produce ATP.
   i) regenerates NAD$^+$ and FAD
   ii) O$_2$ is the final electron acceptor
   iii) occurs across inner mitochondrial membrane

4) Gluconeogenesis synthesizes glucose from glycerol, lactate, amino acids in times of sugar depravation.

5) Pentose phosphate pathway

\[
\text{Glucose-6-phosphate} + 2 \text{NADP}^+ + \text{H}_2\text{O} \rightarrow \text{Ribose-5-phosphate} + 2 \text{NADPH} + 2 \text{H}^+ + \text{CO}_2
\]

   \text{for nucleoside synthesis} \quad \text{for reductive biosynthesis}

6, 7) Urea cycle and fatty acid oxidation feed into the Citric acid cycle and provide compounds for biosynthesis.
Oxidation of fuel molecules

Fats → fatty acids, glycerol
Polysaccharides → glucose, other sugars
Proteins → amino acids

Glycolysis → Acetyl CoA

Oxidative Phosphorylation

Citric Acid Cycle

ATP \rightarrow ADP

O_2 \rightarrow CO_2
## Activated Carriers in Metabolism

<table>
<thead>
<tr>
<th>Carrier molecule</th>
<th>Group carried in activated form</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATP</td>
<td>Phosphoryl</td>
</tr>
<tr>
<td>NADH and NADPH</td>
<td>Electrons</td>
</tr>
<tr>
<td>FADH₂</td>
<td>Electrons</td>
</tr>
<tr>
<td>Coenzyme A</td>
<td>Acyl</td>
</tr>
<tr>
<td>Lipoamide</td>
<td>Acyl</td>
</tr>
<tr>
<td>Thiamine pyrophosphate</td>
<td>Aldehyde</td>
</tr>
<tr>
<td>Biotin</td>
<td>CO₂</td>
</tr>
<tr>
<td>Tetrahydrofolate</td>
<td>One-carbon units</td>
</tr>
<tr>
<td>S-Adenosylmethionine</td>
<td>Methyl</td>
</tr>
<tr>
<td>Uridine diphosphate glucose</td>
<td>Glucose</td>
</tr>
<tr>
<td>Cytidine diphosphate diacylglycerol</td>
<td>Phosphatidate</td>
</tr>
</tbody>
</table>
The glycolytic Pathway

Pyruvate + NAD⁺ + CoA → acetyl CoA + CO₂ + NADH

oxidative decarboxylation of pyruvate by pyruvate dehydrogenase

The Citric Acid Cycle

δ-Aminolevulinate → porphyrins
Oxidative Phosphorylation: final pathway in the oxidative degradation of biomolecules

Free energy produced by oxidation of NADH

(a) $\frac{1}{2} \text{O}_2 + 2 \text{H}^+ + 2e^- \rightleftharpoons \text{H}_2\text{O}$ \hspace{2cm} $E_0' = +0.82 \text{ V}$
(b) $\text{NAD}^+ + \text{H}^+ + 2e^- \rightleftharpoons \text{NADH}$ \hspace{2cm} $E_0' = -0.32 \text{ V}$

Subtracting reaction b from reaction a yields
(c) $\frac{1}{2} \text{O}_2 + \text{NADH} + \text{H}^+ \rightleftharpoons \text{H}_2\text{O} + \text{NAD}^+ \hspace{2cm} \Delta E_0' = +1.14 \text{ V}$

The free energy of oxidation of this reaction is then given by

$$\Delta G'^\circ = -nF\Delta E_0' = -2 \times 23.062 \times 1.14 = -52.6 \text{ kcal/mol}$$

A proton gradient across the inner mitochondrial membrane couples electron transport to ATP
Figure 4-2  The structure of cells. A. Diagram of a typical animal cell. (From De Witt, W.: Biology of the Cell. Philadelphia, W. B. Saunders Co., 1976.) B. Diagram of a typical plant cell.