INTRODUCTION TO METABOLISM

Metabolism refers to all the chemical reactions which occur in life. These reactions are:

1. Catabolic - degradative reactions which:
   a. convert food into twelve, key, low molecular weight intermediates (which can be converted in
      anabolic reactions into low molecular weight precursors of proteins, polysaccharides, lipids, and
      polynucleotides),
   b. oxidize food, generating NADH + H+, which transfers electrons to the electron transport chain,
      with resulting ATP generation,
   c. convert food into low molecular weight compounds which can serve to generate ATP by
      substrate level phosphorylation.

2. Anabolic - biosynthetic reactions which generate amino acids, fatty acids, monosaccharides, and
   mononucleotides and polymerize them into proteins, lipids, polysaccharides, and polynucleotides.

B. Sets of reactions in which the product of one reaction serves as the substrate for the next reaction are called
   pathways. For example, compound A might be converted into compound B by four, successive reactions.

C. Enzymes are necessary to catalyze most biochemical reactions so that the reaction reaches equilibrium within a
   time scale useful for life. Enzymes usually are proteins; they usually catalyze one, specific reaction; usually, every
   reaction requires catalysis by one, specific enzyme.

   Although a given reaction, such as A + B = C + D, might come to equilibrium, in the test tube, with only slightly more C + D formed
   than the amount of A + B remaining, in living organisms, this reaction usually goes to completion. This is possible because C or D is removed, by, for example, conversion to some other product. -if C or D is not removed, the reaction comes to equilibrium.

E. Glycolysis is the conversion of glucose to pyruvate (also called the Embden-Meyerhoff Pathway):

   NAD+ is converted into NADH + H+
   ATP is generated by substrate level phosphorylation

F. Respiration converts pyruvate to CO2 (Krebs's cycle, Citric acid cycle, Tricarboxylic acid cycle) and in the process:

   NADH + H+ are formed, FAD is converted into FADH2. GDP is converted into GTP.

   The reducing compound pool reduces the electron transport chain, generating a pH gradient across the Cytoplasmic
   membrane, the resulting proton motive force is used by ATP synthase to convert ADP + Pi into ATP (Oxidative
   Phosphorylation)

   A terminal electron acceptor is required to accept electrons from the electron transport chain. In aerobic respiration, O2
   accepts electrons and is converted to H2O.

G. Fermentation is a process by which glucose oxidation (glycolysis) can+ be sustained in the absence of a terminal
   electron acceptor. That is the oxidation/reduction reactions are internally balanced. Pyruvate is reduced to
   lactate or ethanol by NADH H+, regenerating NAD+.

H. Microbes have evolved to occupy many niches. Four modes of respiration include aerobic, anaerobic,
   chemolithotrophic, and photosynthetic.
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OVERVIEW - ANABOLISM, CATABOLISM

ENERGY

Free Energy Change
Exergonic, Endergonic
Enzymes - Catalyst, Activation Energy
Enzymes - Bind Substrates
Strain specific bonds in substrates
Lower activation energy

Apoenzyme plus coenzyme = holoenzyme

Example - Aldolase (High Molecular Weight, Protein)
Fructose-1,6-bisphosphate > Dihydroxy acetone phosphate plus
Glyceraldehyde-3-phosphate

OXIDATION/REDUCTION REACTIONS - REDOX

Oxidation - loss of electron - electron donor
Reduction - gain of electron - electron acceptor
Coupled Oxidation/Reduction reactions

ELECTRON CARRIERS

Nicotinamide adenine dinucleotide [NAD] - coenzyme involved in oxidation/reduction
NAD+ plus 2e- plus 2H+ <-> NADH plus H+

Oxidized Reduced [Reducing Power]

ENERGY LEVEL OF PHOSPHATE-CONTAINING COMPOUNDS

Esters - low energy
glucose-6-phosphate

Anhydrides - high energy
ATP, adenosine triphosphate - Universal source of high energy
1,3-diphospho glyceric acid (1,3-diphospho glycerate)

GENERATING ATP

Substrate level phosphorylation -
Phosphate-containing low molecular weight compound plus ADP plus enzyme react to form ATP plus low molecular weight compound
Phospho enol phosphate plus ADP form pyruvate plus ATP

Oxidative phosphorylation -
Reduced NADH plus H+ transfer electrons to Electron Transport Chain
Electron flow is coupled to reaction of ADP plus inorganic phosphate (Pi) to form ATP
Terminal electron acceptor, e.g., oxygen

Photophosphorylation - energy from sunlight excites electron flow from chlorophyll or bacteriochlorophyll to electron transport chain

GLYCOLYSIS - glucose conversion to pyruvate [Embden-Meyerhoff Pathway]

NADH plus H+ generated
Substrate level phosphorylation

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RESPIRATION - pyruvate conversion to carbon dioxide plus water [in aerobic respiration]
NADH plus H+, FADH2, GTP generated
Flow of electrons to Electron Transport Chain
Oxidative Phosphorylation
Terminal Electron Acceptor (Oxygen in aerobic respiration)

FERMENTATION - Pyruvate > Lactic Acid (lactate) Pyruvate > Ethanol Plus CO2 Glycolysis plus fermentation: Allow glucose conversion to lactate or ethanol with internally balanced redox reactions Do not require terminal electron acceptor Result in only partial oxidation of glucose carbons Yield only small amount of potential energy of glucose Allow ATP generation by substrate level phosphorylation

GLYCOLYSIS PATHWAY

FERMENTATION PATHWAYS -Pyruvate to lactate, Pyruvate to ethanol plus carbon dioxide
Carbon/energy
Glucose

\[ \text{G-6-PD} \]

\rightarrow \text{Low mol wt building blocks}

\rightarrow \text{ATP}

\rightarrow \text{Macromolecules}

Chemical synthesis;
Food transport
Motility

Amino acids
Fatty acids
Monosaccharides
Mononucleotides

Proteins—enzymes;
Flagellin; ribosomes etc

Phospholipids
Polysaccharide [peptido glycan]

DNA/RNA [t, t, m]
\[ \Delta G^0 \] change in free energy under standard conditions

Negative \( \Delta G \) - exergonic
- Free energy released
- Reaction occurs spontaneously
- Equilibrium favors right

\[ A + B \rightleftharpoons C + D \]

Large \( -\Delta G \) \( \supseteq \)

Small \( -\Delta G \) \( \supseteq \)
POSITIVE $\Delta G$ - ENDERGONIC

- FREE ENERGY REQUIRED
- REACTION WILL NOT OCCUR SPONTANEOUSLY
- EQUILIBRIUM FAVORS LEFT

$\Delta G$ - DOES NOT PREDICT HOW LONG WILL BE REQUIRED TO REACH EQUILIBRIUM

$\frac{1}{2}O_2 + H_2 \rightarrow H_2O$  
$\Delta G = -237 \text{ kJ/mole}$

[4.2 KILO JOULE = 1 KILO CALORIE]
ENZYMES $10^8 - 10^{20} \times$ RATE

1. BIND SUBSTRATE
2. HOLD SUBSTRATE IN ENZYME CATALYTIC SITE - STRAIN BONDS
3. REDUCE ACTIVATION ENERGY

**Diagram:**
- **Graph:**
  - **NO ENZYME**
  - **+ ENZYME**
  - **SUBSTRATE** → **PRODUCT**
  - **ΔG**
  - **ACTIVATION ENERGY**
  - **ΔG** for **SUBSTRATE**
  - **ΔG** for **PRODUCT**
  - **ENZYME DOES NOT CHANGE:**
    - FREE ENERGY OF SUBSTRATE/PRODUCT
    - EQUILIBRIUM; ΔG IS SAME + / - ENZYME
ENZYME - TURNOVER NUMBER -
NUMBER OF MOLECULES OF
REACTANT (SUBSTRATE)
CONVERTED TO PRODUCT
PER MOLECULE OF ENZYME
PER UNIT TIME (E.G., SECOND)

TYPICAL = 2,000/SECOND =
120,000/MINUTE
FRUCTOSE-1,6-BISPHOSPHATE

ENZYME-ALDOLASE

ENZYME-SUBSTRATE COMPLEX

CH$_2$O-PO$_3$H$_2$

CH$_2$OH

H$_2$C=O

H$_2$C-OH

CH$_2$OPO$_3$H$_2$

ALDOLASE

[359 a.a.;
MW = 39,147]+

DI-HYDROXY ACETONE PHOSPHATE

GLYCER-ALDEHYDE-3-PHOSPHATE
**Fructose-1,6-bisphosphate**

**Aldolase Splits Here**

**Bonds Breaks Two Molecules**

**Forms 2 Molecules**

**Aldolase**

$$[359 \text{ a.a.} ; \text{MW} = 39,147]$$

**Enzyme-Substrate Complex**

**Enzyme-Aldolase**

**Di-Hydroxy Acetone Phosphate**

**Glycer-Aldehyde-3-Phosphate**

$$\text{CH}_2\text{O-PO}_3\text{H}_2$$

$$\text{CH}_2\text{OH}$$

$$\text{HC}=\text{O}$$

$$\text{HC}-\text{OH}$$

$$\text{CH}_2\text{OPO}_3\text{H}_2$$
ATP

Phosphates

Adenosine Triphosphate - A Mononucleotide

Adenine - Nucleic Acid Base

Pentose Ribose
OXIDATION-LOSS OF ELECTRON
REDUCTION-GAIN OF ELECTRON

\[ \text{H}_2 + \frac{1}{2}\text{O}_2 \rightarrow \text{H}_2\text{O} \]

REDDUCING AGENT \quad OXIDIZING AGENT

\[ \text{H}_2 - \text{ELECTRON DONOR} \]
\[ \text{H}_2 \rightarrow 2e^- + 2\text{H}^+ \]

\[ \frac{1}{2}\text{O}_2 - \text{ELECTRON ACCEPTOR} \]
\[ \frac{1}{2}\text{O}_2 + 2e^- \rightarrow \text{O}^{2-} \]

NET CHANGE: \[ 2\text{H}^+ + \text{O}^{2-} \rightarrow \text{H}_2\text{O} \]

SUMMARY
H\textsubscript{2} - REDUCING AGENT
- DONATES ELECTRONS
- BECOMES OXIDIZED

\[ \frac{1}{2}\text{O}_2 - \text{OXIDIZING AGENT} \]
- ACCEPTS ELECTRONS
- BECOMES REDUCED
Nicotinamide adenine dinucleotide (NAD)

\[ \text{NAD}^+ + 2e^- + 2H^+ \rightarrow \text{NADH} + H^+ \]

**Oxidized state**
- Picks up 2e- + 2H+ from food
- Is reduced

**Reduced state**
- Transfers e- to other carriers to generate ATP
- Is oxidized
NAD\(^+\)  \hspace{1cm} \text{NADH} + H^+ \hspace{1cm} +2e^- + 2H^+ \hspace{1cm} \text{REDUCED} \hspace{1cm} \text{OXIDIZED}

Nicotinamide adenine dinucleotide
β-D-Glucose-6-phosphate ester low energy

Adenosine triphosphate anhydride high energy

1,3 di phospho glyceric acid anhydride
GLUCOSE

2 PYRUVATES

GLYCOLYSIS
NAD$^+$ → NADH + H$^+$
ADP → ATP

SUBSTRATE LEVEL PHOSPHORYLATION

CITRIC ACID CYCLE
NAD$^+$ → NADH + H$^+$
FAD → FADH$_2$
GDP → GTP

ELECTRON TRANSPORT CHAIN
NADH + H$^+$ → NAD$^+$
ADP → ATP

OXIDATIVE PHOSPHORYLATION

6O$_2$ → 6 H$_2$O

TERMINAL ELECTRON ACCEPTOR

RESPIRATION
(AEROBIC)
Fermentation

2 lactates or 2 ethanol + 2 CO₂

Note: NAD recycles

\[ \text{NAD}^+ + 2e^- + 2H^+ \rightarrow \text{NADH} + H^+ \]
- **Substrate Level Phosphorylation**
  - Low molecular weight - P<sub>0</sub><sub>4</sub> containing compound + ADP → ATP (plus low mol wt compound)

- **Oxidative Phosphorylation**
  - NADH + H<sup>+</sup> transfer electrons to electron transport chain
  - Electron flow is coupled to ATP synthesis
  - ADP + P<sub>0</sub><sub>4</sub> → ATP
  - Requires terminal electron acceptor
  - e.g., O<sub>2</sub>
SUBSTRATE LEVEL PHOSPHORYLATION

\[ \text{HO-C} - \text{O-} - \text{P}=\text{O} \quad \sim \quad \text{HO-C} - \text{O-} - \text{P}-\text{OH} \quad \rightarrow \quad \text{ATP} \quad + \quad \text{HO-C} - \text{C}=\text{O} \quad \text{HCH} \quad \text{H} \text{C} \\text{H} \quad \text{PYRUVATE} \]

\[ \text{PHOSPHO-ENOL PYRUVATE} \quad + \quad \text{ADP} \quad \quad \quad \quad \quad \quad \text{ENZYME PYRUVATE} \]
GLUCOSE

1 → ATP
ADP

GLUCOSE-6-P0₄

2 → ATP
ADP

FRUCTOSE-6-P0₄

3 → ATP
ADP

FRUCTOSE-1,6-BISPHOSPHATE

4 →

\[ \text{CH}_2\text{O-PO}_3\text{H}_2 \]
\[ \text{C}=\text{O} \]
\[ \text{CH}_2\text{OH} \]
DI HYDROXY ACETONE PHOSPHATE

5 →

\[ \text{HC} = \text{O} \]
\[ \text{HC} - \text{OH} \]
\[ \text{CH}_2\text{OPO}_3\text{H}_2 \]
GLYCERALDEHYDE-3-PHOSPHATE
Glycolysis

1,3 Bisphosphoglycerate

Glyceraldehyde-3-phosphate

NAD^+

Reducing Power

Substrate Level Phosphorylation

ADP

ATP

3 Phosphoglycerate

1,3 Bisphosphoglycerate

NADH + H^+
Glycolysis

2-Phospho Glycerate

Phosphoenol Pyruvate

Pyruvate

Higher energy than anhydride

Substrate level phosphorylation
Lactic Acid Fermentation

Pyruvate \[ \rightarrow \text{Reduced} \rightarrow \text{Lactate} \]

\[ \text{Net} \quad \text{Glucose} \rightarrow 2 \text{Lactate} \]
\[ 2 \text{ADP} + 2 \text{Pi} \rightarrow 2 \text{ATP} \]
**ETHANOL FERMENTATION**

**PYRUVATE**

\[
\begin{array}{c}
\text{O} \\
\text{C} \text{-OH} \\
\text{C} = \text{O} \\
\text{CH}_3
\end{array}
\]

\[
\begin{array}{c}
\cdots \\
\text{H} \text{C} = \text{O} \\
\text{CH}_3
\end{array}
\]

\[
\begin{array}{c}
\text{H} \text{C} \text{-OH} \\
\text{CH}_3
\end{array}
\]

\[\text{CO}_2\]

**ACETALDEHYDE**

\[\text{NADH} + \text{H}^+ \rightarrow \text{NAD}^+\]

**REDUCED TO**

**ETHANOL**

\[\text{NET: GLUCOSE} \rightarrow 2 \text{CO}_2 + 2 \text{ETHANOL} + 2 \text{ADP} + 2 \text{Pi} \rightarrow 2 \text{ATP}\]