Lecture 27: Introduction to Metabolism

Key Points

- Catabolism
- Anabolism
- Glycolysis
- Fatty acid metabolism
- Citric acid (TCA, Krebs) cycle
- Electron transport
- Enzyme nomenclature

ATP energy content**Metabolic pathways are:**

1. Conserved in different organisms.
2. Overall irreversible (but most of the individual steps are not)
3. Consist of a number of small changes.
4. Usually committed after the initial steps
5. Regulated (usually at initial step(s))
6. Compartmentalized in eukaryotes

Catabolism [degradative] – conversion of a diverse set of compounds to a small number of simple compounds for energy production.

Anabolism [synthetic] – conversion of a small number of simple compounds to complex organic molecules.

What you need to know:

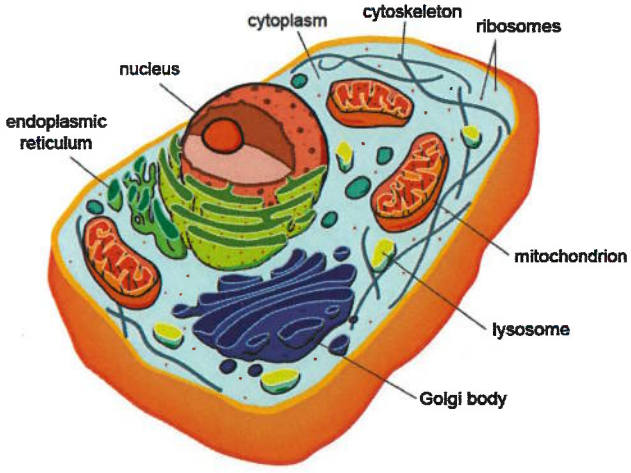
1. Input and output metabolites
2. Steps that control flux
3. How flux through pathway is controlled
4. Cellular location of metabolic steps
5. Selected enzyme mechanisms
6. Selected substrates/products

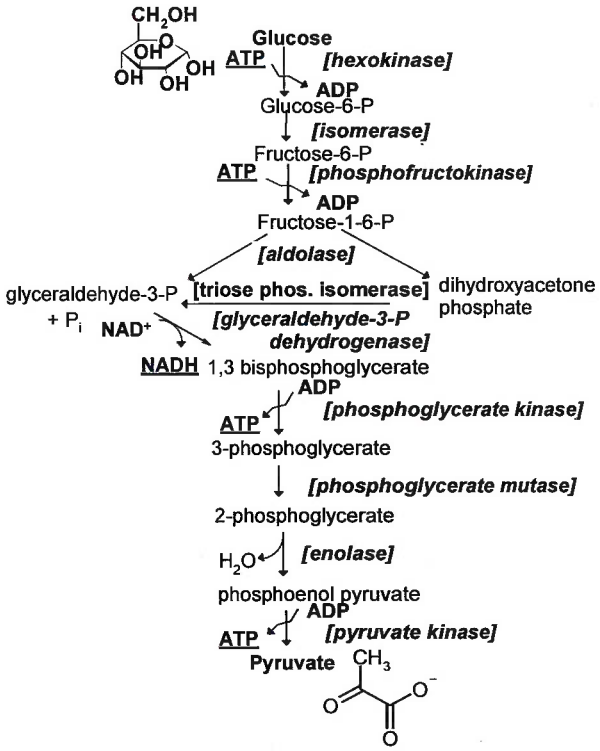
What you should not do: Memorize pathways.

Central Pathways of Energy Production:

Intracellular locations:

- Glycolysis - cytosol
- Fatty Acid Oxidation: Inner matrix of mitochondria
- Citric Acid Cycle (TCA): Inner matrix of mitochondria
- Oxidative Phosphorylation: Inner membrane of mitochondria

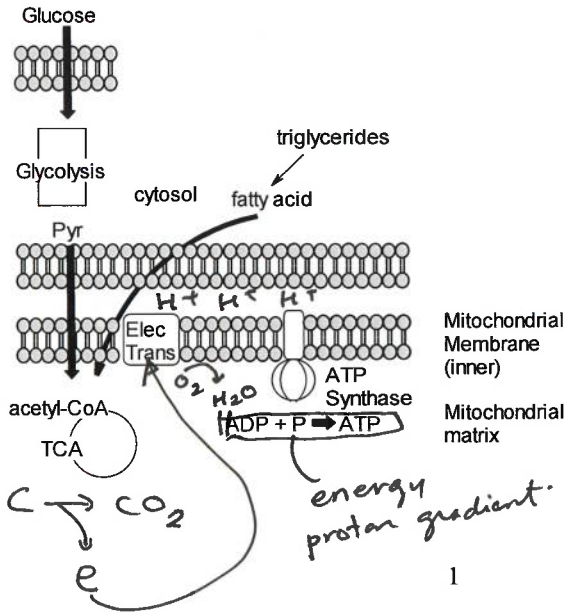




Energy Transactions: Organic compounds (e.g. glucose) → Electron Carriers→Proton Gradient → ATP

Energy Utilization:

- Chemical synthesis reactions (e.g. protein synthesis, DNA synthesis
- Mechanical work (e.g. transport, muscle function)
- Electrical work (e.g. nerve conduction)



Enzyme Nomenclature (Enzyme Commission)

For example, the tripeptide aminopeptidases have the code "EC 3.4.11.4", whose components indicate the following groups of enzymes:

- *EC 3* enzymes are hydrolases (enzymes that use water to break up some other molecule)
- *EC 3.4* are hydrolases that act on peptide bonds
- *EC 3.4.11* are those hydrolases that cleave off the amino-terminal amino acid from a polypeptide
- *EC 3.4.11.4* are those that cleave off the amino-terminal end from a tripeptide

Common Names: hexose kinase

Name - usually consists of three parts:

i) the substrate is used to name the enzyme,

Keep in mind that many enzymatic reactions run in both directions in metabolism, consequently the "product" may be used to name the enzyme.

ii) the nature of the chemical reaction.

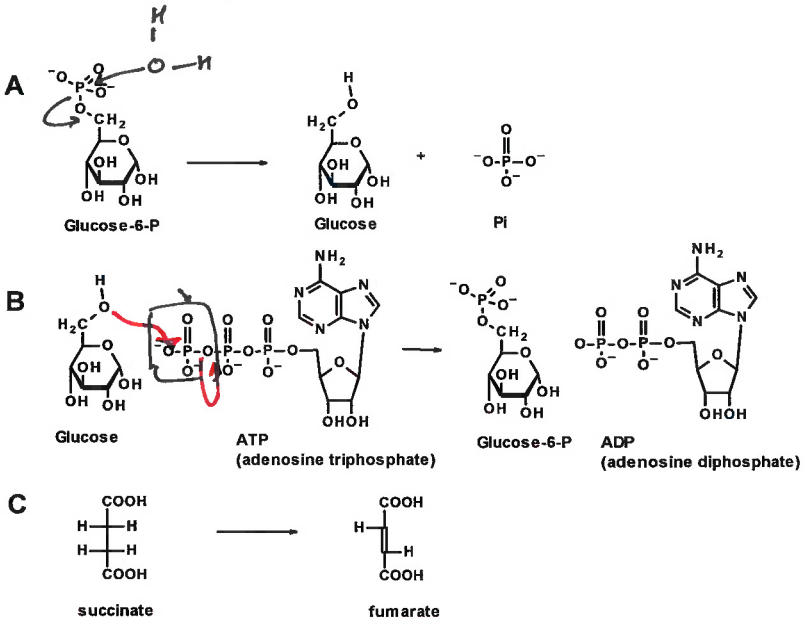
iii) most names end in *"-ase"*

A. Phosphatase: Removes a phosphate group from a substrate, via hydrolysis – no ATP/ADP involved. e.g. glucose-6 phosphatase.

B. Kinase: transfers a phosphate group from ATP to another compound e.g. hexokinase.

C. Dehydrogenase: Removes/adds hydrogens by oxidation/reduction. Usually require NAD^+/NADH or $FAD/FADH_2$ as co-factors/co-substrates. e.g. succinate dehydrogenase.

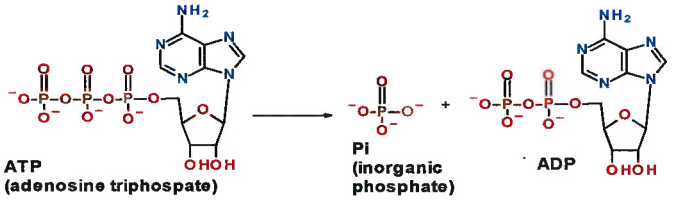
Redox Reactions



Biochemical Energetics:

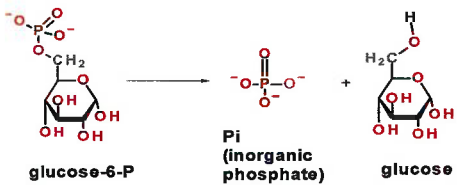
1. Phosphate Hydrolysis:

Consider the following two reactions:



$\Delta G^\circ = -30$ kj/mol

more energy released due to charge repulsion



$\Delta G^\circ = -15$ kj/mol

Reflection: Explain the difference between ΔG° of hydrolysis for ATP and G-6-P.

2. Electrons (Redox Chemistry)

An example of a redox reaction involving metals: $Fe^{3+} + Cu^{+} \leftrightarrow Fe^{2+} + Cu^{2+}$

This reaction can be broken down into two balanced half reactions:

$$Fe^{3+} + e^{-} \leftrightarrow Fe^{2+} \qquad Cu^{+} \leftrightarrow Cu^{2+} + e^{-}$$

The iron is reduced from the 3^+ state to the 2^+ state while the copper is oxidized from the 1^+ state to the 2^+ state.

In biological oxidations and reductions the electrons are often carried by protons (i.e. hydrogen atom). A general rule for oxidation-reduction are:

Loss of electrons or hydrogen atom ($H^+ + e^-$) = oxidation

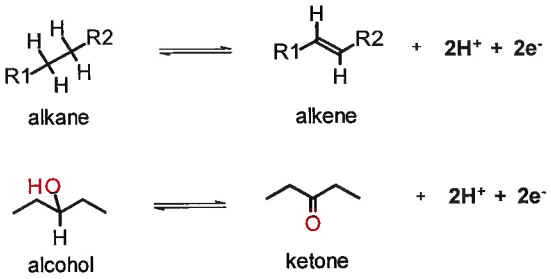
Gain of electrons or hydrogen atom = reduction

There are several common acronyms to help you remember the above, here are two:

LEO GER - lose electrons oxidation, gain electron reduction.

OIL RIG - oxidation involves loss, reduction involves gain.

In the case of biological systems, the redox state of an organic molecule may be difficult to discern. The following shows the oxidation (loss of hydrogen atoms) of two functional groups. Both of these reactions are oxidations since electrons were removed from the reactant, and both are 2 electron oxidations.



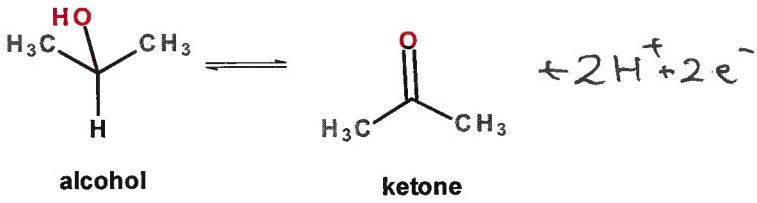
Balancing organic redox reactions.

Method A – Reaction/Product Balancing:

i) If oxygen is needed to balance the reaction, use H_2O.

ii) Use H^+, or $H^+ + e^-$, or e^- to balance hydrogen atoms and/or charge.

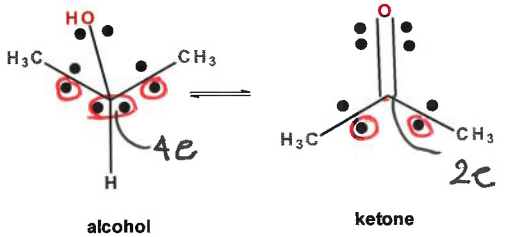
A redox reaction has occurred if electrons appear on one side of the reaction. If they appear on the right side (products) then it is an oxidation – electrons were released from the reactants.



Method B – Determine Oxidation State of Individual Carbons:

Count the number of electrons that are associated with carbon for each bond.

- If the other atom is less electronegative (e.g. H) carbon owns both electrons
- If the other atom is more electronegative (e.g. O) carbon owns none.
- If two carbons are involved, the electrons are equally shared.
- If the carbon has fewer electrons it has been oxidized.
- If the carbon gains electrons, it has been reduced,



Example: Is the conversion of ethene to ethanol a redox reaction?

Method A: