Biology 112 – Ch. 9 Pathways that Release Energy

Five principles govern metabolic pathways:

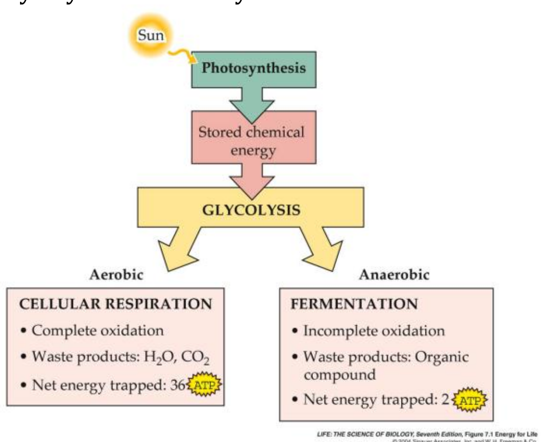
- A complex chemical transformation occurs in a series of separate reactions that form a metabolic pathway
- Each reaction is catalyzed by a specific enzyme
- Most metabolic pathways are similar in all organisms
- In eukaryotes, many metabolic pathways are compartmentalized, with certain reactions occurring inside specific organelles
- Each metabolic pathway is regulated by key enzymes that can be inhibited or activated, thereby determining the rate of reaction

When burned in a flame, glucose releases heat, carbon dioxide, and water

$$C_6H_{12}O_6 + 6\ O_2 \rightarrow 6\ CO_2 + 6\ H_2O + \text{free energy}$$

→ The same equation applies for the biological metabolic use of glucose.
Catabolic pathways are long and complex in order to release energy slowly. Only then can cells use it.
ΔG for the complete oxidation of glucose is -686 kcal/mol (**exergonic**)
About half of the energy from glucose is collected in ATP (**endergonic**)
Two metabolic processes are used in the breakdown of glucose for energy:

- Glycolysis followed by cellular respiration
- Glycolysis followed by fermentation

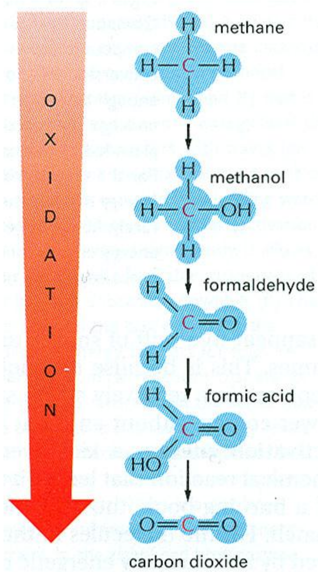


Glycolysis: begins glucose metabolism → **anaerobic process** → yields two molecules of pyruvate
Cellular Respiration: uses oxygen from the environment → **aerobic** → each pyruvate = three molecules of carbon dioxide (through pyruvate oxidation, the citric acid cycle, and an electron transport system)
Fermentation: anaerobic → converts pyruvate into lactic acid or ethyl alcohol = much less energy released than cellular respiration

Redox reactions transfer electrons

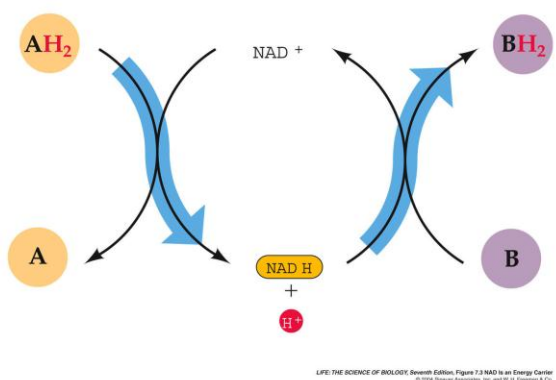
- A gain of electrons or hydrogen atoms is called **reduction**
- The loss of electrons or hydrogen atoms is called **oxidation**
- Whenever one material is reduced, another is oxidized

→ Redox reactions are made up of 2 half-reactions/redox pairs



Rule: Oxidation of organic molecules **decreases** the number of C-H bonds

The cofactor NAD is an essential electron carrier in cellular redox reactions



NAD exists in two chemically distinct forms:

One oxidized (NAD+)

One reduced (NADH)

$$NADH + H^+ + 1/2\ O_2 \rightarrow NAD^+ + H_2O$$

Two half reactions or redox pairs:

$$NADH \rightleftharpoons NAD^+ + H^+ + 2e^- \text{ (oxidation)}$$

$$1/2\ O_2 + 2H^+ + 2e^- \rightleftharpoons H_2O \text{ (reduction)}$$

The oxidation of NADH with oxygen as an electron acceptor is exergonic

→ Conjugated (alternating) double bonds are energetically favored because the electron of all 3 electron pairs form a common electron cloud

The oxidation of NADH with oxygen as an electron acceptor is exergonic:

➔ Tendency to lose or gain electrons is called **redox potential**

- With oxygen present, four major pathways operate
  - Glycolysis
  - Pyruvate oxidation
  - The citric acid cycle
  - The respiratory chain (electron transport chain)
- When no oxygen is available, glycolysis is followed by fermentation

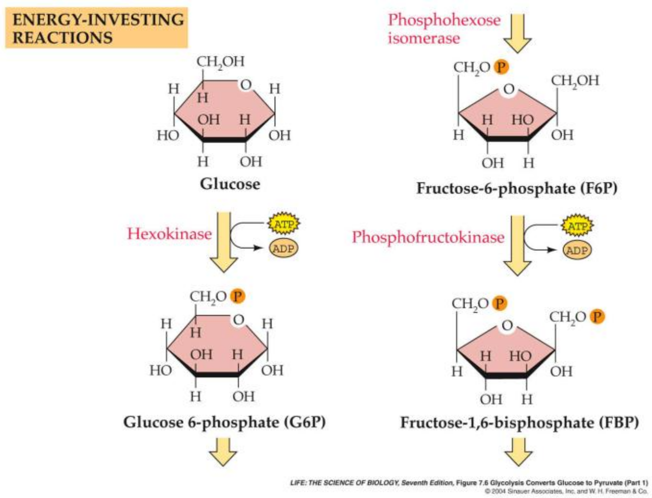
Glycolysis can be divided into two stages:

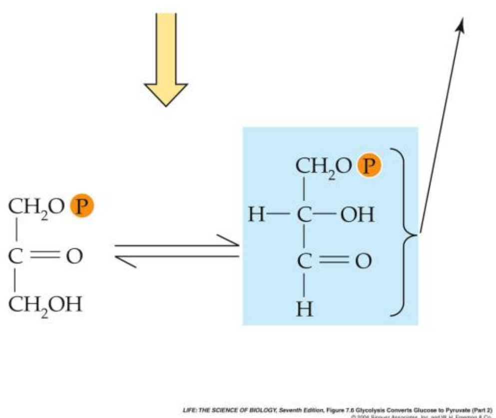
- Investment of ATP to activate the sugar followed by splitting of C6 into 2x C3

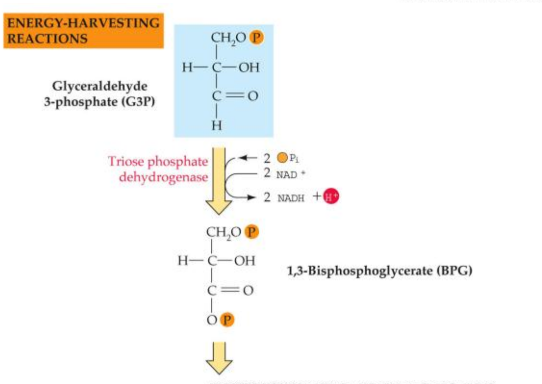
- Oxidation of C3 giving NADH + H^+ and ATP followed by recovery of initital ATP investment

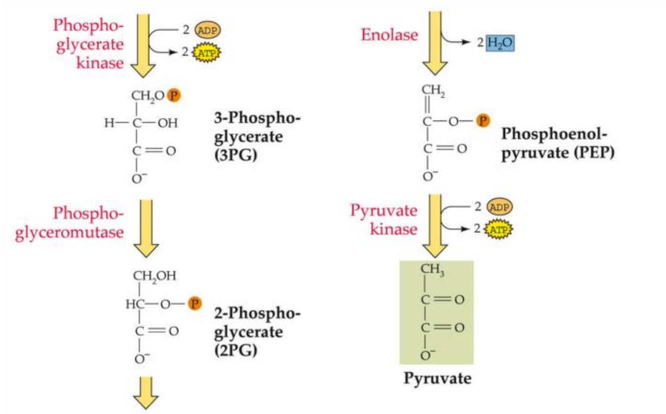
The energy harvesting reaction of glycolysis (takes place in the ctyosol):

- The first reaction (a redox reaction) makes one NADH + H^+ per G3P molecule, and releases enough energy to be coupled to the formation of an energy-rich P-bond per G3P
- Two other reactions each yield one ATP per G3P molecule. This part of the patherway is called **substrate-level phosphorylation**
- The final product is two 3 carbon molecules of **pyruvate**





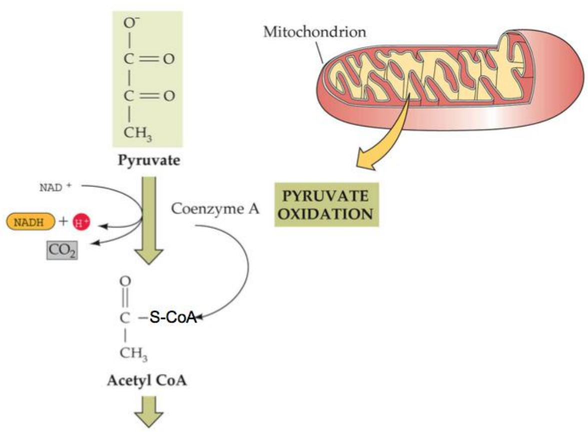




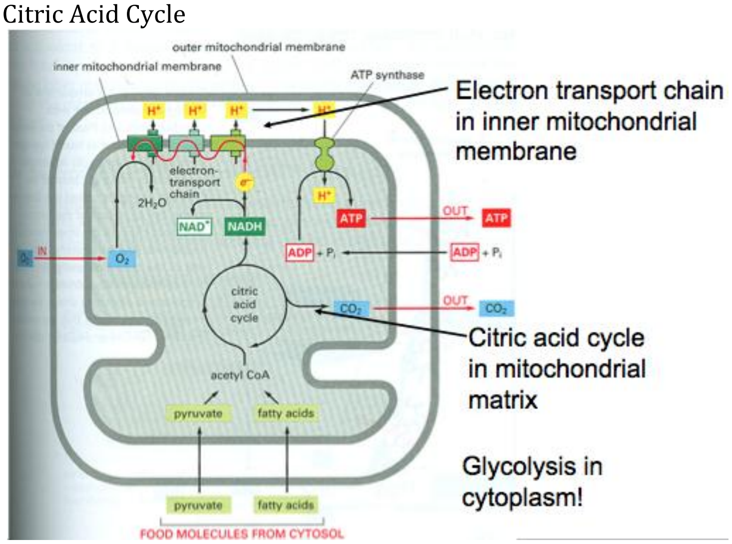
For sequential reaction, ΔG values are additive

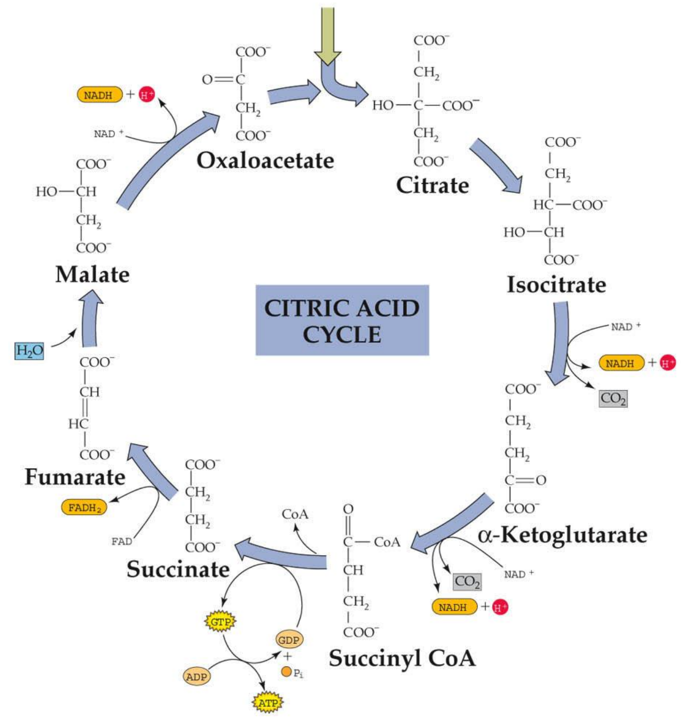
Unfavorable reactions (positive ΔG°) can be directly coupled to favorable ones (hydrolysis of ATP) or indirectly, by sequential coupling

- Pyruvate is oxidized to acetate which is converted to acetyl CoA, which is fed into the citric acid cycle
- Pyruvate oxidation is a multistep reaction catalyzed by an enzyme complex (60 subunits) in the mitochondrial matrix
- The acetyl group is added to coenzyme A to form acetyl CoA – One NADP + H+ is generated during this reaction



Citric Acid Cycle





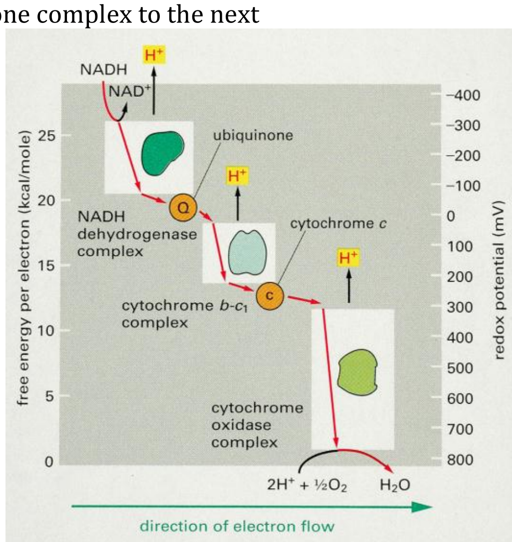
LIFE: THE SCIENCE OF BIOLOGY, Seventh Edition, Figure 7.8 Pyruvate Oxidation and the Citric Acid Cycle (Part 2)

Electron Transport Chain

- The respiratory chain (or electron transport chain) uses NADH + H^+ and $FADH_2$ generated during sugar oxidation
- The flow of electrons in a series of redox reactions causes the active transport of protons across the inner mitochondrial membrane, creating a proton concentration gradient
- The protons then diffuse through proton channels down the concentration and electrical gradient back into the matrix of the mitochondria, creating ATP in the process
- ATP synthesis by electron transport is called **oxidative phosphorylation**

→ The electron transport chain consists of three large protein complexes bound to the inner mitochondrial membrane, plus **cytochrome c** and **ubiquinone**

Cytochrome c and **ubiquinone** are hydrophobic carriers that shuttle hydrogen atoms or electrons from one complex to the next



A series of redox reactions is coupled to hydrogen transport

➔ The electron transport chain produces a proton gradient

How is hydrogen transported?

For example, cytochrome c reduces cytochrome c oxidase by passing on its electrons. **Oxidation of the enzyme induces a conformational change resulting in the transport of H+**

What happens with the protons?

- NADH + H^+ or $FADH_2$ yield energy upon oxidation
- As electrons pass through the respiratory chain, protons are pumped by active transport into the intermembrane space against their concentration gradient
- This transport results in a difference in electric charge and in a pH difference across the membrane
- The potential energy generated is called the **proton – motive force**

The pumping of protons in the electron transport chain followed by ATP synthesis is called **oxidative phosphorylation** (in aerobic respiration in mitochondria and prokaryotes)

The same mechanism occurs during photosynthesis in chloroplasts and prokaryotes **(photophosphorylation)**

➔ ATP synthesis is reversible – If ATP accumulates in the matrix or proton-motive force drops, ATP synthase reverses; occurs in bacteria when they grow without oxygen

Can a hydrogen gradient drive ATP synthesis in isolated mitochondria?

1. Place isolated mitochondria or bacteria in test tube
2. Add cyanide
3. Measure [ATP] before and after lowering pH

Electron transport chain can be uncoupled from ATP production by hydrogen channel to produce heat (when flow of 3 H+ is coupled to ATP production, only -2kcal/mole of heat/disorder is released. Without ATP production ΔG is -14kcal/mole)

Regulation

The main control point in Glycolysis is the kinase that adds the second phosphate to the C6.

- This enzyme is inhibited by high [ATP] and activated by high [ADP]

The main control point of the citric acid cycled is the first **dehydrogenase** in the cycle

- High [NAD+] activate this dehydrogenase; high [NADP + H+] inhibits

Electron transport chain is regulated by H+ gradient: low electrochemical gradient results in faster electron transport

→ In absence of oxygen…

Electron transport chain shuts down because there is no electron acceptor; ATP synthase stops

In Pyruvate oxidation and citric acid cycle → they can no longer operate because they need a lot of NAD+, which is provided by NADH + H+ oxidation in the electron transport chain

Fermentation

→ Some cells under anaerobic conditions continue glycolysis and produce a limited amount of ATP if **fermentation** regenerates the NAD+ to keep glycolysis going

➔ Occurs in the cytoplasm (like glycolysis)

Lactic acid fermentation (essentially a step back: you have to reduce pyruvate in order to replenish NAD+; pyruvate replaces oxygen as electron acceptor)

Lactic acid fermentation occurs in some microorganisms (yogurt; cheese; salami, etc)

Anabolic interconversions:

- **Glyconeogensis** is the process by which intermediate of glycolysis and the citric acid cycle are used to form glucose
- Acetyl CoA can form fatty acids
- Intermediates can form amino acids and purines/pyrimidines

What happens if inadequate food molecules are available?

- Glycogen stores in muscle and liver are used first
- Fats are used next; but the brain can only use glucose, so it must be synthesized by **gluconeogensis**
- After fates are depleted, proteins alone provide energy