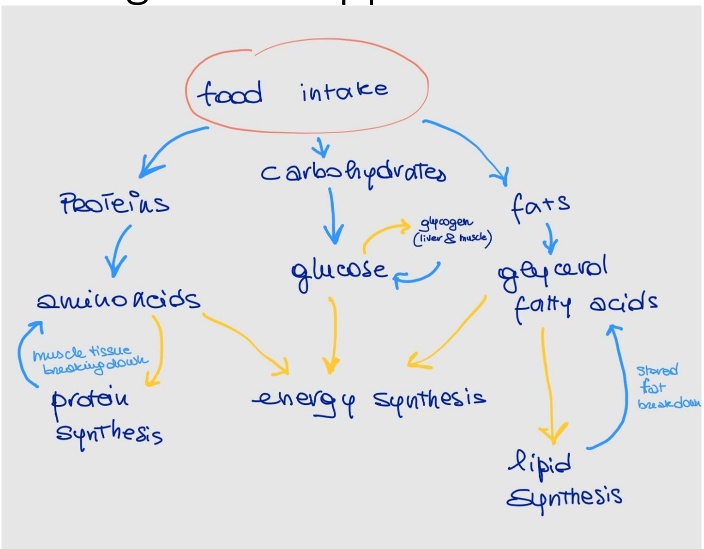
Metabolism
energetic strategies and applications



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Most, although not all, of the biochemical processes of bacteria also occur in eukaryotic microbes and in the cells of multicellular organisms, including humans.

reactions that are unique to bacteria allow microorganisms to do unique processes

chemical reactions that either produce energy (the catabolic reactions) or use energy (the anabolic reactions) in microorganisms.

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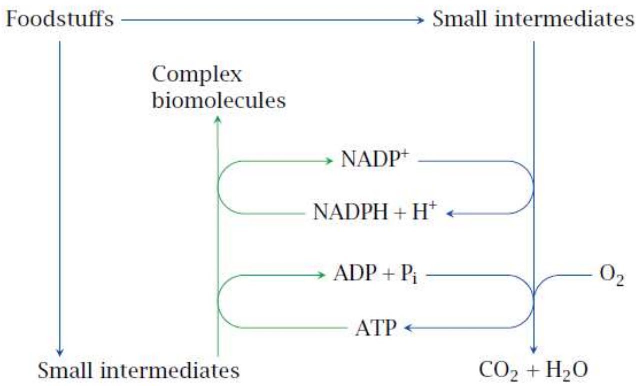
Food made of building blocks:
- carbohydrates
- protein
- fat
- nucleic acids



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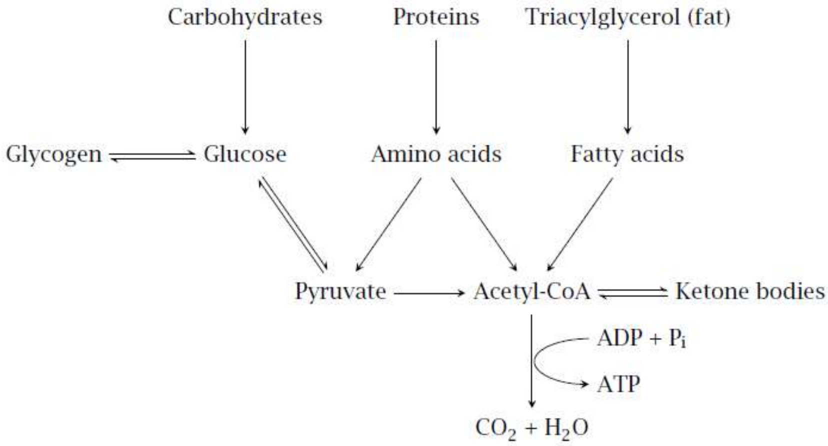

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Cellular metabolism

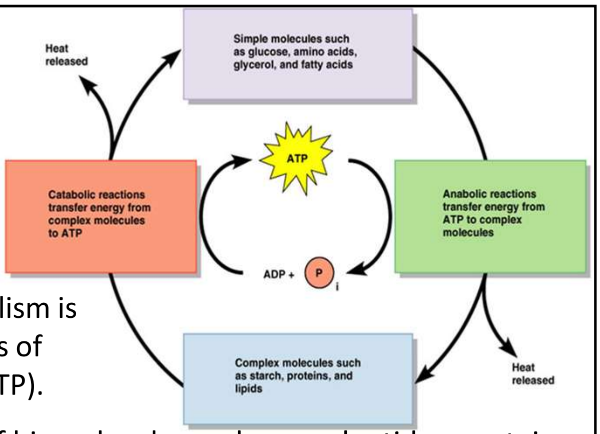
reactions and pathways by which biomolecules are synthesized and degraded

Highly coordinated cellular activity

It is needed to:

1. Obtain energy for the cell.
2. Convert nutrients into macromolecules.
3. Assemble macromolecules into cellular structures.
4. Degrade macromolecules as required for biological function.

Catabolism: degradation pathways to salvage components and energy from biomolecules such as nucleotides, proteins, lipids and polysaccharides. It generates energy. Energy liberated by catabolism is stored in energy-rich bonds of adenosine triphosphate (ATP).

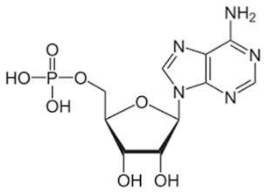


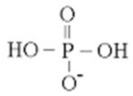
Anabolism: biosynthesis of biomolecules such as nucleotides, proteins, lipids and polysaccharides from simple precursor molecules. It requires energy.

Some pathways can function both in a catabolic and an anabolic context.

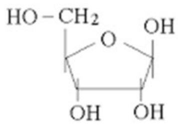
An example is the citric acid cycle, which breaks down acetyl-CoA but also participates in the synthesis of amino acids. Such pathways are sometimes referred to as *amphibolic*.

Biomolecules: examples

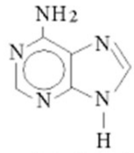




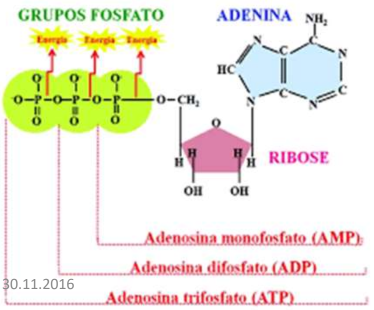
acido fosforico



ribosio



base azotata (adenina)



All living things require a source of energy, carbon, oxygen and nitrogen

Energy and Carbon

Autotrophs: prokaryotes that can produce all of their cellular components from simple molecules such as H_2O, CO_2, NH_3 and H_2S.

These are self sufficient cells that utilize CO_2 from the atmosphere as the carbon source.

Chemolithotrophs obtain free energy via the oxidation of inorganic compounds such as NH_3, H_2S or Fe^{+2}.

Photoautrophs obtain free energy from light photons via photosynthesis.

Heterotrophs: obtain energy by oxidation of organic compounds (carbohydrates, lipids, or protein).

Heterotrophs obtain carbon from glucose, proteins and lipids.

Oxygen
obtainable from the atmosphere or from water.

Aerobes live in the presence of oxygen. They use oxygen to oxidize organic nutrients.

Anaerobes live in the absence of oxygen. Catabolize nutrients without molecular oxygen.

Obligate anaerobes are poisoned by oxygen.

Facultative Some organisms can live in either aerobic or anaerobic conditions (yeast and *E. coli*).

Nitrogen

All living things require nitrogen.

Most animals obtain nitrogen from amino acids. Plants are able to use ammonia or nitrates as nitrogen sources.

Only a few organisms can fix N_2 (cyanobacteria and blue-green algae and symbiotic relationship).

Take home message

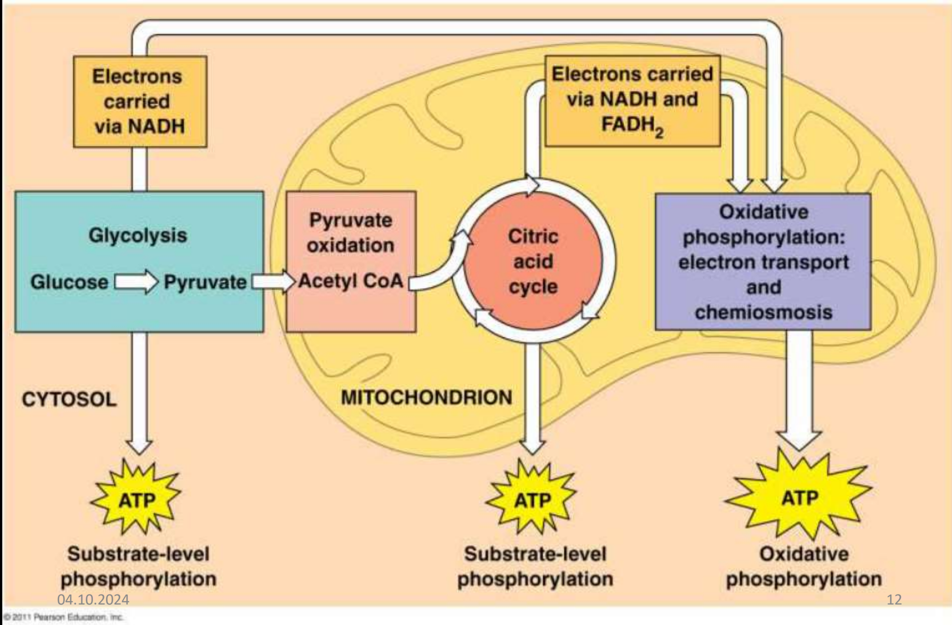
Metabolism is the sum of all chemical reactions within a living organism, including anabolic (biosynthetic) reactions and catabolic (degradative) reactions.

Anabolism is the combination of simpler substances into complex substances and requires energy.

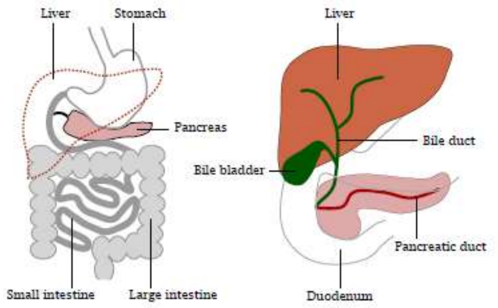
Catabolism releases energy stored in organic molecules, for example, and yields energy.

Energy liberated by catabolism is stored in energy-rich bonds of adenosine triphosphate (ATP).

General overview



Digestive system



Organ	Function
stomach	killing of microbes contained in the food; protein denaturation
small intestine	breakdown of macromolecules to small molecules, uptake of the latter
large intestine	fluid and ion reuptake
pancreas	production of digestive enzymes and of hormones
liver	production of bile; metabolic homeostasis

From food to ATP

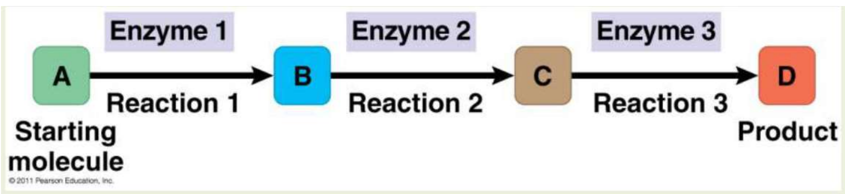
- **Amylas**e in saliva starts to break down starches to disaccharides
- **Stomach acid** breaks apart large structures such as cells and intercellular structures
- **Amylase** in the small intestine completes the breakdown of all carbohydrates to disaccharides
- **Maltases, lactases, and sucrases** break down disaccharides into monosaccharides
- **Glucose** is brought to all the cells in the body through the circulatory system

Metabolic pathway

a sequence of enzymatically catalyzed chemical reactions in a cell.

Metabolic pathways are determined by enzymes and consist of sequential steps.

The substrates of these enzymes are called metabolites.

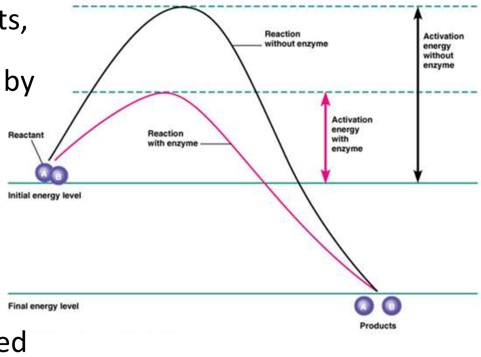


Enzymes

proteins that function as catalysts, substances that speed up a reaction without being changed by it; they lower the activation energy needed.

An enzyme has a three-dimensional structure, with an active site that reacts with the surface of a substrate .

The **turnover number** is the number of molecules metabolized per enzyme molecule per second.



Enzymes generally are named after the substrate they react with or the type of reaction they perform, using the suffix -ase.

Examples
dehydrogenase for enzymes that remove hydrogen
oxidase for enzymes that add oxygen.

The Mechanism of Enzymatic Action

The surface of the substrate contacts a specific region of the surface of the enzyme molecule, called the active site.

1. A temporary intermediate compound forms *enzyme–substrate complex*.
2. The substrate molecule is transformed by the rearrangement of existing atoms, the breakdown of the substrate molecule, or in combination with another substrate molecule.
3. The transformed substrate molecules *products of the reaction* are released from the enzyme molecule as they no longer fit in the active site of the enzyme.
4. The unchanged enzyme is now free to react with other substrate molecules.
5. As a result of these events, an enzyme speeds up a chemical reaction.

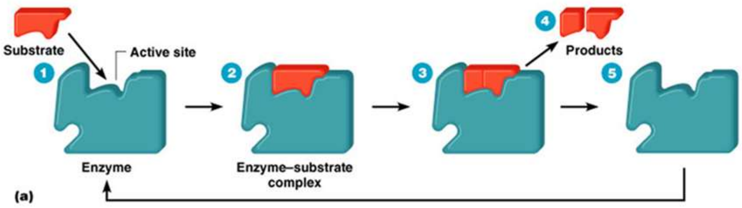
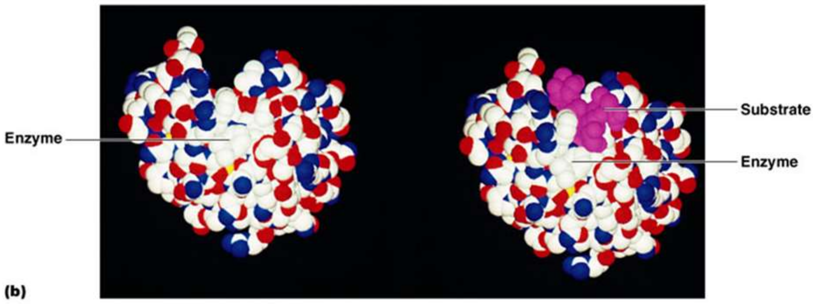


Table 5.1	Enzyme Classification Based on Type of Chemical Reaction Catalyzed	
Class	**Type of Chemical Reaction Catalyzed**	**Examples**
Oxidoreductase	Oxidation-reduction, in which oxygen and hydrogen are gained or lost	Cytochrome oxidase, lactate dehydrogenase
Transferase	Transfer of functional groups, such as an amino group, acetyl group, or phosphate group	Acetate kinase, alanine deaminase
Hydrolase	Hydrolysis (addition of water)	Lipase, sucrase
Lyase	Removal of groups of atoms without hydrolysis	Oxalate decarboxylase, isocitrate lyase
Isomerase	Rearrangement of atoms within a molecule	Glucose-phosphate isomerase, alanine racemase
Ligase	Joining of two molecules (using energy usually derived from the breakdown of ATP)	Acetyl-CoA synthetase, DNA ligase



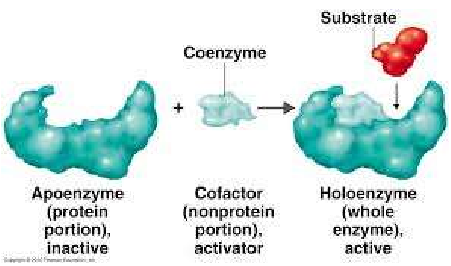
Enzyme structure

Many enzymes contain an **apoenzyme**, a protein that is inactive without a **cofactor**, a nonprotein component.

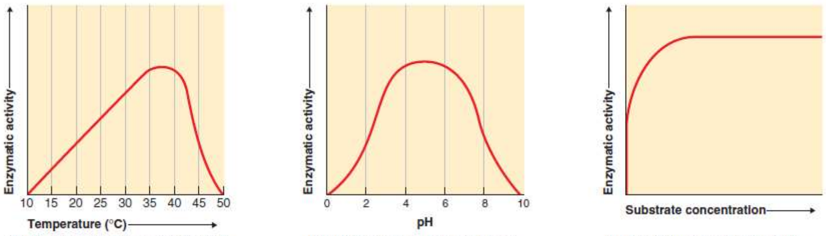
Together, they are an activated **holoenzyme** (whole enzyme).

Cofactors may serve as a bridge binding enzyme and substrate together.

Cofactors may be metal ions or organic molecules called coenzymes.



Factors Influencing Enzymatic Activity



(a) Temperature. The enzymatic activity (rate of reaction catalyzed by the enzyme) increases with increasing temperature until the enzyme, a protein, is denatured by heat and inactivated. At this point, the reaction rate falls steeply.

(b) pH. The enzyme illustrated is most active at about pH 5.0.

(c) Substrate concentration. With increasing concentration of substrate molecules, the rate of reaction increases until the active sites on all the enzyme molecules are filled, at which point the maximum rate of reaction is reached.

Denaturation of an enzyme changes the arrangement of the amino acids in the active site, altering its shape and causing the enzyme to lose its catalytic ability.

Inhibitors

An effective way to control the growth of bacteria is to control their enzymes. Certain poisons, such as cyanide, arsenic, and mercury, combine with enzymes and prevent them from functioning.

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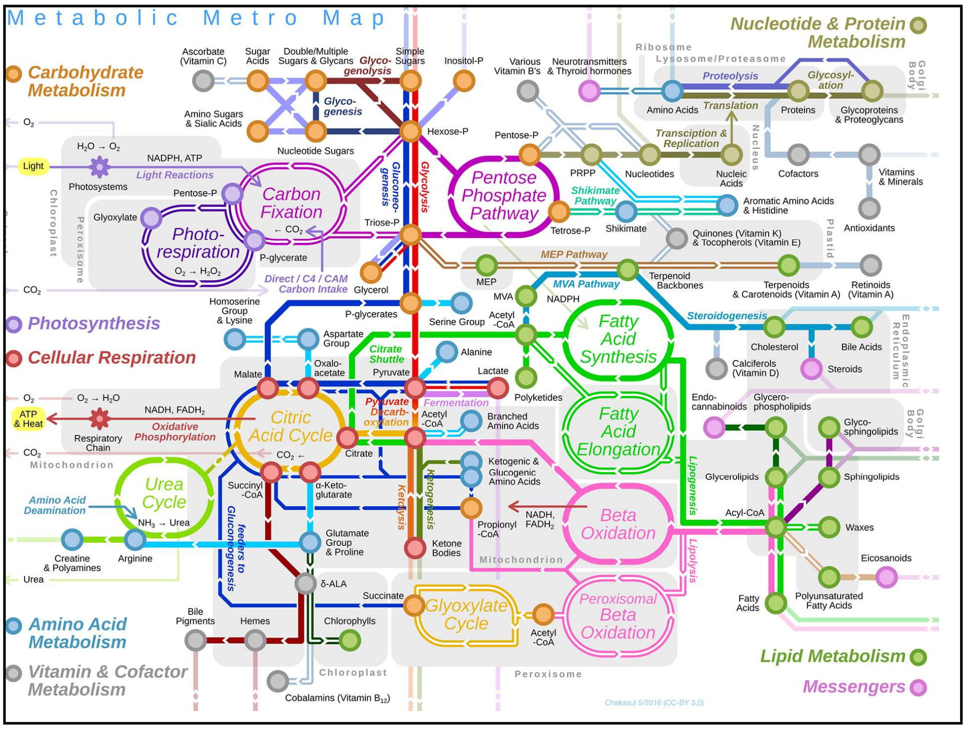

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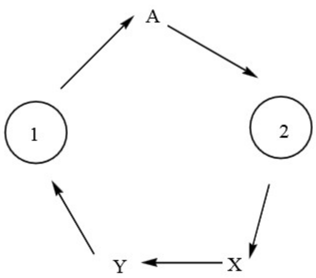
- http://www.metabolic-pathway.com/fullMap.html

Metabolic pathways: properties

Metabolic pathways are irreversible

Metabolic pathways are highly exergonic which gives the pathway direction. Consequently if two metabolites are interconvertible, the pathway from the first to the second must be different than the pathway of the second back to the first. This independent interconversion allows the two pathways to be independently regulated.



Every metabolic pathway has a first committed step

Most of the reactions in a metabolic pathway are close to equilibrium, but every pathway has an irreversible highly exergonic reaction that commits the intermediate it produces to continue down the pathway.

All metabolic pathways are regulated

The control of the metabolic flux of metabolites through a pathway is accomplished by regulating the rate determining step of the pathway which often is the first committed step of the pathway.

Compartmentalization of Metabolic Pathways

Eukaryotes use organelles to compartmentalize pathways to occur in specific locations.

Mitochondrion - Citric acid cycle, oxidative phosphorylation, amino acid catabolism.

Cytosol – Glycolysis, pentose phosphate pathway, fatty acid biosynthesis, gluconeogenesis.

Nucleus – DNA replication, RNA transcription, RNA processing.

Lysosomes – Enzymatic digestion of cellular components.

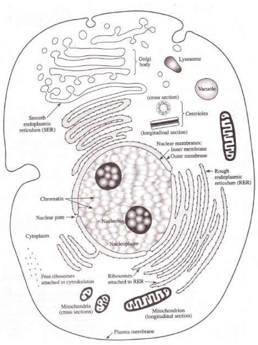
Golgi Apparatus – Post translational modification of membrane and secretory proteins, formation of plasma membranes and secretory vesicles.

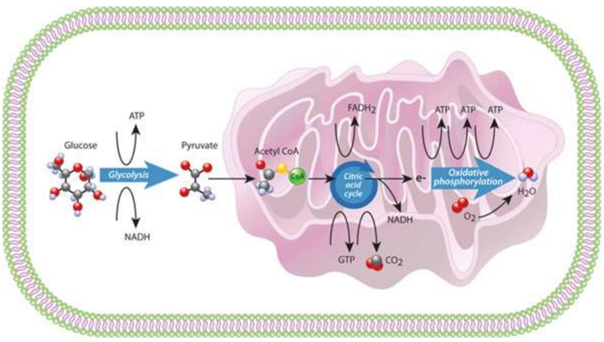
Rough Endoplasmic Reticulum – Synthesis of membrane-bound and secretory proteins.

Smooth Endoplasmic Reticulum – Lipid and steroid biosynthesis.

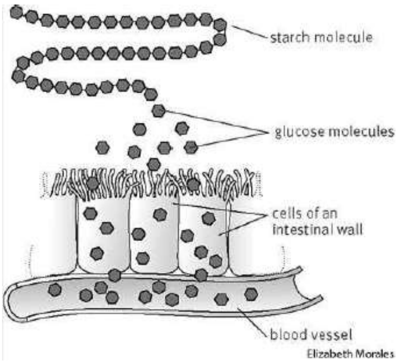
Peroxisomes - Oxidative reactions involving amino acid oxidases and catalase, glyoxylate cycle reactions in plants.

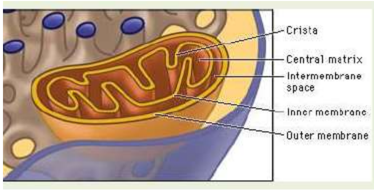
Where is the energy produced inside the cell?





- Glucose is brought inside the cell by cotransport with sodium
- The mitochondria are where ATP is produced





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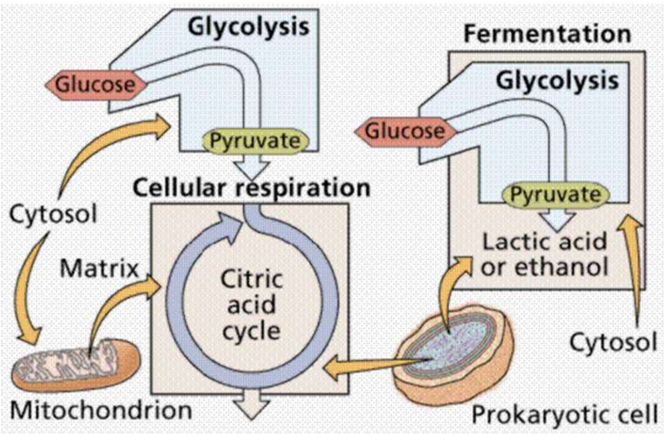

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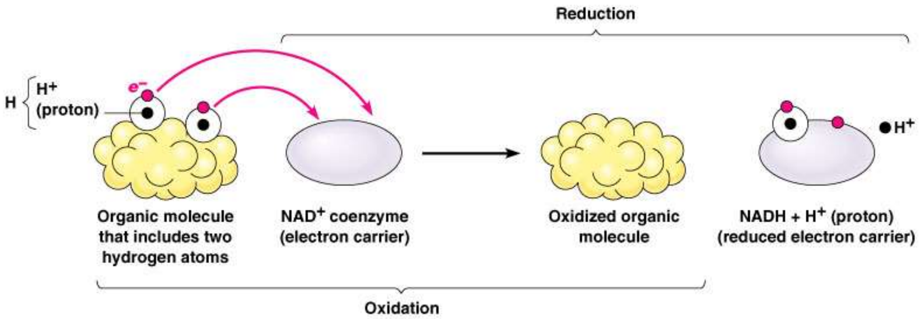
Energy transfer

Oxidation-Reduction and Phosphorylation-Dephosphorylation reactions

In biological systems, the electrons are often associated with hydrogen atoms.

Biological oxidations are often dehydrogenations.



Free Energy and ATP

The energetics of biochemical reactions are best described in terms of the thermodynamic function called **Gibbs free energy** (G)

The change in free energy (ΔG) of a reaction combines the effects of changes in **enthalpy** (the heat that is released or absorbed during a chemical reaction) and **entropy** (the degree of disorder resulting from a reaction) to predict whether a reaction is energetically favorable.

All chemical reactions spontaneously proceed in the energetically favorable direction, accompanied by a decrease in free energy ($\Delta G < 0$).

$A \rightleftharpoons B$

$\longrightarrow$

If ΔG < 0, this reaction will proceed in the forward direction, as written.

If ΔG > 0, however, the reaction will proceed in the reverse direction and B will be converted to A.

Standard conditions are considered to be a 1M concentration of all reactants and products, and 1 atm of pressure
The ΔG of a reaction is defined under standard conditions.
The standard free-energy change (ΔG°) of a reaction is directly related to its equilibrium position because the actual ΔG is a function of both ΔG° and the concentrations of reactants and products

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$A \rightleftharpoons B$

The free-energy change for this reaction can be written as

$$\Delta G = \Delta G^\circ + RT \ln [B]/[A]$$

where R is the gas constant and T is the absolute temperature.

At equilibrium, ΔG= 0 and the reaction does not proceed in either direction. The equilibrium constant for the reaction (K= [B]/[A] at equilibrium) is thus directly related to ΔG° by the above equation, which can be expressed as follows:

$$0 = \Delta G^\circ + RT \ln K \qquad \Delta G^\circ = -RT \ln K$$

If the actual ratio [B]/[A] is greater than the equilibrium ratio (K), ΔG > 0 and the reaction proceeds in the reverse direction (conversion of B to A). On the other hand, if the ratio [B]/[A] is less than the equilibrium ratio, ΔG < 0 and A is converted to B.

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For biochemical reactions, the standard free-energy change is usually expressed as ΔG°′, which is the standard free-energy change of a reaction in aqueous solution at pH= 7, approximately the conditions within a cell.

Many biological reactions (such as the synthesis of macromolecules) are thermodynamically unfavorable (ΔG > 0) under cellular conditions.
In order for such reactions to proceed, an additional source of energy is required.

For example, consider the reaction

$$A \rightleftharpoons B \qquad \Delta G = +10 \text{ kcal/mol}$$

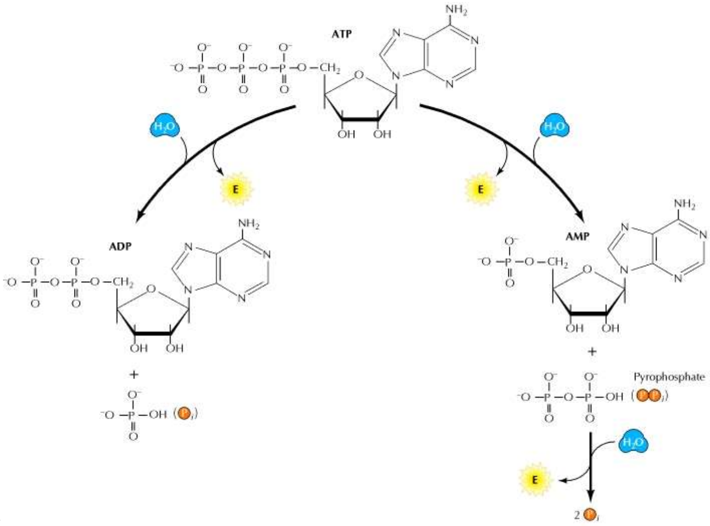
The conversion of A to B is energetically unfavorable, so the reaction proceeds in the reverse rather than the forward direction.
However, the reaction can be driven in the forward direction by coupling the conversion of A to B with an energetically favorable reaction, such as:

$$C \rightleftharpoons D \qquad \Delta G = -20 \text{ kcal/mol}$$

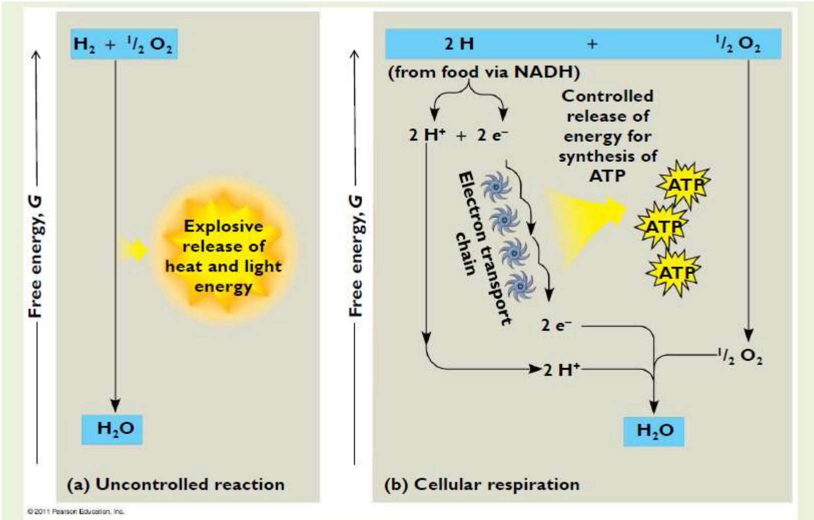
If these two reactions are combined, the coupled reaction can be written as follows:

$$A + C \rightleftharpoons B + D \qquad \Delta G = -10 \text{ kcal/mol}$$

Adenosine 5′-triphosphate (ATP) as a store of free energy within the cell



Role of ATP



The chemical reactions in respiration

- Redox reactions
- Phosphorylation/dephosphorylation
  - Carried out by kinases and phosphatases
  - Phosphorylation increases chemical potential energy and "primes" the molecule for work

Redox (*again…*)

chemistry definition

Oxidation and **reduction** are the reaction occurring in respiration OIL RIG

Oxidation is "losing" Reduction is "gaining"

What is being lost and gained? Electrons!

Electrons are usually lost to oxygen

Oxygen is highly electronegative

Oxidation and reduction reactions are often coupled, and together are called **redox** reactions

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Redox (*again…*)

biology definition

Oxidation and **reduction**

Losing a hydrogen atom Gaining a hydrogen atom

In biochemical reactions, hydrogen is what usually gets swapped around

Hydrogen almost always bonds to an atom that is more electronegative (C, O, N, P), and so loses its electron

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The bonds between the phosphates in ATP are known as high-energy bonds because their hydrolysis is accompanied by a relatively large decrease in free energy.

In the hydrolysis of ATP to ADP plus phosphate (Pi), $\Delta G°' = -7.3$ kcal/mol. **ΔG°′ refers to "standard conditions," in which the concentrations of all products and reactants are 1 M.**

Actual intracellular concentrations of Pi are approximately 10^{-2}M, and intracellular concentrations of ATP are higher than those of ADP. These differences between intracellular concentrations and those of the standard state favor ATP hydrolysis, so for ATP hydrolysis within a cell, ΔG is approximately -12 kcal/mol.

ATP can be hydrolyzed to AMP plus pyrophosphate (PPi). This reaction yields about the same amount of free energy as the hydrolysis of ATP to ADP does. However, the pyrophosphate produced by this reaction is then itself rapidly hydrolyzed, with a ΔG similar to that of ATP hydrolysis. Thus, the total free-energy change resulting from the hydrolysis of ATP to AMP is approximately twice that obtained by the hydrolysis of ATP to ADP. For comparison, the bond between the sugar and phosphate group of AMP, rather than having high energy, is typical of covalent bonds; for the hydrolysis of AMP, $\Delta G°' = -3.3$ kcal/mol.

The Generation of ATP

Three main ways:

- <u>Photophosphorylation</u> - using light energy to phosphorylate ADP to ATP
- <u>Substrate level phosphorylation</u> - a transfer of a phosphate group from one molecule to another
  - 1,3-diphosphoglyceric acid + ADP → ATP + 3-phosphoglyceric acid
- <u>Oxidative phosphorylation</u> - energy released from the transfer of electrons (oxidation) of one compound to another (reduction) can used to generate ATP by **chemiosmosis**.

Photophosphorylation

- Light causes chlorophyll to give up electrons. Energy released from the transfer of electrons (oxidation) of chlorophyll through a system of carrier molecules is used to generate ATP.

Phosphorylation and Dephosphorylation

Transferring a phosphate group.

- Adding is Phosphorylation - storing energy
- Removing is Dephosphorylation - releasing energy
  - ATP is generated by the phosphorylation of ADP.

$$\overbrace{\text{Adenosine}-\text{P}\sim\text{P}}^{\text{ADP}} + \text{Energy} + \text{P} \rightarrow \underbrace{\text{Adenosine}-\text{P}\sim\text{P}\sim\text{P}}_{\text{ATP}}$$

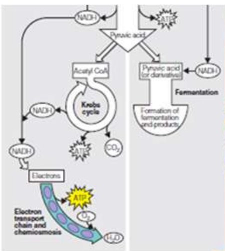
The Generation of ATP

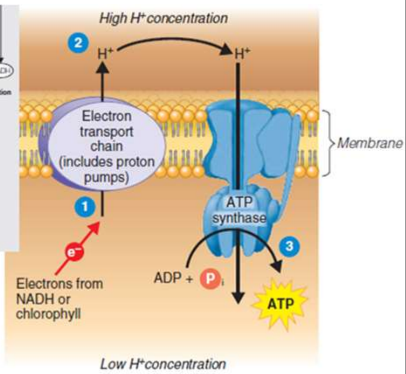
- Substrate-level phosphorylation is the transfer of a high-energy PO_4^- to ADP.

$$\mathrm{C{-}C{-}C} \sim \text{Ⓟ} + \mathrm{ADP} \longrightarrow \mathrm{C{-}C{-}C} + \mathrm{ATP}$$

chemiosmosi

As energetic electrons from NADH (or chlorophyll) pass down the electron transport chain, some of the carriers in the chain pump—actively transport—protons across the membrane.





Such carrier molecules are called *proton pumps.* The phospholipid membrane is normally impermeable to protons, so this one-directional pumping establishes a **proton gradient** (a difference in the concentrations of protons on the two sides of the membrane).
In addition to a concentration gradient, there is an electrical charge gradient.
The excess H+ on one side of the membrane makes that side positively charged compared with the other side. The resulting electrochemical gradient has potential energy, called the *proton motive force.* The protons on the side of the membrane with the higher proton concentration can diffuse across the membrane only through special protein channels that contain an enzyme called *ATP synthase.* When this flow occurs, energy is released and is used by the enzyme to synthesize ATP from ADP and Pi.

Because of the accompanying decrease in free energy, the hydrolysis of ATP can be used to drive other energy-requiring reactions within the cell. For example, the first reaction in glycolysis (discussed in the next section) is the conversion of glucose to glucose-6-phosphate. The reaction can be written as follows:

$$\text{Glucose} + \text{Phosphate } (HPO_4^{2-}) \rightarrow \text{Glucose-6-phosphate} + H_2O$$

Because this reaction is energetically unfavorable as written ($\Delta G°' =$ +3.3 kcal/mol), it must be driven in the forward direction by being coupled to ATP hydrolysis ($\Delta G°' =$ -7.3 kcal/mol):

$$ATP + H_2O \rightarrow ADP + HPO_4^{2-}$$

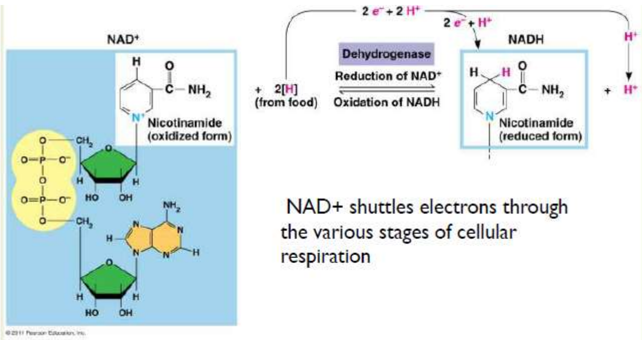
The combined reaction can be written as follows:

$$\text{Glucose} + ATP \rightarrow \text{Glucose-6-phosphate} + ADP$$

The free-energy change for this reaction is the sum of the free-energy changes for the individual reactions, so for the coupled reaction $\Delta G°' =$ -4.0 kcal/mol, favoring glucose-6-phosphate formation.

Electron carriers (shuttles)

- NAD+ and NADH coenzyme derived from niacin
- FAD and $FADH_2$ derived from riboflavin



NAD+ accepts electrons and becomes NADH

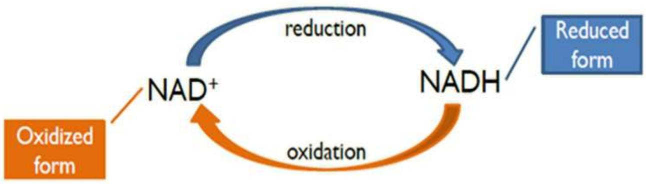
NAD+ is reduced into NADH

NADH is a reducing agent, and is recycled back to

NAD+ through oxidation

Each NADH (the reduced form of NAD+) represents stored energy that is tapped to synthesize ATP.

Each NADH produces 3 ATPs in the e- transport chain



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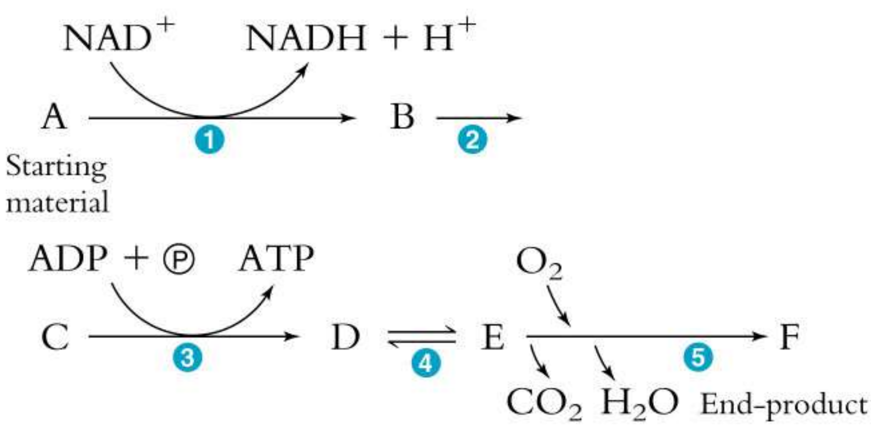
Metabolic Pathways



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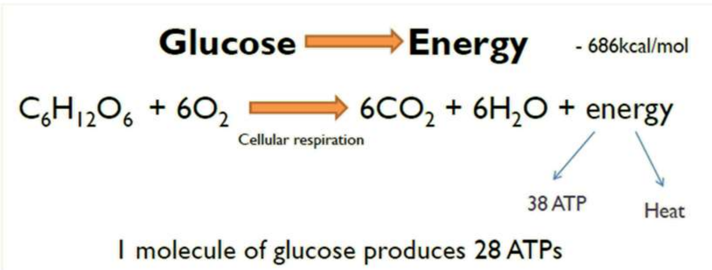
Carbohydrate Catabolism

- The breakdown of carbohydrates to release energy
  - Glycolysis
    - Fermentation
  - Krebs cycle
  - Electron transport chain

Cellular respiration is the step-by-step release and harness of the chemical potential energy in glucose

To produce energy from glucose, microorganisms use two general processes: cellular respiration and fermentation.



$$C_6H_{12}O_6 + 6\ O_2 \longrightarrow 6\ CO_2 + 6\ H_2O + \text{Energy}$$

Redox reactions in cellular respiration

cellular respiration

- Aerobic respiration – takes place in the presence of oxygen
- Anaerobic respiration – takes place in the absence of oxygen

– Fermentation is a type of anaerobic respiration where sugars are partially degraded

– Consumes compounds other than oxygen

The breakdown of organic molecules is always exergonic

Breaks glucose in half	**glycolysis**	-2 ATP +4 ATP
Half glucose rearrangement	**Citric acid cycle** **Aka** **TCA** **Aka** **Krebbs cycle**	+2 ATP
Glucose electrons are passed	**Electron transport chain**	+34ATP

glycolysis

Who:
- Glucose
- Pyruvate
- ADP/ATP
- Enzymes

what:
- Substrate-level phosphorylation

where:
- Cytoplasm

The production of ATP from ADP by direct transfer of a phosphate group from a phosphorylated protein

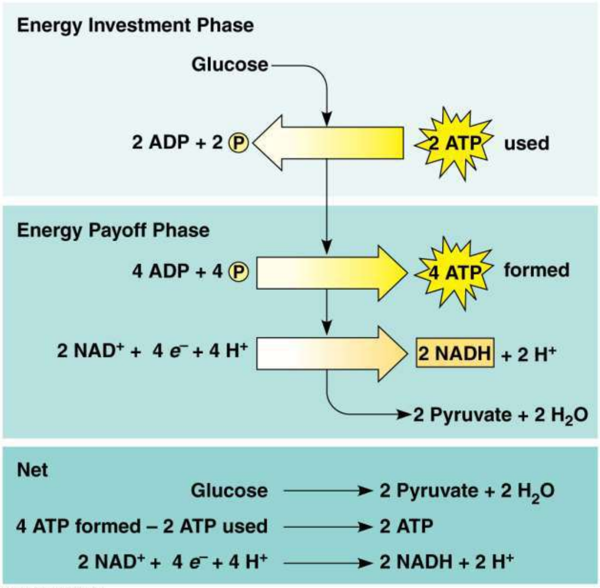
Glycolysis

Glycolysis, the initial stage in the breakdown of glucose, is common to virtually all cells.

Glycolysis occurs in the absence of oxygen and can provide all the metabolic energy of anaerobic organisms.

In aerobic cells, however, glycolysis is only the first stage in glucose degradation

The net reaction (Phase 1 + Phase 2) produces 2 molecules of ATP and 2 molecules of NADH per molecule of glucose



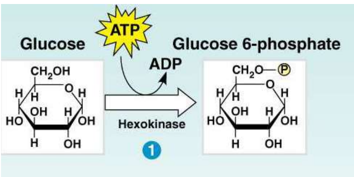
The reactions of glycolysis result in the breakdown of glucose into pyruvate, with the net gain of two molecules of ATP.

The initial reactions (first phase) in the pathway actually consume energy, using ATP to phosphorylate glucose to glucose-6-phosphate and then fructose-6-phosphate to fructose-1,6-bisphosphate.

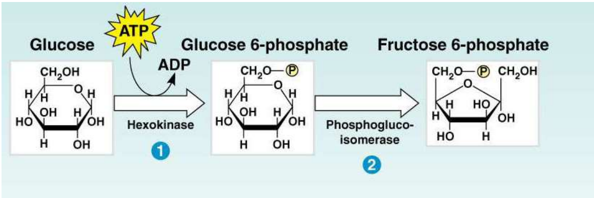
The enzymes that catalyze these two reactions—hexokinase and phosphofructokinase, respectively—are important regulatory points of the glycolytic pathway.

The key control element is phosphofructokinase, which is inhibited by high levels of ATP. Inhibition of phosphofructokinase results in an accumulation of glucose-6-phosphate, which in turn inhibits hexokinase. **Thus, when the cell has an adequate supply of metabolic energy available in the form of ATP, the breakdown of glucose is inhibited.**

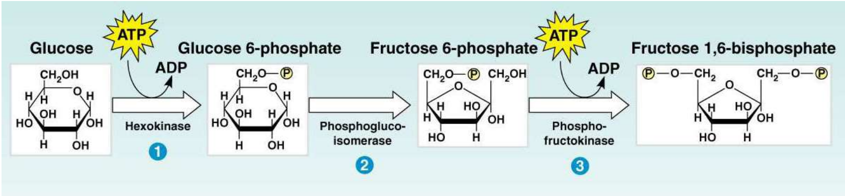
Phase 1 energy investment



Phase 1 energy investment



Phase 1 energy investment



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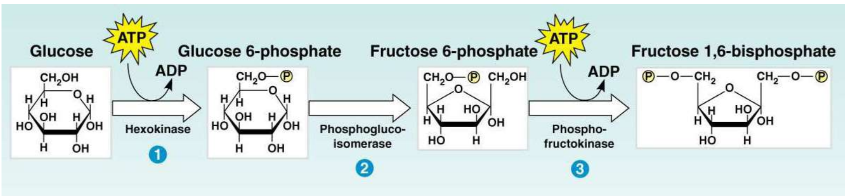
Phase 1 energy investment



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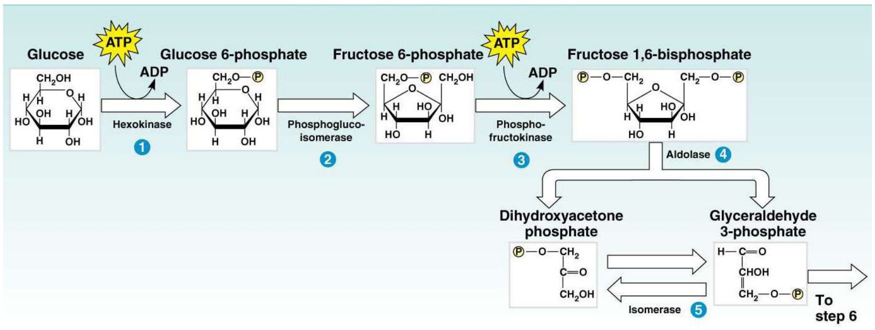
Phase 1 energy investment



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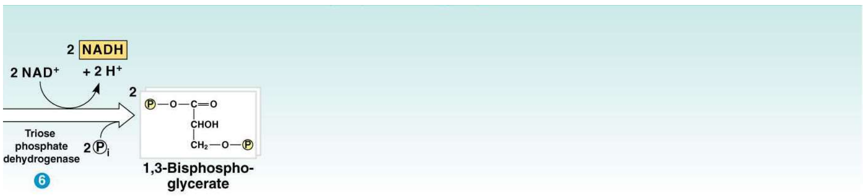
Phase 2 energy pay off



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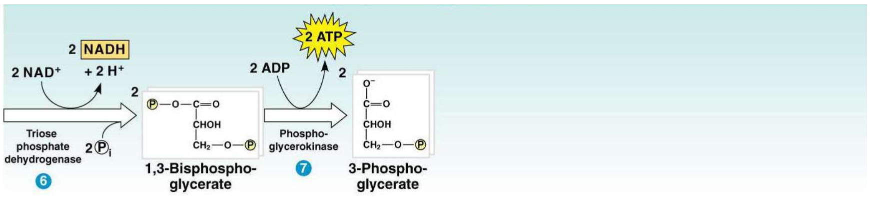
Phase 2 energy pay off



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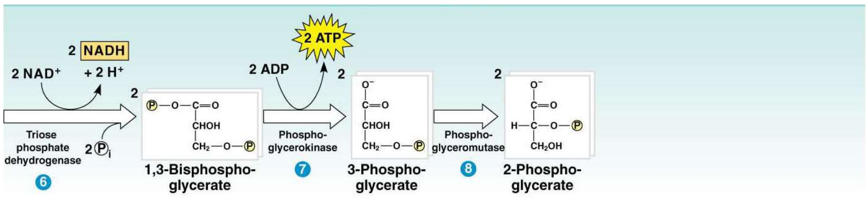
Phase 2 energy pay off



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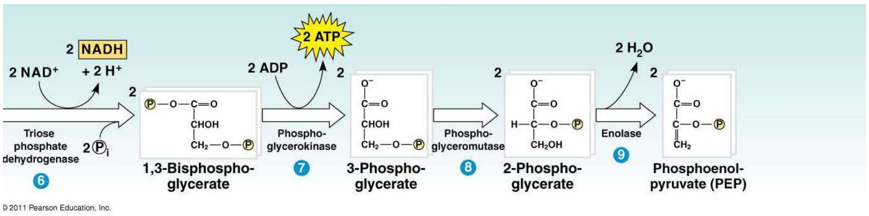
Phase 2 energy pay off



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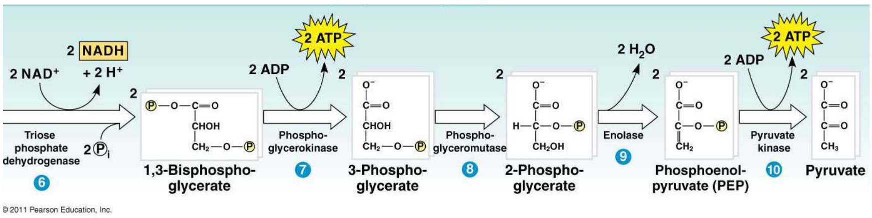
Phase 2 energy pay off



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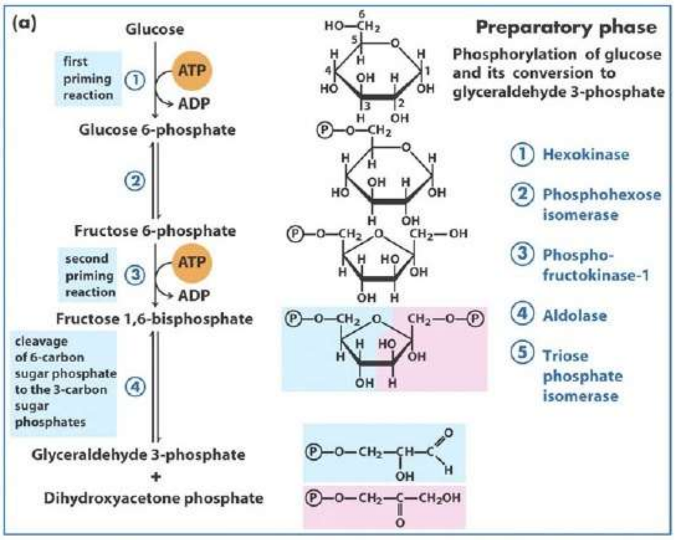
Glycolysis Phase 1



1. the transfer of a phosphoryl group from ATP to glucose.
2. isomerization of glucose 6-phosphate to fructose 6-phosphate.
3. **<u>first committed step of glycolysis</u>** transfer of a second phosphoryl group from ATP to fructose 6-phosphate.
4. aldolytic cleavage of the C3-C4 bond to yield two triose phosphates.
5. rapid isomerization of the triose phosphates

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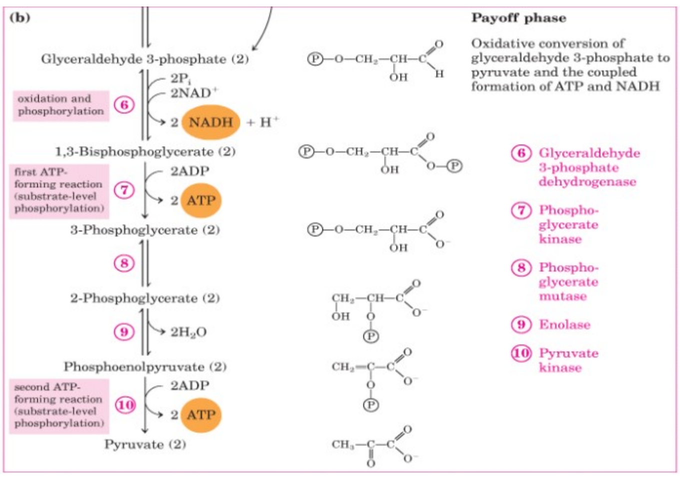
Glycolysis Phase 2



a total of 4 ATP molecules are made. 2 of these are "paid back" because they were used in the first phase of glycolysis (the Preparatory Phase). This leaves 2 molecules of ATP to be gained from this entire phase

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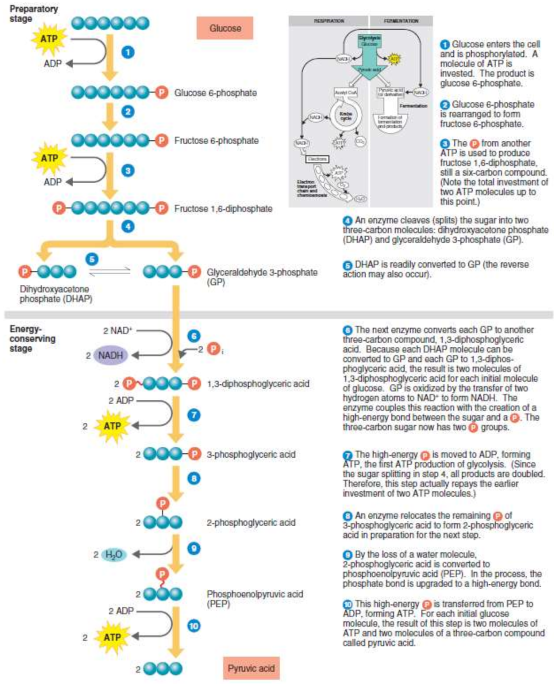

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Glycolysis

We start with
– Glucose
– NAD+
– ADP
We finish with
- – 2 pyruvate
- – 2 NADH
- – 2 ATP

Most of glucose's original energy is still present in pyruvate!

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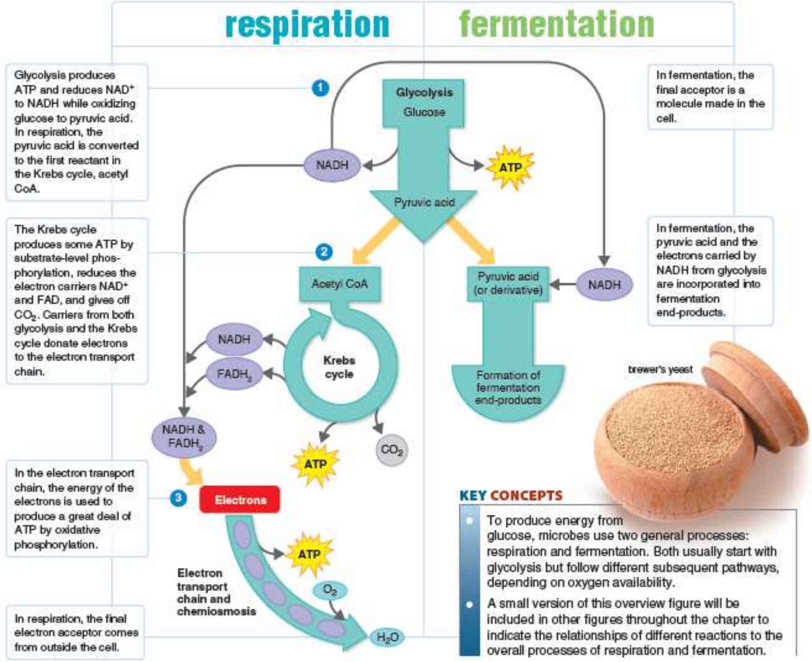

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Fate of Pyruvate

- NADH is formed from NAD+ during glycolysis.
- The redox balance of the cell has to be maintained for further cycles of glycolysis to continue.
- NAD+ can be regenerated by one of the following reactions /pathways:
- Absence of O_2 *fermentation*
  - Pyruvate is converted to lactate
  - Pyruvate is converted to ethanol
- In the presence of O_2,
- NAD+ is regenerated by ETC. pyruvate enters the mitochondrion is converted to acetyl CoA which enters TCA cycle and gets completely oxidized to CO2.

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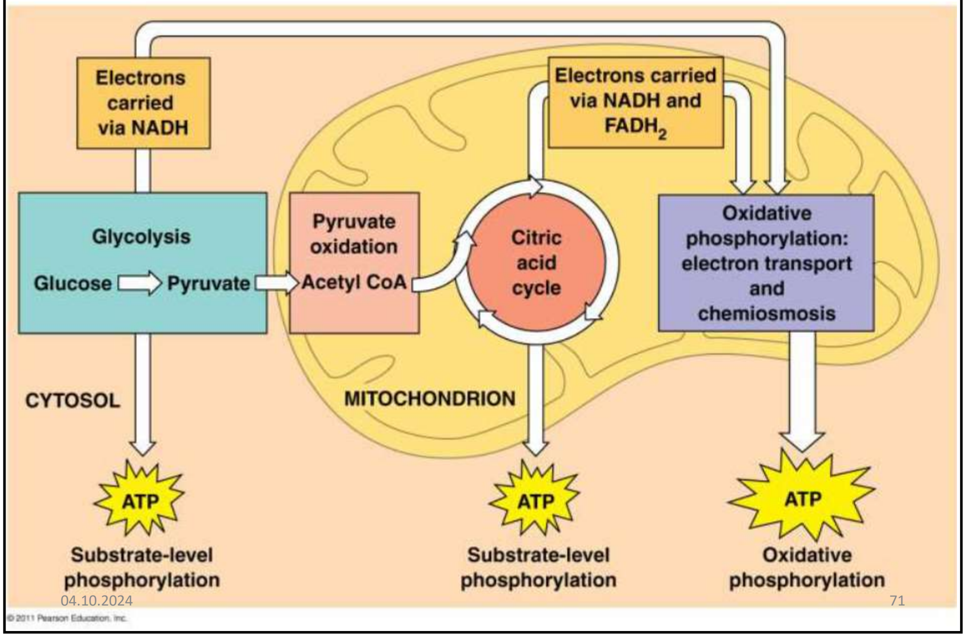
General overview

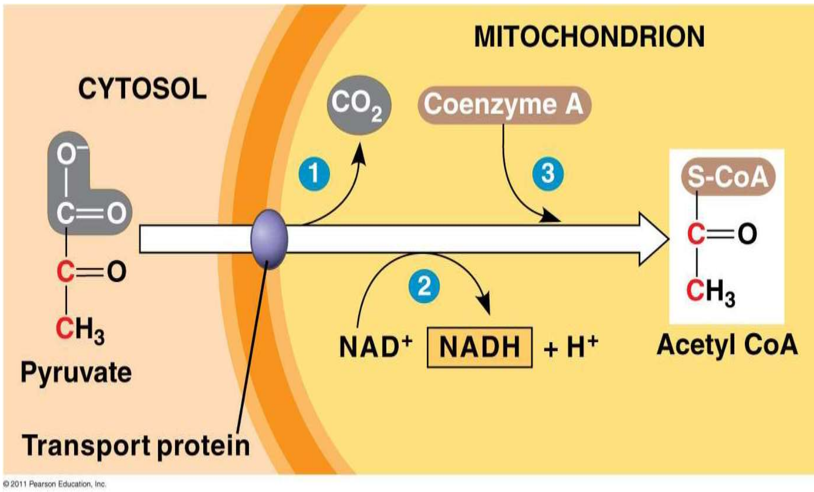


Pyruvate oxidation

Before pyruvate can be fed into TCA cycle, it has to be oxidated to **acetyl-CoA** (acetyl-coenzyme A)

– Produces one NADH from NAD+

– Three-carbon pyruvate is converted into two-carbons + acetyl-CoA



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- Acetyl-CoA couples with oxaloacetate, the
- first molecule in TCA cycle
- • Acetyl-CoA + oxaloacetate = citrate

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Citric acid cycle

Who:
- Acetyl-CoA
- Oxaloacetate
- Plus many more carbon skeleton intermediates
- Enzymes

what:
- Hydrolysis
- Redox reactions

where:
- Mitochondrial matrix

- In eukaryotes, the citric acid cycle takes place in the matrix of the mitochondria, just like the conversion of pyruvate to acetyl CoA.
- In prokaryotes, these steps both take place in the cytoplasm.

TCA

We start with:

Oxaloacetate

1 ADP

3 NAD+

1 FAD

We finish with:

Oxaloacetate

1ATP

3 NADH

1 FADH2

The citric acid cycle, also called the Krebs cycle, completes the break down of pyruvate to CO_2

TCA

The citric acid cycle is the entry point for other catabolic pathways

Acetyl-CoA can be derived from carbohydrates, proteins, and fats

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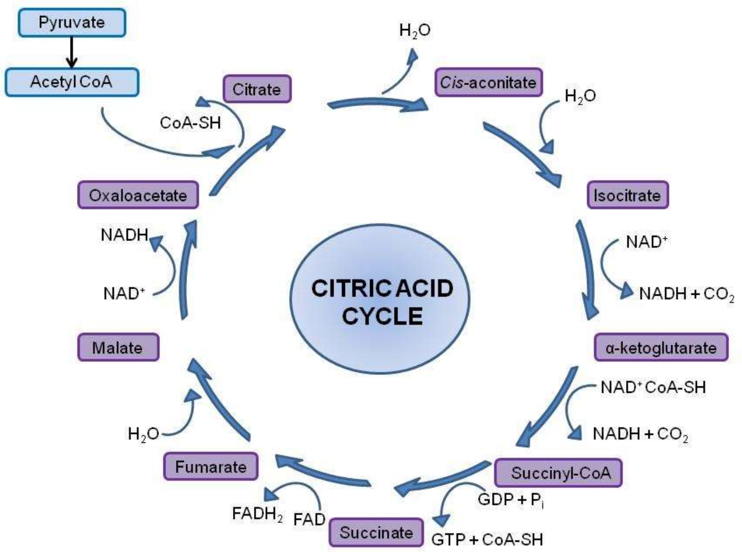

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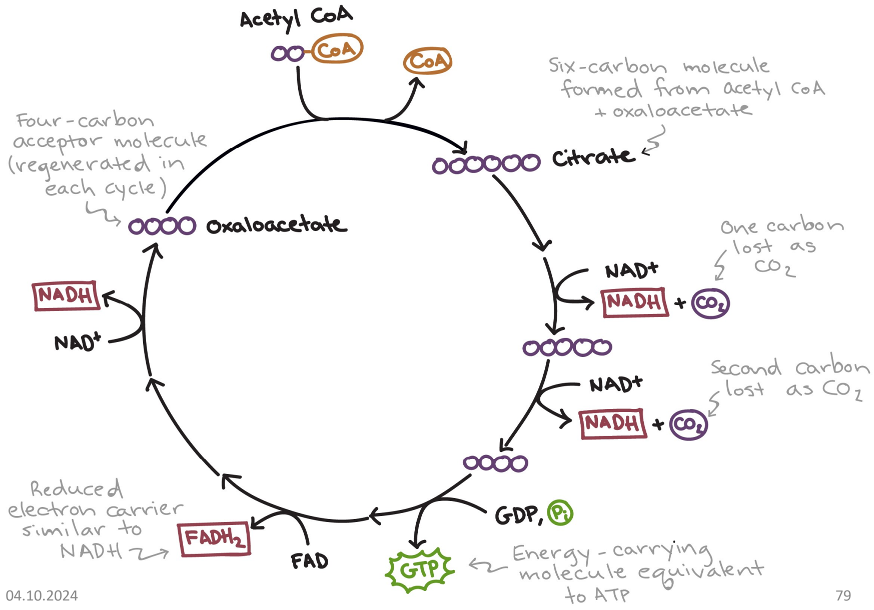

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- <u>Glycolysis</u>
  4 made - 2 used**= 2 ATP** substrate level
  2 NADH x 2= **4 ATP** (enters at complex II)

  <u>Pyruvate Decarboxylation</u>
  1 NADH x two pyruvate= 2 NADH x 3= **6 ATP**

  <u>Krebs Cycle</u>
  3 NADH x two pyruvate= 6 x 3= **18 ATP**
  1 GTP x two pyruvate= 2 GTP= **2 ATP**
  1 FADH2 x two pyruvate= 2 FADH2 x2= **4 ATP**

  Total: 2+4+6+18+2+4= 36 ATP

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electron transport chain

BUT: wasn't it about ATP?

Why are we interested in NADH and FADH2?

These molecules then get oxidized in the electron transport chain

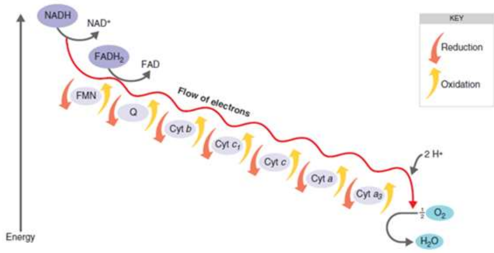
– Every NADH will produce 3 ATP

– Every FADH2 will produce 2 ATP

electron transport chain

the electrons pass along the chain in a gradual and stepwise fashion, so energy is

released in manageable quantities



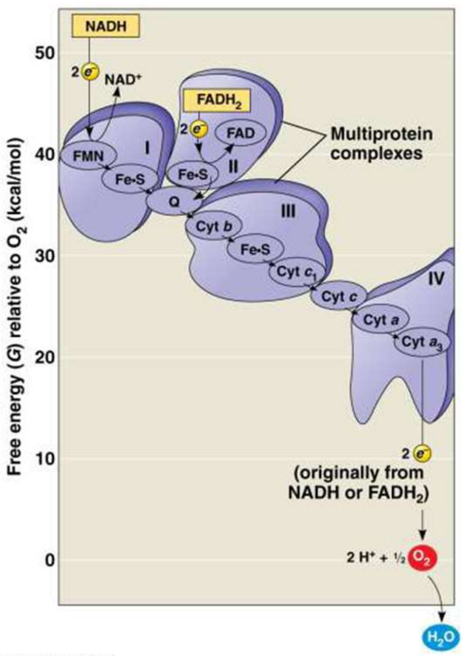
As electrons are passed through the chain, there occurs a stepwise release of energy, which is used to drive the chemiosmotic generation of ATP.

The final oxidation is irreversible.

In eukaryotic cells, the electron transport chain is contained in the inner membrane of mitochondria; in prokaryotic cells, it is found in the plasma membrane.

electron transport chain

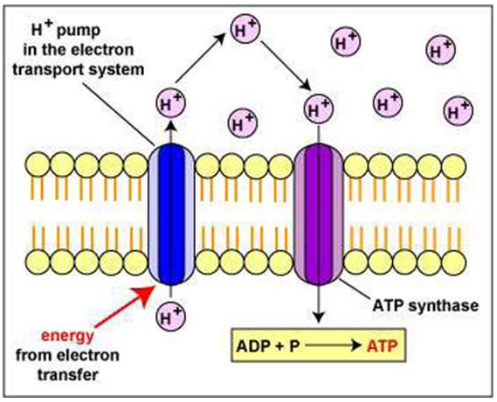
Who:
– FADH2, NADH, ADP
– ATP Synthase
– Cytochromes and membrane proteins
What:
– Chemiosmosis
where:
– Intermembrane space of the mitochondria euk
– plasmamembrane prok



The transport proteins alternate reduced and oxidized states as they accept and donate electrons

FADH2’s electrons are lower energy than NADH, and so enter the electron transport chain at a protein further along in the Chain
Oxygen accepts those now very-low energy electrons.

Oxygen is the terminal electron acceptor



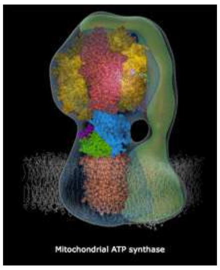
The release of energy is used to pump H+ across the matrix membrane into the intermembrane space

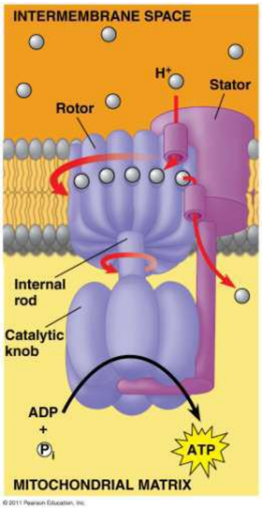
H+ are pumped against their gradient using the energy released from passing electrons to lower and lower energy states

This creates an electrochemical gradient

ATP synthase is a turbine that connects the flow of protons to ADP-> ATP phosphorylation

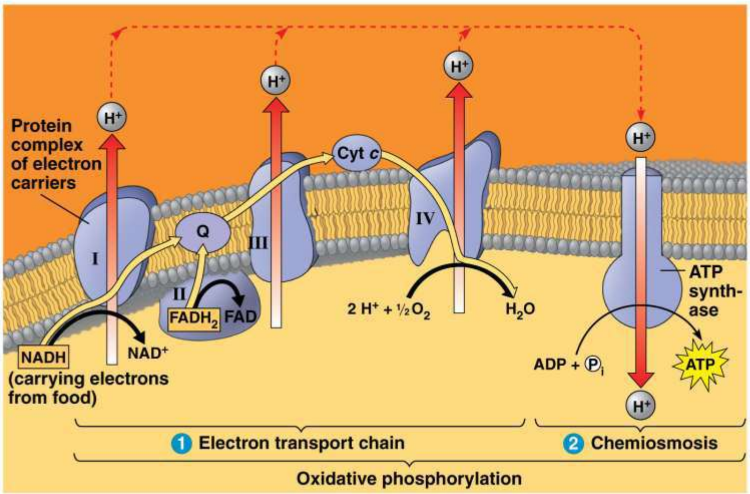
chemiosmosis





As the turbine turns with the “current” of protons flowing past, it phosphorylates ADP into ATP

Electron transport chain and chemiosmosis



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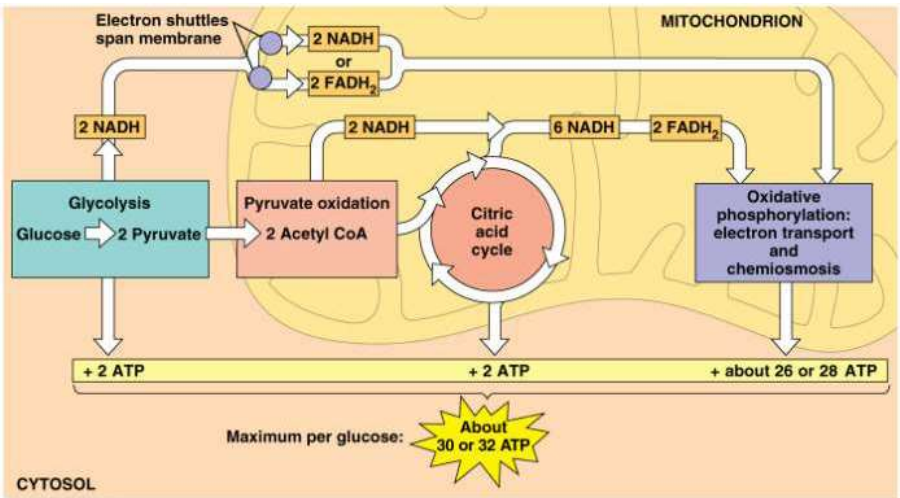

glucose -> NADH ->electron transport chain -> proton-motive force -> ATP

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And if there is no oxygen?

Anaerobic respiration uses an electron transport chain with a final electron acceptor other than O_2, for example sulfate

• Produces much less energy than aerobic respiration

– Only source of ATP is substrate-level phosphorylation

fermentation

Two common types of fermentation:

– **Lactic acid** fermentation

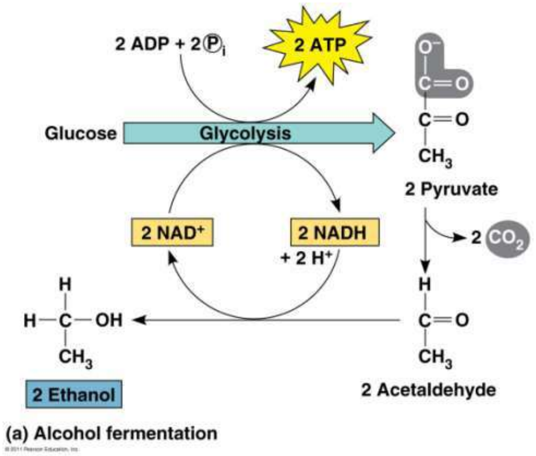
Lactic acid fermentation by some fungi and bacteria is used to make cheese and yogurt

Human muscle cells use lactic acid fermentation to generate ATP when O_2 is scarce

– **Alcohol** fermentation

Alcohol fermentation by yeast is used in brewing, winemaking, and baking

Alcohol fermentation



Pyruvate is converted to ethanol in two steps

– NADH produced in glycolysis is oxidized to NAD+

– Glucose is not completely digested

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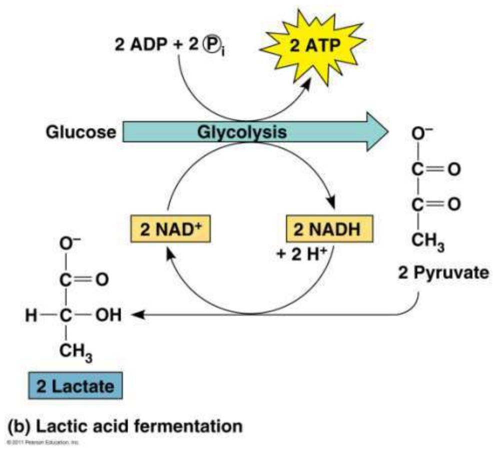
Lactic acid fermentation



Pyruvate is converted to lactate in one step

– NADH produced during glycolysis is oxidized to NAD+

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Aerobic vs anaerobic respiration

	Aerobic Respiration	Anaerobic Respiration
Glycolysis	Yes	Yes
Krebs Cycle	Yes	No
Electron Transport Chain	Yes	No
ATP Production	32 per glucose	2 per glucose
NADH production	Yes	Yes
$FADH_2$ production	Yes	No
Terminal electron acceptor	O_2	Pyruvate or acetaldehyde

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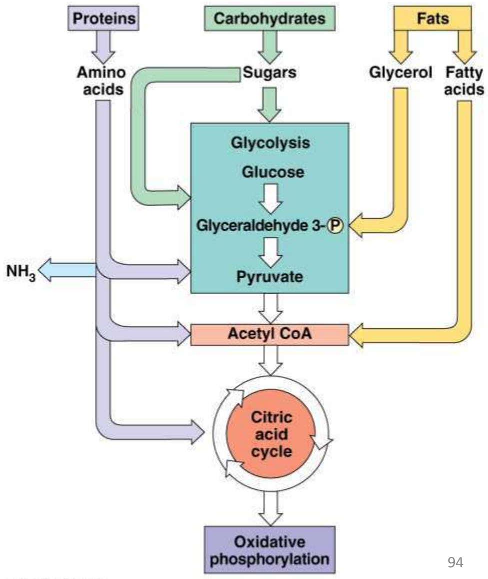
Proteins fats and carbohydrates

- Proteins must be digested to amino acids; amino groups can feed glycolysis or the citric acid cycle
- Fats are digested to glycerol (used in glycolysis) and fatty acids (used in generating acetyl CoA)
- Fatty acids are broken down by **beta oxidation** and yield acetyl CoA
- An oxidized gram of fat produces more than twice as much ATP as an oxidized gram of carbohydrate



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