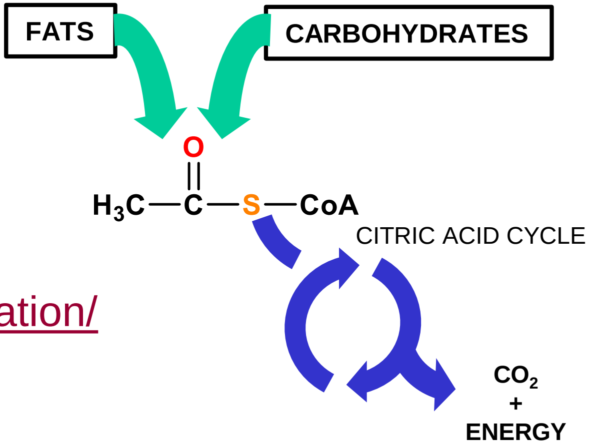
School of Industrial and Information Engineering

Course 096125 (095857)

Introduction to Green and Sustainable Chemistry

POLITECNICO DI MILANO

Cell Metabolism.



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The processes of energy transduction are carried out by a highly integrated network of chemical reactions called metabolism.

A. Metabolism is composed of many coupled, interconnecting reactions

B. The oxidation of carbon "fuels" is an important source of cellular energy

C. Metabolic pathways contain many recurring motifs.

TERMS:

- **The reactions that occurs in cells are collectively known as *metabolism***
- **Pathways that break down larger molecules into smaller ones are called *catabolism***
- **Pathways that synthesise larger molecules from smaller ones are called *anabolism***
- **Catabolic pathways usually release energy whereas anabolic pathways usually absorb energy.**

Primary and Secondary Metabolism.

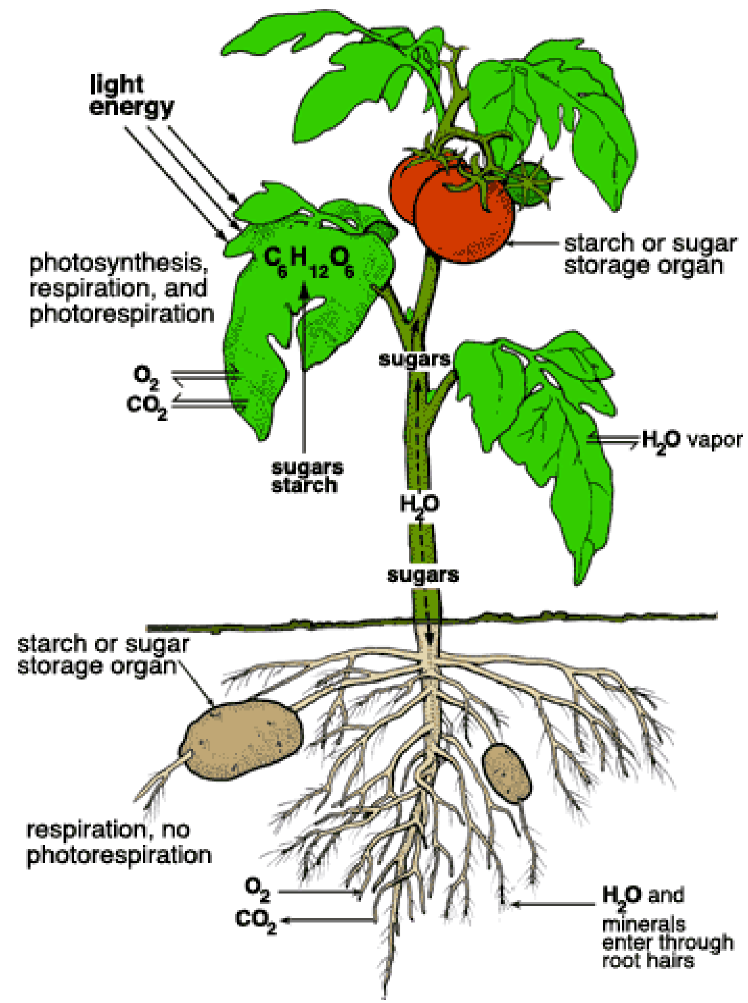
Metabolism: (Gr. *metabole* = change) the totality of the chemical changes in living cells which involves the buildup and breakdown of chemical compounds.

Primary metabolism: biosynthesis, utilization and breakdown of the essential compounds and structural elements of the living organism, such as: sugars and polysaccharides; amino acids, peptides and proteins (including enzymes); fatty acids; and nucleotides. The starting materials are CO_2, H_2O and NH_3. All organisms possess similar primary metabolic pathways and use similar primary metabolites.

Secondary metabolism: refers to the biosynthesis, utilization and breakdown of smaller organic compounds found in the cell. These compounds, called ***secondary metabolites***, arise from a set of intermediate building blocks : acetyl coenzyme A (acetyl-CoA), mevalonic acid (MVA) and methyl erythritol phosphate (MEP), shikimic acid, and the amino acids phenylalanine/tyrosine, tryptophan, ornithine and lysine.

Plant Metabolism: Primary Metabolites.

- Primary metabolites are compounds that are commonly produced by all plants and that are directly used in plant growth and development.
- The main primary metabolites are:
  - **carbohydrates,**
  - **proteins,**
  - **nucleic acids**
  - **lipids**.



Photosynthesis, respiration, leaf water exchange, and translocation of sugar (photosynthate) in a plant.
(photosynthate) in a plant.

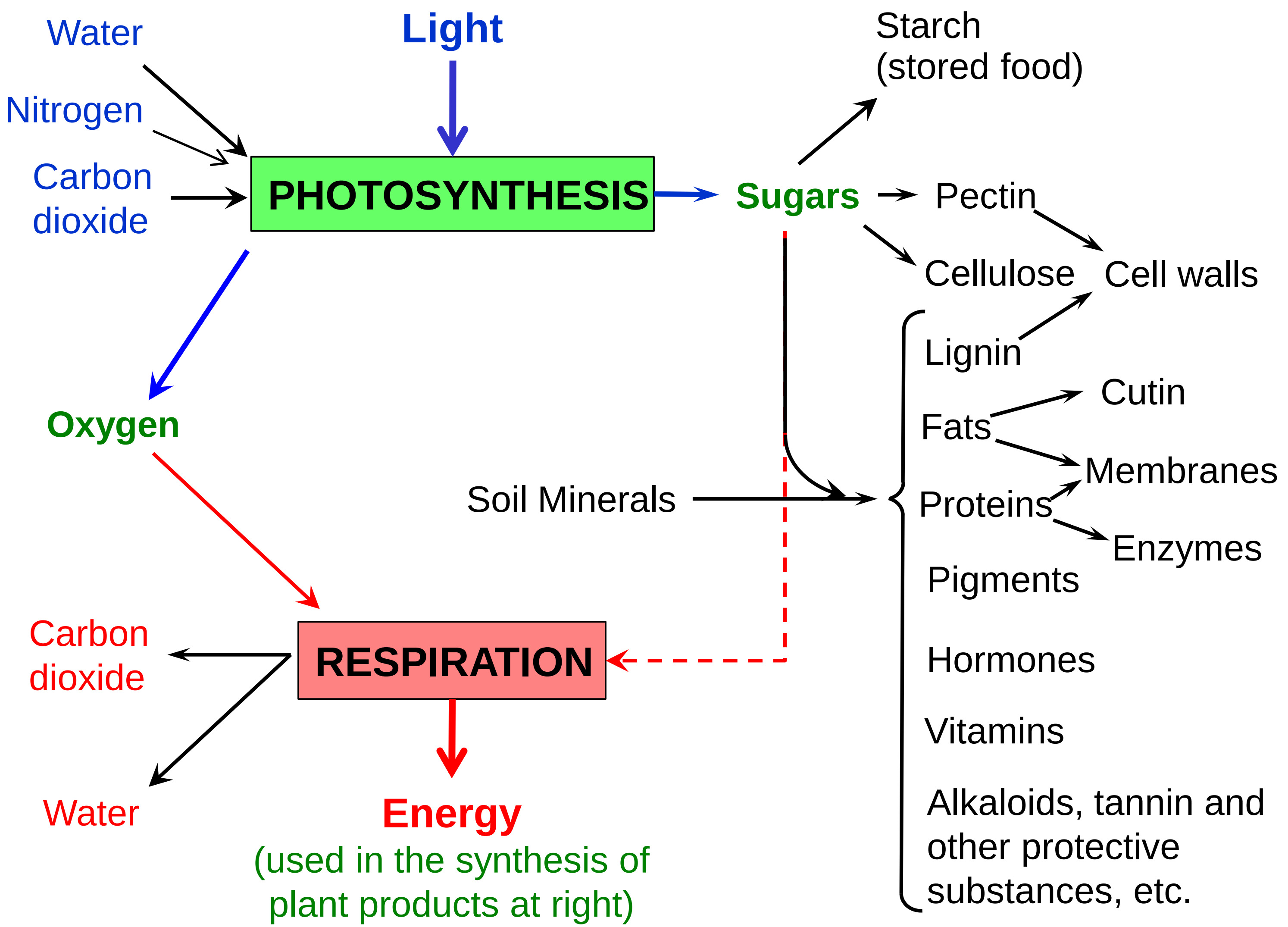
Relationship Between Primary and Secondary Metabolism.

- The processes and products of primary metabolism are similar in most organisms, while those of secondary metabolism are more specific.
- In plants, primary metabolism is made up of photosynthesis, respiration, etc., using CO_2, H_2O, and NH_3 as starting materials, and forming products such as glucose, amino acids, nucleic acids. These are similar among different species.
- In secondary metabolism, the biosynthetic steps, substrates and products are characteristic of families and species. Species which are taxonomically close display greater similarities (and metabolites); those which are distant have greater differences.

Biogenesis: overview of the origin of compounds starting from the set of intermediate building blocks: acetyl-CoA, MEP, shikimic acid, and the amino acids phenylalanine and tyrosine, tryptophan, ornithine and lysine.

Biosynthesis: study of the step-wise formation of metabolites. The specific enzymes, genes and signals are identified.

An Outline of Plant Metabolism.



Metabolism: Complexity & Design.

- *E. coli* metabolism has more than 1000 chemical reactions
- This vast array is simplified by the use of a coherent design containing many common motifs.
- Motifs include the use of an energy currency (ATP), and the repeated appearance of a limited number of activated intermediates (acetyl-CoA, MEP, shikimic acid). A group of about 100 molecules play central roles in all forms of life
- The number of reactions is large, the number of kinds is small, and the mechanisms are usually quite simple
- Metabolic pathways are regulated in common ways.

Classification of Biosynthetic Transformations.

All metabolites, no matter how complex, are biosynthesized *via* discrete chemically-reasonable steps. The biosynthetic transformations are classified as follows:

1. Hydrolysis
2. Esterification
3. Oxidation: hydroxylation, epoxidation or oxygenation of alkene, dehydrogenation, halogenation
4. Reduction: hydrogenation, deoxygenation
5. Carbon-carbon bond formation: aromatic radical coupling, Claisen condensation, aldol condensation
6. Cationic rearrangement: 1,2-migration, Wagner-Meerwein
7. Rearrangement under control of orbital symmetry
8. S*n*2 displacement
9. *E*2 elimination
10. Carboxylation / decarboxylation

Enzymes Involved in the Metabolism.

Each **step** is presumed to be **mediated by a specific enzyme**. All chemical transformations are accounted for by the system of six enzyme classes:

1. oxidoreductase
2. transferase
3. hydrolase
4. lyase
5. isomerase
6. ligase

3. The enzymes are located in specific parts of the cell, and in some cases may be immobilized on a membrane.

4, The enzymes are coded for in the plant’s genome whose expression can be controlled at the level of the gene.

Cells Transform Different Types of Energy.

Living organisms require a persistent input of free energy for three major purposes:

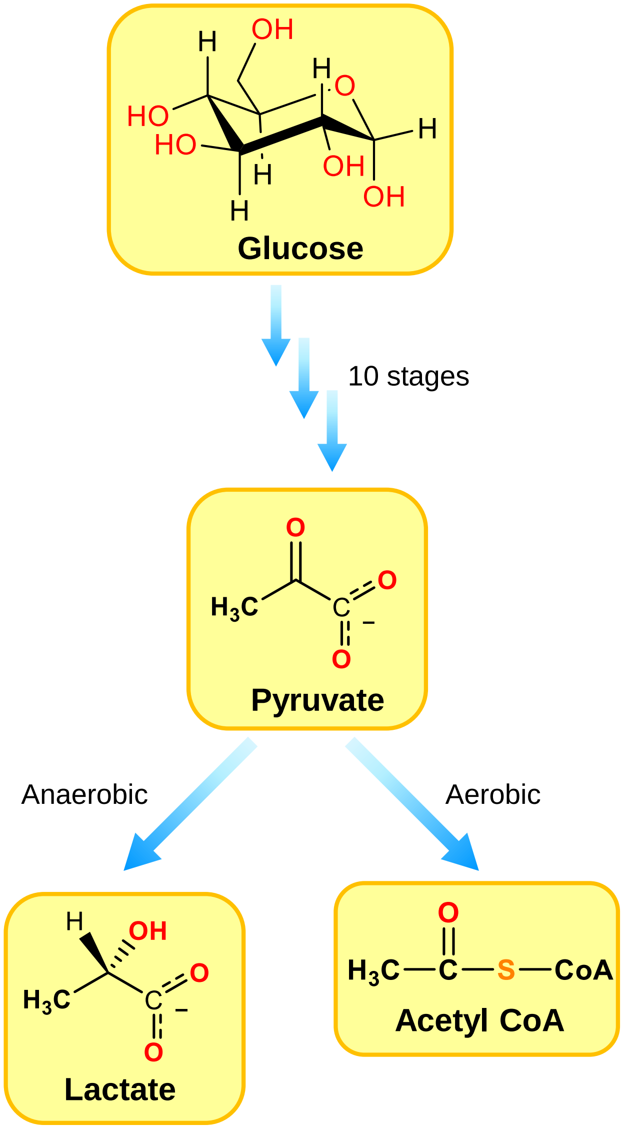
- To perform mechanical work, e.g. muscle contraction, and other cellular movements
- The active transport of molecules and ions
- The synthesis of macromolecules and other biomolecules from simple precursors.

Energy conversions:

- ✓ Photosynthetic organisms (phototrophs) use sunlight energy to convert simple energy-poor molecules into more complex energy-rich molecules that serve as fuels. They transform light to chemical bonds
- ✓ Chemotrophs, e.g. humans, obtain chemical energy through oxidation of foodstuffs generated by phototrophs
- ✓ Chemical energy transformed to other energy forms.

Simplified Example: Metabolism of Glucose.

Glucose to Pyruvate in 10 linked reactions

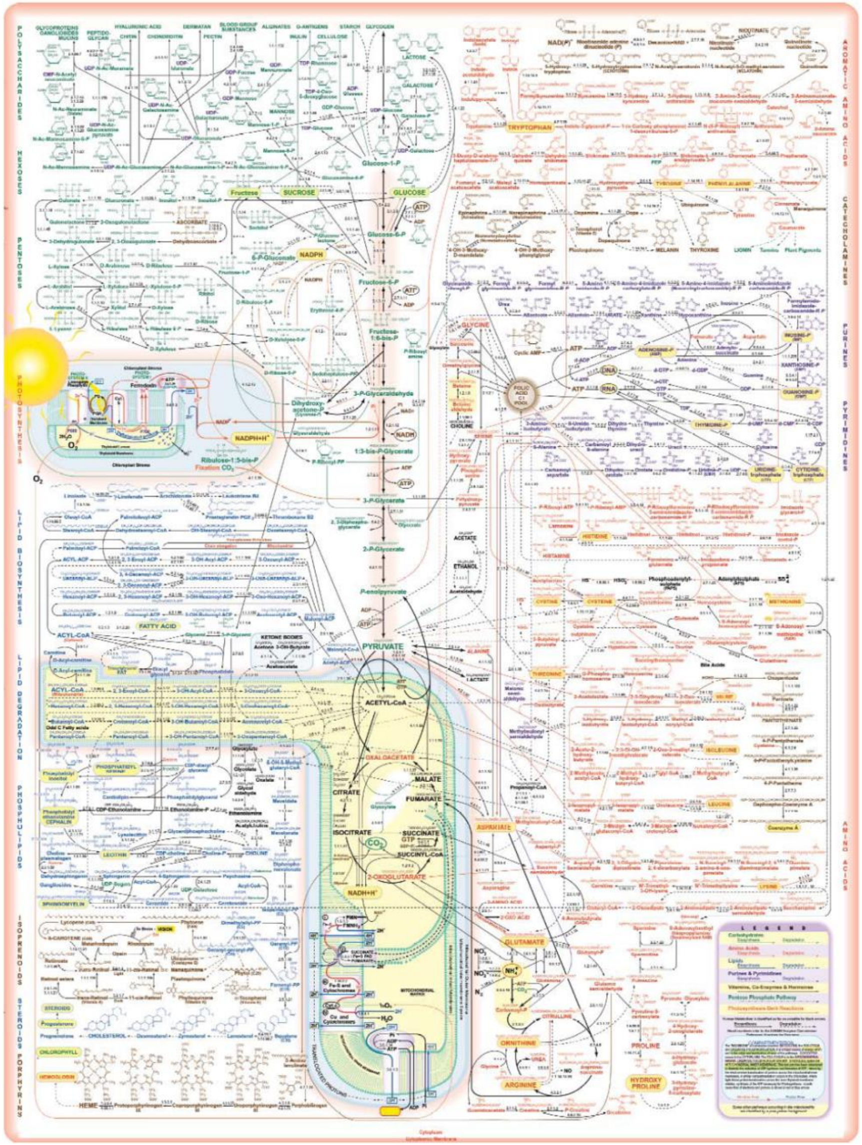


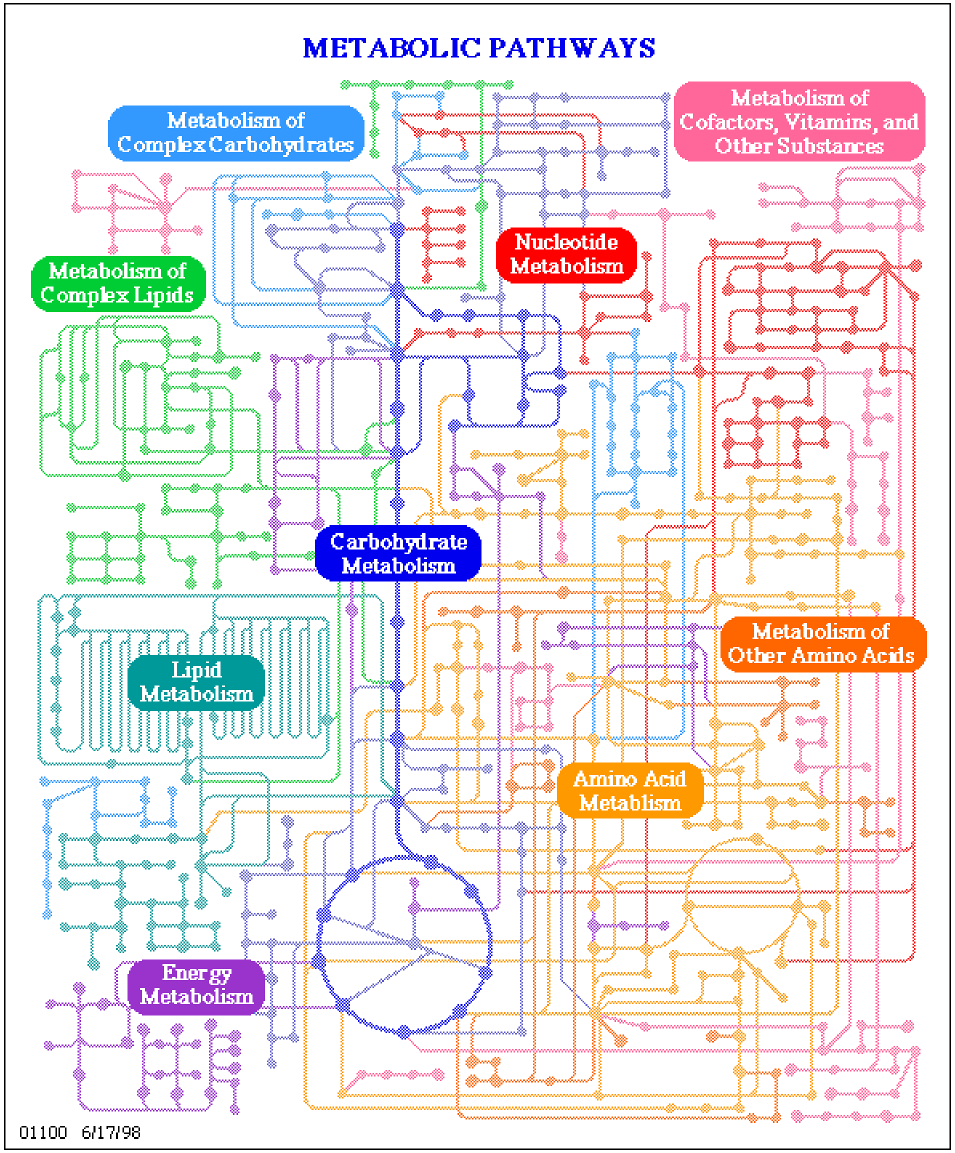
Metabolism:
a linked series of chemical reaction

Anaerobic conditions

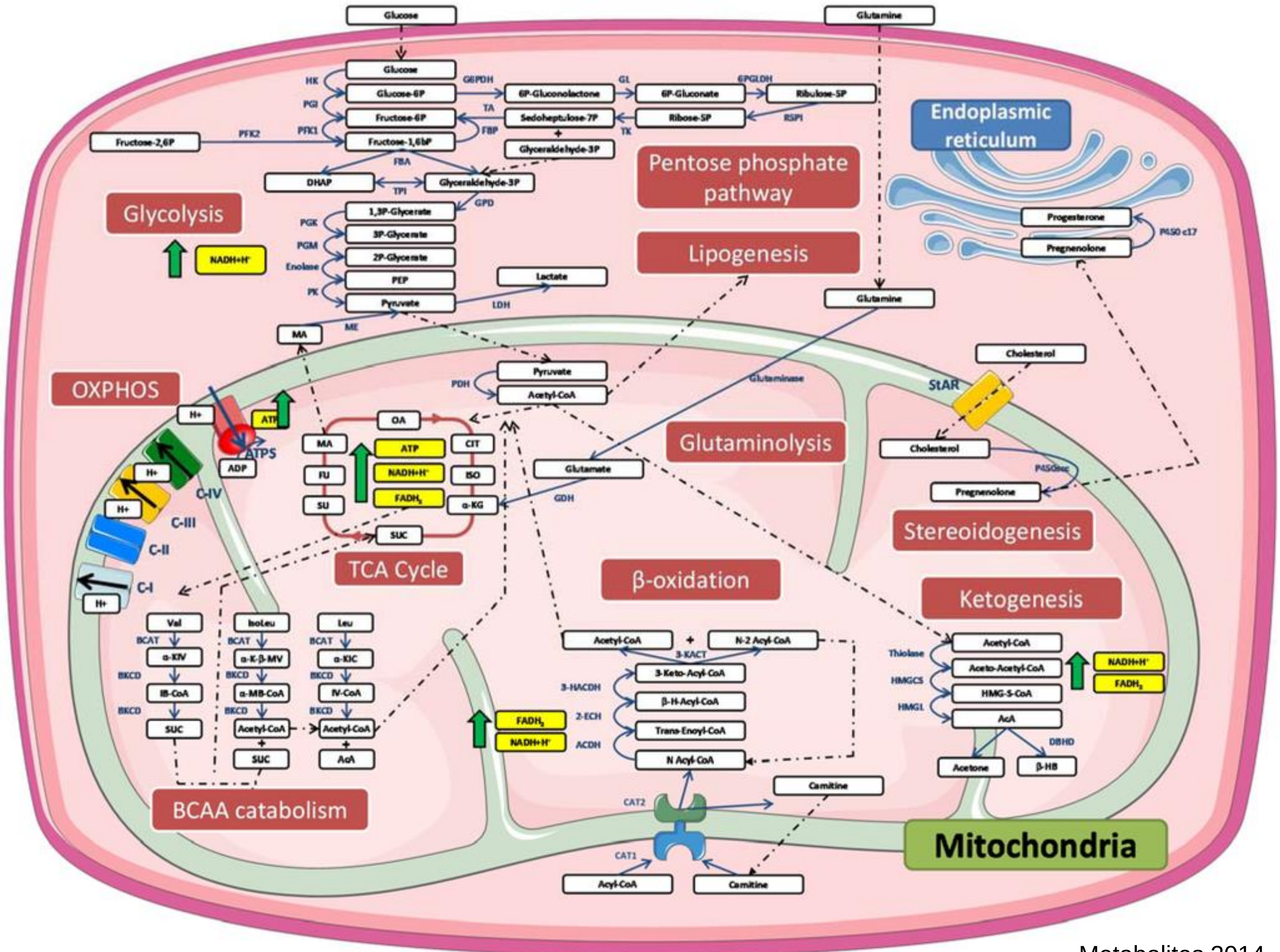
Aerobic conditions

Metabolic Pathways.





Simplified Representation of Biochemical Pathways Related to Mitochondria.



Metabolites 2014, 4(3), 831-878

Metabolic Pathways.

Two broad classes:

a) catabolic pathways: convert energy into biologically useful forms

“Fuels” (carbs & fats) → CO_2 + H_2O + useful energy: **catabolism**

b) anabolic pathways: require inputs of energy to proceed

Useful energy + small molecules → complex mol. : **anabolism**

Pathways that can be either anabolic or catabolic are referred to as **amphibolic pathways**.

Coupling Favorable and Unfavorable Reactions.

A pathway must satisfy minimally two criteria:

1. The individual reactions must be specific, yielding only one particular product or set of products.
   - Enzymes provide specificity
2. The entire set of reactions in a pathway must be thermodynamically favored
   - A reaction can occur spontaneously only if ΔG, the change in free energy, is negative.
3. An important thermodynamic fact: the overall free energy change for a chemically coupled series of reactions is equal to the sum of the free-energy changes of the individual steps:

$$A \rightleftarrows B + C \qquad \Delta G^{0'} = +5\ \text{kcal}\cdot\text{mol}^{-1}$$

$$B \rightleftarrows D \qquad \Delta G^{0'} = -8\ \text{kcal}\cdot\text{mol}^{-1}$$

$$A \rightleftarrows C + D \qquad \Delta G^{0'} = -3\ \text{kcal}\cdot\text{mol}^{-1}$$

ATP is the Universal Currency of Free Energy.

Metabolism is facilitated by the use of a common energy currency

Part of the free energy derived from the oxidation of foodstuffs and from light is transformed into ATP - the energy currency ATP is the universal currency of free energy A large amount of free energy is liberated when ATP is hydrolyzed to ADP and phosphate (P_i), or ATP to AMP and PP_i

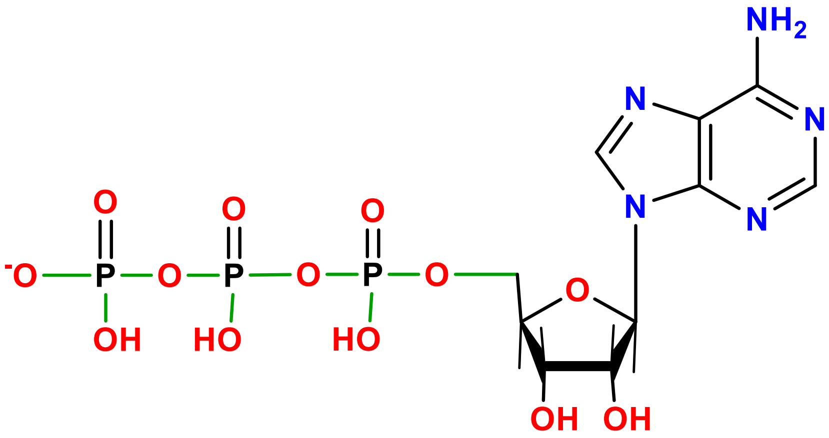
$$ATP + H_2O \rightleftarrows ADP + P_i \qquad \Delta G^{0'} = -7.3\ kcal \cdot mol^{-1}$$

$$ATP + H_2O \rightleftarrows AMP + PP_i \qquad \Delta G^{0'} = -10.9\ kcal \cdot mol^{-1}$$

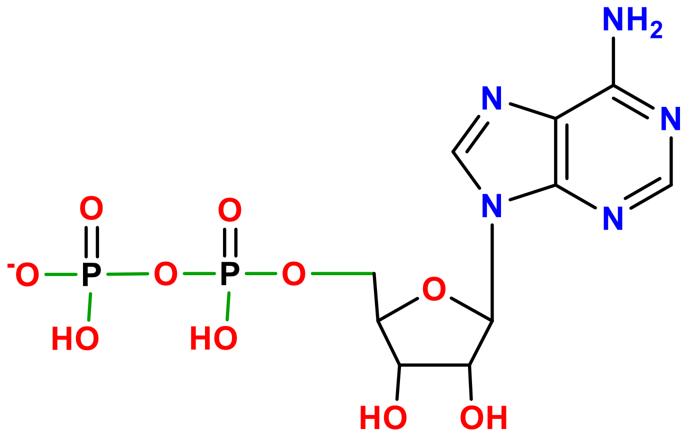
Under typical cellular conditions, the actual **ΔG** for these hydrolyses is approximately **$-12\ kcal \cdot mol^{-1}$**.

ATP hydrolysis drives metabolism by shifting the equilibrium of coupled reactions: by a factor of approximately **10^8**.

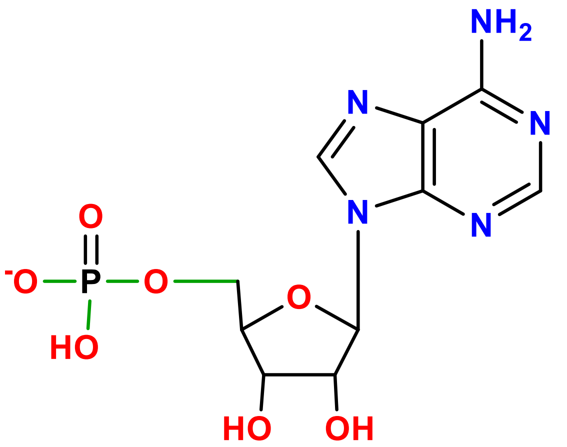
Structures of ATP, ADP, and AMP.



Adenosine triphosphate (ATP)



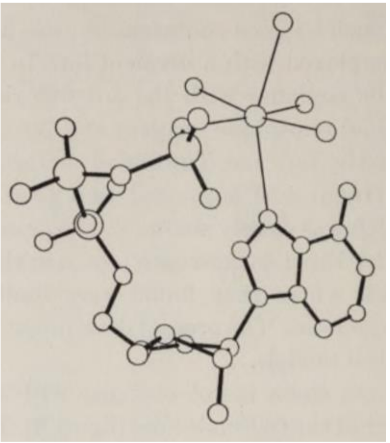
Adenosine diphosphate (ADP)



Adenosine monophosphate (AMP)

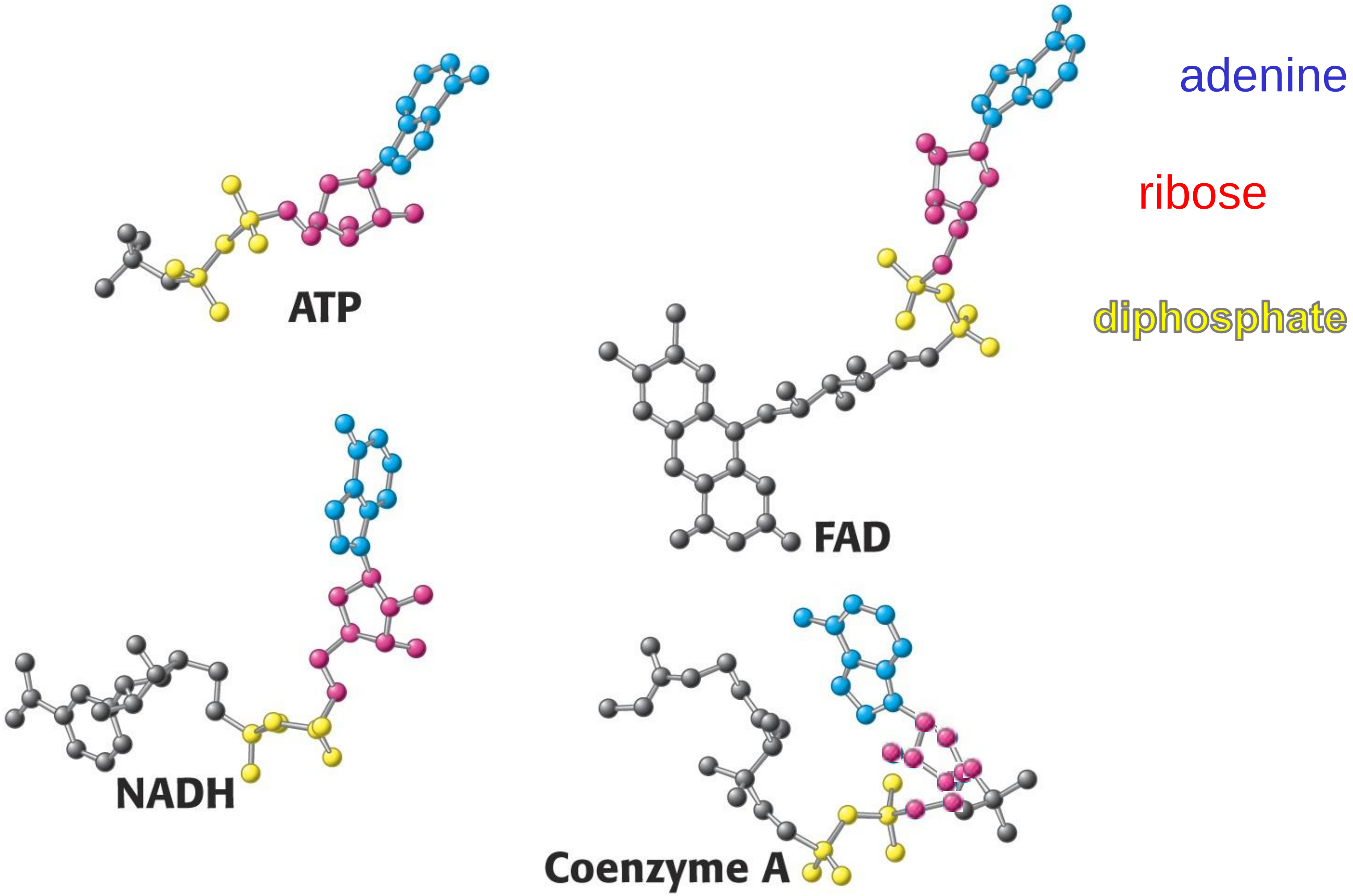
Raggi X del sale ATP Na

A. Kennard et al. Proc. R. Soc. London, 325, ,401 (1978)

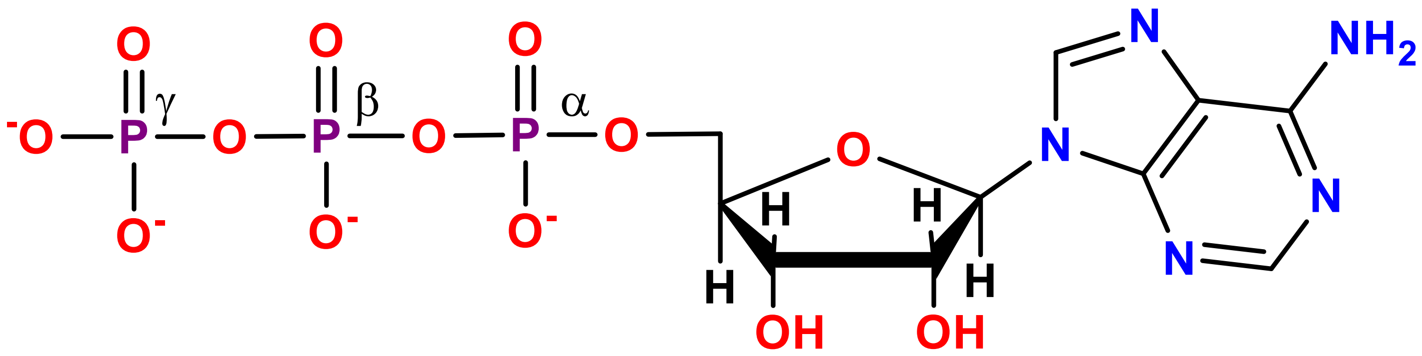


Adenosine Diphosphate (ADP) is an Ancient Module.

in metabolism. Evolved from early RNA catalysts?



ATP is an energy-rich molecule because its triphosphate units contain two phosphoanhydridic bonds (β and γ).



Adenosine triphosphate (ATP)

ATP has an high potential of phosphoryl group transfer ($\Delta G = -12\ kcal \cdot mol^{-1}$)

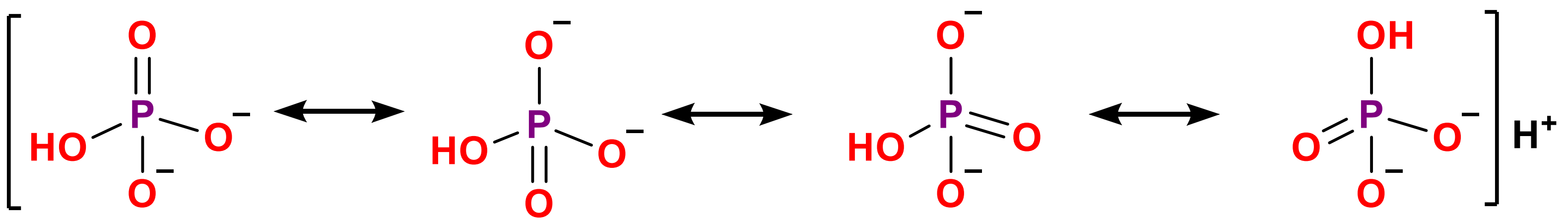
Resonance Structures of Orthophosphate.

Why does ATP have a high phosphoryl transfer potential?

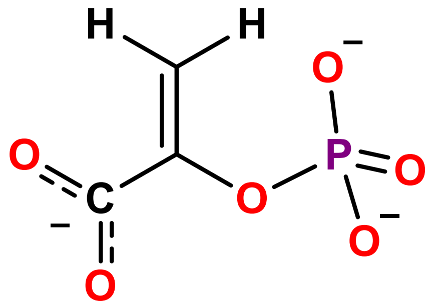
$\Delta G^{0'}$ depends on the difference in free energies of products and reactants, therefore, both must be considered.

Four factors are important:

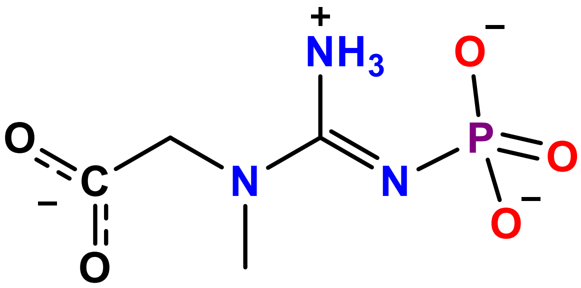
1. Resonance stabilization
2. Electrostatic repulsion
3. Stabilization due to hydration
4. Increase of entropy due to the formation of 2 species from 1



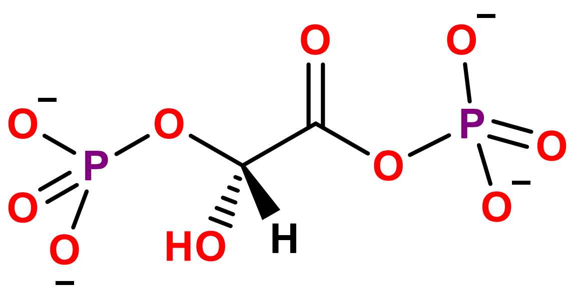
Compounds with High Phosphoryl Transfer Potential.



Phosphoenolpyruvate



Creatine phosphate



1,3-Bisphosphoglycerate

Phosphoryl transfer potential is an important form of cellular energy transformation.

These compounds can transfer a phosphoryl group to ADP to form ATP.

They couple carbon oxidation to ATP synthesis.

Intermediate Position of ATP.

Enables ATP to function efficiently as a carrier of phosphoryl groups

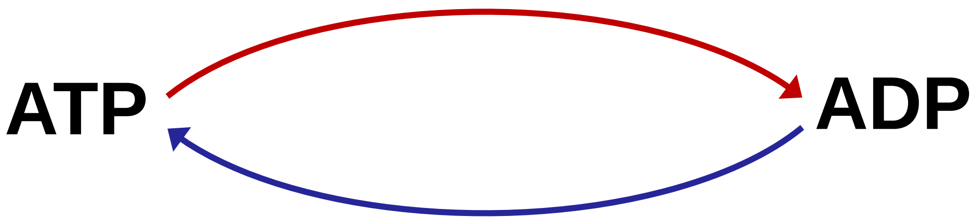
$$R\text{-}OPO_3^{2-} + H_2O \rightarrow ROH + HOPO_3^{2-} \qquad \Delta G°_{hydrolysis}$$

Standard free energy of hydrolysis of some phosphorylated compounds

Compound	kcal·mol^{-1}	kJ·mol^{-1}
Phosphoenolpyruvate	- 14.8	- 61.9
1,3-Bisphosphoglycerate	- 11.8	- 49.4
Acetyl phosphate	- 10.3	-43.1
Creatine phosphate	- 10.3	- 43.1
ATP (to ADP + P_i)	- 7.3	- 30.5
Glucose-1-phosphate	- 5.0	- 20.9
Pyrophosphate	- 4.6	- 19.3
Glucose-6-phosphate	- 3.3	- 13.8
Glycerol-3-phosphate	- 2.2	- 9.2

ATP-ADP Cycle.

Motion
Active transport
Biosyntheses
Signal amplification



Oxidation of fuel molecules
or
Photosynthesis

100 g of ATP in the body, turnover is very high.

Resting human consumes 40 kg of ATP in 24 hours.

Strenuous exertion: 0.5 kg / minute.

2 h run: 60 kg utilized

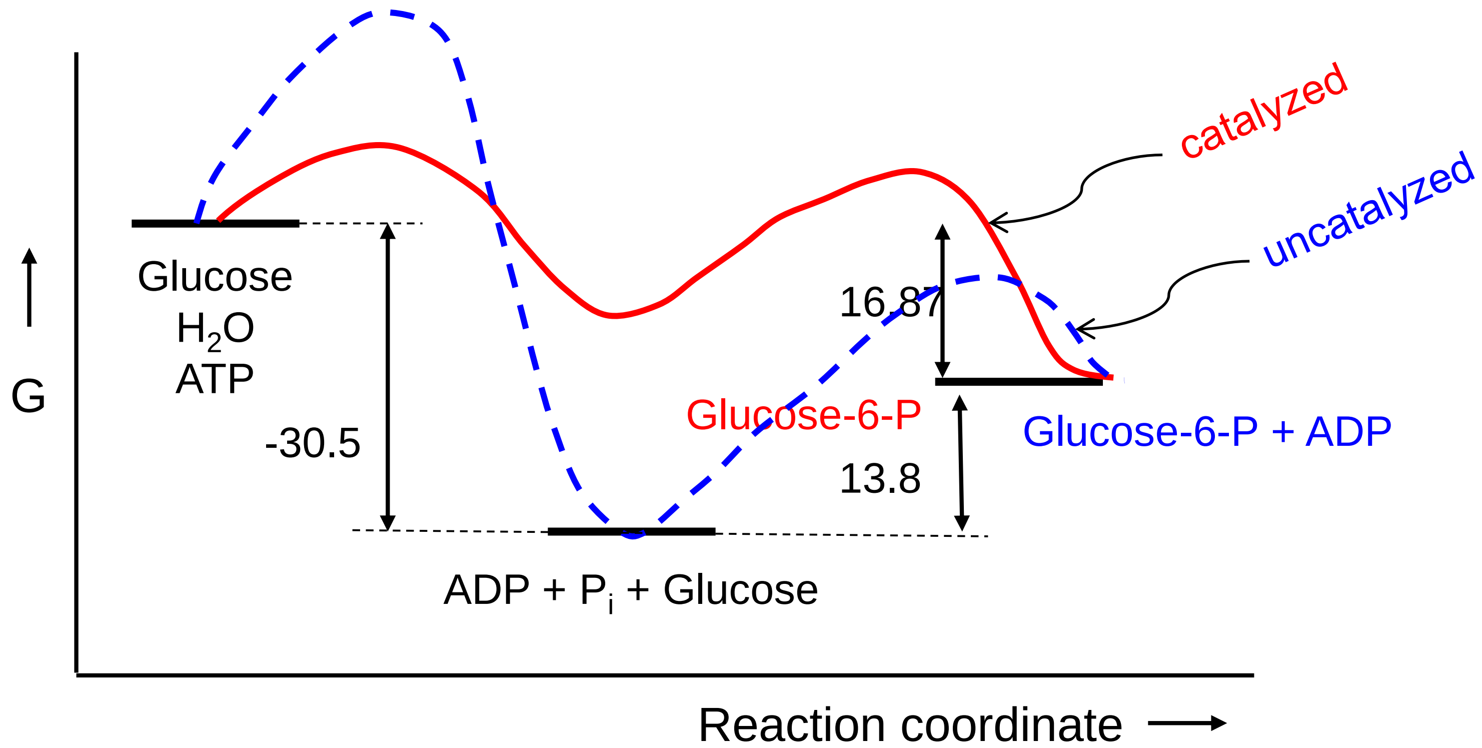
Fundamental mode of energy exchange in biological systems

The oxidation of carbon “fuels” is an important source of cellular energy.

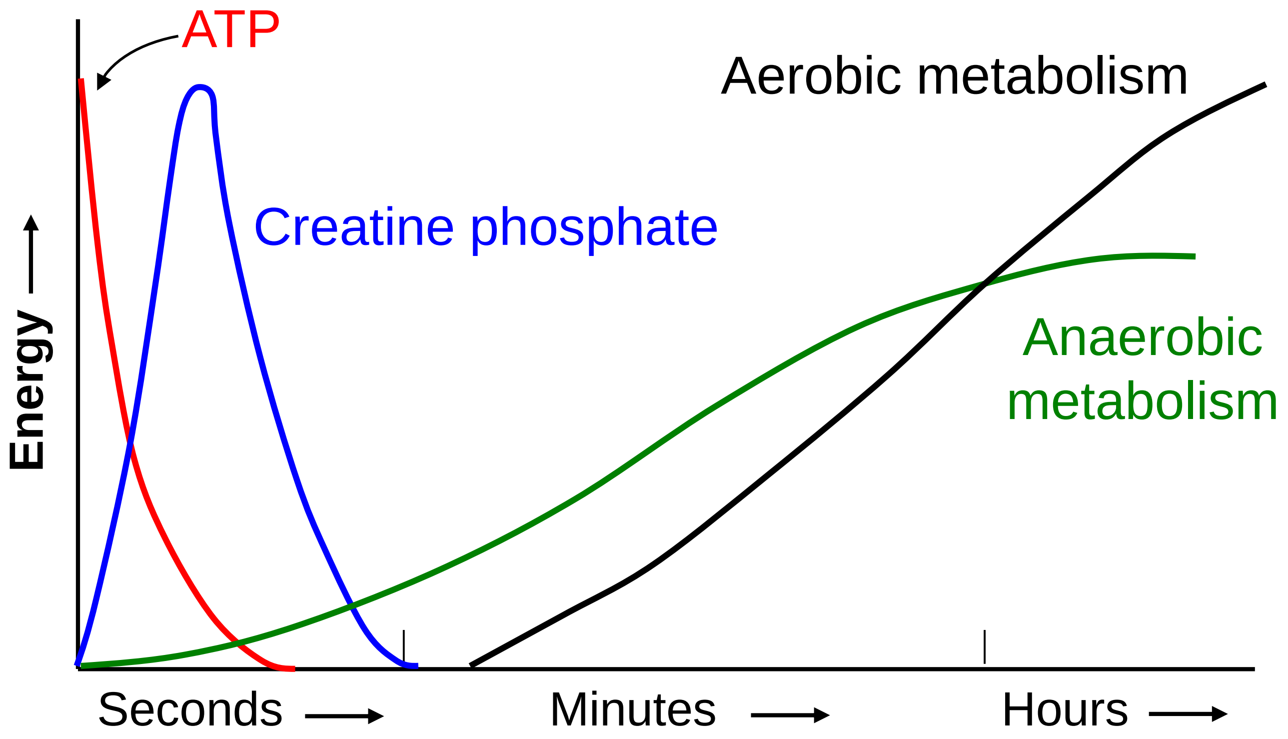
ATP-Coupled Reactions.

Many reactions cannot be made favorable under cellular or physiological conditions. But these reactions can be coupled to ATP hydrolysis to go.

ATP + Glucose → Glucose-6-P + ADP
Actual cellular reaction → (P)-transfer



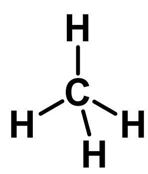
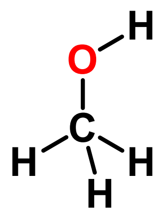
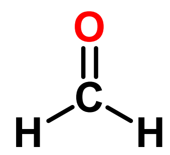
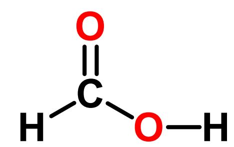
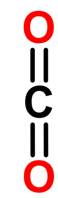
Sources of ATP During Exercise.



In resting muscle, [ATP] = 4 mM, [creatine phosphate] = 25 mM
[ATP] sufficient to sustain 1 second of muscle contraction.

Free Energy of Oxidation of Single-carbon Compounds.

most energy → least energy

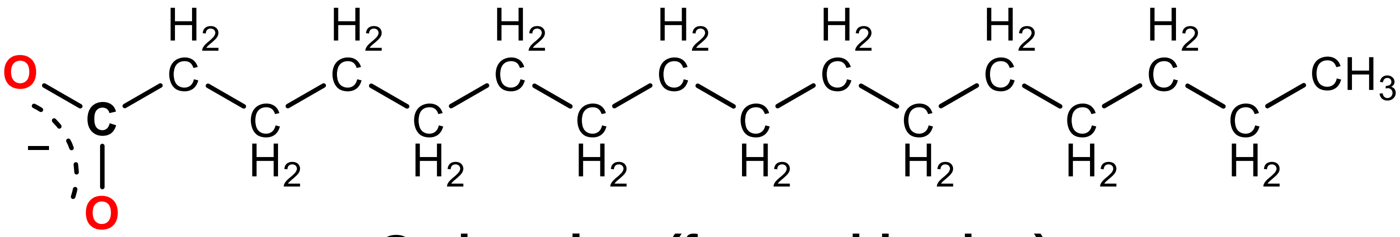
	Methane	Methanol	Formaldehyde	Formic acid	Carbon dioxide
$\Delta G°_{oxidation}$ ($kcal\cdot mol^{-1}$)	-195	-168	-125	-68	0
$\Delta G°_{oxidation}$ ($kJ\cdot mol^{-1}$)	-820	-703	-523	-285	0

In aerobic organisms, the ultimate electron acceptor in the oxidation of carbon is O_2, and the oxidation product is CO_2.

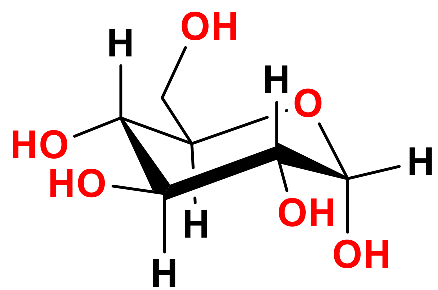
The more reduced a carbon is, the more energy from its oxidation.

Common Biological Fuels.

Fats are more efficient “fuels” than carbohydrates (e.g. Glucose)



Carboxylate (fatty acid anion)



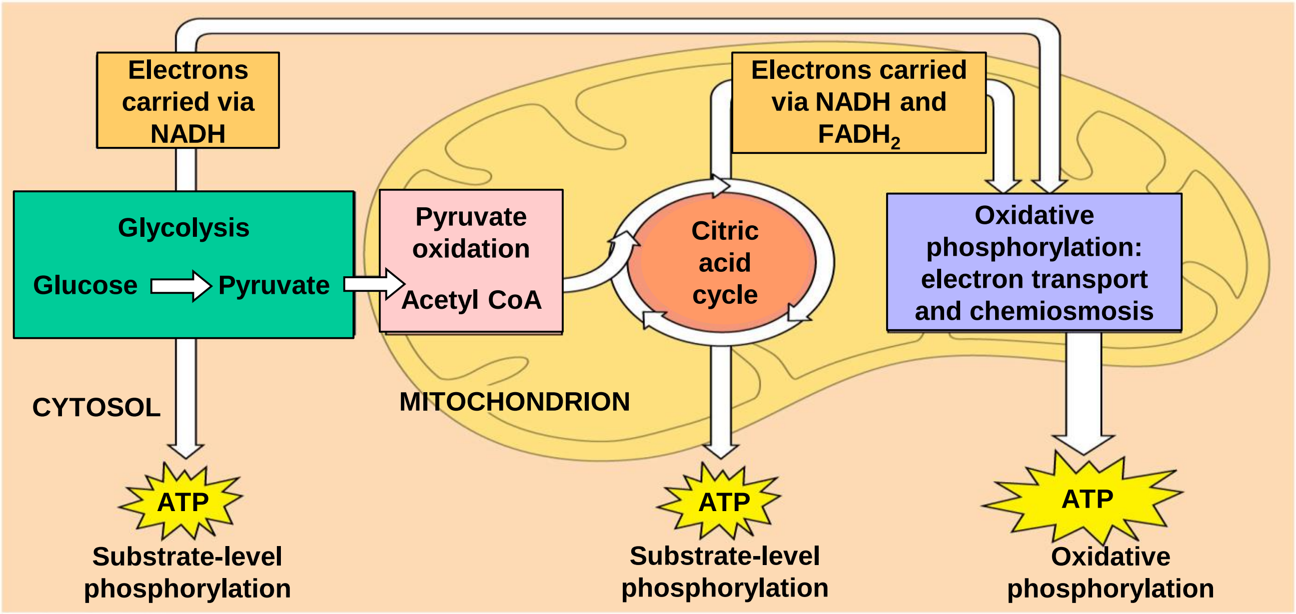
Glucose

Because carbon in fats is more reduced (except the COOH carbon).

The Stages of Cellular Respiration.

Harvesting of energy from glucose has three stages

- **Glycolysis** (breaks down glucose into two molecules of pyruvate)
- The **citric acid cycle** (completes the breakdown of glucose)
- **Oxidative phosphorylation** (accounts for most of the ATP synthesis).



Oxidative Phosphorylation and Glycolysis.

The process that generates most of the ATP is called oxidative phosphorylation because it is powered by redox reactions

- Oxidative phosphorylation accounts for almost 90% of the ATP generated by cellular respiration
- A smaller amount of ATP is formed in glycolysis and the citric acid cycle by **substrate-level phosphorylation**
- For each molecule of glucose degraded to CO_2 and water by respiration, the cell makes up to 32 molecules of ATP.

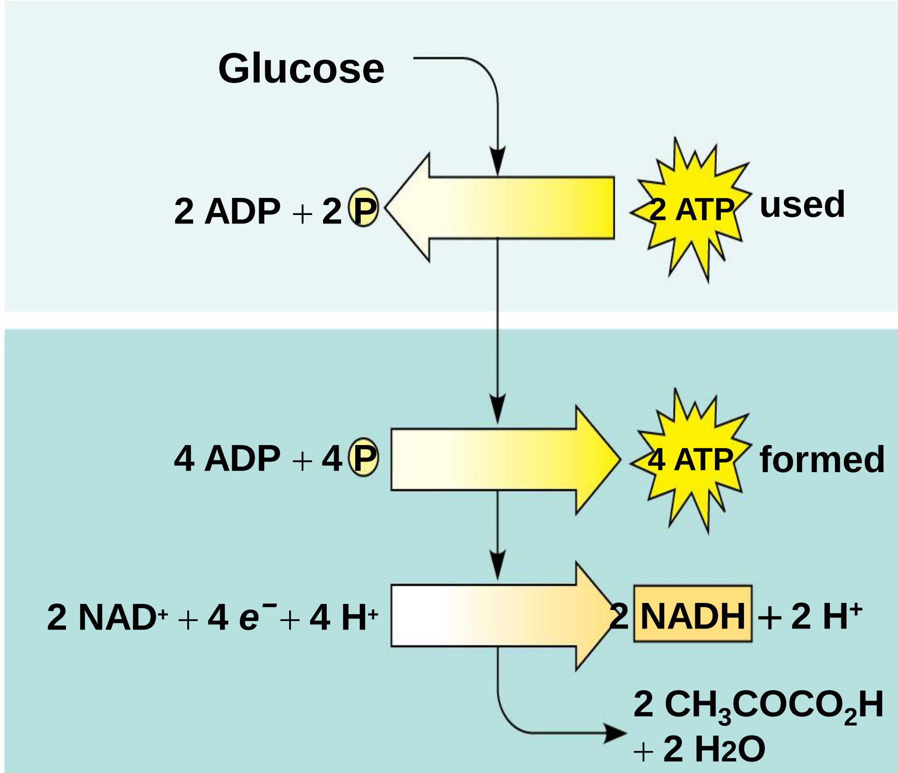
Glycolysis ("splitting of sugar") breaks down glucose into two molecules of pyruvate

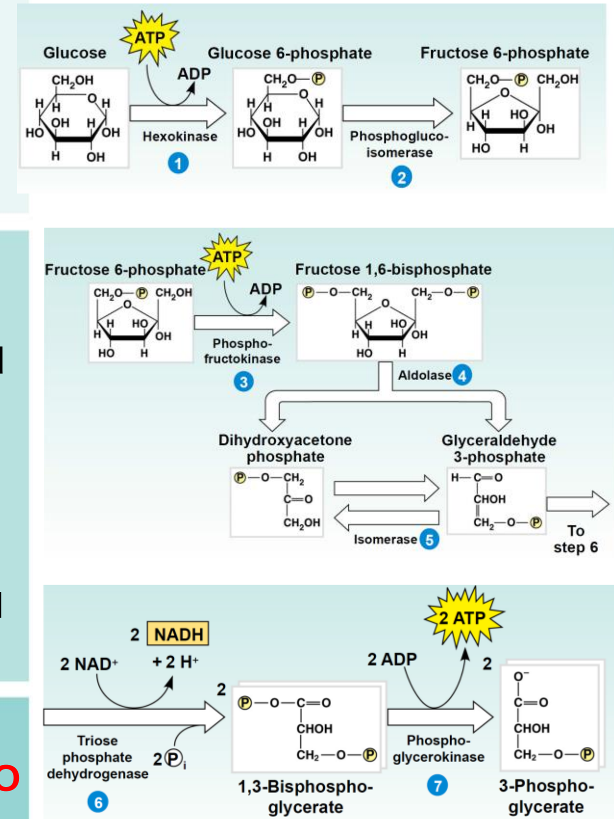
- • Glycolysis occurs in the cytoplasm and has two major phases
  - Energy investment phase
  - Energy payoff phase
- Glycolysis occurs whether or not O_2 is present.

Glycolysis.

Energy Investment Phase

Energy Payoff Phase





Net

$$\text{Glucose} \longrightarrow 2\ \text{Pyruvate} + 2\ H_2O$$

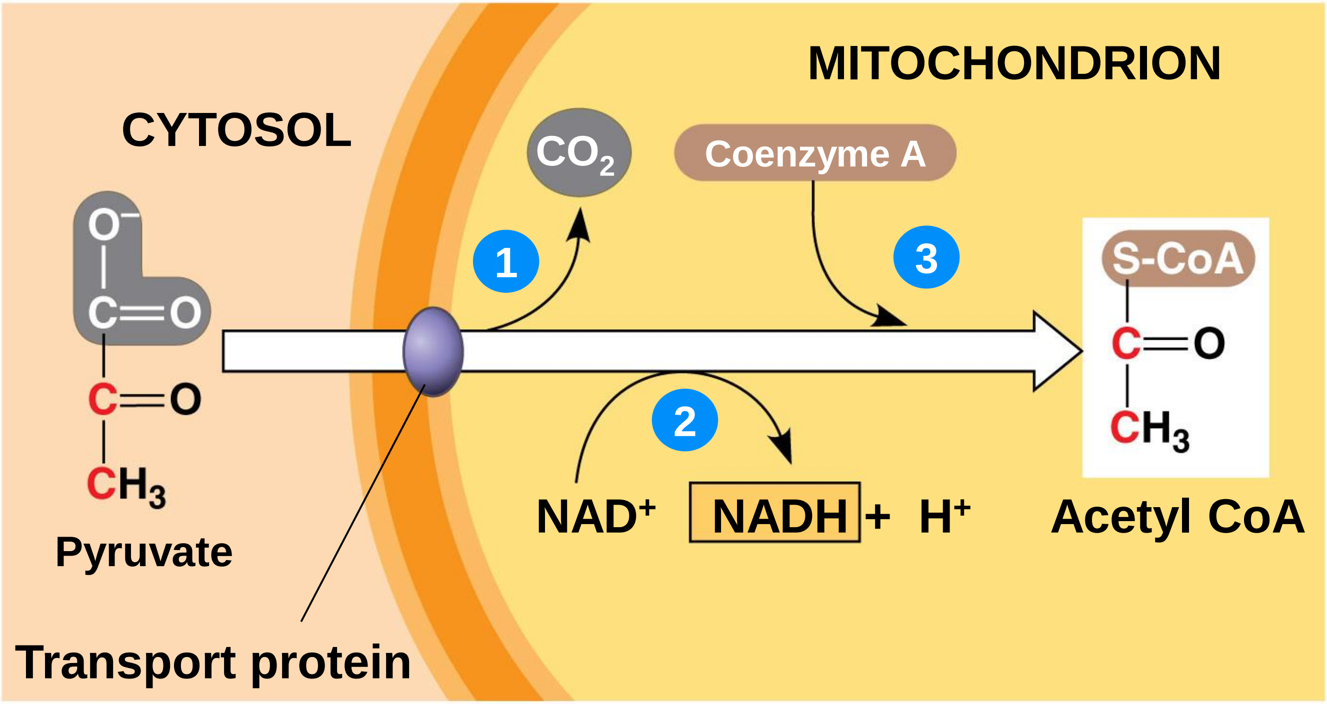
$$4\ \text{ATP formed} - 2\ \text{ATP used} \longrightarrow 2\ \text{ATP}$$

$$2\ NAD^{+} + 4\ e^{-} + 4\ H^{+} \longrightarrow 2\ NADH + 2\ H^{+}$$

Conversion of Pyruvate into Acetyl CoA.

After pyruvate is oxidized, the citric acid cycle completes the energy-yielding oxidation of organic molecules

In the presence of O_2, pyruvate enters the mitochondrion (in eukaryotic cells) where the oxidation of glucose is completed. Before the citric acid cycle can begin, pyruvate must be converted to acetyl Coenzyme A (**acetyl CoA**), which links glycolysis to the citric acid cycle.



Stages of Catabolism: Citric Acid, Cycle – CTA.

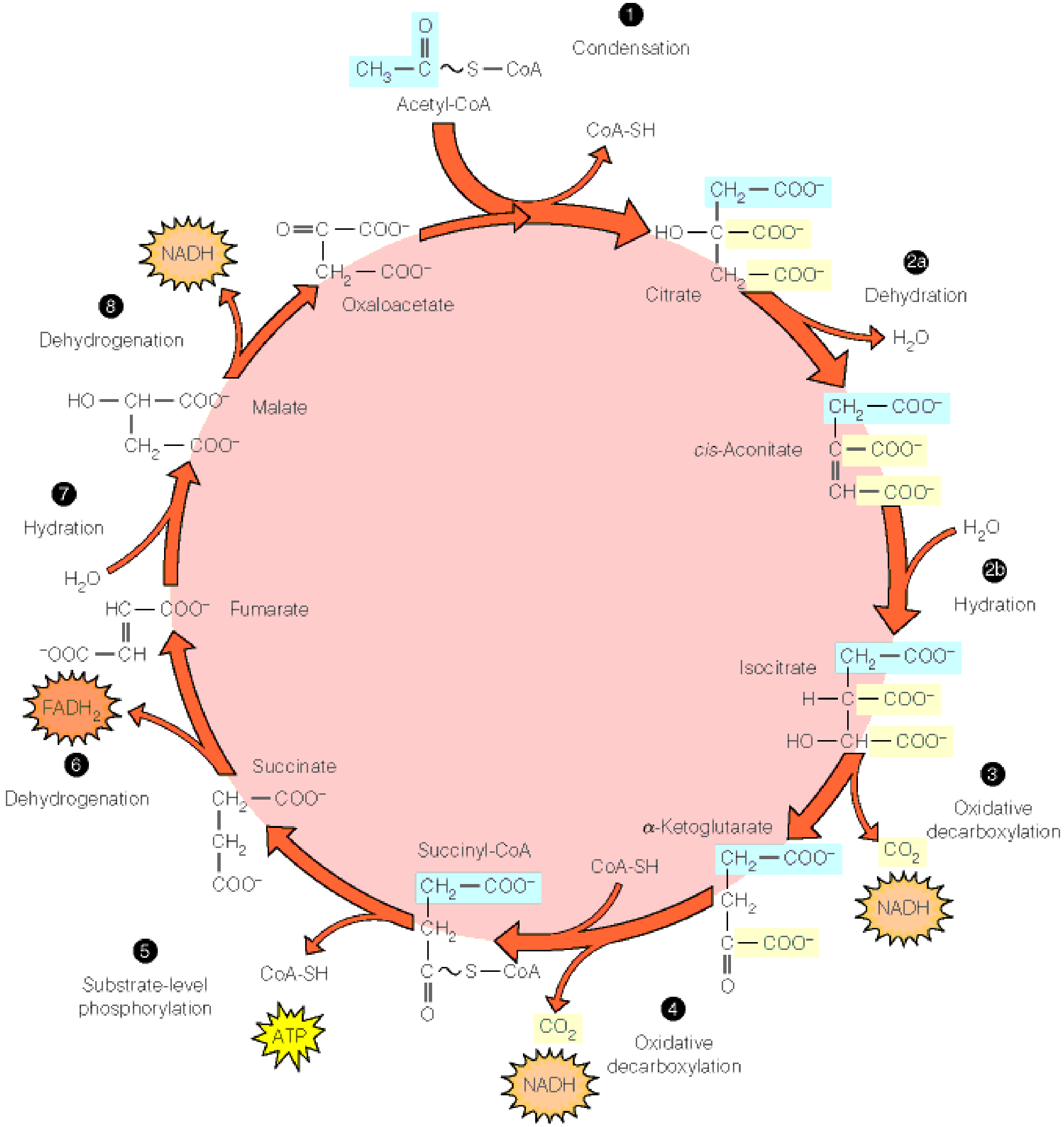
After pyruvate is oxidized, the citric acid cycle completes the energy-yielding oxidation of organic molecules

The oxidation of substrates is a 8 steps process, summarized in 3:

- incorporation into acetyl-CoA
- Oxidation to CO_2, reduction of electron-transfer agents and a small amount of ATP
- The reduced electron transfer agents are reoxidized producing energy for the synthesis of further ATP (oxidative phosphorylation)

The activity of TCA cycle is favored by low ratio of NADH/NAD$^+$

1 mole of glucose yields 30 moles of ATP !



During oxidative phosphorylation, chemiosmosis couples electron transport to ATP synthesis.

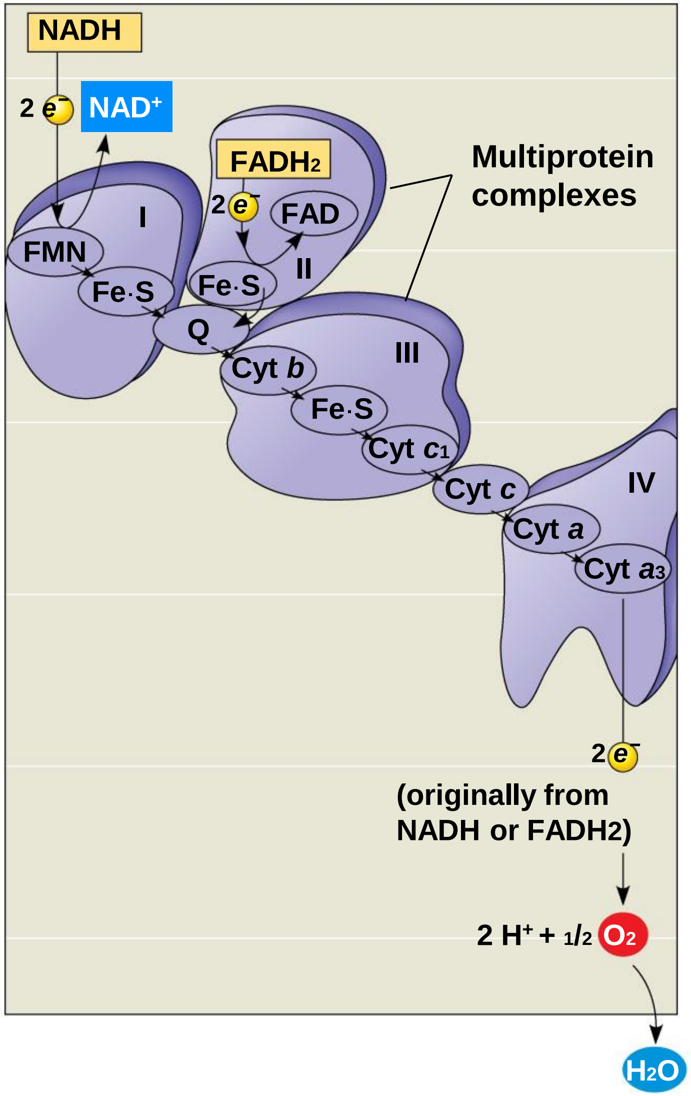
Following glycolysis and the citric acid cycle, NADH and $FADH_2$ account for most of the energy extracted from food

- These two electron carriers donate electrons to the electron transport chain, which powers ATP synthesis via oxidative phosphorylation
- Electrons are transferred from NADH or $FADH_2$ to the electron transport chain
- Electrons are passed through a number of proteins including **cytochromes** (each with an iron atom) to O_2
- The electron transport chain generates no ATP directly
- It breaks the large free-energy drop from food to O_2 into smaller steps that release energy in manageable amounts.

The Pathway of Electron Transport.

The electron transport chain is in the inner membrane (cristae) of the mitochondrion

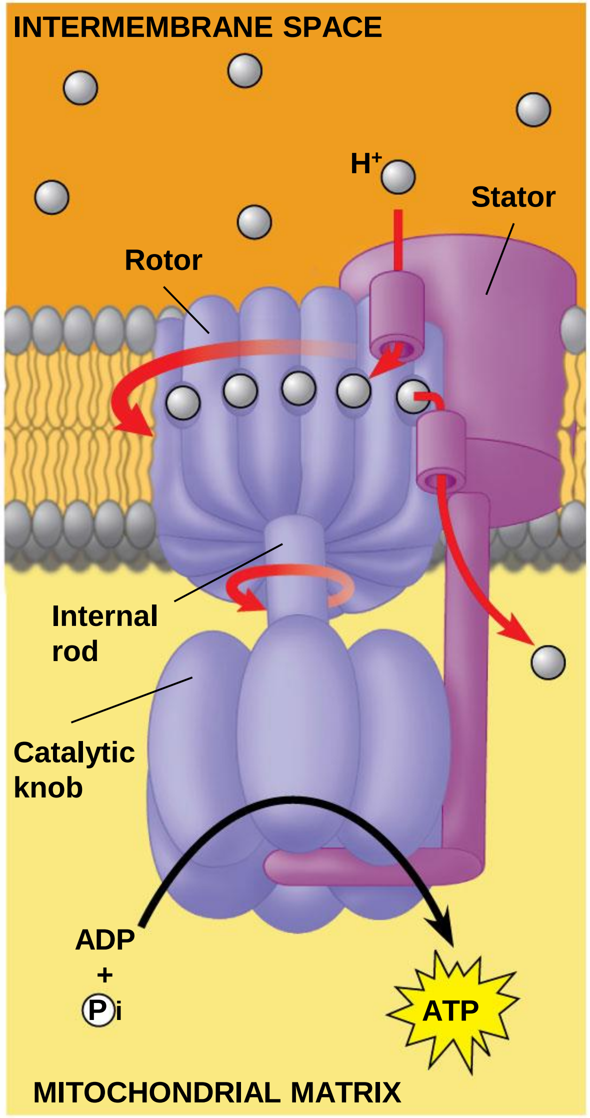
- Most of the chain's components are proteins, which exist in multiprotein complexes
- The carriers alternate reduced and oxidized states as they accept and donate electrons
- Electrons drop in free energy as they go down the chain and are finally passed to O_2, forming H_2O.



Energy-Coupling Mechanism.

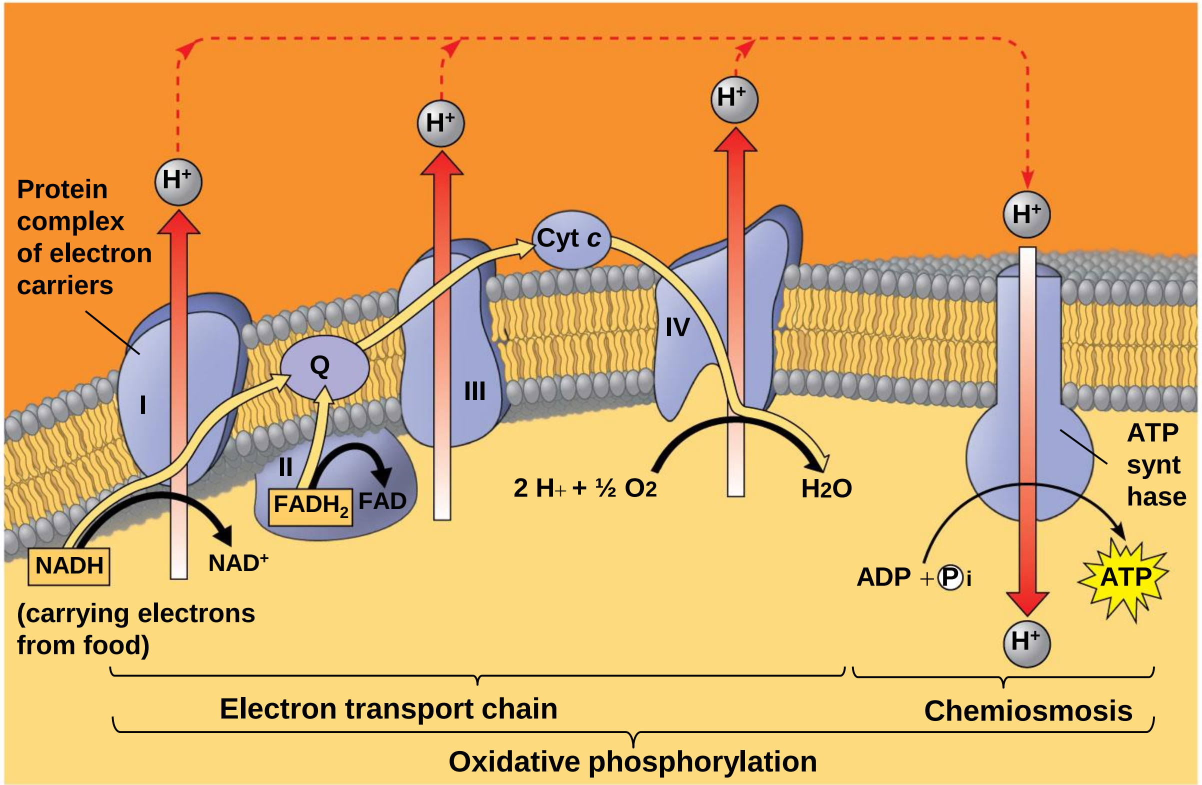
Electron transfer in the electron transport chain causes proteins to pump H^+ from the mitochondrial matrix to the intermembrane space

- H^+ then moves back across the membrane, passing through the proton, **ATP synthase**
- ATP synthase uses the exergonic flow of H^+ to drive phosphorylation of ATP
- This is an example of **chemiosmosis**, the use of energy in a H^+ gradient to drive cellular work.

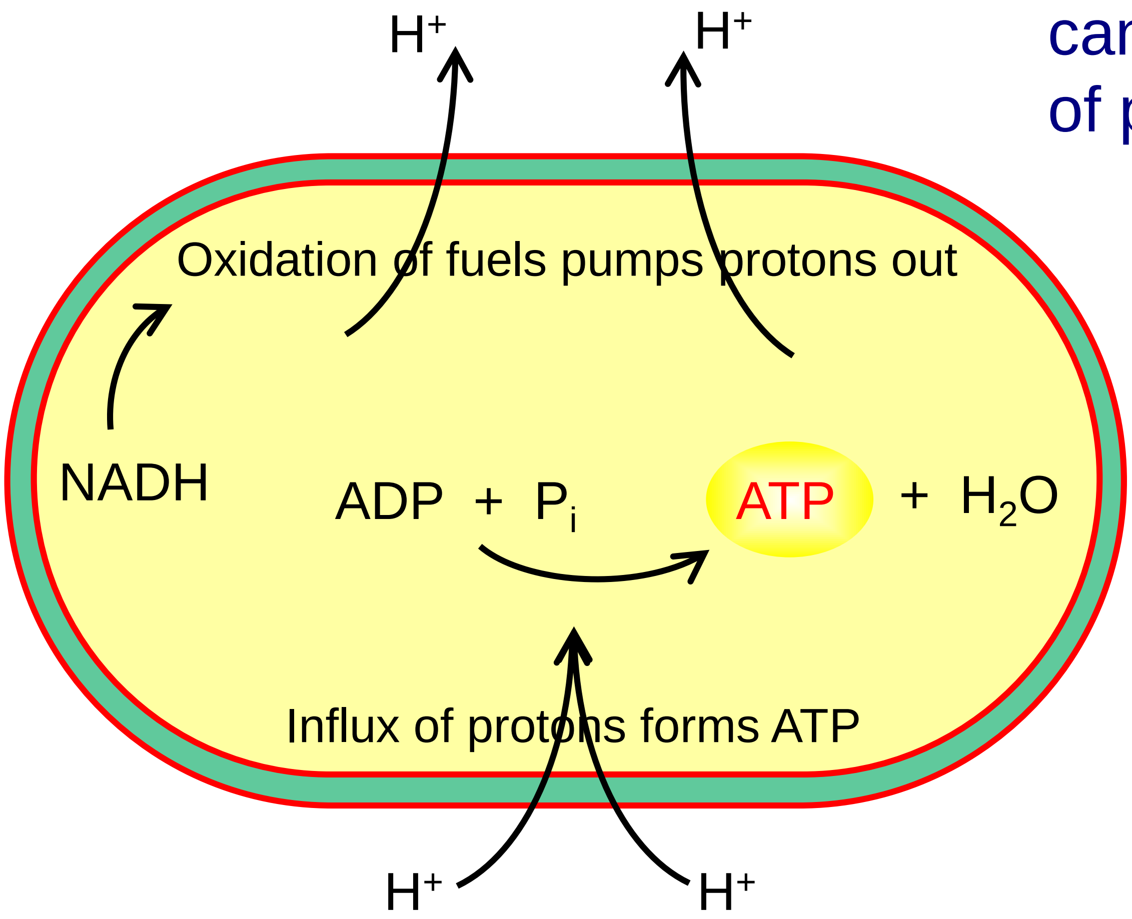


Proton Gradients in Respiration.

- The energy stored in a H^+ gradient across a membrane couples the redox reactions of the electron transport chain to ATP synthesis
- The H^+ gradient is referred to as a **proton-motive force**, emphasizing its capacity to do work (about 32 mol of ATP for mole of glucose).



Oxidation of “fuels” can power formation of proton gradients



Proton gradients can in turn drive ATP synthesis

Fermentation and Anaerobic Respiration.

Fermentation and anaerobic respiration enable cells to **produce ATP without the use of oxygen**

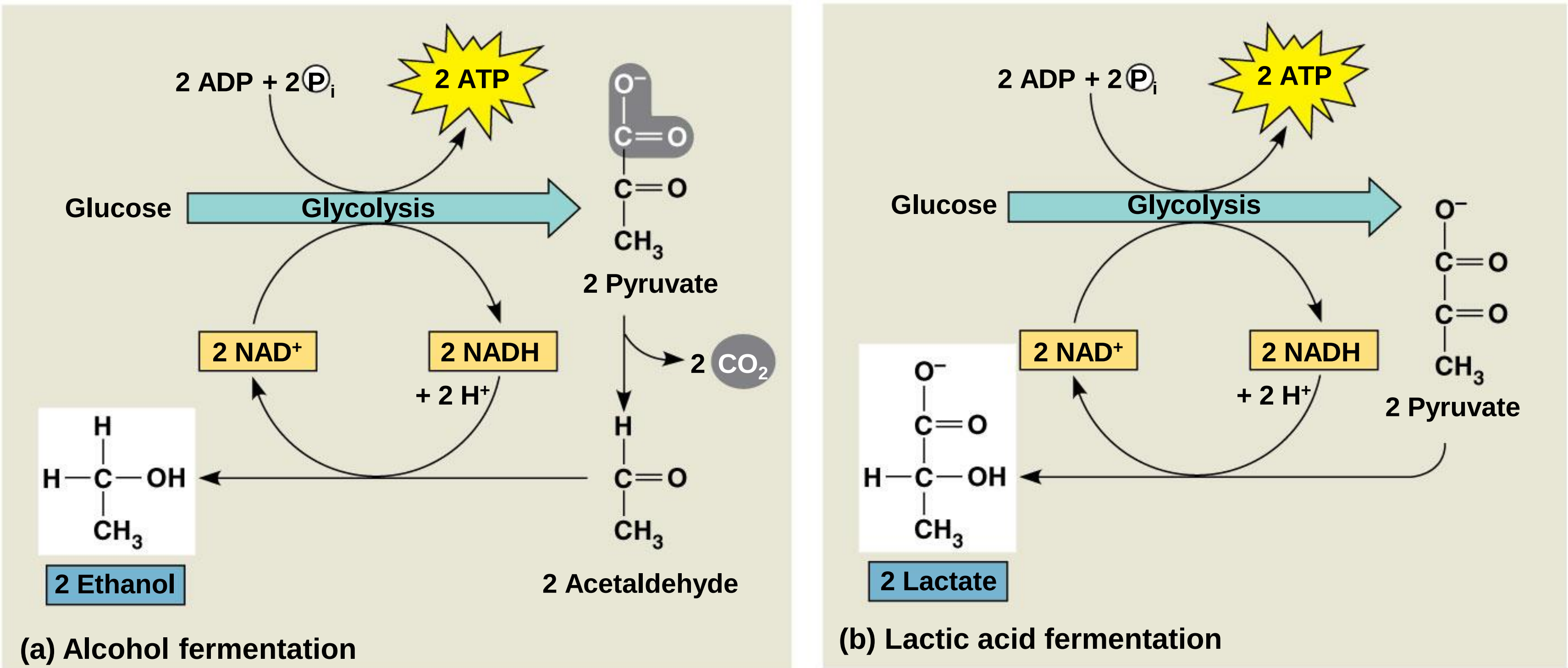
- Most cellular respiration requires O_2 to produce ATP
- Without O_2, the electron transport chain will cease to operate
- In that case, glycolysis couples with fermentation or anaerobic respiration to produce ATP
- Anaerobic respiration uses an electron transport chain with a final electron acceptor other than O_2, for example sulfate
- Fermentation uses substrate-level phosphorylation instead of an electron transport chain to generate ATP.

Types of Fermentation.

Fermentation consists of glycolysis plus reactions that regenerate NAD^+, which can be reused by glycolysis

- Two common types are alcohol fermentation and lactic acid fermentation
- In alcohol fermentation, pyruvate is converted to ethanol in two steps, with the first releasing CO_2
- Alcohol fermentation by yeast is used in brewing, winemaking, and baking
- In lactic acid fermentation, pyruvate is reduced to NADH, forming lactate as an end product, with no release of CO_2
- 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.

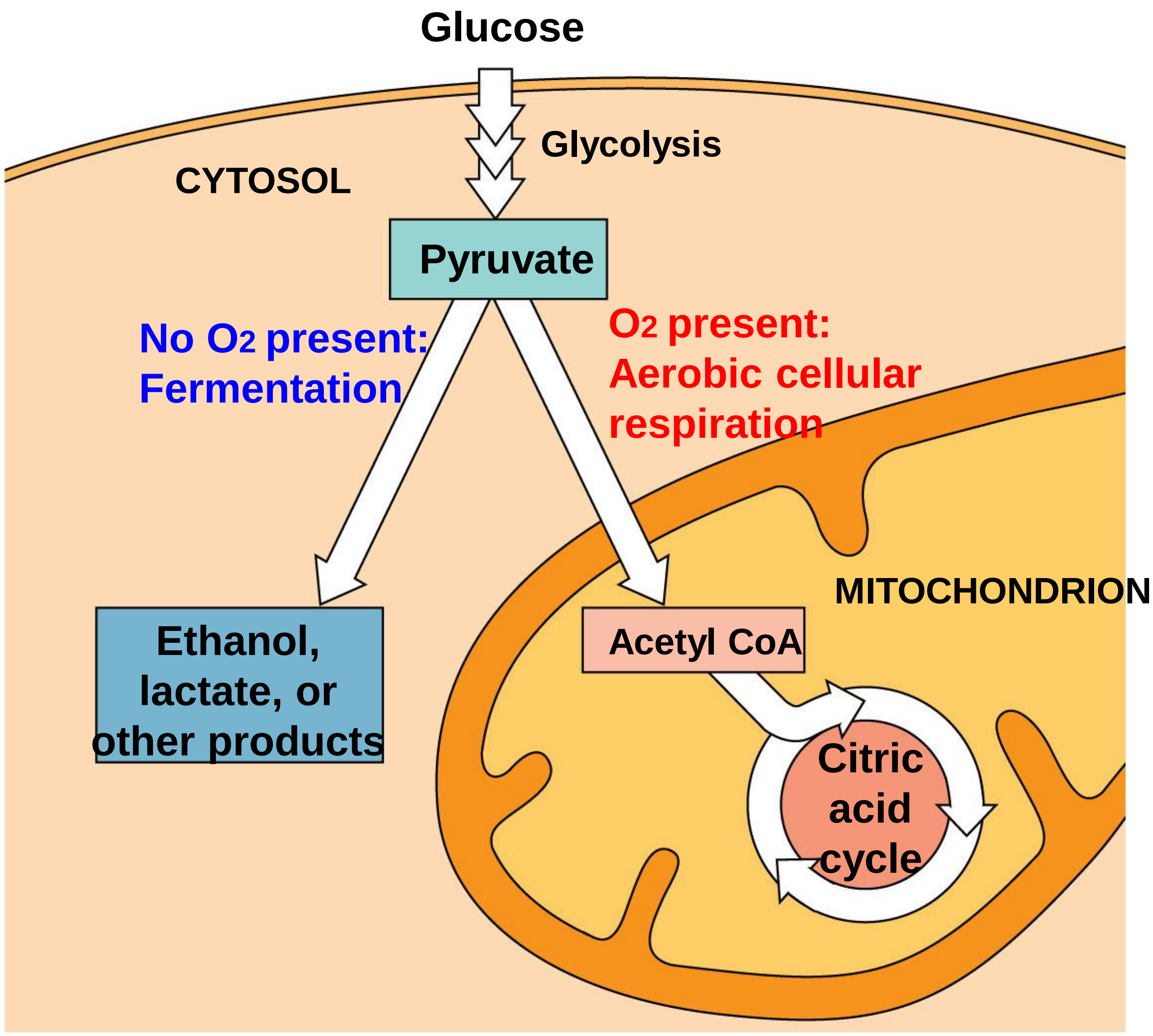
Two Common Type of Fermentation.



Comparing Fermentation with Anaerobic and Aerobic Respiration.

- All use glycolysis (net ATP = 2) to oxidize glucose and harvest chemical energy of food
- In all three, NAD^+ is the oxidizing agent that accepts electrons during glycolysis
- The processes have different final electron acceptors: an organic molecule (such as pyruvate or acetaldehyde) in fermentation and O_2 in cellular respiration
- Cellular respiration produces 32 ATP per glucose molecule; fermentation produces 2 ATP per glucose molecule
- Obligate anaerobes carry out fermentation or anaerobic respiration and cannot survive in the presence of O_2
- Yeast and many bacteria are facultative anaerobes, meaning that they can survive using either fermentation or cellular respiration
- In a facultative anaerobe, pyruvate is a fork in the metabolic road that leads to two alternative catabolic routes.

Divergent Metabolic Pathways.

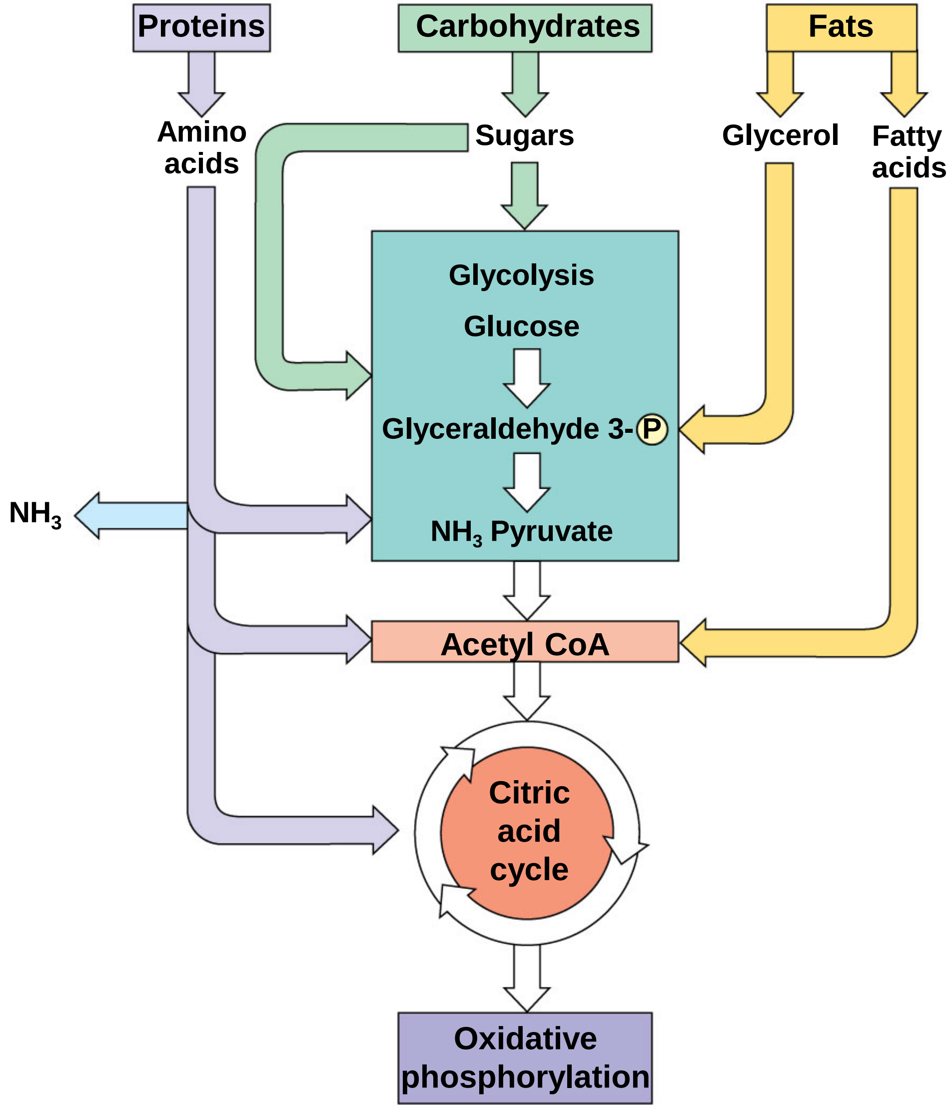


Glycolysis and the citric acid cycle connect to many other metabolic pathways.

- Glycolysis and the citric acid cycle are major intersections to various catabolic and anabolic pathways
- Catabolic pathways funnel electrons from many kinds of organic molecules into cellular respiration
- Glycolysis accepts a wide range of 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.

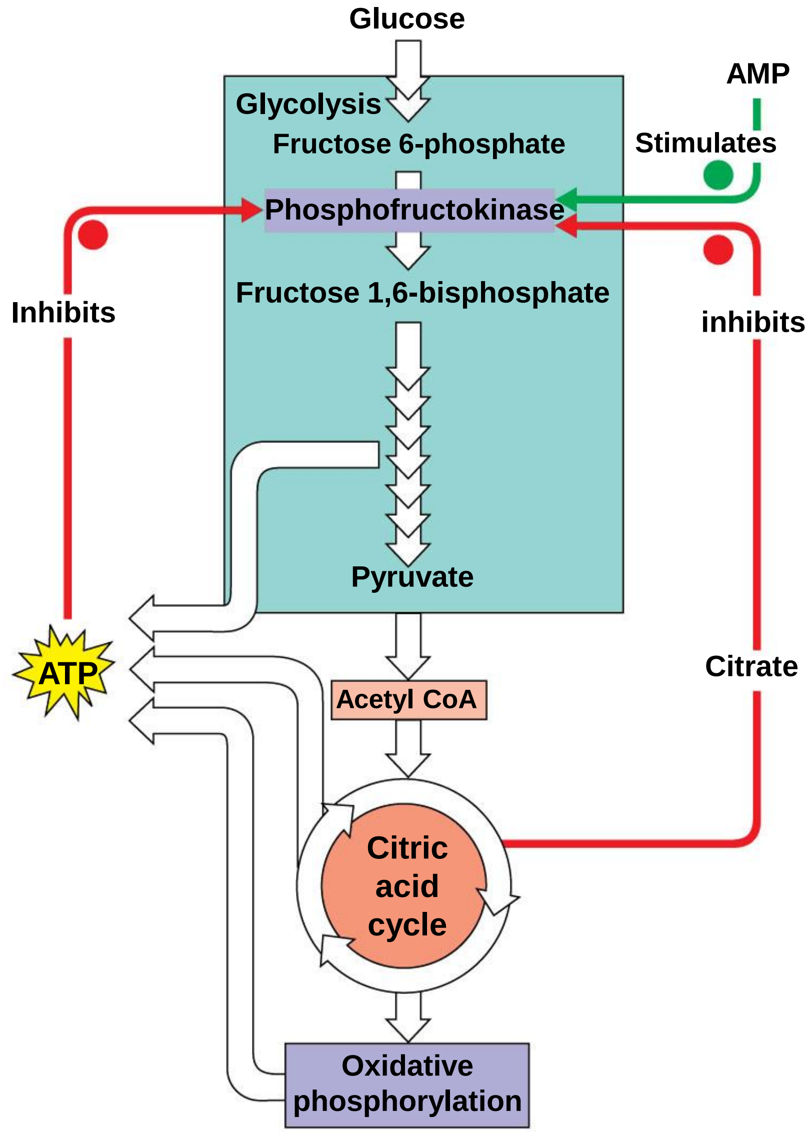
Key Small Molecules (Metabolites) from Food.

- The body uses small molecules to build other substances.
- These small molecules may come directly from food, from glycolysis, or from the citric acid cycle.

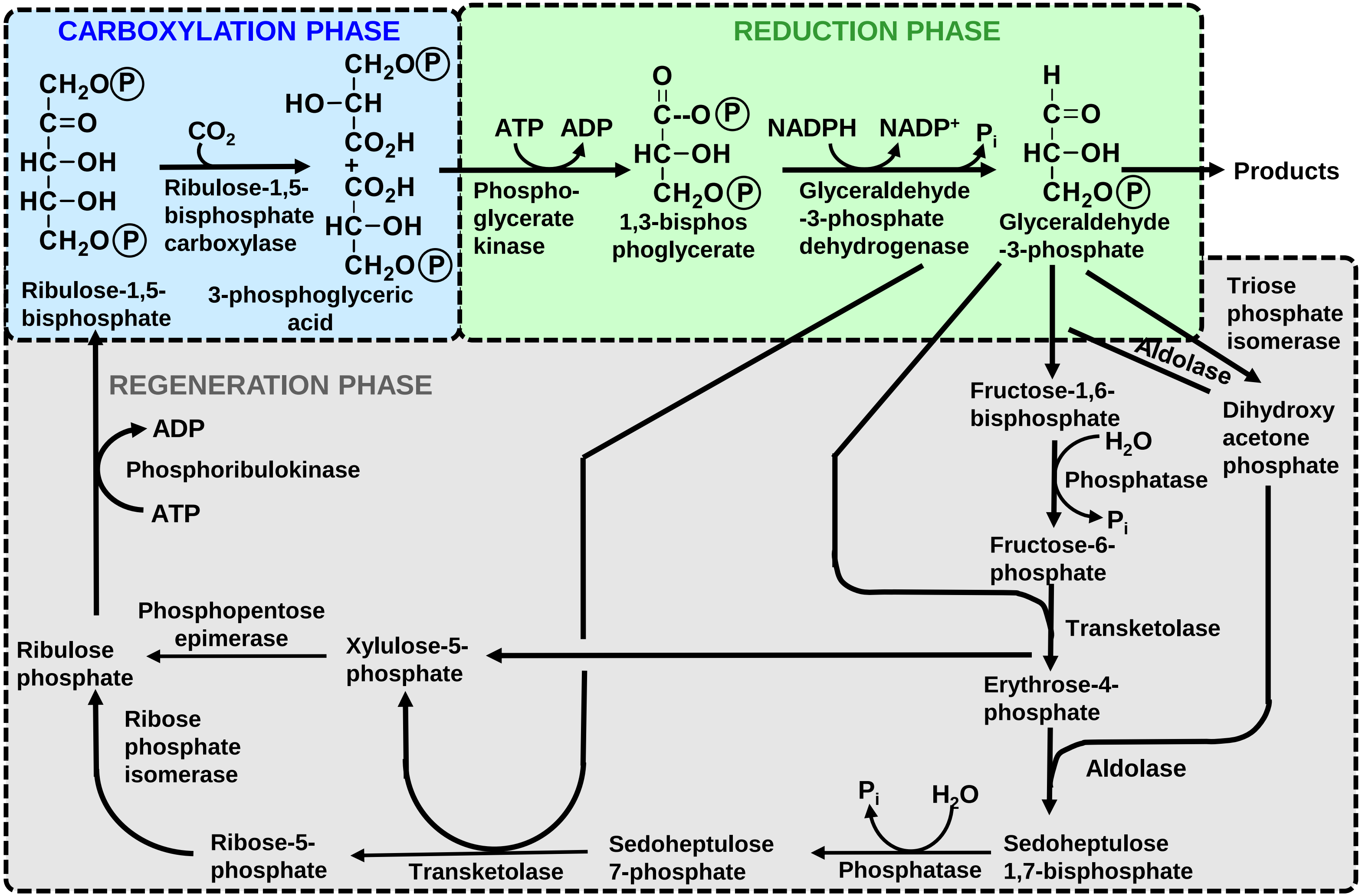


Regulation of Cellular Respiration via Feedback Mechanisms.

- Feedback inhibition is the most common mechanism for control
- If ATP concentration begins to drop, respiration speeds up; when there is plenty of ATP, respiration slows down.
- Control of catabolism is based mainly on regulating the activity of enzymes at strategic points in the catabolic pathway.



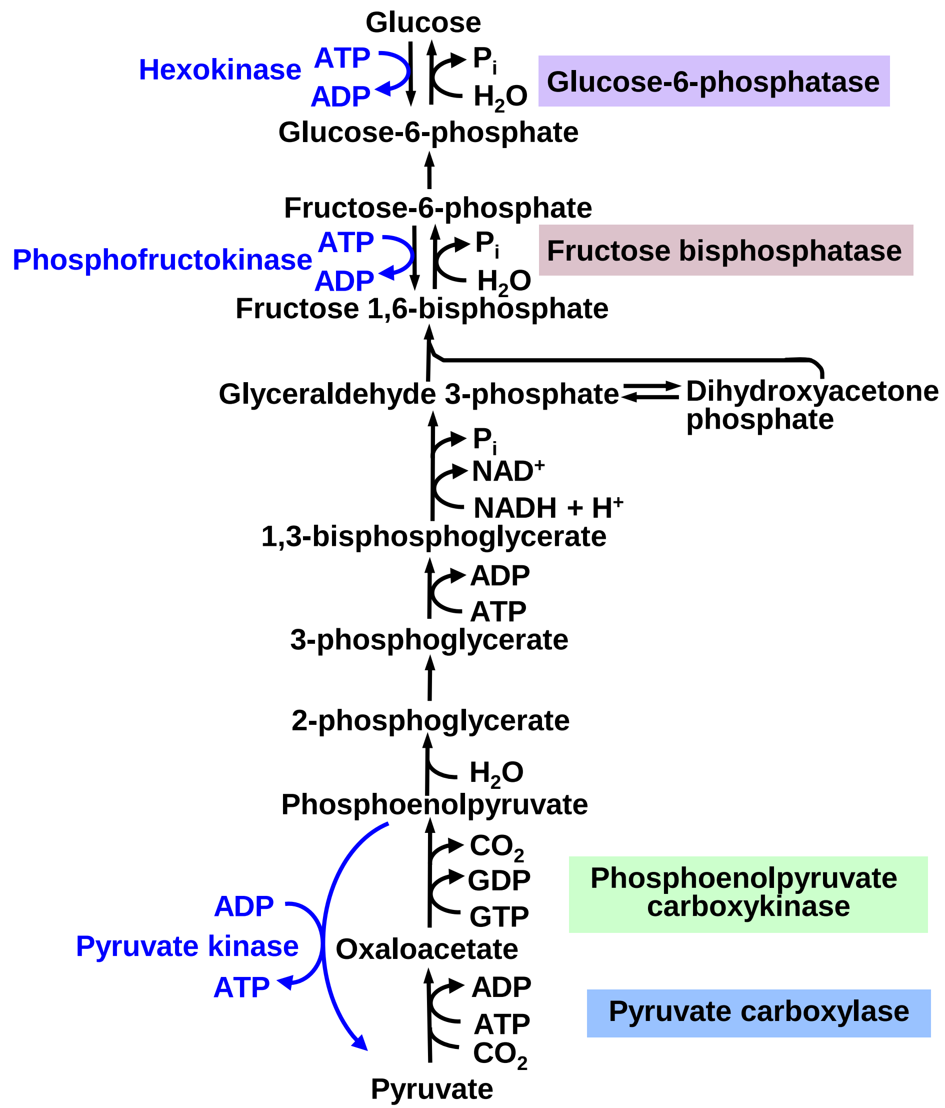
The Calvin Cycle.



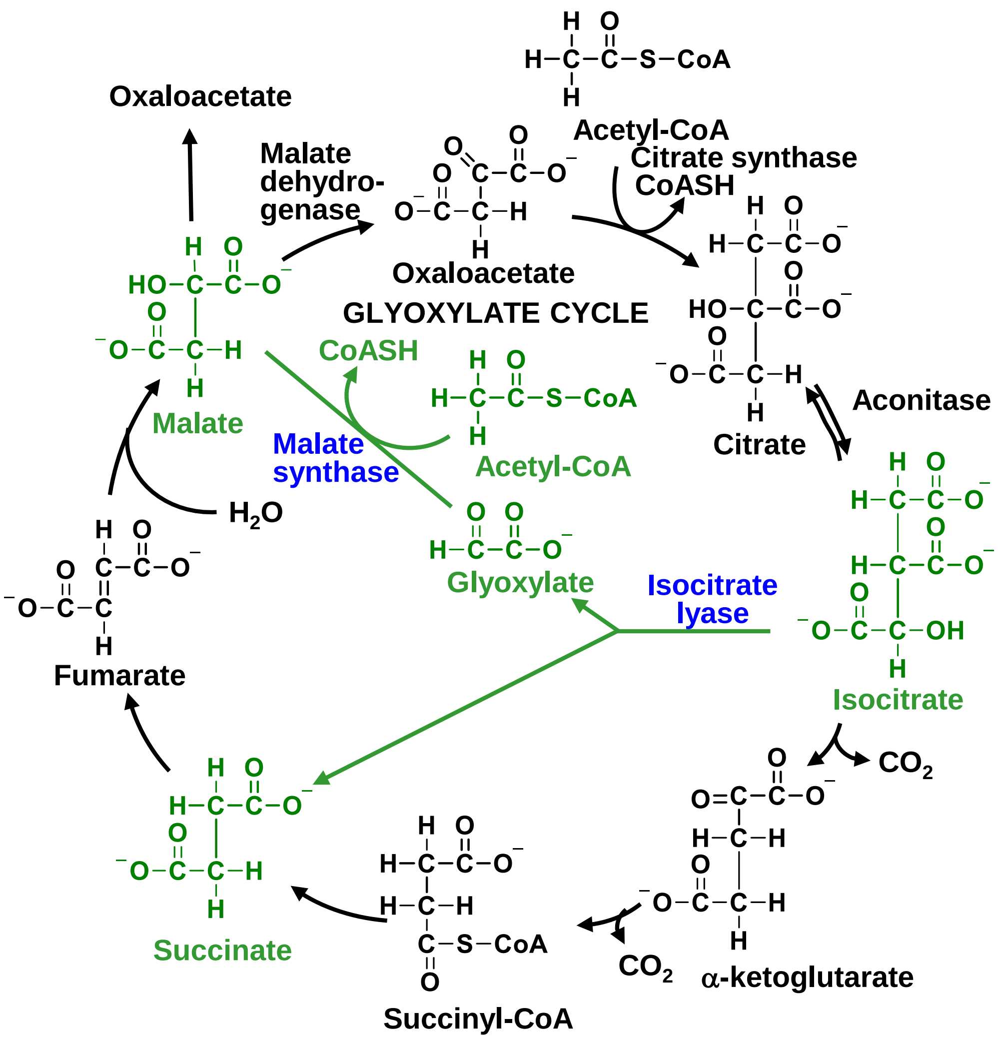
Gluconeogenesis.

Cells use this route to synthesize 6-C sugars from fatty acids, proteins, etc.

Mainly, the same processes of glycolysis



The Glyoxalate Cycle.



Overall equation:

2 Acetyl-CoA + FAD + 2NAD$^+$+ 3H_2O $\rightarrow$ Oxaloacetate + 2CoA + $FADH_2$ + 2NADH +2H

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Metabolic Pathways.

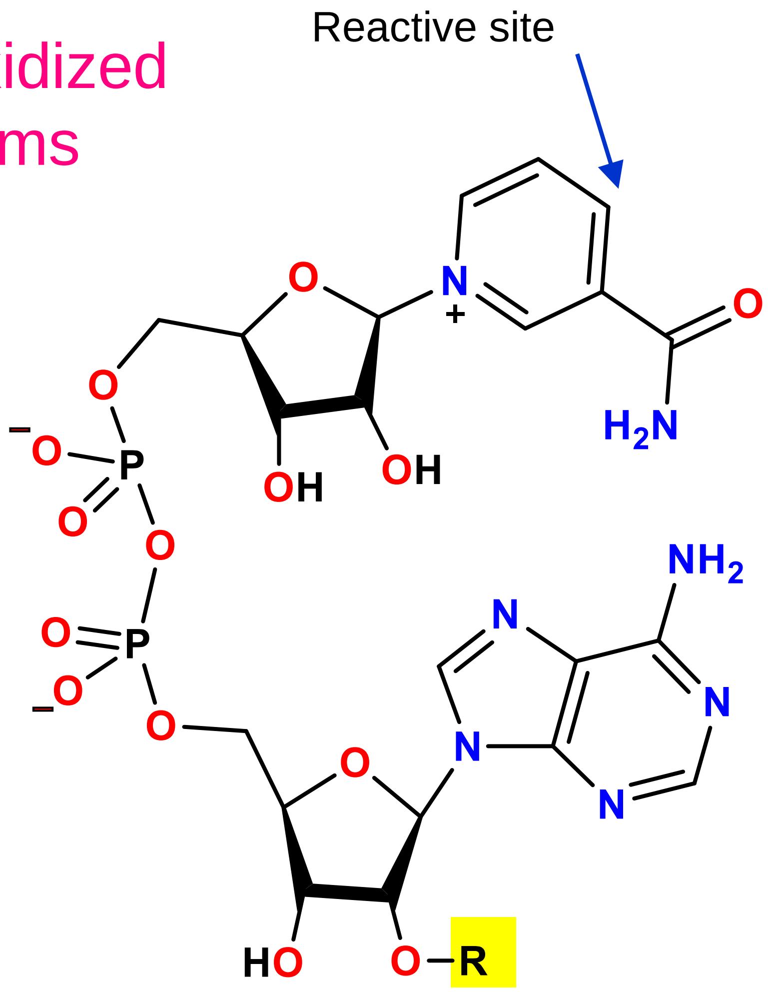
Unifying themes include, common metabolites, reactions, and regulatory schemes.

Activated carriers exemplify modular design and economy of metabolism, *e.g.* ATP is an activated carrier of phosphoryl groups:

1. Activated carriers of electrons for fuel oxidation
   NAD^+ / NADH and FAD / $FADH_2$
2. An activated carrier of electrons for reductive biosynthesis
   $NADP^+$ / NADPH
3. An activated carrier of two-carbon fragments
   Coenzyme A, *e.g.* Acetyl CoA

Structure of Nicotinamide-derived Electron Carriers.

Oxidized forms

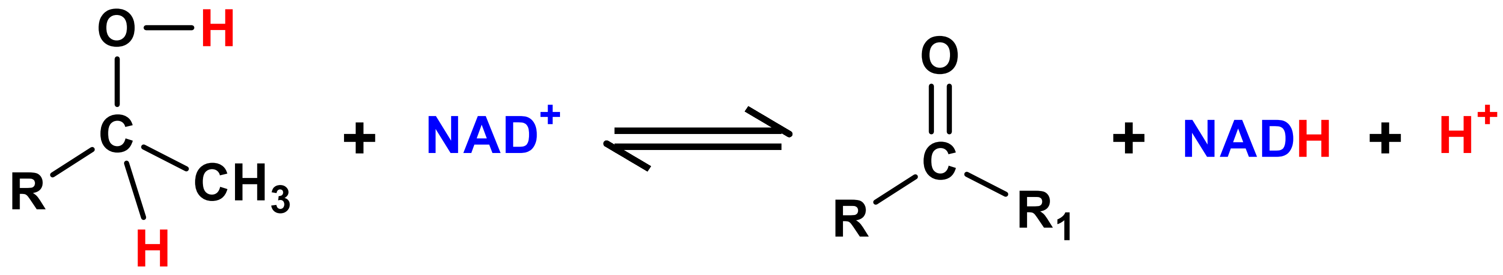


Nicotinamide adenine dinucleotide (NAD^+), R = H

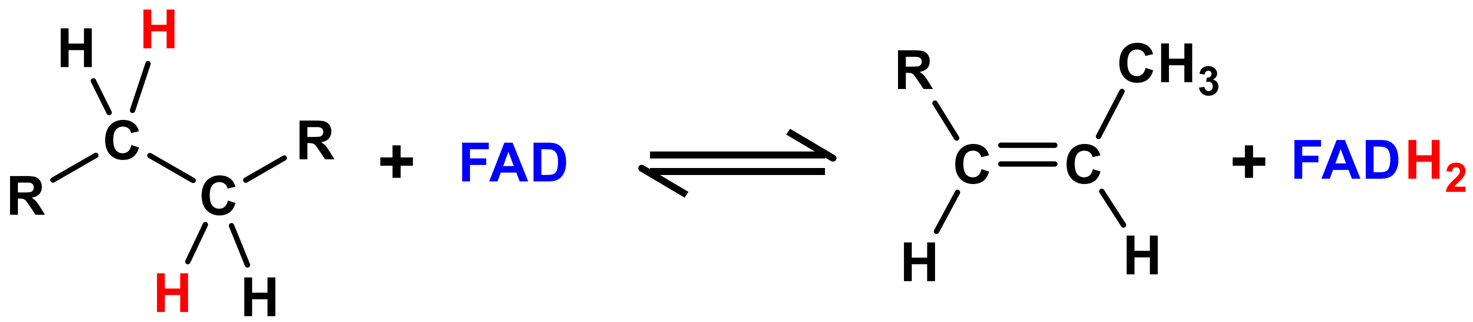
Nicotinamide adenine dinucleotide phosphate ($NADP^+$), $R = PO_3^{2-}$

Prominent carriers of high-energy electrons.

Reaction Type for NAD^+ as Electron Acceptor.

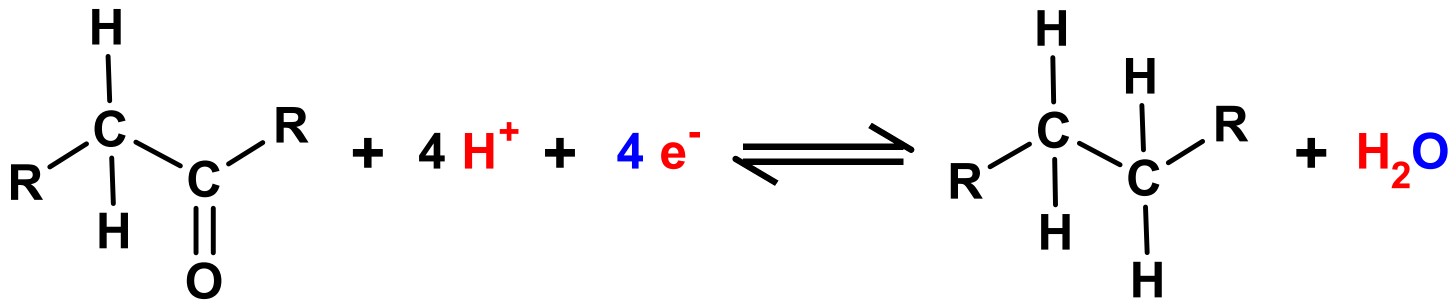


Reaction Type for FAD as Electron Acceptor.



Reductive Biosynthesis: Fatty Acids.

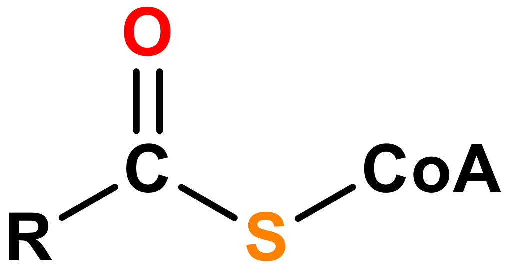
Keto group to methylene group reduction, several steps, requires an input of 4 electrons:



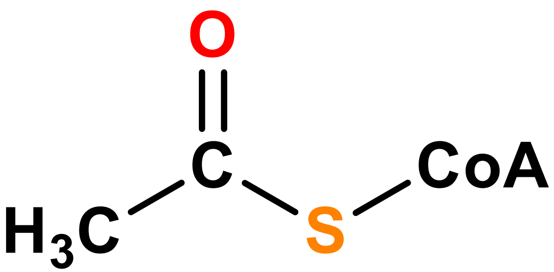
NADPH is the electron donor

Coenzyme A.

Activated carrier of two-carbon fragments.



Acyl CoA

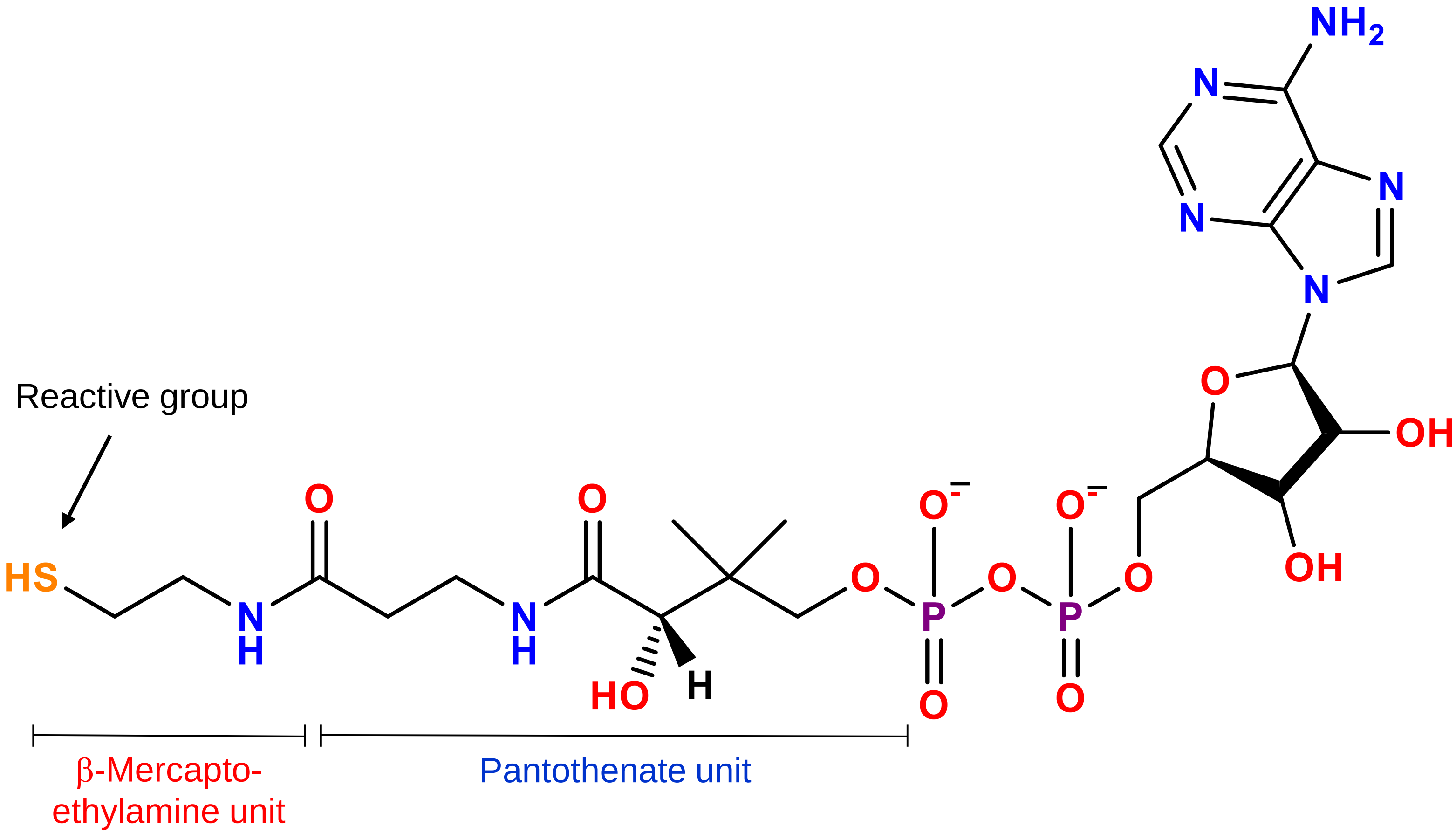


Acetyl CoA

Acyl groups linked to CoA by thioester bonds: high acyl group-transfer potential (transfer is exergonic).

Acetyl CoA carries an activated acetyl group just like ATP carries an activated phosphoryl group.

Structure of Coenzyme A.



B vitamin

Main Activated Carriers in Metabolism.

Carrier molecule in activated form	Group carried	Vitamin Precursor
ATP	Phosphoryl	
NADH and NADPH	Electrons	Nicotinate (niacin)
$FADH_2$	Electrons	Riboflavin (vit. B_2)
$FMNH_2$	Electrons	Riboflavin (vit. B_2)
Coenzyme A	Acyl	Pantothenate
Lipoamide	Acyl	
Thiamine pyrophosphate	Aldehyde	Thiamine (vitamin B_1)
Biotin	CO_2	Biotin
Tetrahydrofolate	One-carbon units	Folate
S-Adenosylmethionine	Methyl	
Uridine diphosphate glucose	Glucose	
Cytidine diphosphate diacylglycerol	Phosphatidate	
Nucleoside triphosphates	Nucleosides	

A small set of carriers responsible for most interchanges of activated groups in metabolism

Thousands of Metabolic Reactions.

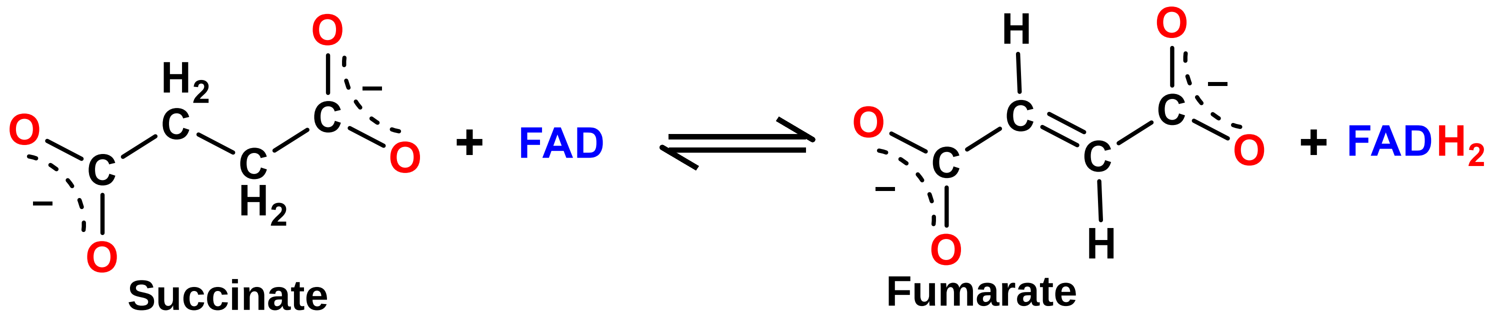
Can be subdivided into six types.

Types of chemical reactions in metabolism:

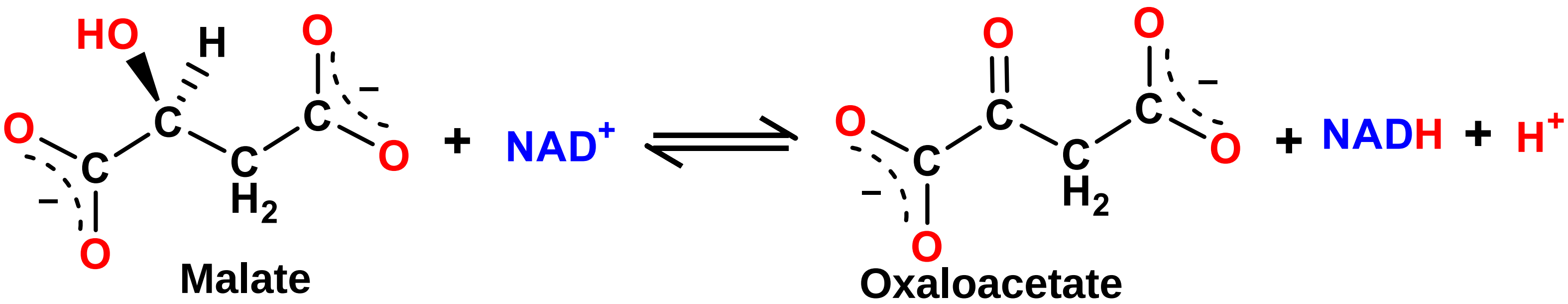
Type of reaction	Description
Oxidation-reduction	Electron-transfer
Ligation requiring ATP cleavage	Formation of covalent bond (i.e. carbon-carbon bonds)
Isomerization	Rearrangement of atoms to form isomers
Group transfer	Transfer of a functional group from one molecule to another
Hydrolytic	Cleavage of bonds by the addition of water
Addition or removal of functional groups	Addition of functional groups to double bonds or their removal to form double bonds.

1. Oxidation-reduction Reactions.

The two reactions are components of the citric acid cycle, which completely oxidizes the activated two-carbon fragment of acetyl CoA to two molecules of CO_2:



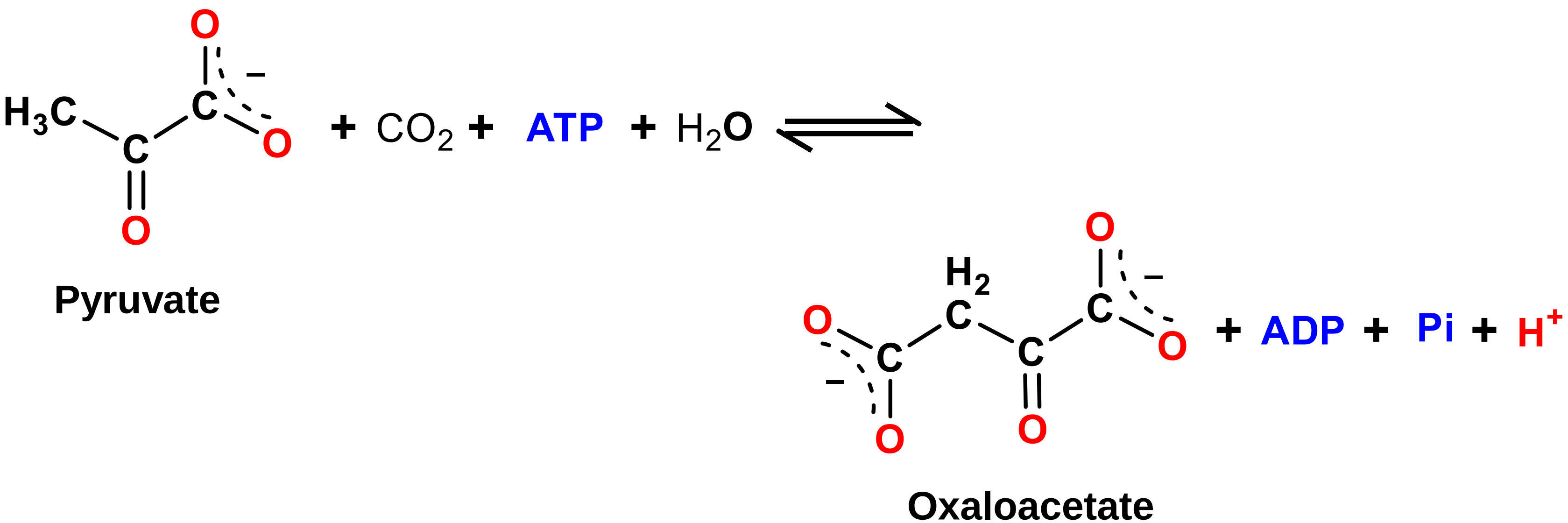
(1)



(2)

Oxidation of succinate and malate generates useful energy by transferring electrons to carriers FAD and NAD^+.

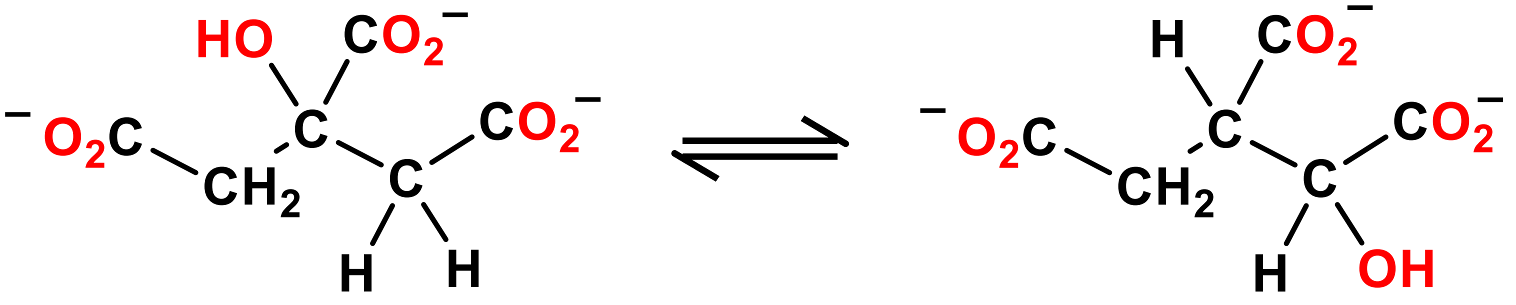
Form bonds by using energy from ATP cleavage:



Oxaloacetate can be used in the citric acid cycle, or converted into amino acids such as aspartic acid.

3. Isomerization Reactions.

Rearrange particular atoms within the molecule, often in preparation for subsequent reactions, e.g. oxidation-reduction:



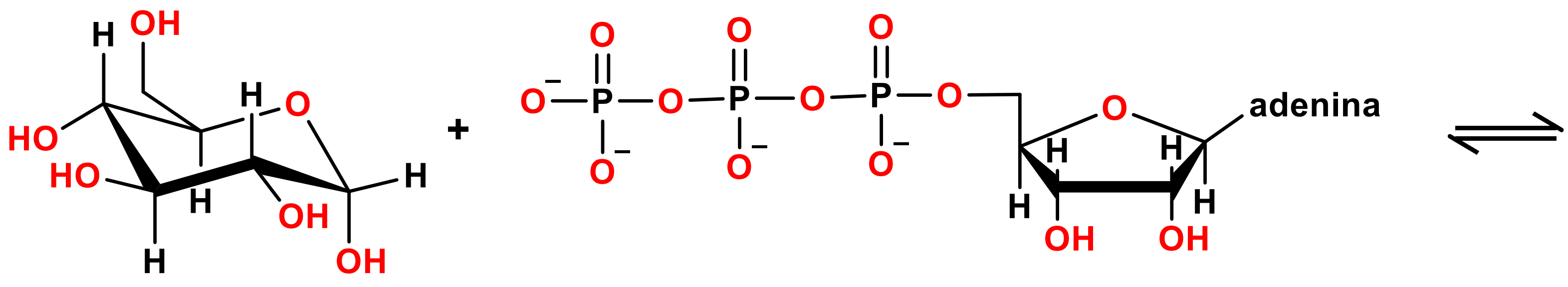
Citrate

Isocitrate

Component of citric acid cycle. Hydroxyl group of citrate moved from tertiary to secondary position followed by oxidation-reduction and decarboxylation.

4. Group Transfer Reactions.

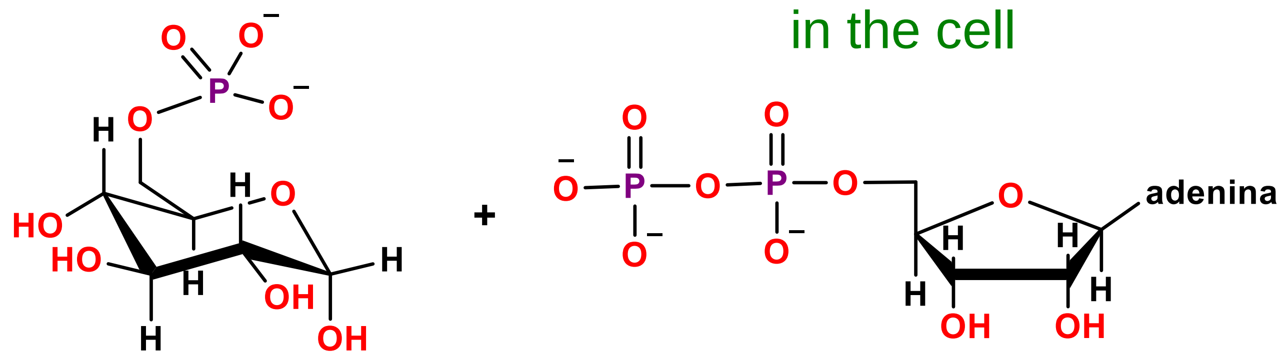
Play a variety of roles, e.g. phosphoryl group transfer to glucose:



Glucose

ATP

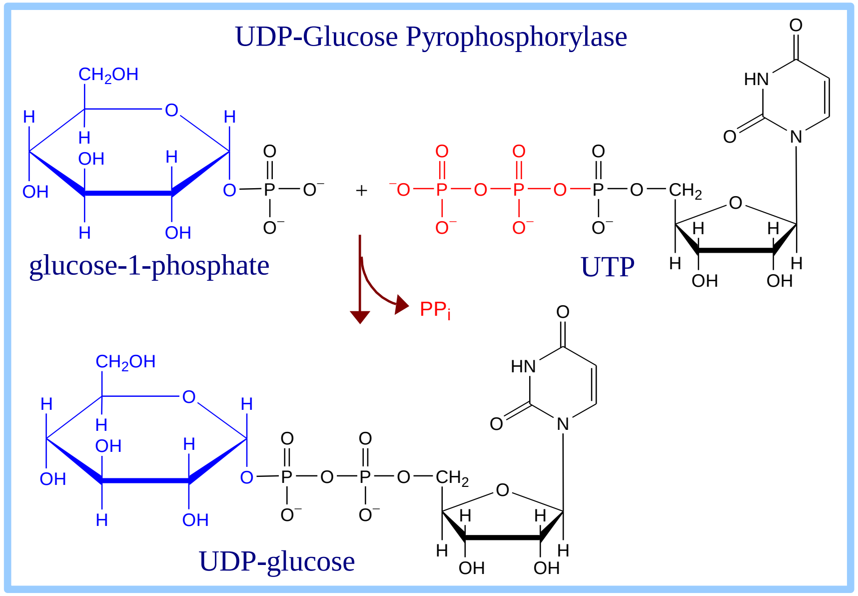
Reaction traps glucose in the cell



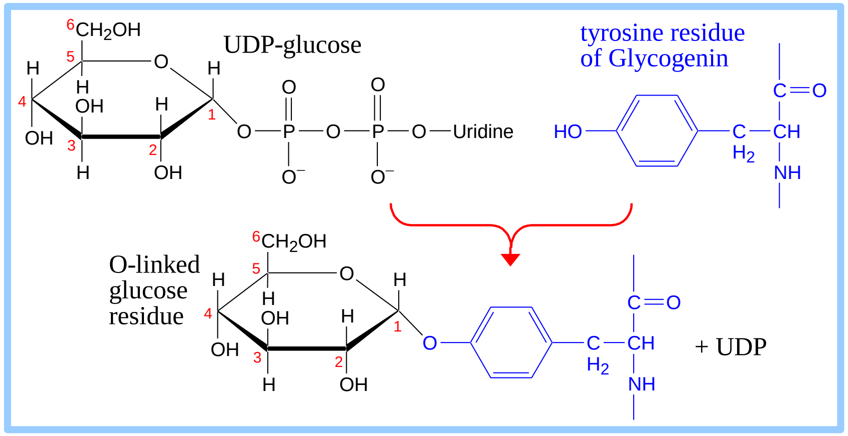
Glucose-6-phosphate ($G\text{-}6P_i$)

ADP

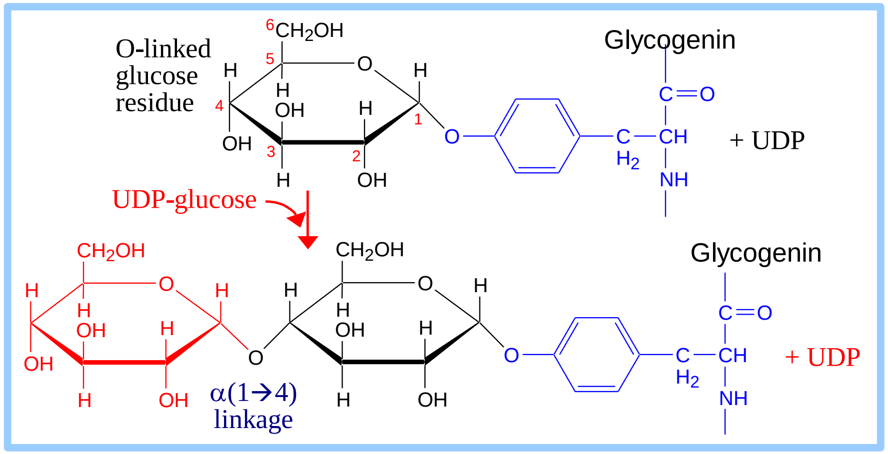
Group Transfer Reactions - Glycogen Synthesis.



Uridine diphosphate (UDP)



Glycogen Synthase



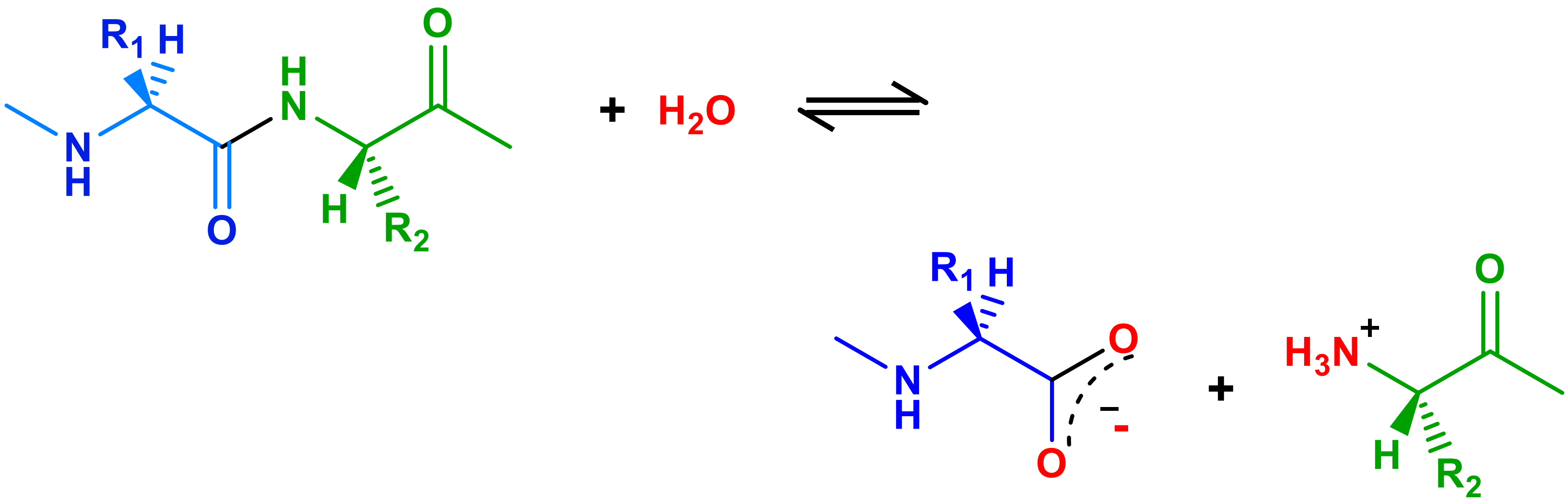
This is repeated until a short linear glucose polymer with α(1,4) glycosidic linkages is built up on Glycogenin.

A branching enzyme transfers a segment from the end of a glycogen chain to the C6 hydroxyl of a glucose residue of glycogen to yield a branch with an α(1,6) linkage.

5. Hydrolytic Reactions.

Cleave bonds by the addition of water:

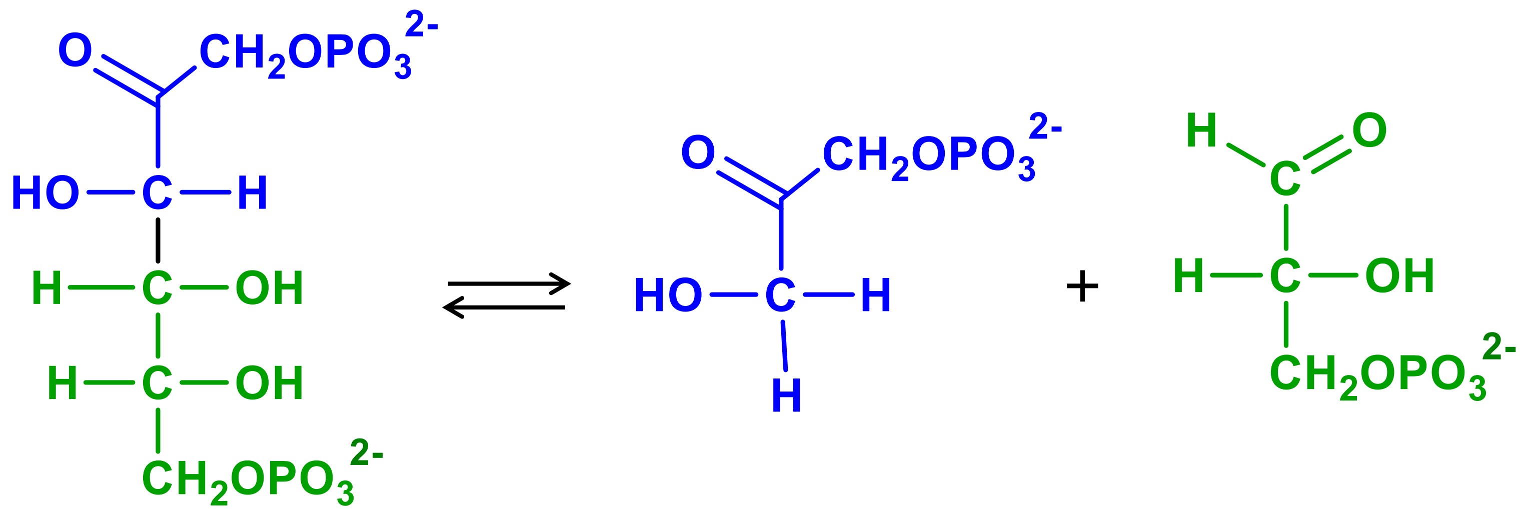
- common means employed to break down large molecules



Illustrates hydrolysis of a peptide bond.

6. The Addition of Functional Groups.

To double bonds or the removal of groups to form double bonds, catalyzed by lyases. Example from glycolysis in the reaction:

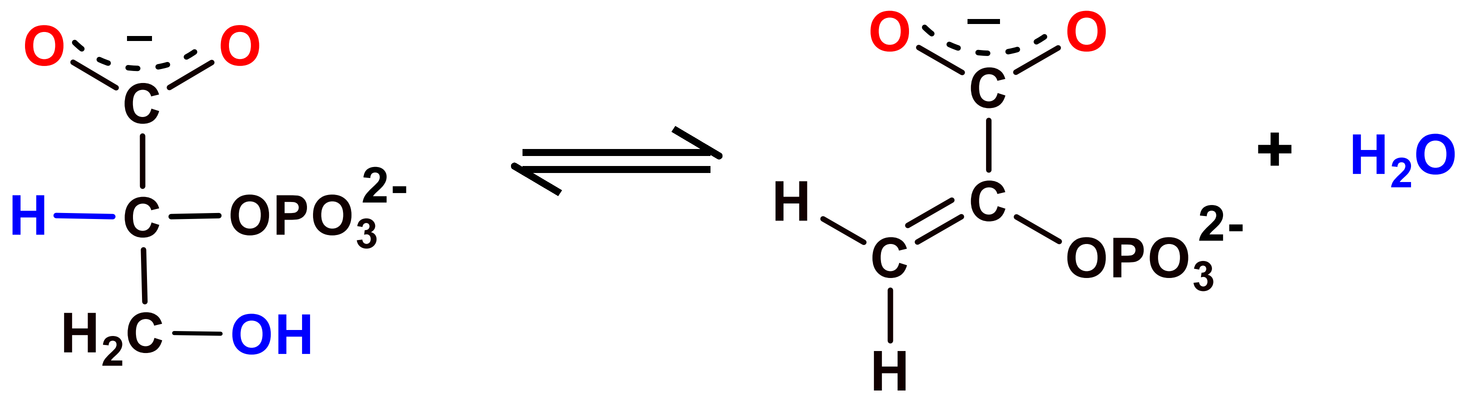


Fructose 1,6-bisphosphate (F-1,6-BP) **Dihydroxyacetone phosphate (DHAP)** **Glyceraldehyde 3-phosphate (GAP)**

The reverse reaction is typical of aldolic condensation between a ketone and an aldehyde. The enzyme catalyzing the equilibrium is an aldolase.

2nd Example of Group Removal.

Dehydration step sets up the next step in the pathway,



2-Phosphoglycerate

Phosphoenolpyruvate (PEP)

a group-transfer reaction that uses high phosphoryl transfer potential of PEP to form ATP from ADP

Metabolic Motifs.

Pathways have reactions in common: oxidation, addition of a functional group to double bond, and another oxidation