BIO102-Foundations of Biology (I)

Glucose metabolism

INDRAPRASTHA INSTITUTE *of* INFORMATION TECHNOLOGY **DELHI**

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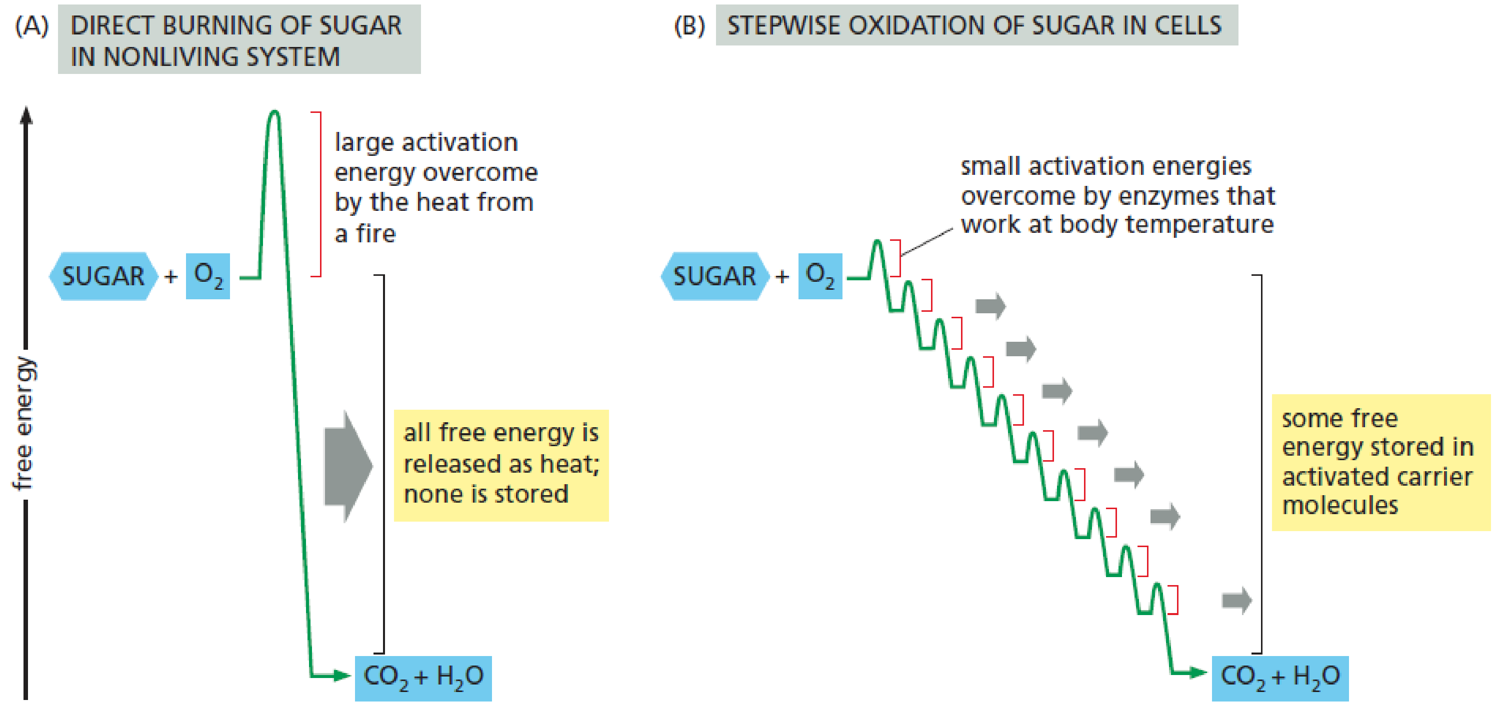
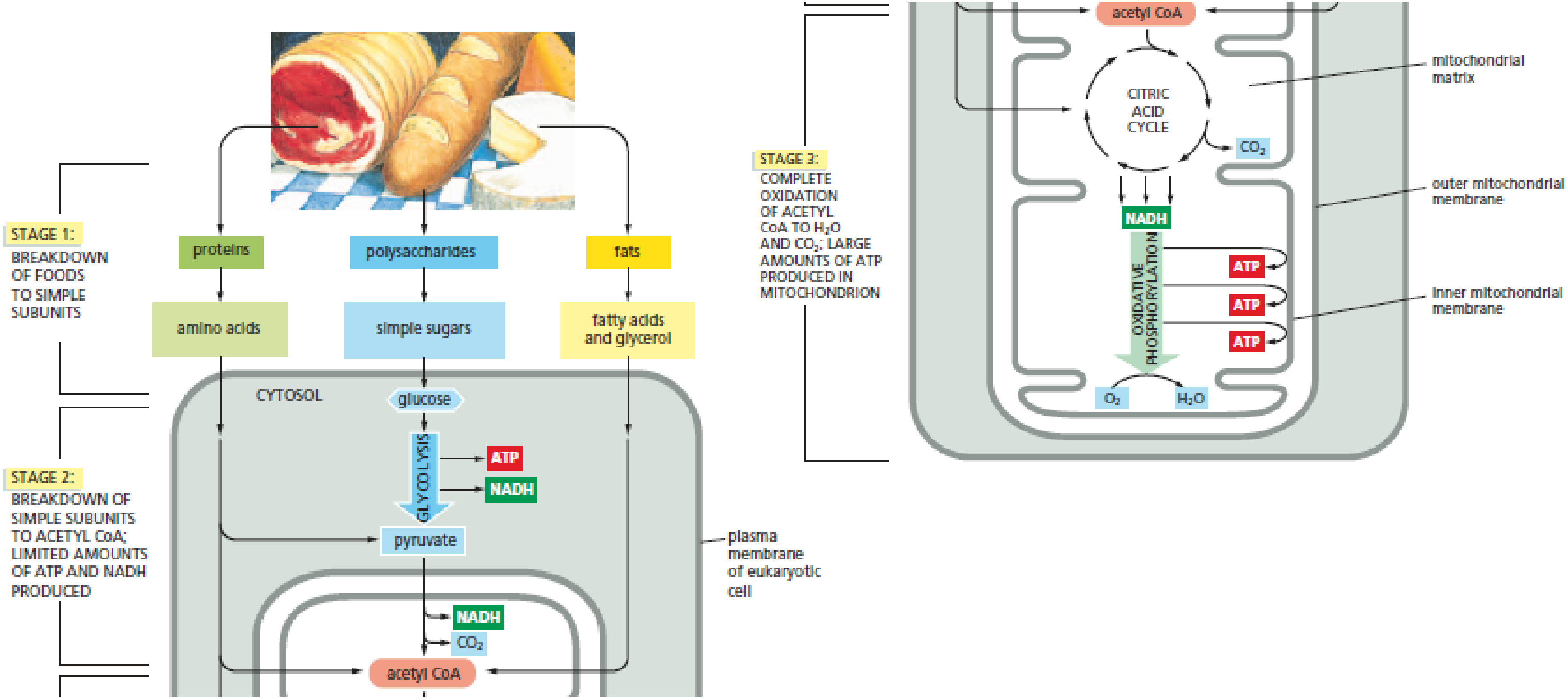
Oxidation of sugar takes place in multiple steps



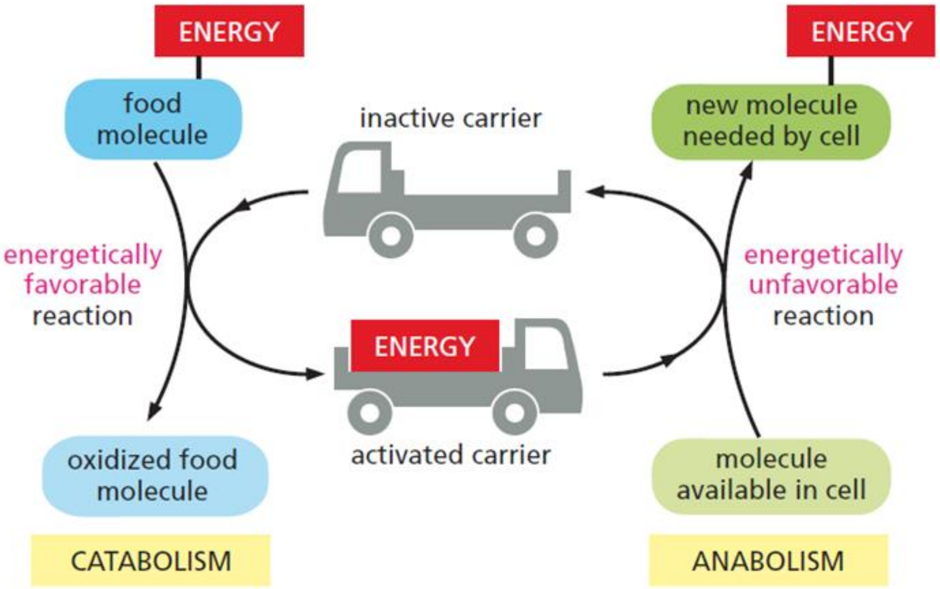
Food molecules are broken down in three stages



Activated carriers

Activated carriers

- In most cases, the energy is stored as chemical-bond energy in a set of activated carriers, small organic molecules that contain one or more energy-rich covalent bonds.
- These molecules diffuse rapidly and carry their bond energy from the sites of energy generation to the sites where energy is used for biosynthesis or for other energy-requiring cell activities.

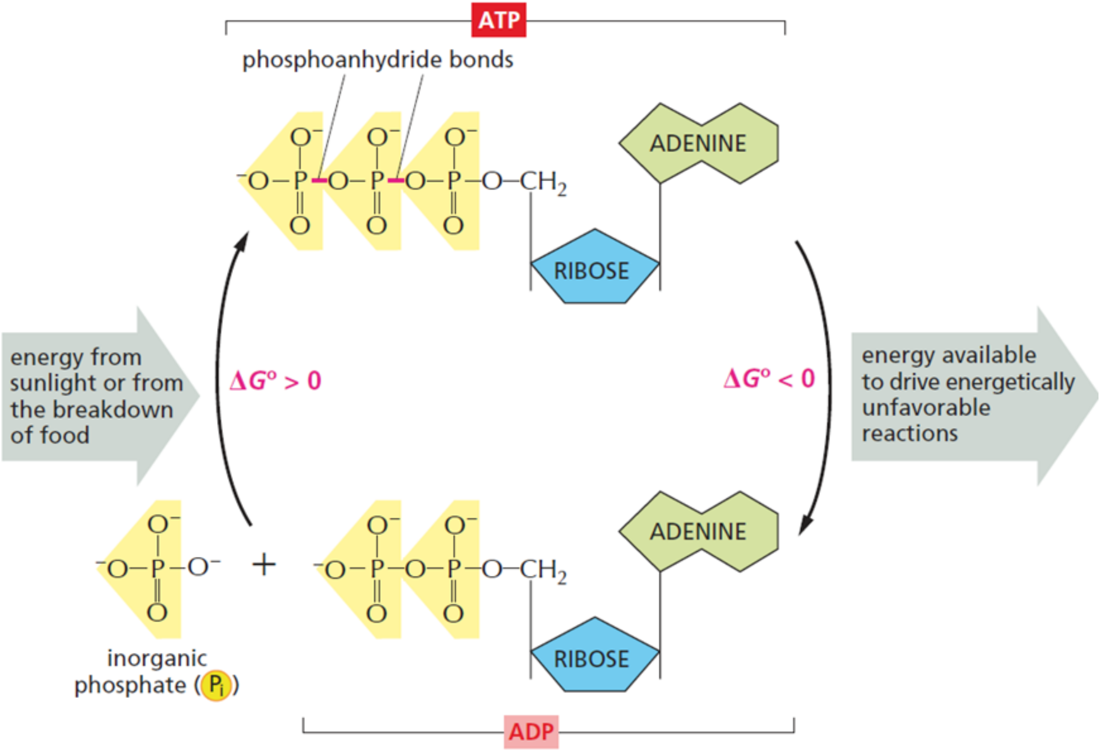


Activated carriers

- Activated carriers store energy in an easily exchangeable form, either as a readily transferable chemical group or as readily transferable (“high energy”) electrons.
- They can serve a dual role as a source of both energy and chemical groups for biosynthetic reactions. The most important activated carriers are ATP and two molecules that are closely related to each other, NADH and NADPH.
- Cells use activated carriers like money to pay for the energetically unfavorable reactions that otherwise would not take place.
- The formation of an activated carrier is coupled to an energetically favorable reaction.

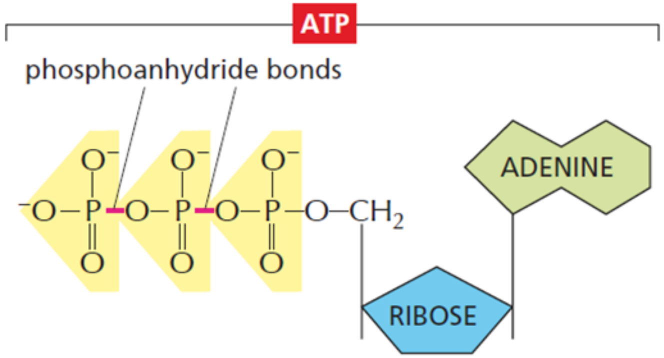
ATP is the most widely used activated carrier

- The most important and versatile of the activated carriers in cells is ATP (adenosine 5′-triphosphate).
- It can be used to drive a variety of chemical reactions in cells.
- ATP is synthesized in an energetically unfavorable phosphorylation reaction, in which a phosphate group is added to ADP (adenosine 5′-diphosphate).



ATP is the most widely used activated carrier

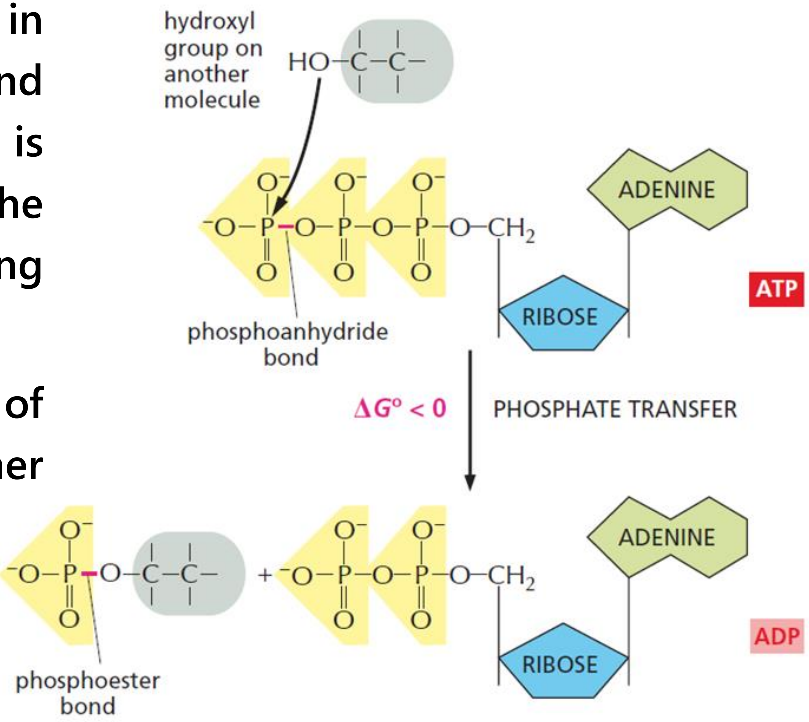
- The two outermost phosphate groups in ATP are held to the rest of the molecule by high-energy phosphoanhydride bonds and are readily transferred to other organic molecules. Water can be added to ATP to form ADP and inorganic phosphate (Pi).



- Inside a cell, this hydrolysis of the terminal phosphate of ATP yields between 11 and 13 kcal/mole of usable energy. Although the ΔGº of this reaction is –7.3 kcal/mole, the ΔG is much more negative, because the ratio of ATP to the products ADP and Pi is so high inside the cell.

ATP is the most widely used activated carrier

- When required, ATP gives up this energy packet in an energetically favorable hydrolysis to ADP and inorganic phosphate (Pi). The regenerated ADP is then available to be used for another round of the phosphorylation reaction that forms ATP, creating an ATP cycle in the cell.
- ATP hydrolysis is often coupled to the transfer of the terminal phosphate in ATP to another molecule.
- Any reaction that involves the transfer of a phosphate group to a molecule is termed a phosphorylation reaction.



ATP is the most widely used activated carrier

- ATP is the most abundant activated carrier in cells.
- ATP molecules activate substrates, mediate the exchange of chemical energy, and serve as key constituents of intracellular signaling pathways.
- It is used to supply energy for many of the pumps that actively transport substances into or out of the cell.
- It also powers the molecular motors that enable muscle cells to contract.
- Provides energy for transport materials along their lengthy axons.

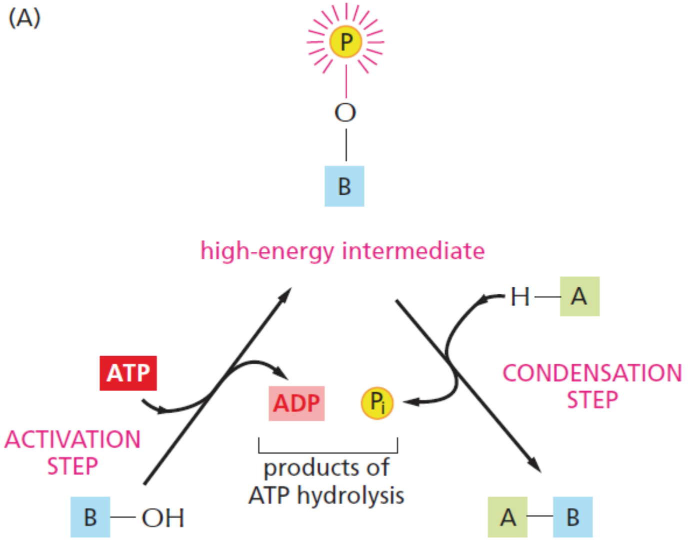
ATP helps in joining two molecules together

$A–H + B–OH \rightarrow A–B + H_2O$

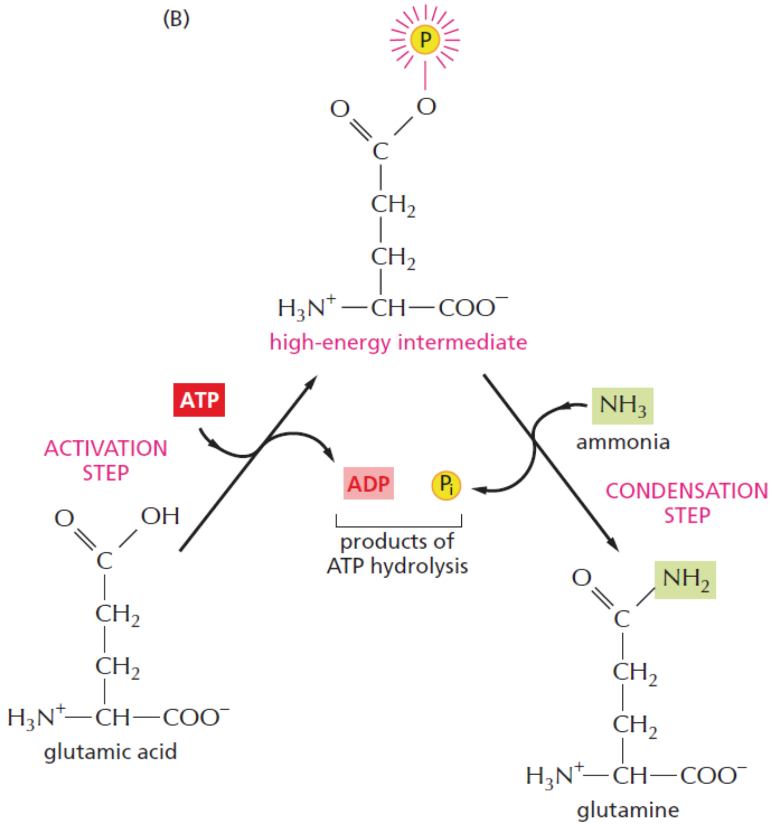
1. $B–OH + ATP \rightarrow B–O–PO_3 + ADP$
2. $A–H + B–O–PO_3 \rightarrow A–B + P_i$

Net result: $B–OH + ATP + A–H \rightarrow A–B + ADP + P_i$

(A)

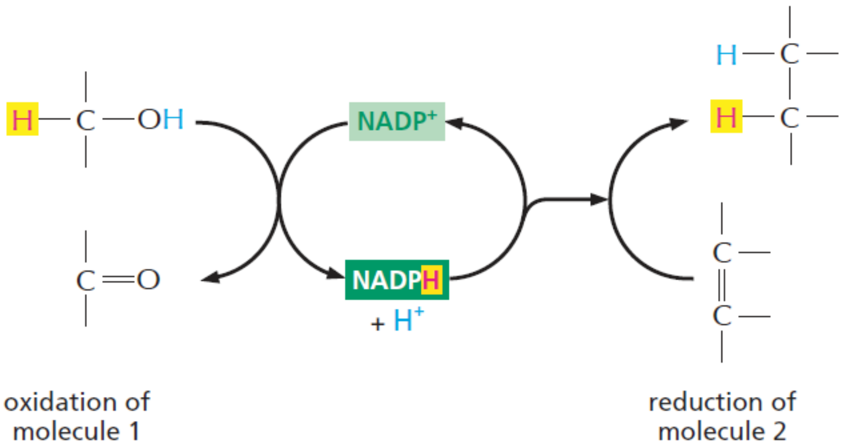


(B)

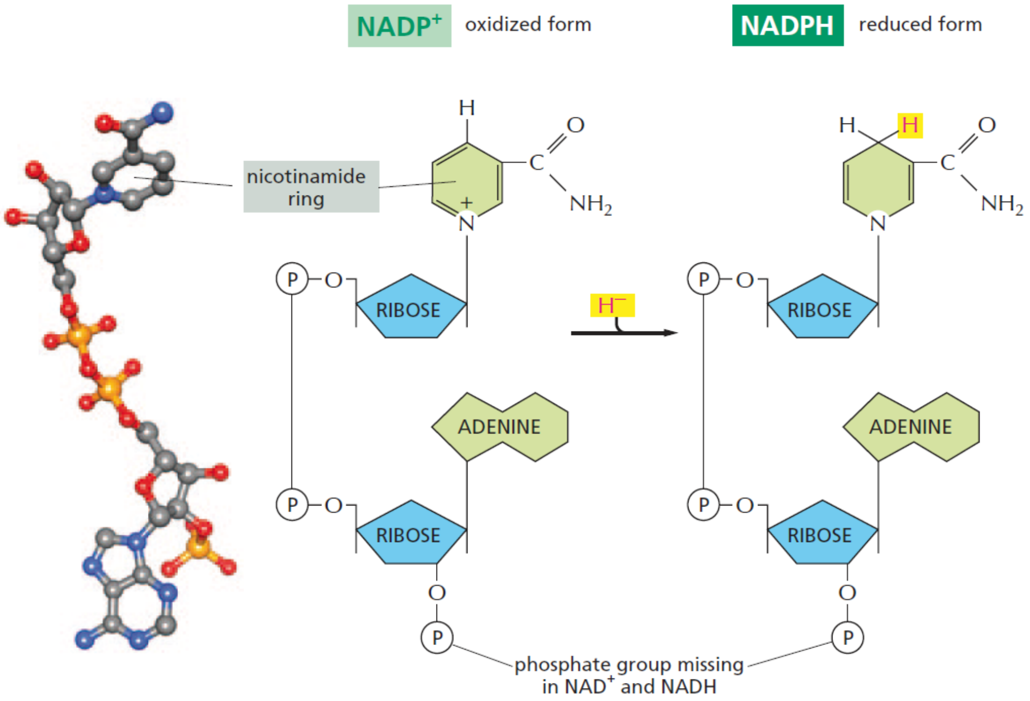


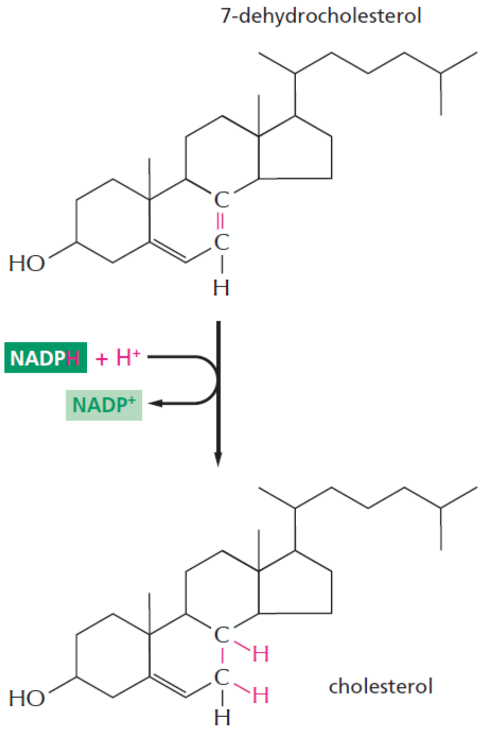
NADH and NADPH are both activated carriers of electrons

- NADH (nicotinamide adenine dinucleotide) and the closely related molecule NADPH (nicotinamide adenine dinucleotide phosphate) are the activated carriers that participate in oxidation–reduction reactions and are also commonly part of coupled reactions in cells.
- Both NADH and NADPH carry energy in the form of two high-energy electrons plus a proton (H^+), which together form a hydride ion (H^-). When these activated carriers pass their energy (in the form of a hydride ion) to a donor molecule, they become oxidized to form NAD^+ and $NADP^+$, respectively.



NADH and NADPH are both activated carriers of electrons





NADPH and NADH differ in a single phosphate group, which is located far from the region involved in electron transfer in NADPH.

NADPH and NADH have different roles in cells

- The phosphate group in NADPH has no effect on the electron-transfer properties, when compared with NADH. It gives NADPH a slightly different shape from NADH. This subtle difference in conformation makes it possible for the two carriers to bind as substrates to different sets of enzymes and thereby deliver electrons (in the form of hydride ions) to different target molecules.
- NADPH operates chiefly with enzymes that catalyze anabolic reactions, supplying the high-energy electrons needed to synthesize energy-rich biological molecules.
- NADH has a special role as an intermediate in the catabolic system of reactions that generate ATP through the oxidation of food molecules.

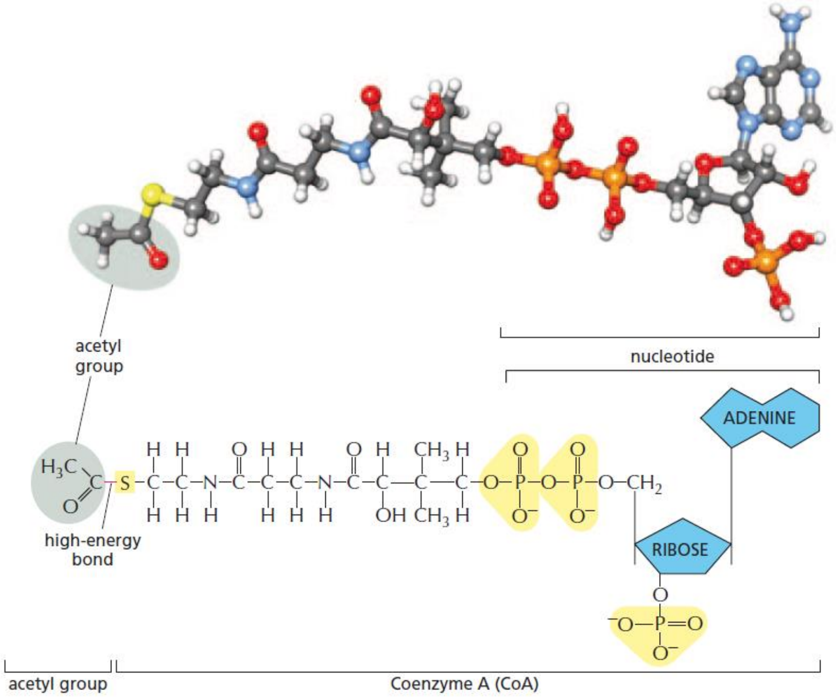
NADPH and NADH have different roles in cells

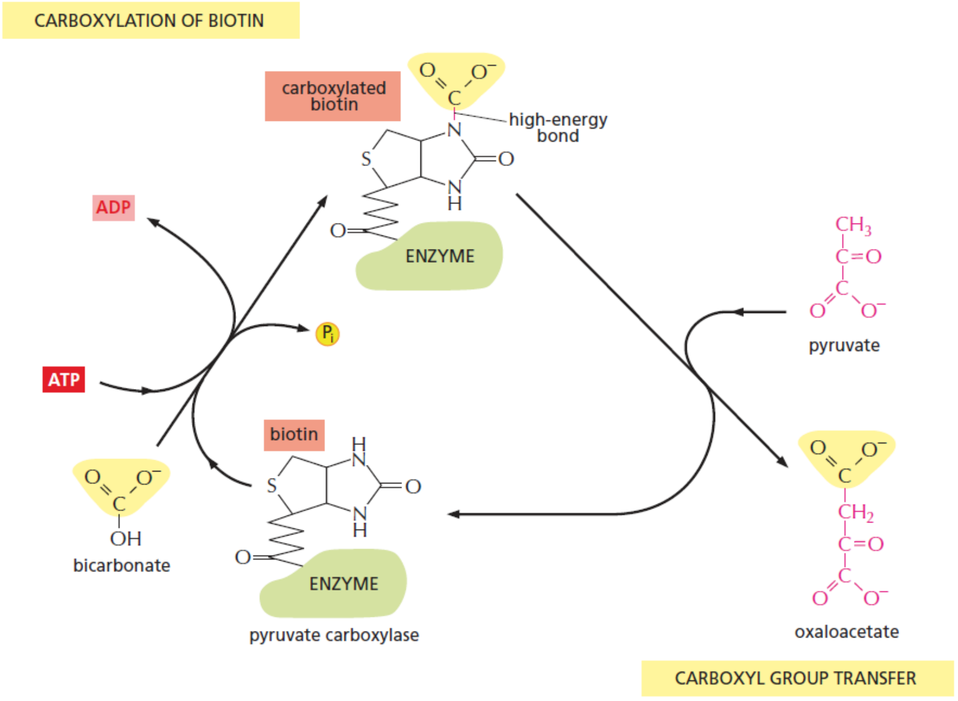
- The genesis of NADH from NAD^+ and that of NADPH from $NADP^+$ occurs by different pathways that are independently regulated, so that the cell can adjust the supply of electrons for these two contrasting purposes.
- Inside the cell, the ratio of NAD^+ to NADH is kept high, whereas the ratio of $NADP^+$ to NADPH is kept low.
- This arrangement provides plenty of NAD^+ to act as an oxidizing agent and plenty of NADPH to act as a reducing agent—as required for their special roles in catabolism and anabolism, respectively.

Cells make use of many other activated carriers

- Cells make use of other activated carriers that pick up and carry a chemical group in an easily transferred, high-energy linkage.
- $FADH_2$, like NADH and NADPH, carries hydrogen and high-energy electrons. But other important reactions involve the transfers of acetyl, methyl, carboxyl, and glucose groups from activated carriers for the purpose of biosynthesis.
- Coenzyme A, for example, can carry an acetyl group in a readily transferable linkage. This activated carrier, called acetyl CoA (acetyl coenzyme A) is used, for example, to add sequentially two carbon units in the biosynthesis of the hydrocarbon tails of fatty acids.
- Activated carriers are usually generated in reactions coupled to ATP hydrolysis. Therefore, the energy that enables their groups to be used for biosynthesis ultimately comes from the catabolic reactions that generate ATP.

Cells make use of many other activated carriers



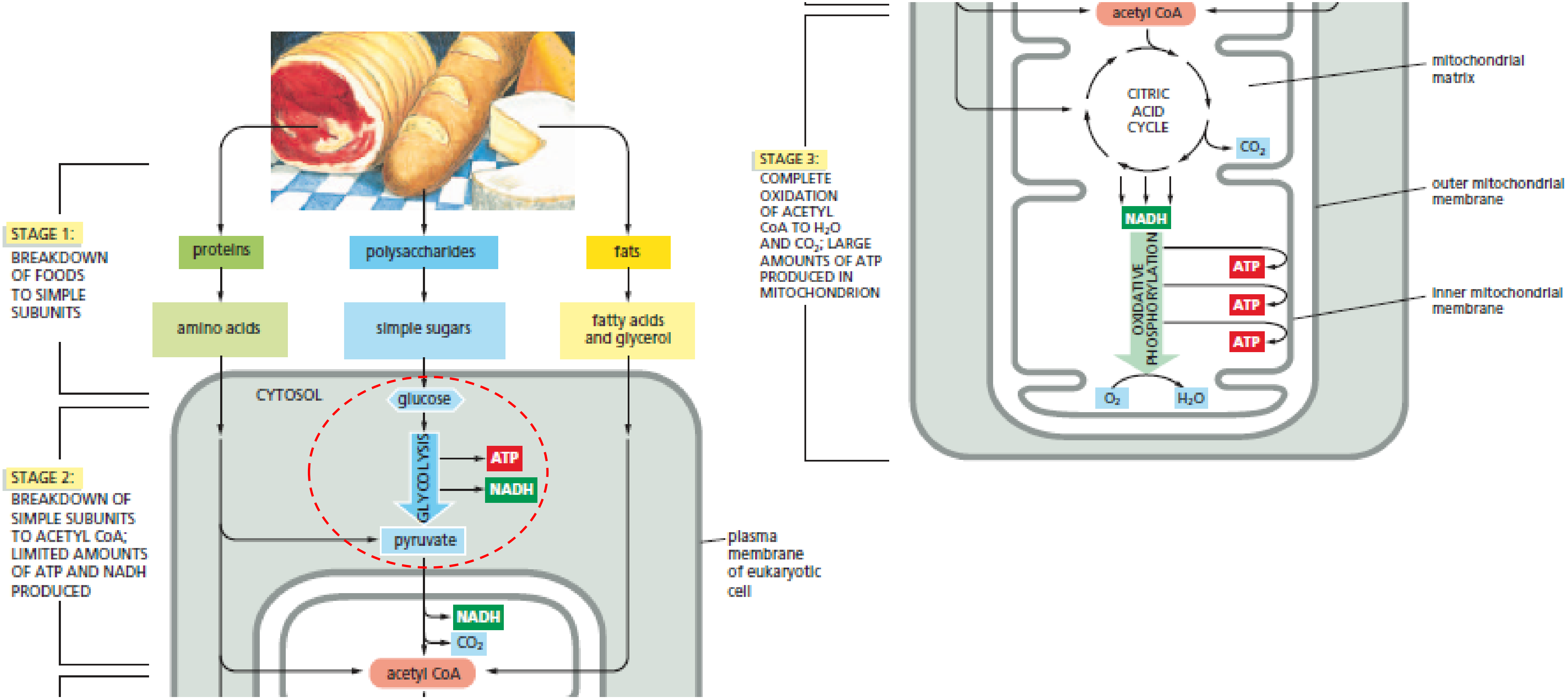


Cells make use of many other activated carriers

SOME ACTIVATED CARRIERS WIDELY USED IN METABOLISM	
Activated Carrier	**Group Carried in High-Energy Linkage**
ATP	phosphate
NADH, NADPH, $FADH_2$	electrons and hydrogens
Acetyl CoA	acetyl group
Carboxylated biotin	carboxyl group
S-adenosylmethionine	methyl group
Uridine diphosphate glucose	glucose

Glycolysis

Food molecules are broken down in three stages



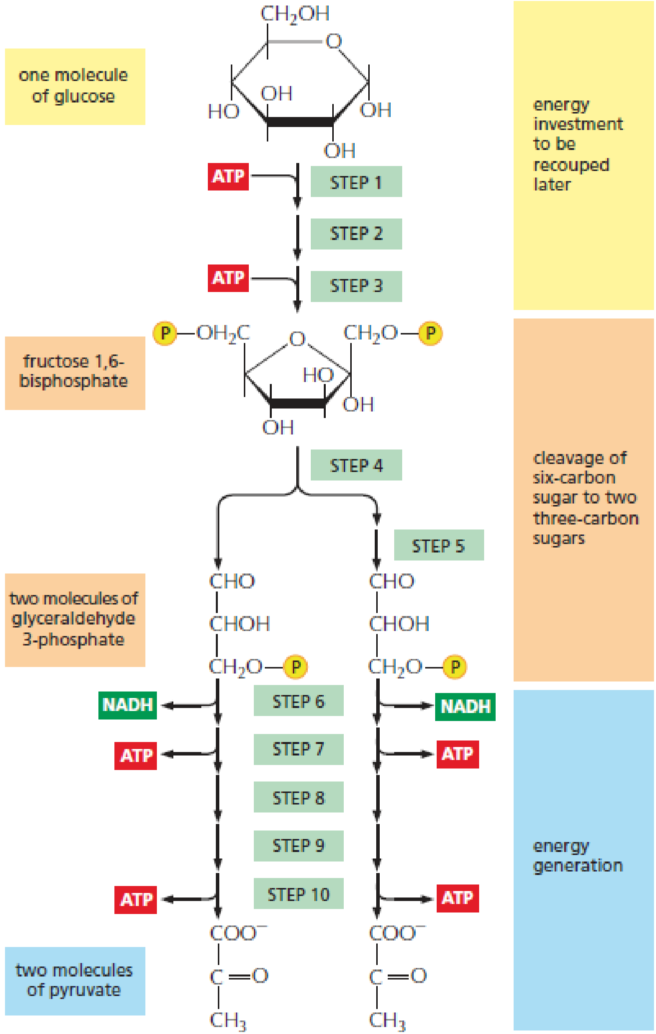
Glycolysis extracts energy from the splitting of sugar

- The central process in stage 2 of catabolism is the oxidative breakdown of glucose in the sequence of reactions known as glycolysis.
- Glycolysis produces ATP without the involvement of oxygen. It occurs in the cytosol of most cells, including many anaerobic microorganisms that thrive in the absence of oxygen.
- The term “glycolysis” comes from a Greek word meaning, “sweet,” and lysis means “splitting.” It is an appropriate name, as glycolysis splits a molecule of glucose, which has six carbon atoms, to form two molecules of pyruvate, each of which contains three carbon atoms.
- The series of chemical rearrangements that ultimately generate pyruvate release energy because the electrons in a molecule of pyruvate are, overall, at a lower energy state than those in a molecule of glucose.

Glycolysis - overview

- Glycolysis as the pathway consists of a sequence of 10 separate reactions, each producing a different sugar intermediate and each catalyzed by a different enzyme.

SOME TYPES OF ENZYMES INVOLVED IN GLYCOLYSIS		
Enzyme type	**General function**	**Role in glycolysis**
Kinase	catalyzes the addition of a phosphate group to molecules	a kinase transfers a phosphate group from ATP to a substrate in steps 1 and 3; other kinases transfer a phosphate to ADP to form ATP in steps 7 and 10
Isomerase	catalyzes the rearrangement of bonds within a single molecule	isomerases in steps 2 and 5 prepare molecules for the chemical alterations to come
Dehydrogenase	catalyzes the oxidation of a molecule by removing a hydrogen atom plus an electron (a hydride ion, H^-)	the enzyme glyceraldehyde 3-phosphate dehydrogenase generates NADH in step 6
Mutase	catalyzes the shifting of a chemical group from one position to another within a molecule	the movement of a phosphate by phosphoglycerate mutase in step 8 helps prepare the substrate to transfer this group to ADP to make ATP in step 10



Glycolysis - overview

- Glycolysis is also sometimes referred to as the Embden–Meyerhof pathway.
- Much of the energy released by the breakdown of glucose is used to drive the synthesis of ATP molecules from ADP and Pi. This form of ATP synthesis, which takes place in steps 7 and 10 in glycolysis, is known as substrate-level phosphorylation because it occurs by the transfer of a phosphate group directly from a substrate molecule—one of the sugar intermediates—to ADP. By contrast, most phosphorylations in cells occur by the transfer of phosphate from ATP to a substrate molecule.

NET RESULT: GLUCOSE → 2 PYRUVATE + 2 ATP + 2 NADH