BIO 311C
Spring 2010

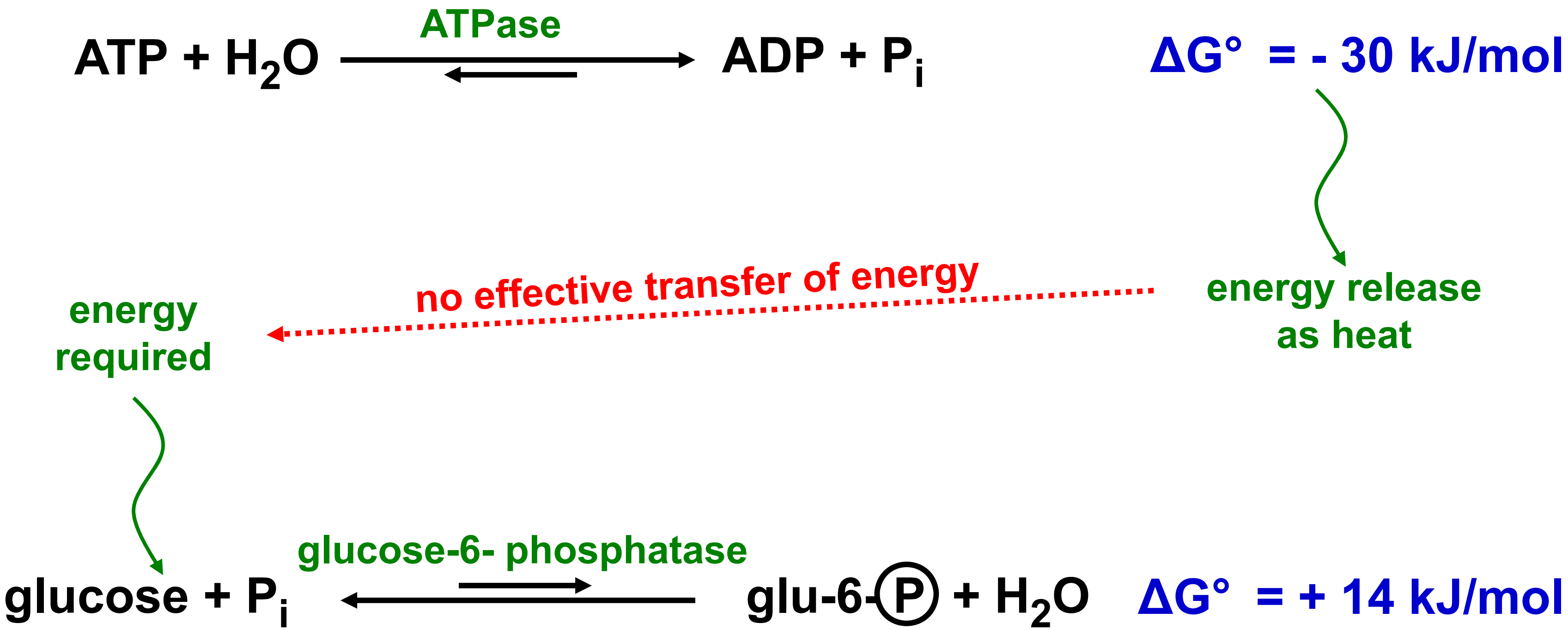
I (JB) made two errors on the answer key for Exam 2.
Multiple Questions 2 and 5 were incorrectly keyed.

To compensate, we have added 4 points (= 4 percentage points) to all scores.
Thus your recorded grade is 4 percent higher than the grade written on your exam.

The correct key is now posted on the course web site and on Blackboard.

Lecture 23 – Friday 26 Mar.

Consider two reactions: one exergonic, the other endergonic



$$\mathrm{ATP} + \mathrm{H_2O} \xrightleftharpoons{\text{ATPase}} \mathrm{ADP} + \mathrm{P_i} \qquad \Delta G° = -30\ \mathrm{kJ/mol}$$

energy release
as heat

no effective transfer of energy

energy required

$$\text{glucose} + \mathrm{P_i} \xrightleftharpoons{\text{glucose-6- phosphatase}} \text{glu-6-}\textcircled{P} + \mathrm{H_2O} \qquad \Delta G° = +14\ \mathrm{kJ/mol}$$

Generally energy cannot be transferred from one reaction to another unless the two reactions are <u>coupled</u> together in some way. Thus, the energy released in the reaction catalyzed by ATPase cannot be directed to the reaction catalyzed by glucose-6-phosphatase in order to produce glucose-6-phosphate unless the reactions occur in a very confined space such that the ATPase-catalyzed reaction substantially increases the concentration of P_i, thereby increasing the ΔG value of glu-6-phosphate-catalyzed reaction.

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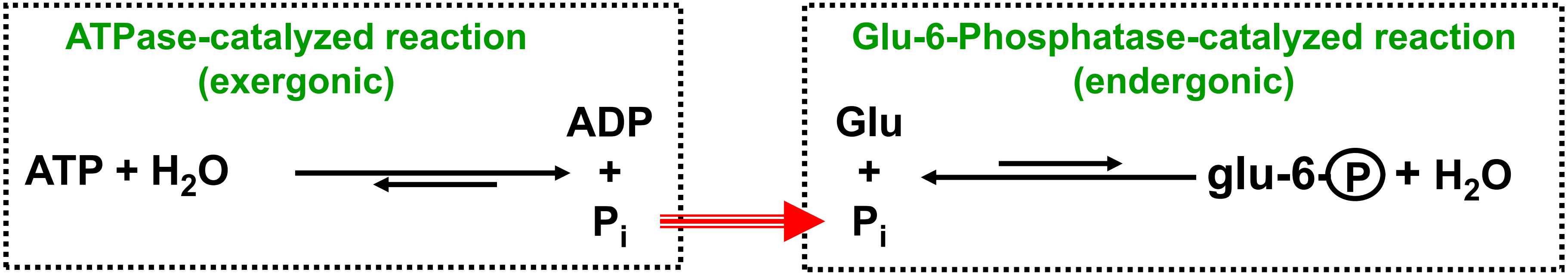
note: The names of many enzymes end in “ase".

“Loose” coupling of two reactions together



ATPase-catalyzed reaction (exergonic)

$ATP + H_2O \rightleftharpoons ADP + P_i$

Glu-6-Phosphatase-catalyzed reaction (endergonic)

$Glu + P_i \rightleftharpoons glu\text{-}6\text{-}\textcircled{P} + H_2O$

pushing reaction

pushing effect

Reaction that is being pushed

In order for a pushing reaction to produce this effect on a second reaction:

(1) both reactions must occur in the same compartment,

(2) a product of the pushing must be a reactant of the reaction to be pushed,

(3) the pushing reaction must be more exergonic than the is the reaction that is loosely coupled to it.

*

Some enzymes are capable of coupling an exergonic reaction to an endergonic reaction as a single coupled reaction, in order to drive the endergonic reaction in the forward direction.

loosely coupled reactions

$$\left\{\begin{array}{ll} \text{ATP} + \cancel{H_2O} \overset{\text{ATPase}}{\rightleftharpoons} \text{ADP} + \cancel{P_i} & \Delta G° = -30 \text{ kJ/mol} \\ \text{glucose} + \cancel{P_i} \overset{\text{glucose-6- phosphatase}}{\leftrightharpoons} \text{glu-6-}\textcircled{P} + \cancel{H_2O} & \Delta G° = +14 \text{ kJ/mol} \end{array}\right.$$

sum

$$\text{ATP} + \text{glucose} \rightleftharpoons \text{ADP} + \text{glu-6-}\textcircled{P} \qquad \Delta G° = -16 \text{ kJ/mol}$$

A single <u>tightly</u> <u>coupled</u> reaction

$$\text{ATP} + \text{glucose} \overset{\text{hexokinase}}{\rightleftharpoons} \text{ADP} + \text{glu-6-}\textcircled{P} \qquad \Delta G° = -16 \text{ kJ/mol}$$

Hexokinase is the name of an enzyme that activates glucose so that it can undergo further reactions, by transferring a phosphate functional group from ATP to glucose.

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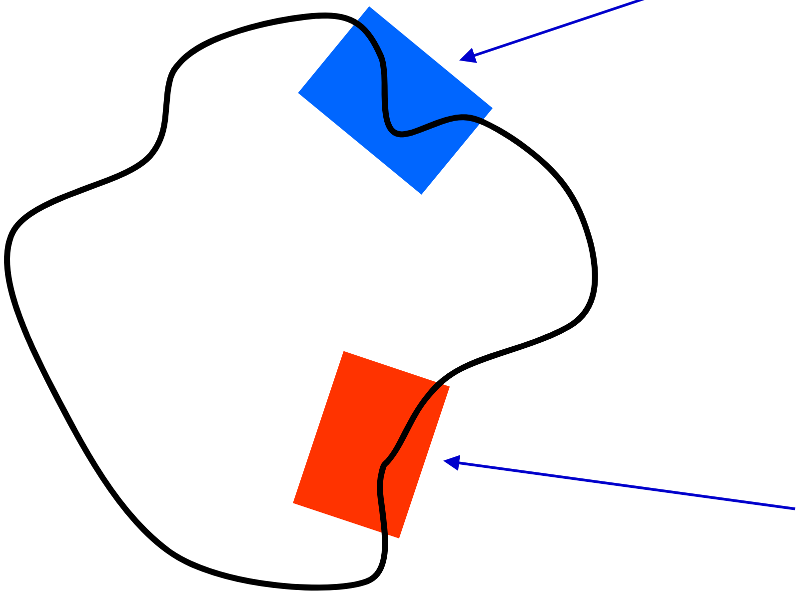
Domains of a Regulatory Enzyme



catalytic site
(substrate-binding domain)

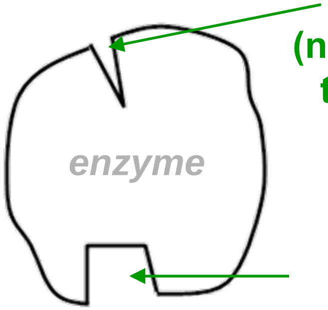
Allosteric site
(binding domain for a
regulatory molecule)

An allosteric enzyme contains one or more regulatory (allosteric) sites in addition to its active site.

*

Illustration of An Allosteric Enzyme that Utilizes an Allosteric Activator to "turn on" its Reaction

(1)

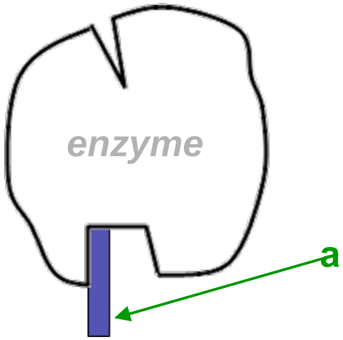


active site
(not accessible
to substrate

allosteric site
(can bind to an
activator)

inactive enzyme

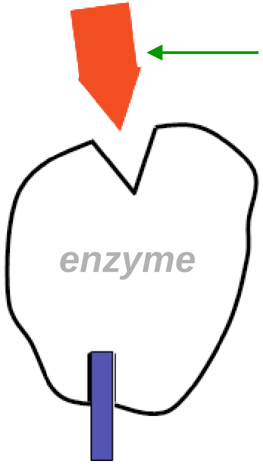
(2)



allosteric activtor at
allosteric site

allosteric activator binds to the enzyme

(3)



substrate

enzyme changes to shape that fits substrate

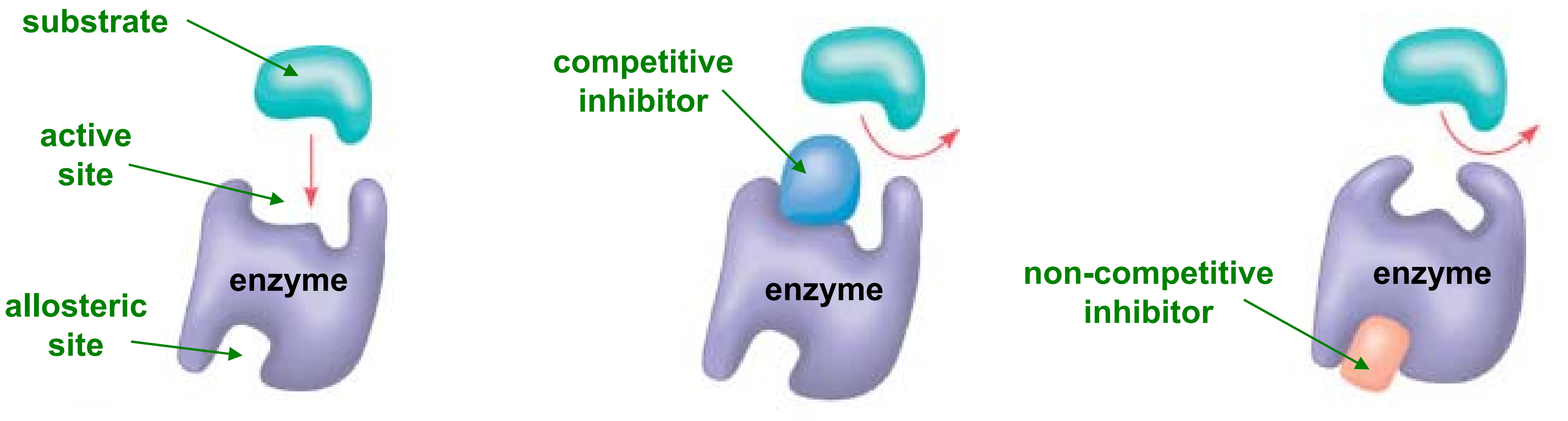
➡ substrate molecule

▬ regulatory molecule
(allosteric activator)

*

Inhibition of Enzyme Activity by a Competitive Inhibitor or by a Noncompetitive Inhibitior

From textbook Fig. 8.19, p. 155



No inhibition (substrate binds to active site)

Competitive inhibition (inhibitor molecule binds to active site)

Noncompetitive inhibition (inhibitor molecule binds to allosteric site)

*

A large fraction of all chemical reactions that occur in cells fall into one of four broad categories:

- Protonation / de-protonation[*]
- isomerization
- Hydrolysis / dehydration
- oxidation-reduction

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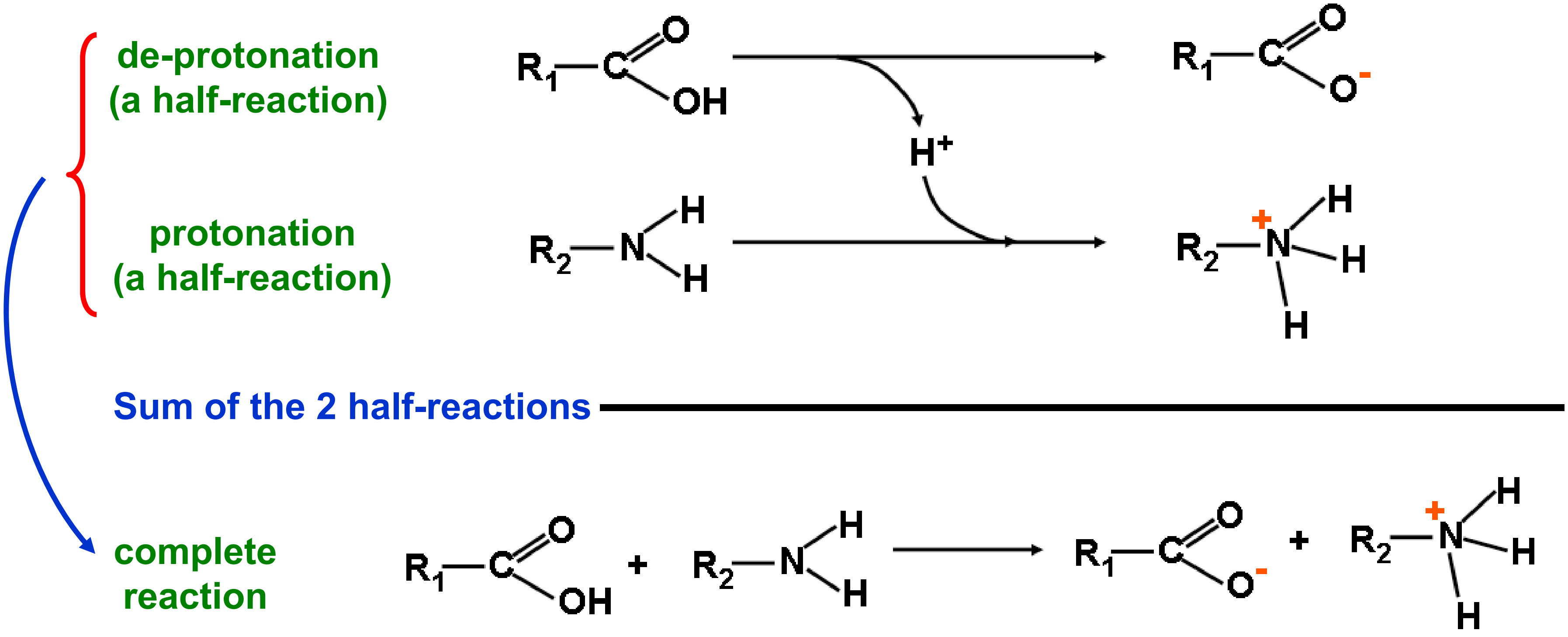
[*] Protonation and de-protonation reactions are sometimes not treated as chemical reactions since they require the movement of only a single proton. However, the protonated and de-protonated forms of functional groups have very different physical and chemical properties, and therefore act very different from each other biologically.

Thus, in this course we will consider protonation and de-protonation processes to be chemical reactions.

*

Example of a Protonation / De-protonation:



de-protonation
(a half-reaction)

protonation
(a half-reaction)

Sum of the 2 half-reactions

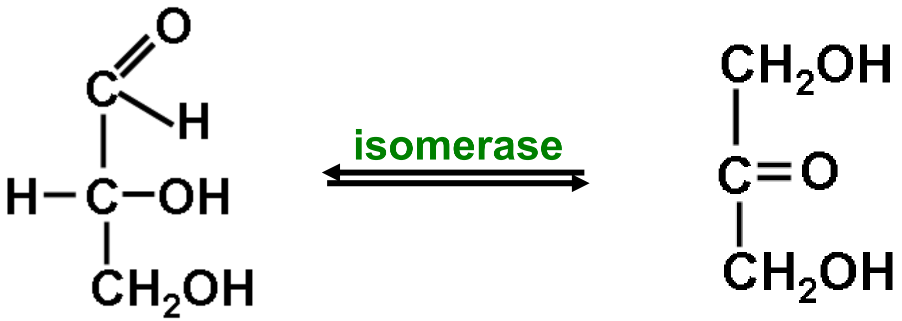
complete
reaction

A protonation half-reaction always must be coupled to a de-protonation half-reaction in order to produce the complete reaction.

Protonation/de-protonation reactions do not need an enzyme to proceed rapidly.

*

Example of an Isomerization:



D-glyceraldehyde
(an aldotriose)

dihydroxyacetone
(a ketotriose)

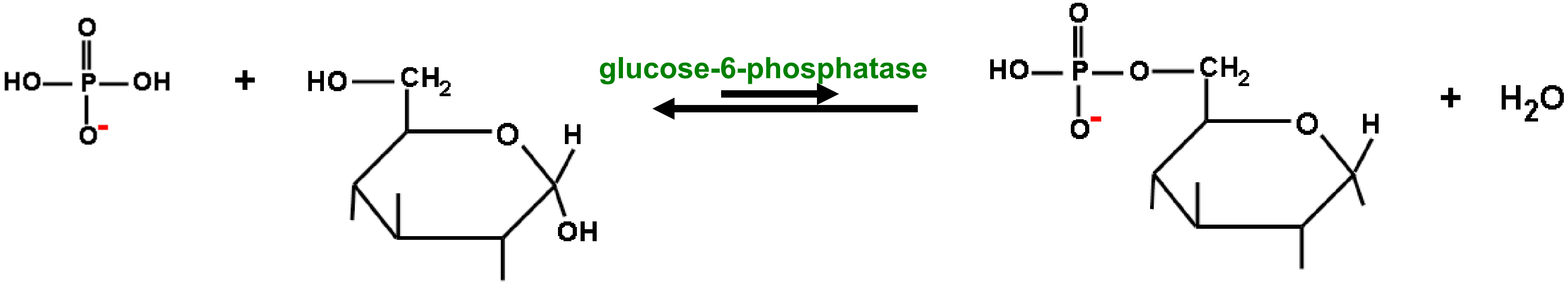
$C_3H_6O_3$

$C_3H_6O_3$

Isomerase enzymes rearrange atoms in a substrate molecule, but do not change the atomic composition of the molecule (i.e. the chemical formula of the molecule is not changed). Most isomerization metabolic reactions require an isomerase enzyme in order to proceed.

*

Example of a Hydrolysis/Dehydration:



This dehydration reaction is endergonic. Thus its reverse, a hydrolysis, is exergonic.

An alternative way of illustrating the reaction shown above:

$$\text{glucose} + P_i \;\; \underset{\textit{hydrolysis}}{\overset{\textit{dehydration}}{\underset{\text{glucose-6-phosphatase}}{\rightleftharpoons}}} \;\; \text{glucose-6-}\textcircled{P} + H_2O$$

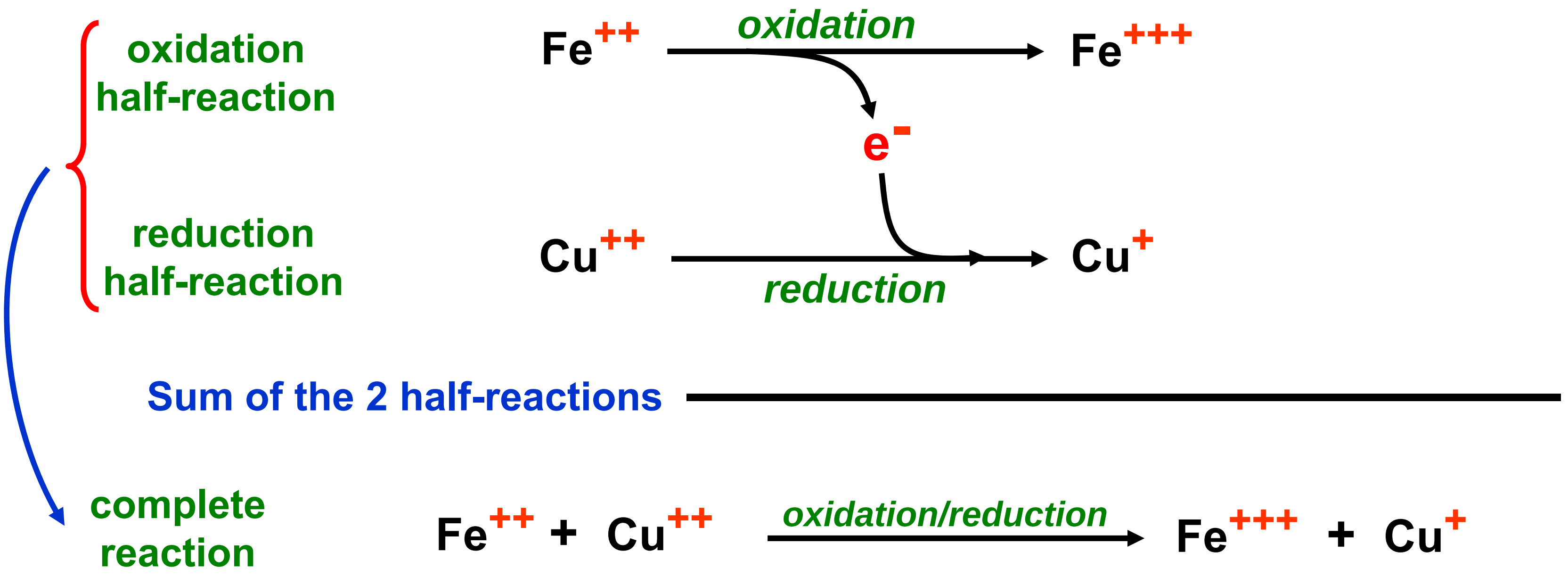
Dehydration reactions are the reverse of hydrolysis reactions.

Most dehydration/hydrolysis metabolic reactions require an enzyme in order to proceed at a reasonably rapid rate.

*

A molecular species is said to be oxidized if it loses one or more electrons.

A molecular species is said to be reduced if it gains one or more electrons.



oxidation half-reaction

$Fe^{++} \xrightarrow{\text{oxidation}} Fe^{+++}$

e^{-}

reduction half-reaction

$Cu^{++} \xrightarrow[\text{reduction}]{} Cu^{+}$

Sum of the 2 half-reactions

complete reaction

$Fe^{++} + Cu^{++} \xrightarrow{\text{oxidation/reduction}} Fe^{+++} + Cu^{+}$

We define a molecular species as any atom, ion or molecule.

Molecular biologists refer to oxidation/reduction reactions as "redox" reactions.

As with a proton, an electron leaves one molecular species only if it can simultaneously become attached to another. Thus, a molecular species only becomes oxidized if another molecular species becomes reduced.

Many oxidation-reduction reactions that involve only moving an electron from one molecular species to another do not require an enzyme.

*

Definitions and Descriptions:

An organic molecule is oxidized if it loses one or more hydrogen atoms, or if it gains one or more oxygen atoms.

An organic molecule is reduced if it gains one or more hydrogen atoms, or if it loses one or more oxygen atoms.

A hydrogen atom represents one unit of reduction. An oxygen atom represents two units of oxidation.

Biological molecules are nearly always oxidized or reduced two units at a time.

Note: A molecular species can be reduced by two units by the addition of two electrons, or by the addition of two hydrogen atoms, or by the removal of one oxygen atom.

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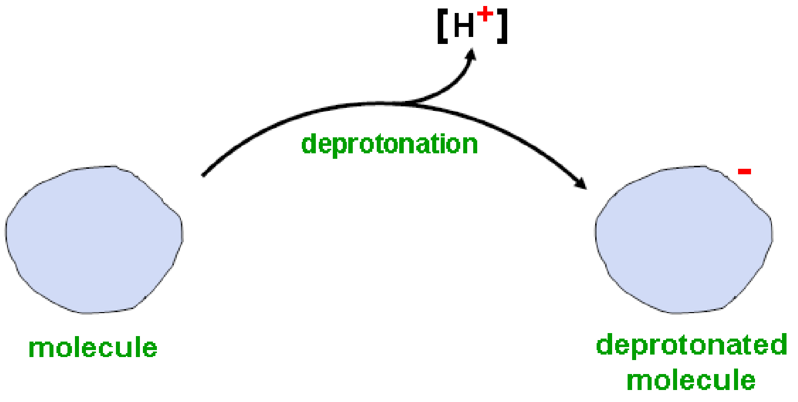
Comparison of a Deprotonation half-reaction and an Oxidation half-reaction

Deprotonation half-reaction



$[H^+]$

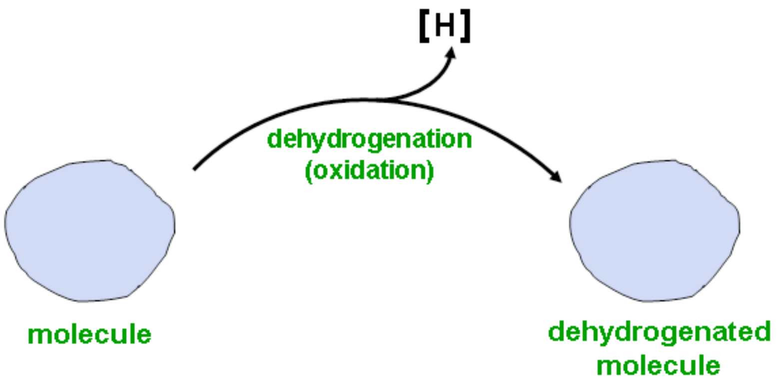
deprotonation

molecule

-

deprotonated molecule

Dehydrogenation half-reaction



[H]

dehydrogenation (oxidation)

molecule

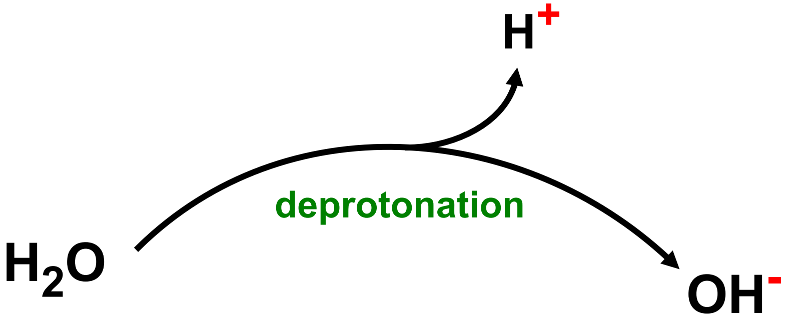
dehydrogenated molecule

Note: a hydrogen atom consists of a proton and an electron. The electron is the component of the of hydrogen atom that facilitates oxidation or reduction.

*

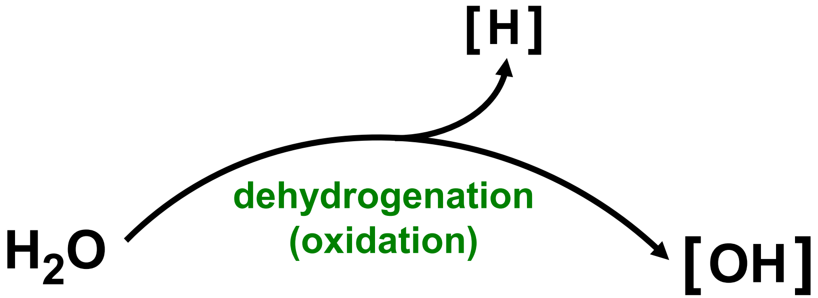
Example: Comparison of deprotonation of water half-reaction and oxidation of water half-reaction.

Deprotonation of water



This half-reaction can occur very rapidly without any enzyme.

Dehydrogenation of water

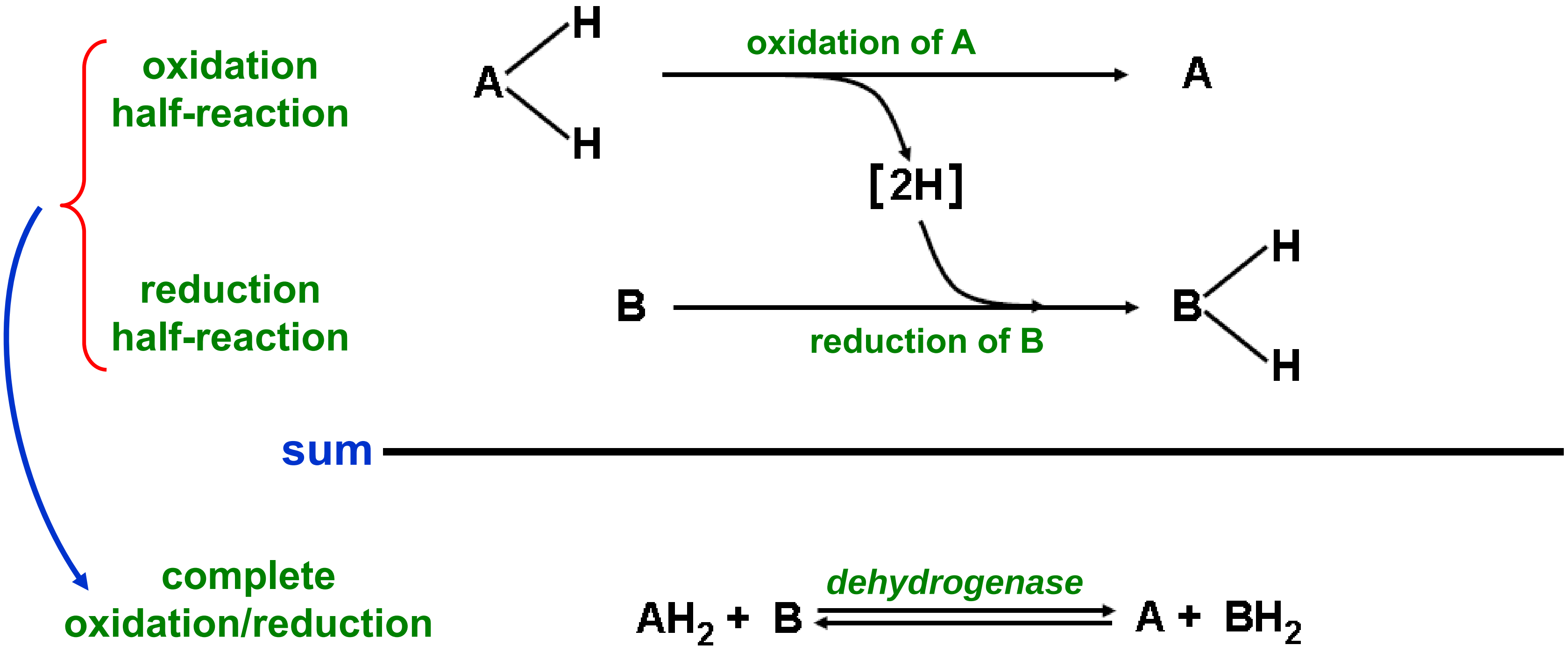


Dehydrogenation of water is a very endergonic half-reaction under most conditions and requires considerable energy to proceed in the forward direction. It is a unique metabolic process of photosynthesis.

The [OH] product of the dehydrogenation of water is not a stable molecular species; it must undergo further reaction to become stabilized.

*

Example of oxidation and reduction of organic molecules



oxidation half-reaction

reduction half-reaction

sum

complete oxidation/reduction (redox) reaction

$$AH_2 + B \underset{}{\overset{\textit{dehydrogenase}}{\rightleftharpoons}} A + BH_2$$

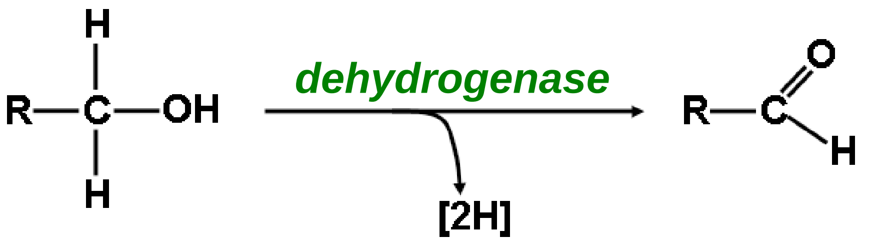
Hydrogen atoms don't exist free in nature; they are lost by one molecular species only if they are simultaneously accepted by another.

Metabolic reactions involving the transfer of a pair of hydrogen atoms from one molecular species to another require an enzyme. Many of these enzymes are called dehydrogenases or transhydrogenases.

*

Example of an Oxidation of an Organic Functional Group

Oxidation of an Alcohol



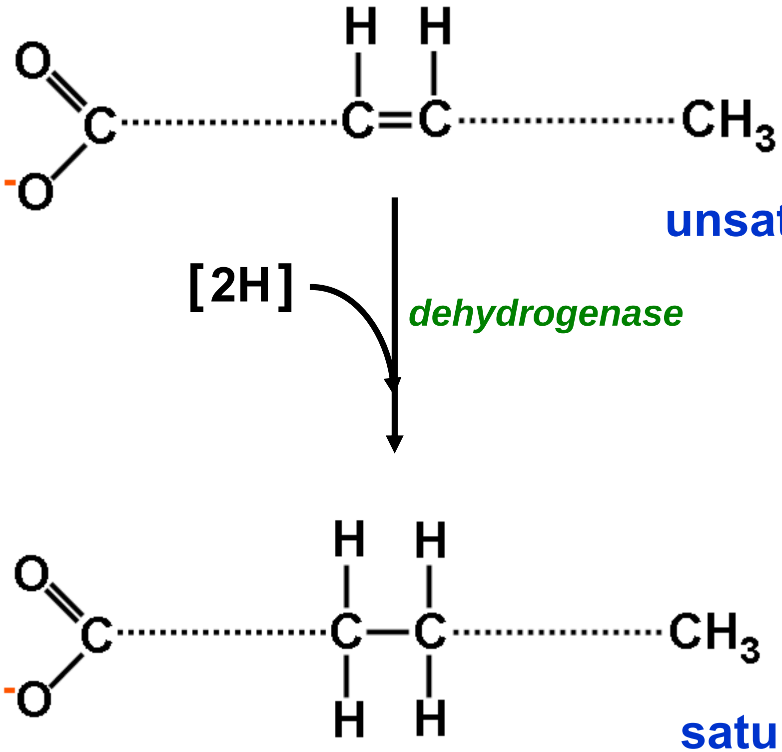
alcohol

aldehyde

Biological molecules are nearly always oxidized or reduced two units at a time.

*

Example of a Reduction of an Organic Molecule



oxidized

unsaturated fatty acid

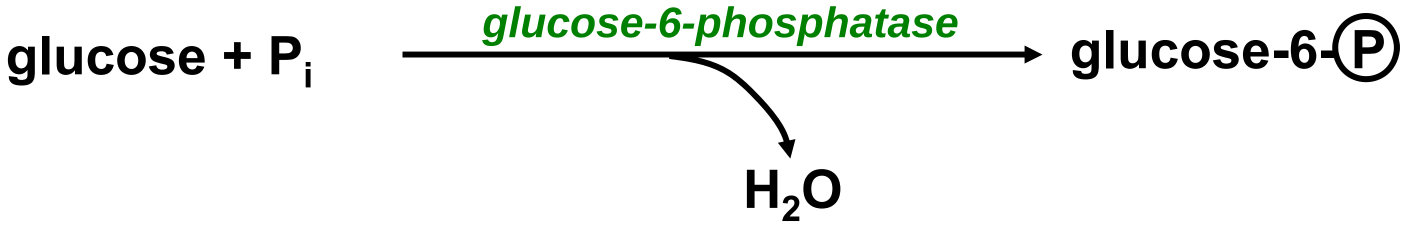
reduced

saturated fatty acid

*

Hydrolysis/dehydration reactions are not oxidation or reduction.

dehydration reaction



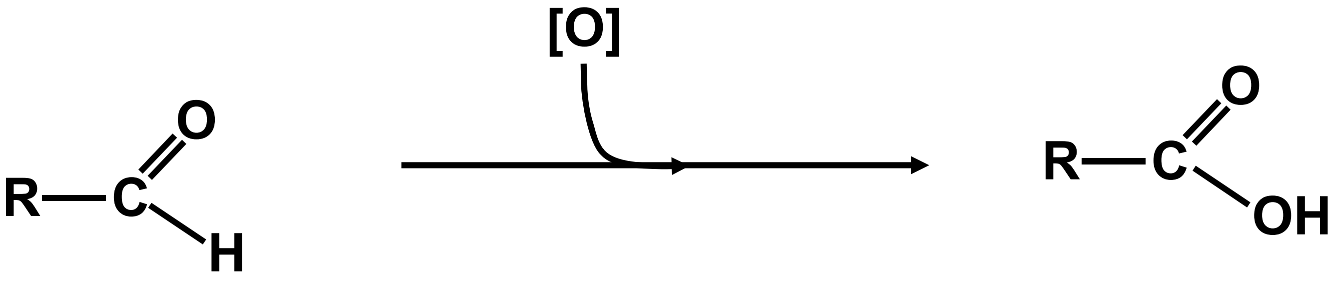
$$\text{glucose} + P_i \xrightarrow{\textit{glucose-6-phosphatase}} \text{glucose-6-Ⓟ} + H_2O$$

Note: this reaction represents two units of oxidation (removal of 2 hydrogen atoms) and two units of reduction (removal of one oxygen atom) at the same time, so there is no net oxidation or reduction.

*

Oxidation of an Aldehyde in an enzyme-catalyzed reaction

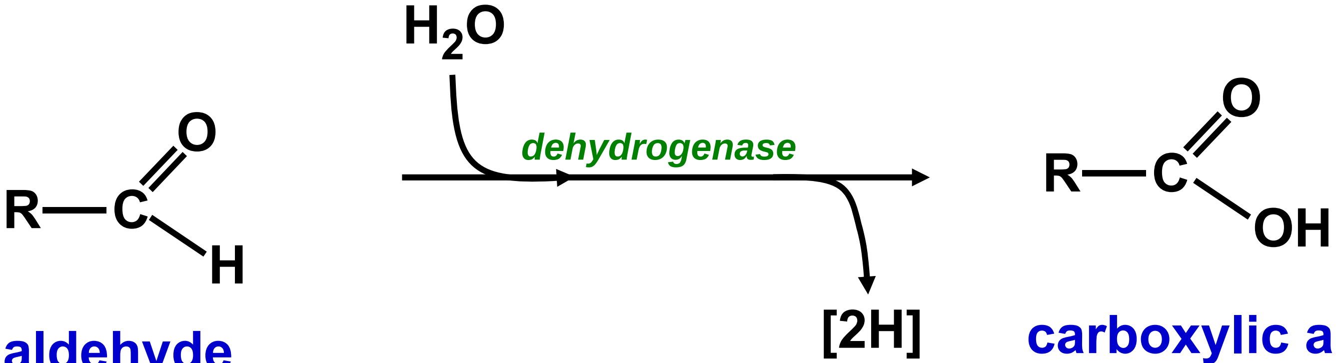
net effect



aldehyde

carboxylic acid

actual process



aldehyde

carboxylic acid

*