Bioenergetics (634 فح ج)

Lecture 4

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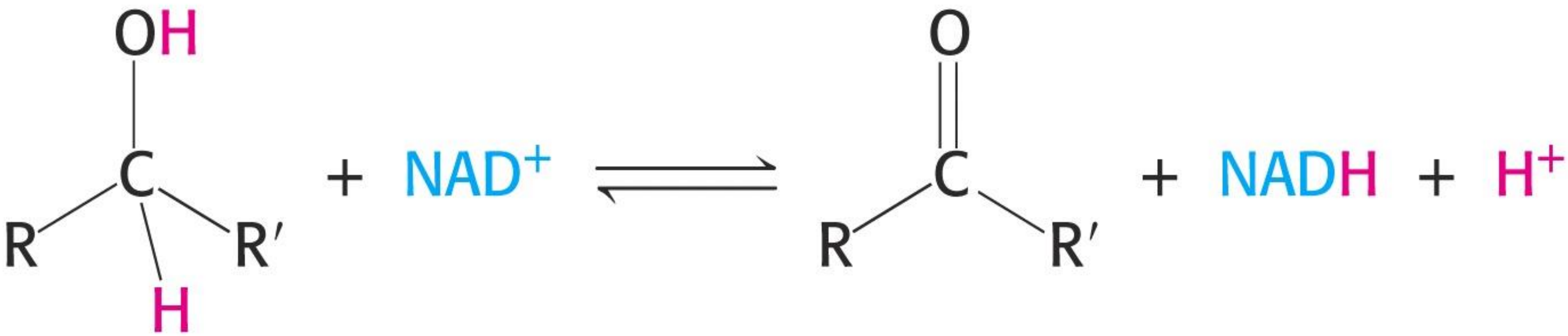
Topics:

- Coenzymes.
- NAD+ as co-enzyme
- Glycolysis
  - Regulation of Glycolysis
- Digestion is depolymerization
- Convergent and divergent metabolic pathways

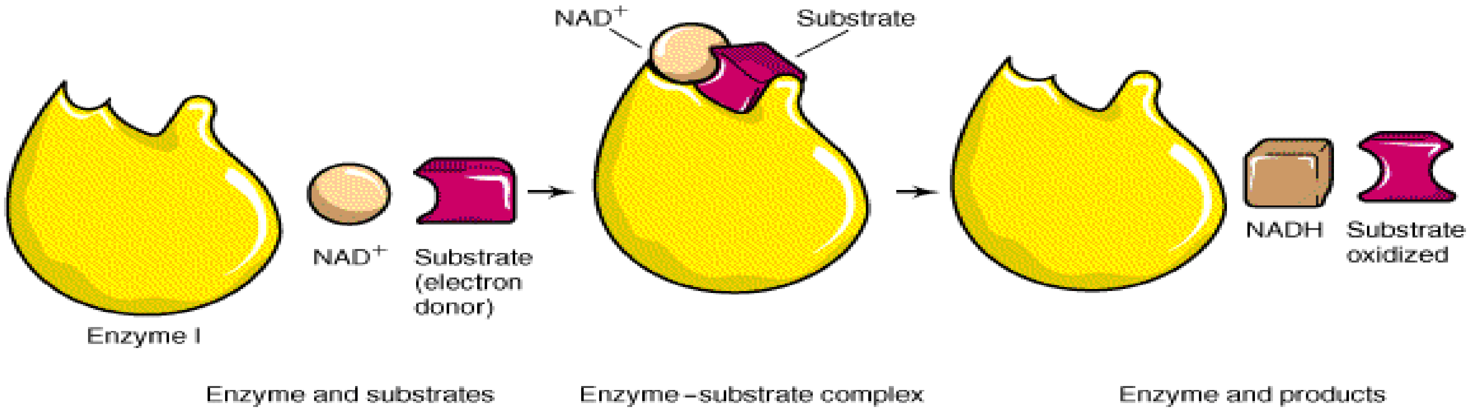
Coenzymes

- coenzymes are organic molecules that are required by certain enzymes to carry out catalysis. They bind to the active site of the enzyme and participate in catalysis but are not considered substrates of the reaction.
- coenzymes often function as intermediate carriers of electrons, specific atoms or functional groups that are transferred in the overall reaction.
- An example of this would be the role of NAD in the transfer of electrons in certain coupled oxidation reduction reactions.

NAD^+ as co-enzyme

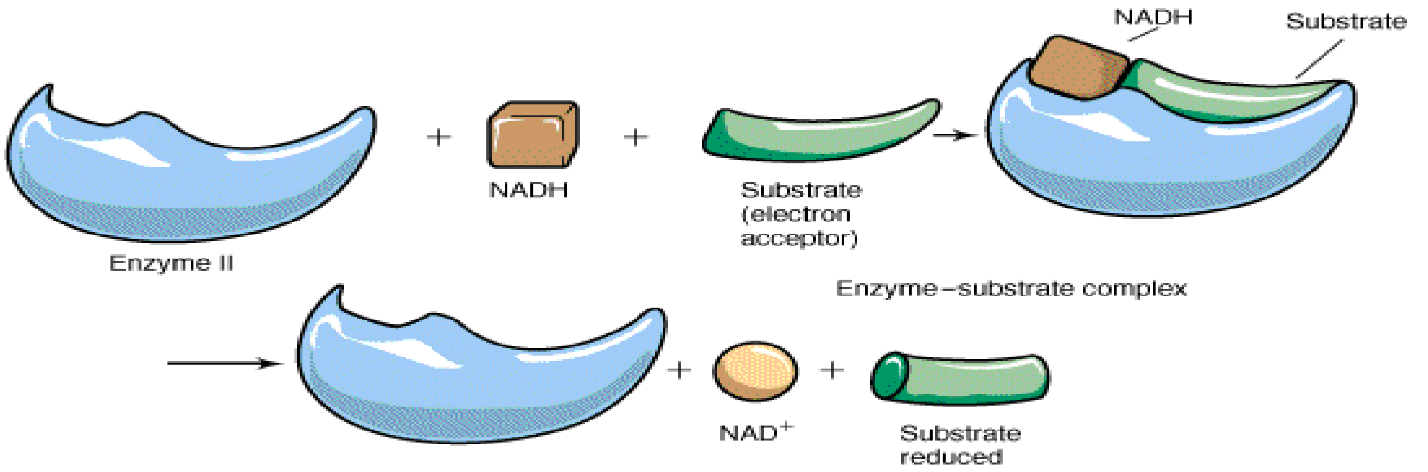


NAD^+ as co-enzyme (continued)

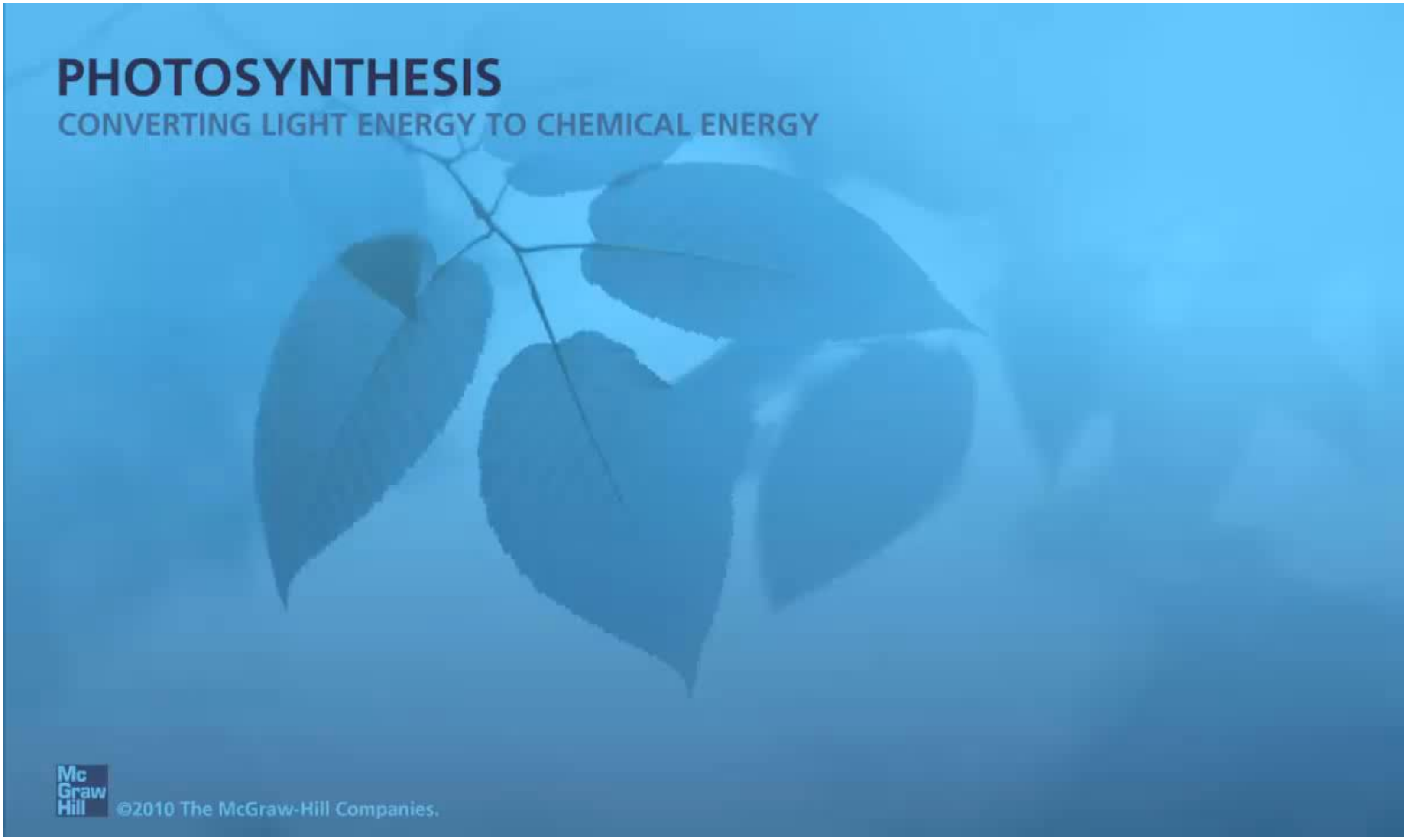


Reaction 1. Enzyme I reacts with substrate (electron donor) and oxidized form of coenzyme, NAD^+.

NAD+ as co-enzyme (continued)



Reaction 2. Enzyme II reacts with substrate (electron acceptor) and reduced form of coenzyme, NADH.


PHOTOSYNTHESIS
CONVERTING LIGHT ENERGY TO CHEMICAL ENERGY
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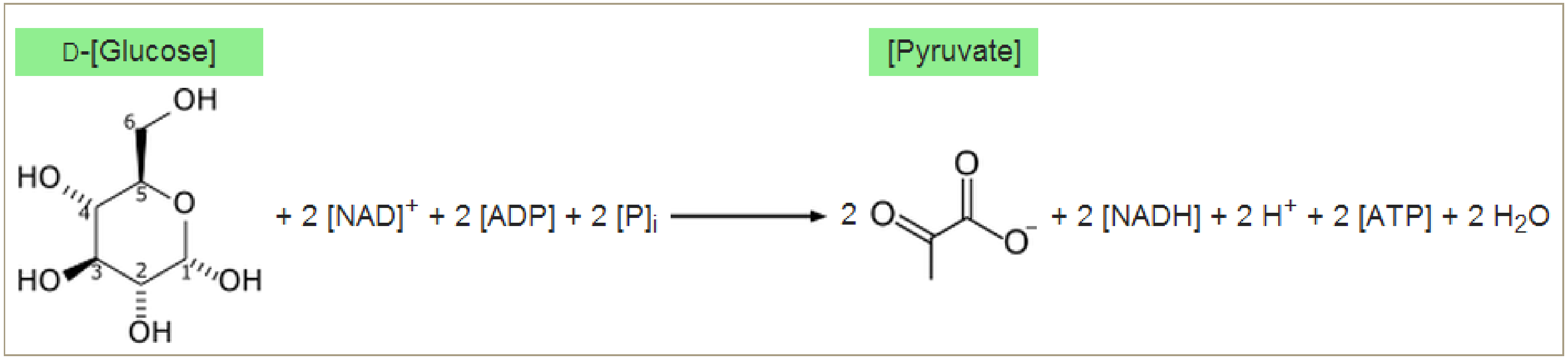
Glycolysis

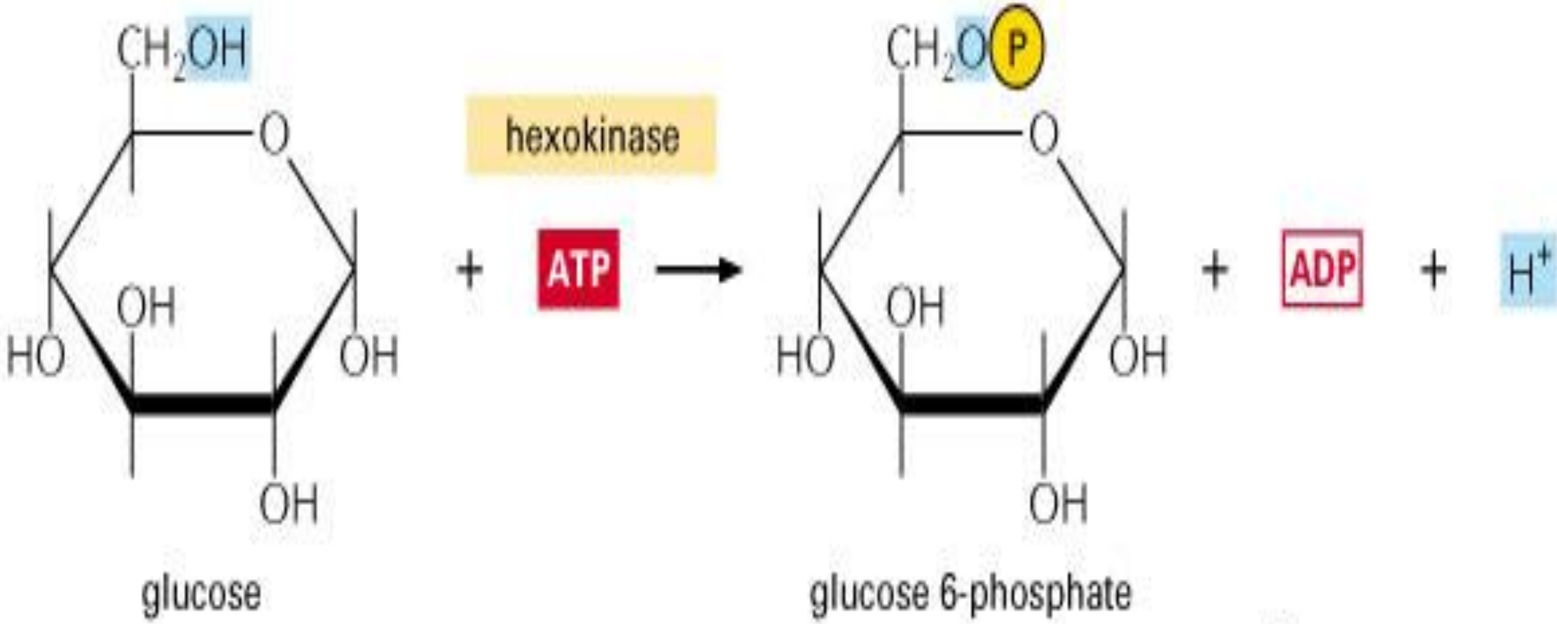
https://highered.mcgraw-hill.com/sites/0072507470/student_view0/chapter25/animation__how_glycolysis_works.html

- Glycolysis is the metabolic pathway that converts glucose $C_6H_{12}O_6$, into pyruvate, $CH_3COCOO^- + H^+$.
- The free energy released in this process is used to form the high-energy compounds ATP and NADH

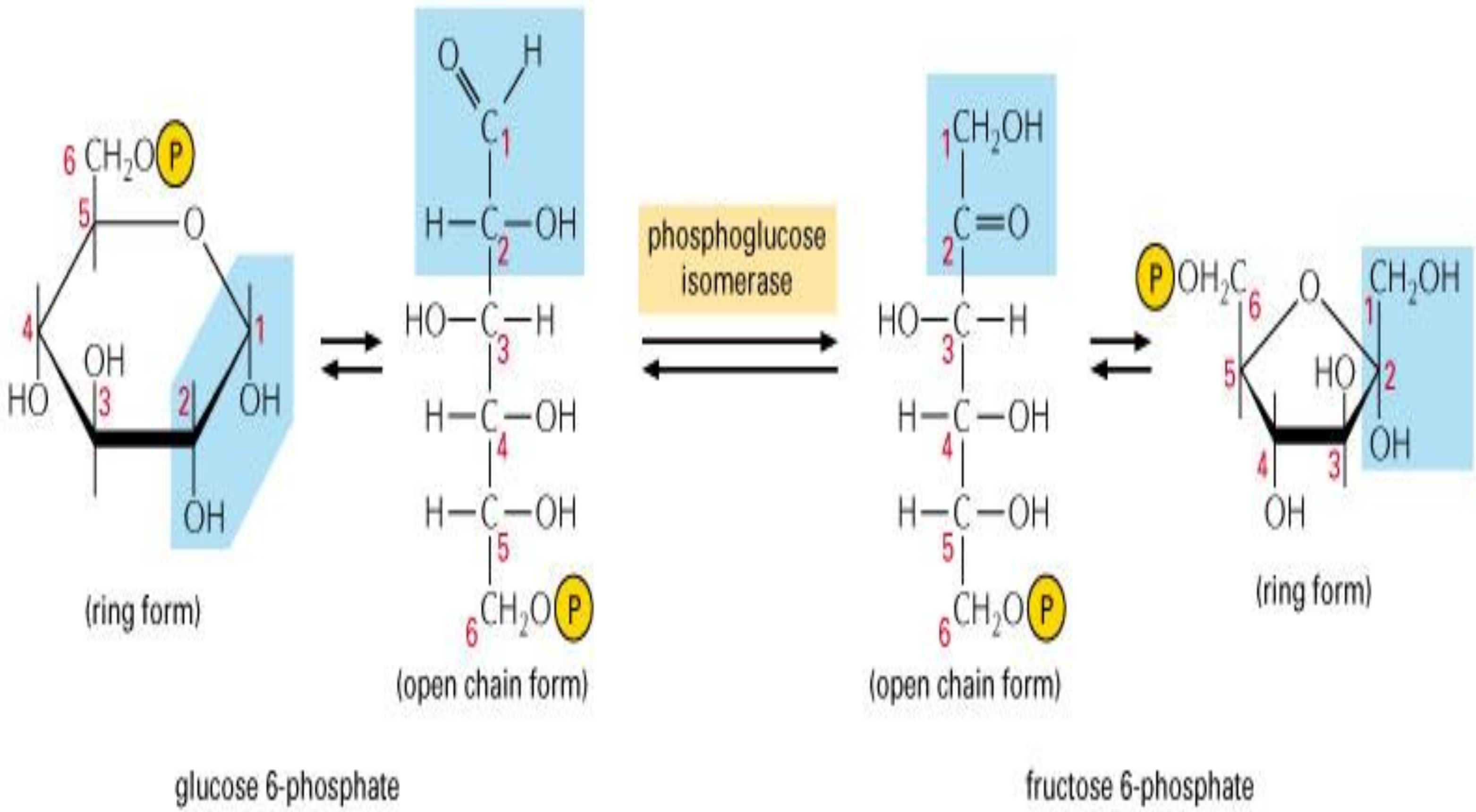


Step 1

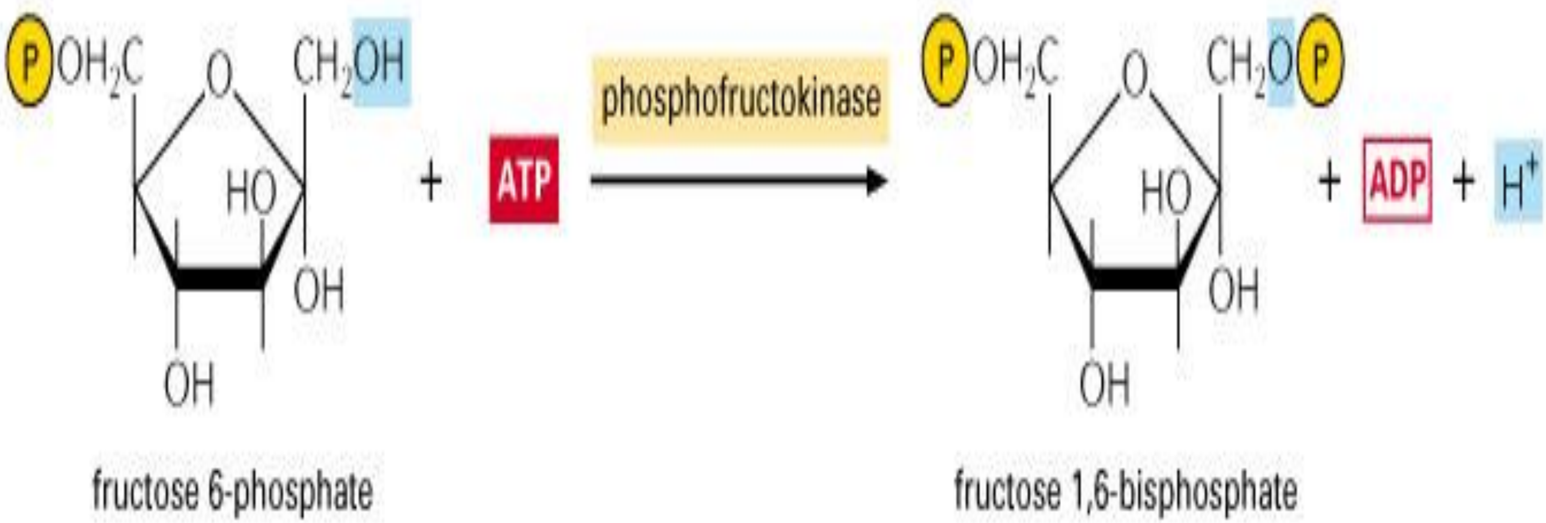
Glucose is phosphorylated by ATP to form a sugar phosphate. The negative charge of the phosphate prevents passage of the sugar phosphate through the plasma membrane, trapping glucose inside the cell.

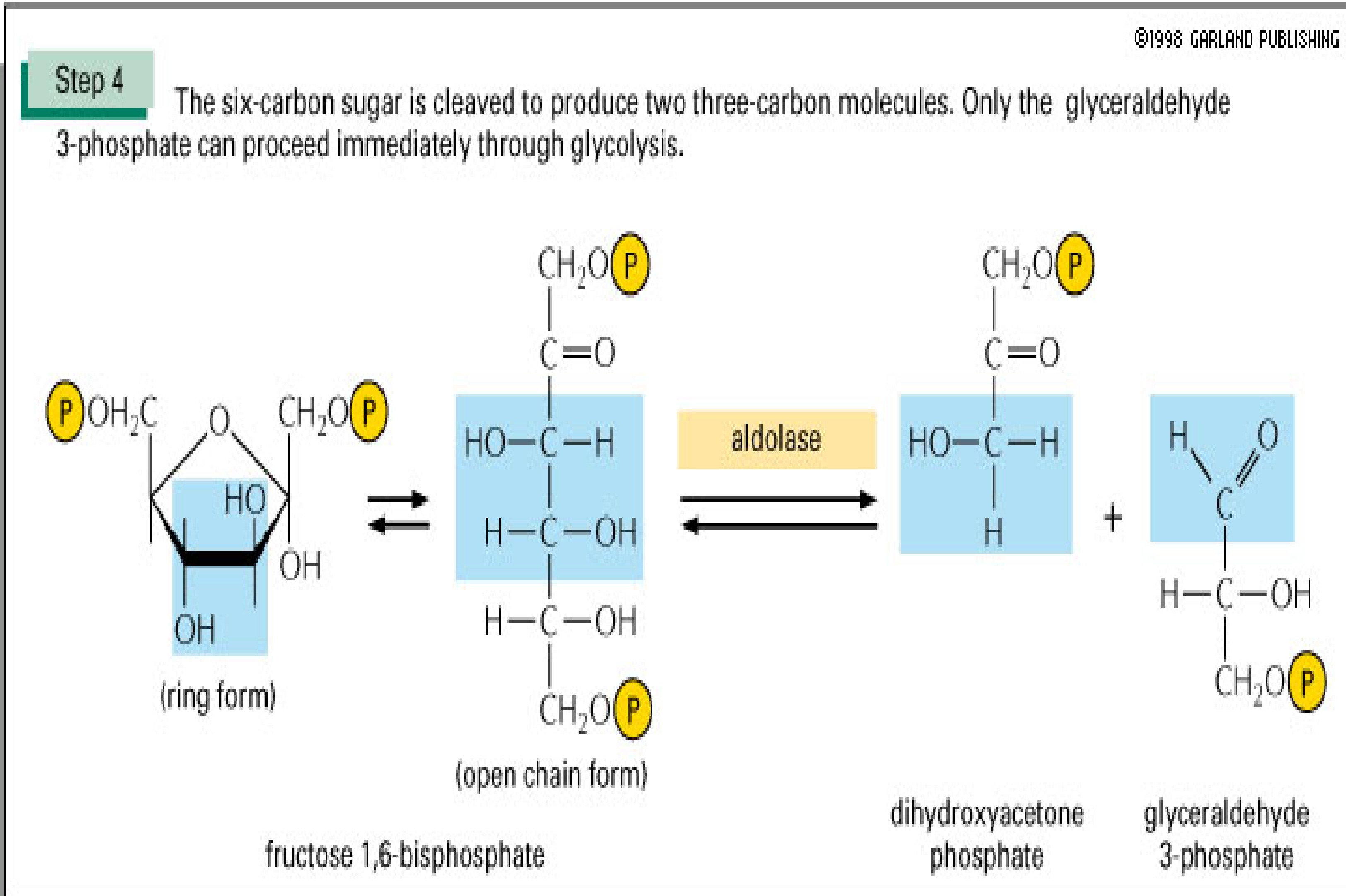


Step 2 A readily reversible rearrangement of the chemical structure (isomerization) moves the carbonyl oxygen from carbon 1 to carbon 2, forming a ketose from an aldose sugar. (See Panel 2-3, pp. 56–57.)



Step 3 The new hydroxyl group on carbon 1 is phosphorylated by ATP, in preparation for the formation of two three-carbon sugar phosphates. The entry of sugars into glycolysis is controlled at this step, through regulation of the enzyme *phosphofructokinase*.

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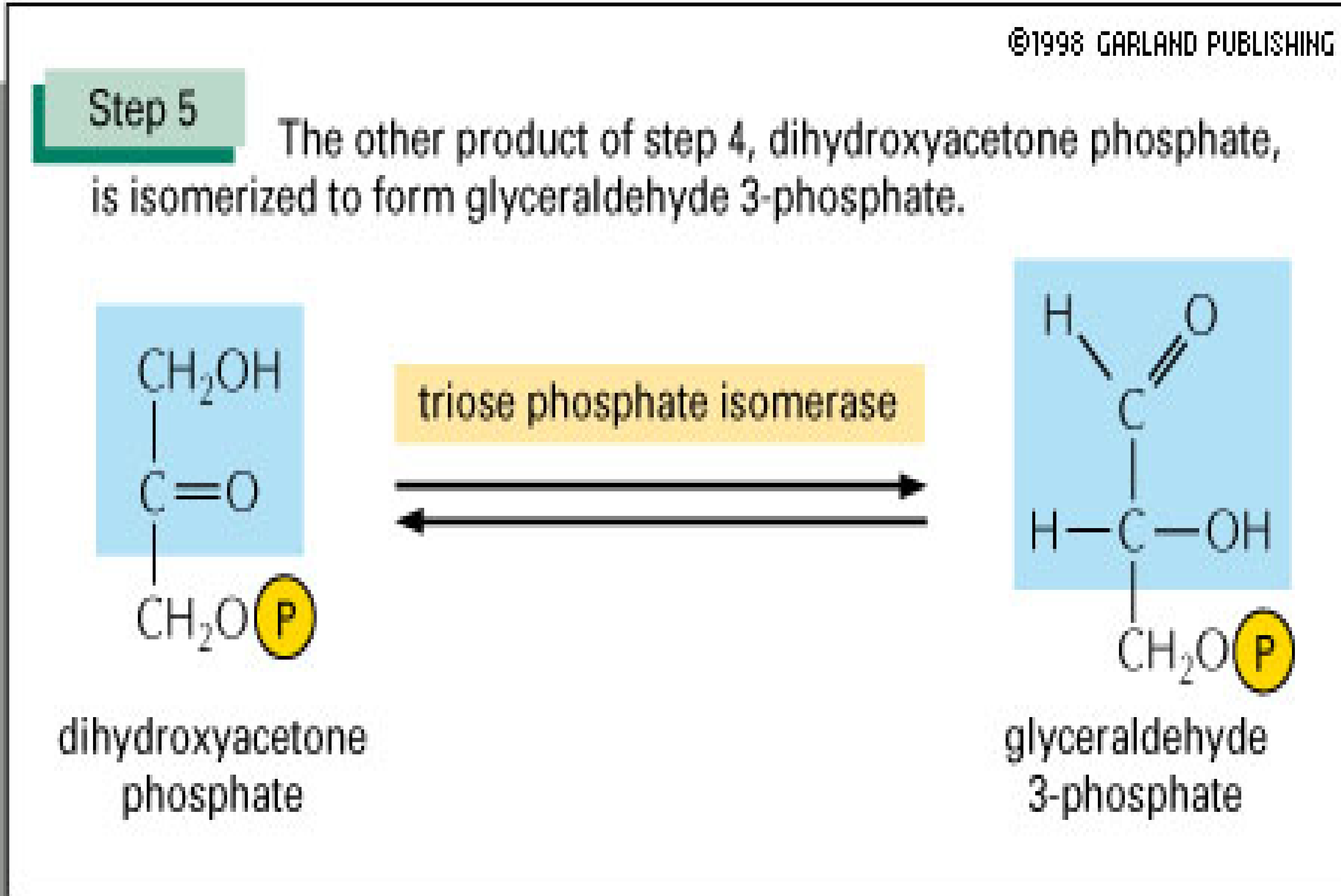
Step 4
The six-carbon sugar is cleaved to produce two three-carbon molecules. Only the glyceraldehyde 3-phosphate can proceed immediately through glycolysis.
(ring form)
(open chain form)
fructose 1,6-bisphosphate
aldolase
dihydroxyacetone phosphate
glyceraldehyde 3-phosphate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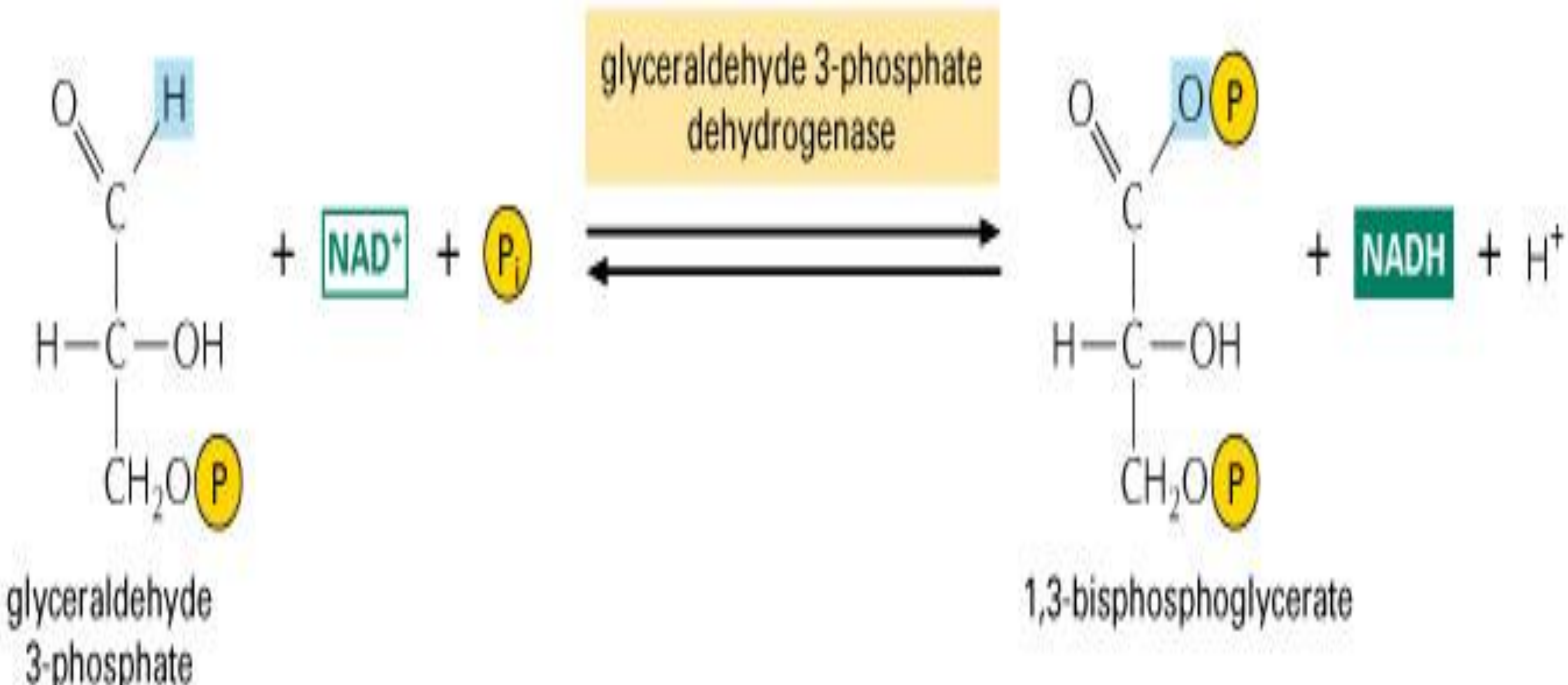
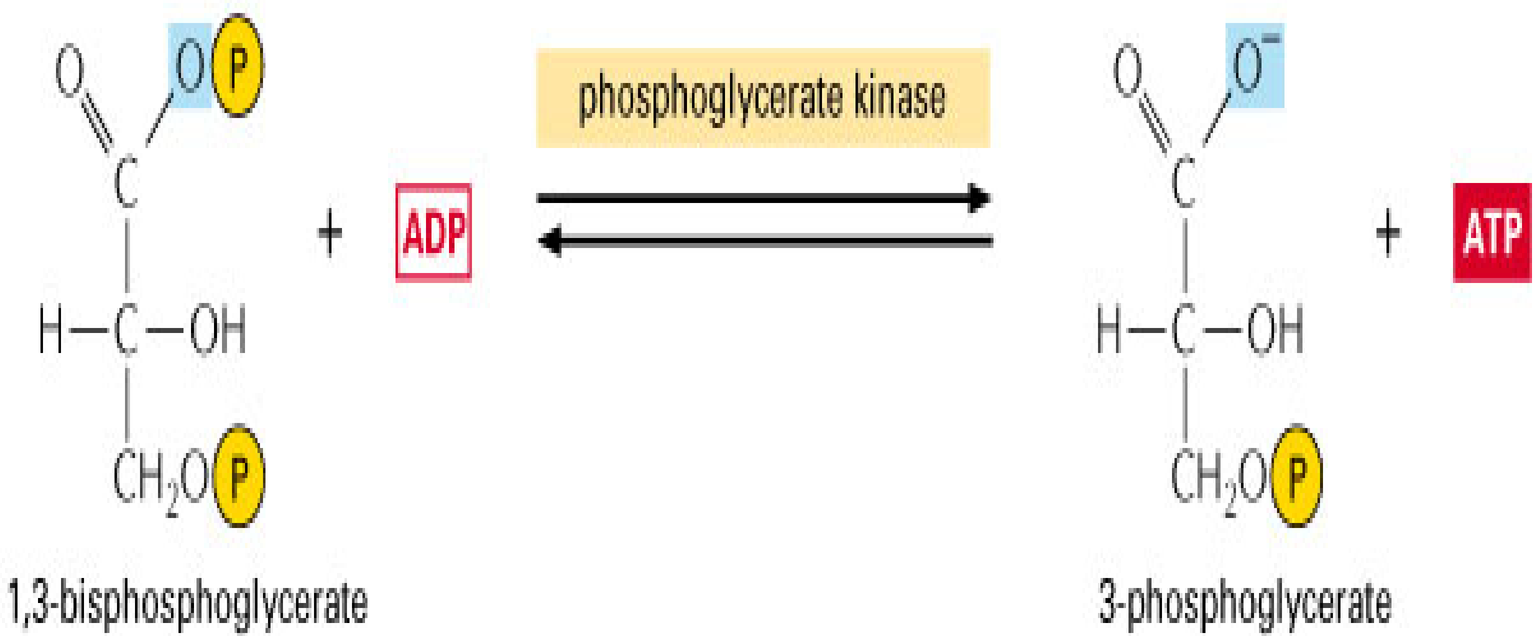
Step 5
The other product of step 4, dihydroxyacetone phosphate, is isomerized to form glyceraldehyde 3-phosphate.
CH2OH
C=O
CH2O P
triose phosphate isomerase
H
O
C
H—C—OH
CH2O P
dihydroxyacetone phosphate
glyceraldehyde 3-phosphate

Step 6

The two molecules of glyceraldehyde 3-phosphate are oxidized. The energy generation phase of glycolysis begins, as NADH and a new high-energy anhydride linkage to phosphate are formed (see Figure 4–5).

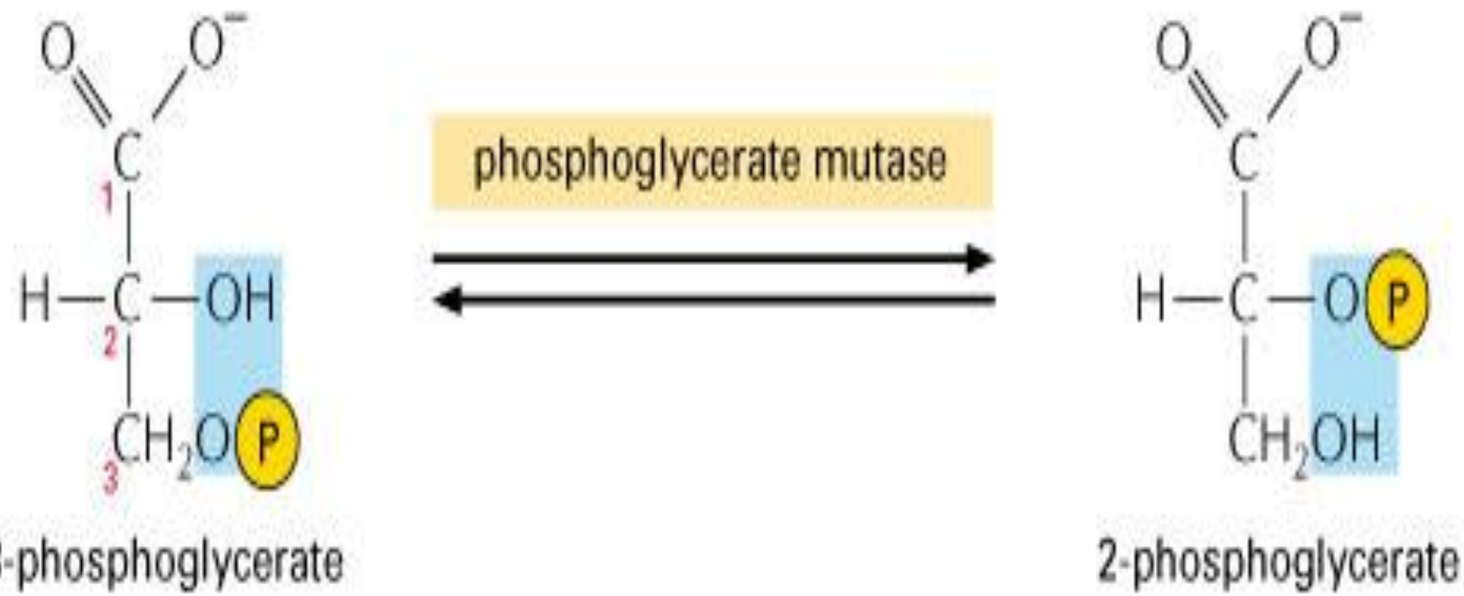


Step 7 The transfer to ADP of the high-energy phosphate group that was generated in step 6 forms ATP.

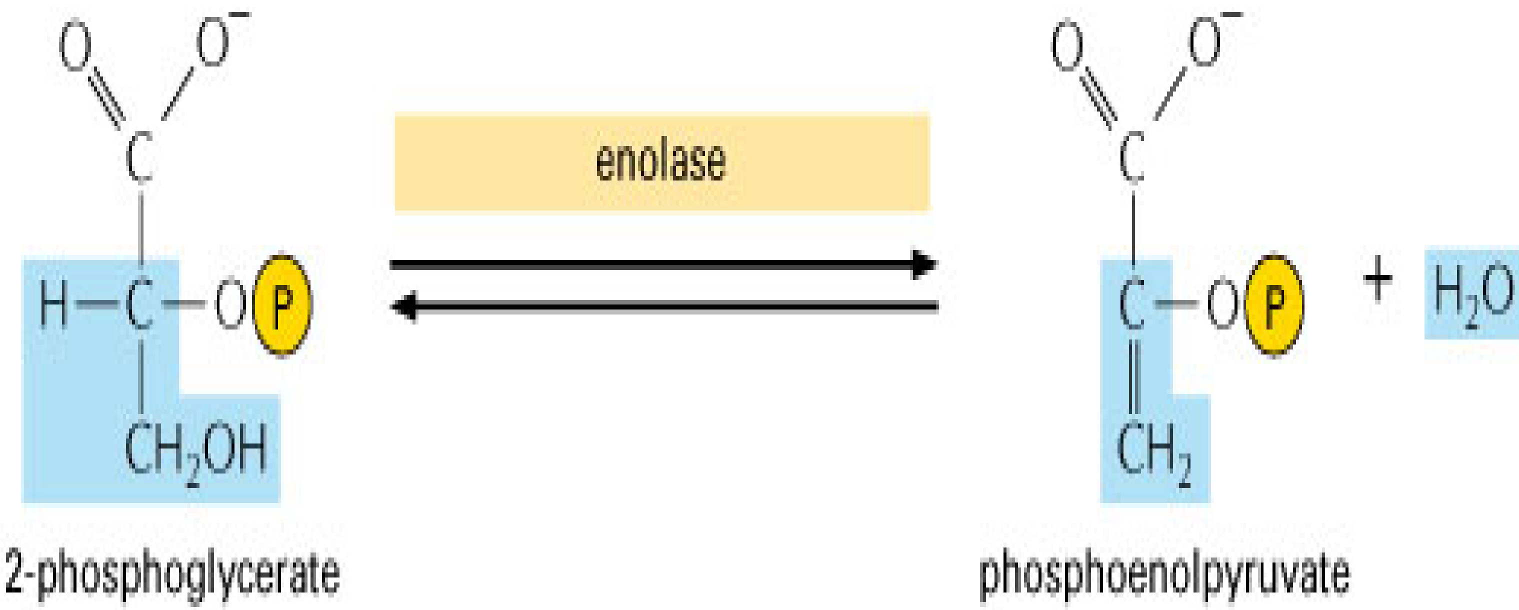


Step 8

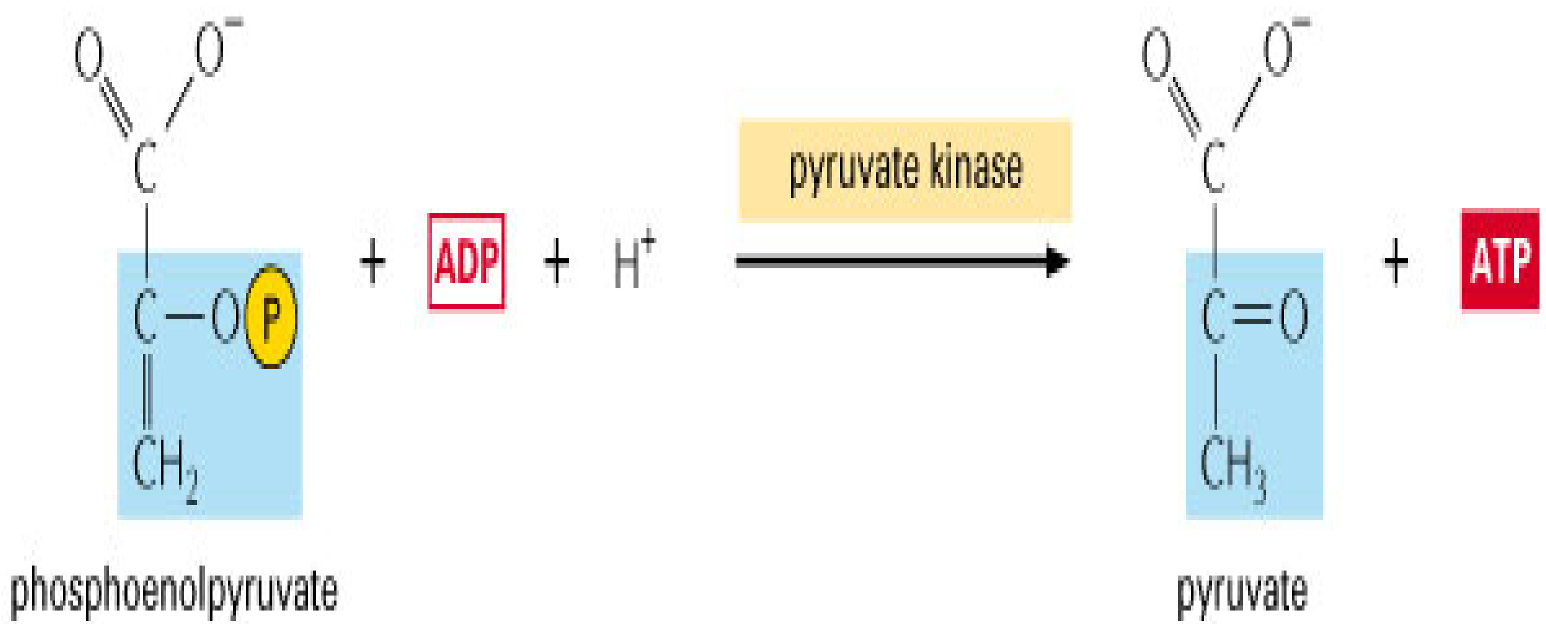
The remaining phosphate ester linkage in 3-phosphoglycerate, which has a relatively low free energy of hydrolysis, is moved from carbon 3 to carbon 2 to form 2-phosphoglycerate.

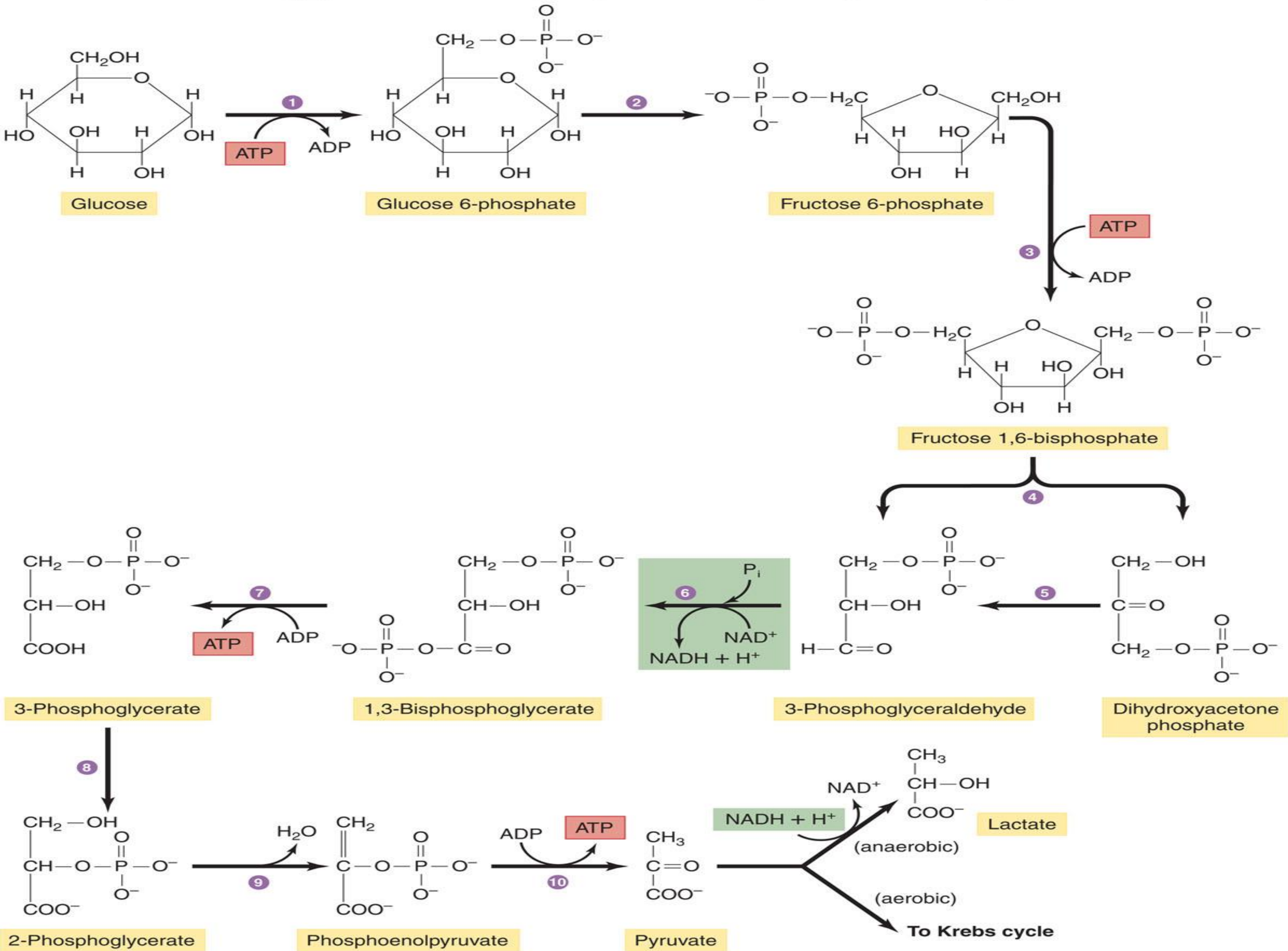


Step 9 The removal of water from 2-phosphoglycerate creates a high-energy enol phosphate linkage.



Step 10 The transfer to ADP of the high-energy phosphate group that was generated in step 9 forms ATP, completing glycolysis.




Glucose
ATP
ADP
Glucose 6-phosphate
Fructose 6-phosphate
ATP
ADP
Fructose 1,6-bisphosphate
3-Phosphoglyceraldehyde
Dihydroxyacetone phosphate
P_i
NAD^+
$NADH + H^+$
1,3-Bisphosphoglycerate
ADP
ATP
3-Phosphoglycerate
2-Phosphoglycerate
H_2O
Phosphoenolpyruvate
ADP
ATP
Pyruvate
$NADH + H^+$
NAD^+
(anaerobic)
Lactate
(aerobic)
To Krebs cycle

Regulation of Glycolysis

- Glycolysis is regulated by slowing down or speeding up certain steps in the glycolysis pathway. This is accomplished by inhibiting or activating the enzymes that are involved.
- The steps that are regulated may be determined by calculating the change in free energy, ΔG, for each step.

Regulation of Glycolysis (Continued)

- If a step's products and reactants are in equilibrium, then the step is assumed not to be regulated. Since the change in free energy is zero for a system at equilibrium, any step with a free energy change near zero is not being regulated.

Regulation of Glycolysis (Continued)

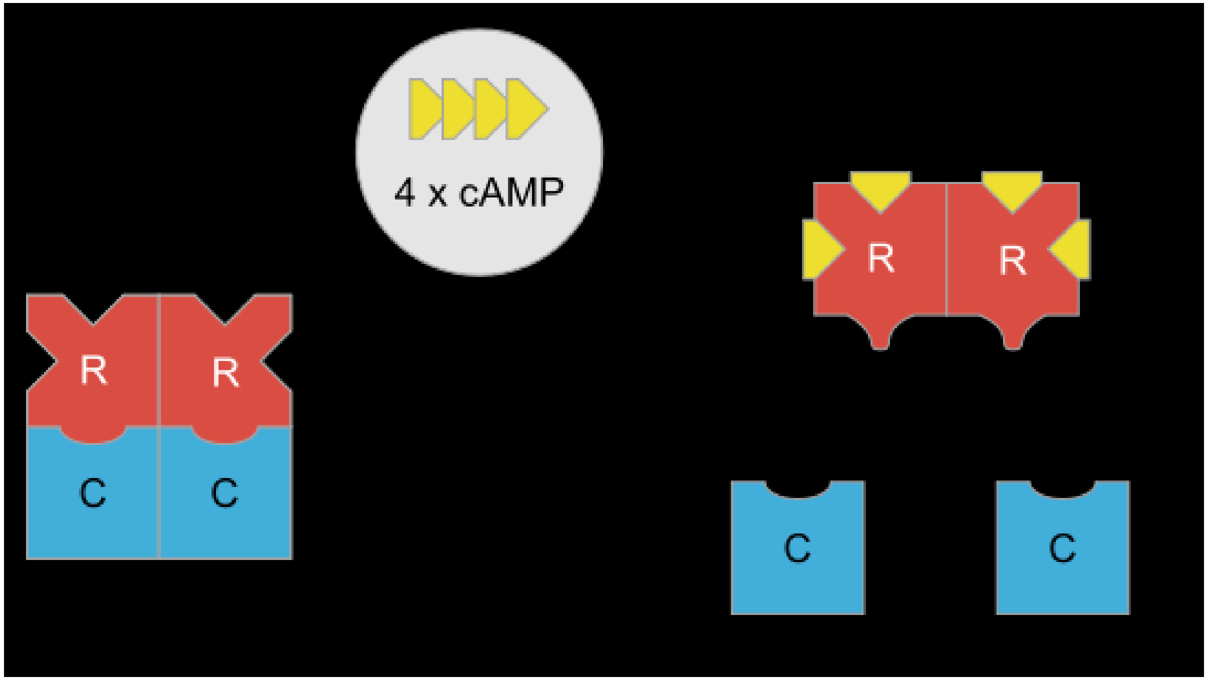
- If a step is being regulated, then that step's enzyme is not converting reactants into products as fast as it could, resulting in a build-up of reactants, which would be converted to products if the enzyme were operating faster.
- Since the reaction is thermodynamically favorable, the change in free energy for the step will be negative. A step with a large negative change in free energy is assumed to be regulated.

Regulation of Glycolysis (Continued)

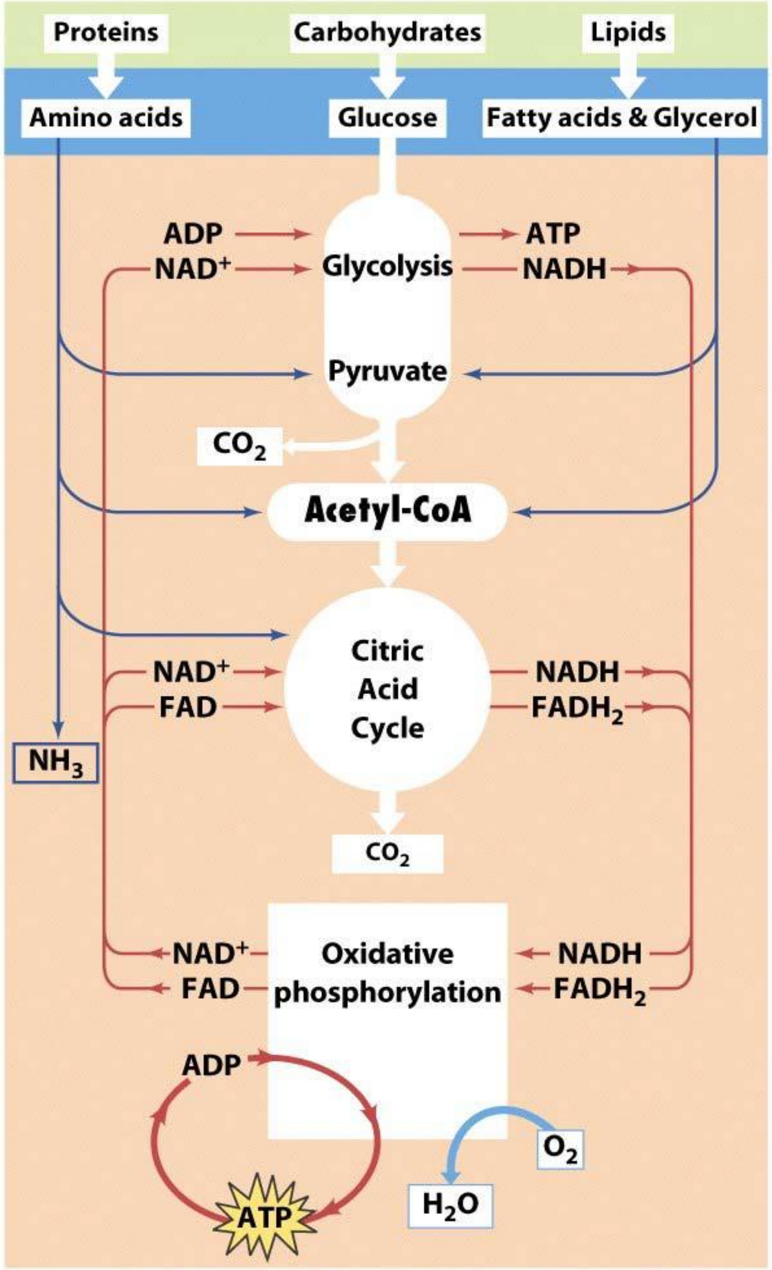
Example:

- Protein kinase A (PKA) is an enzyme that is regulated by cyclic AMP (cAMP). This is common in the "flight or fight response".
- The hormone Epinephrine signals the synthesis for cAMP which subsequently activates PKA. The kinase regulates target proteins through phosphorylation of serine and threonine.
- PKA is not activated until cAMP binds to the regulatory subunit. This stops inhibition of PKA. The complex (R2C2) has a pseudosubstrate sequence of R that occupies the active site of PKA. When cAMP binds, the R chains move so it is no longer inhibiting the active site.

Regulation of Glycolysis (Continued)



Regulating Activity: Intracellular concentration of cyclic AMP provides a very simple control mechanism over activity of protein kinase A.

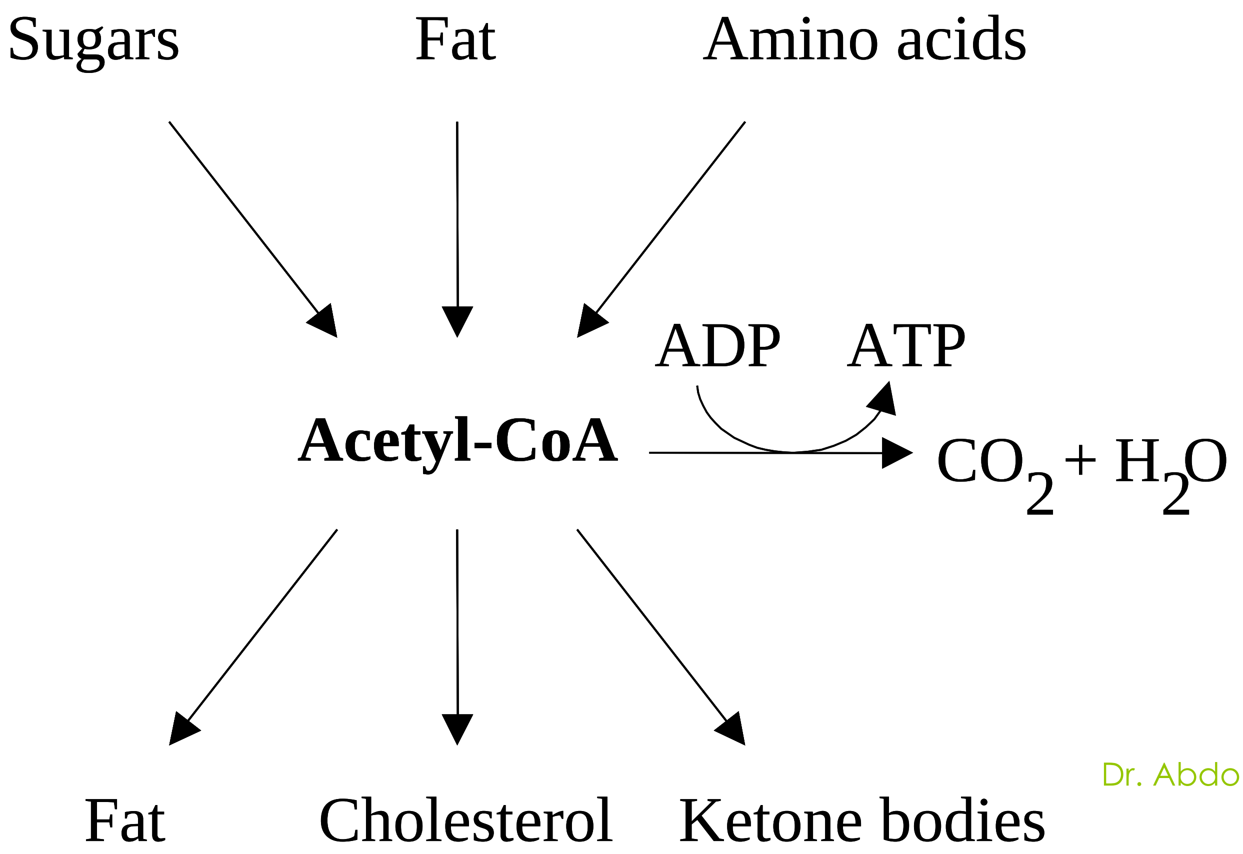


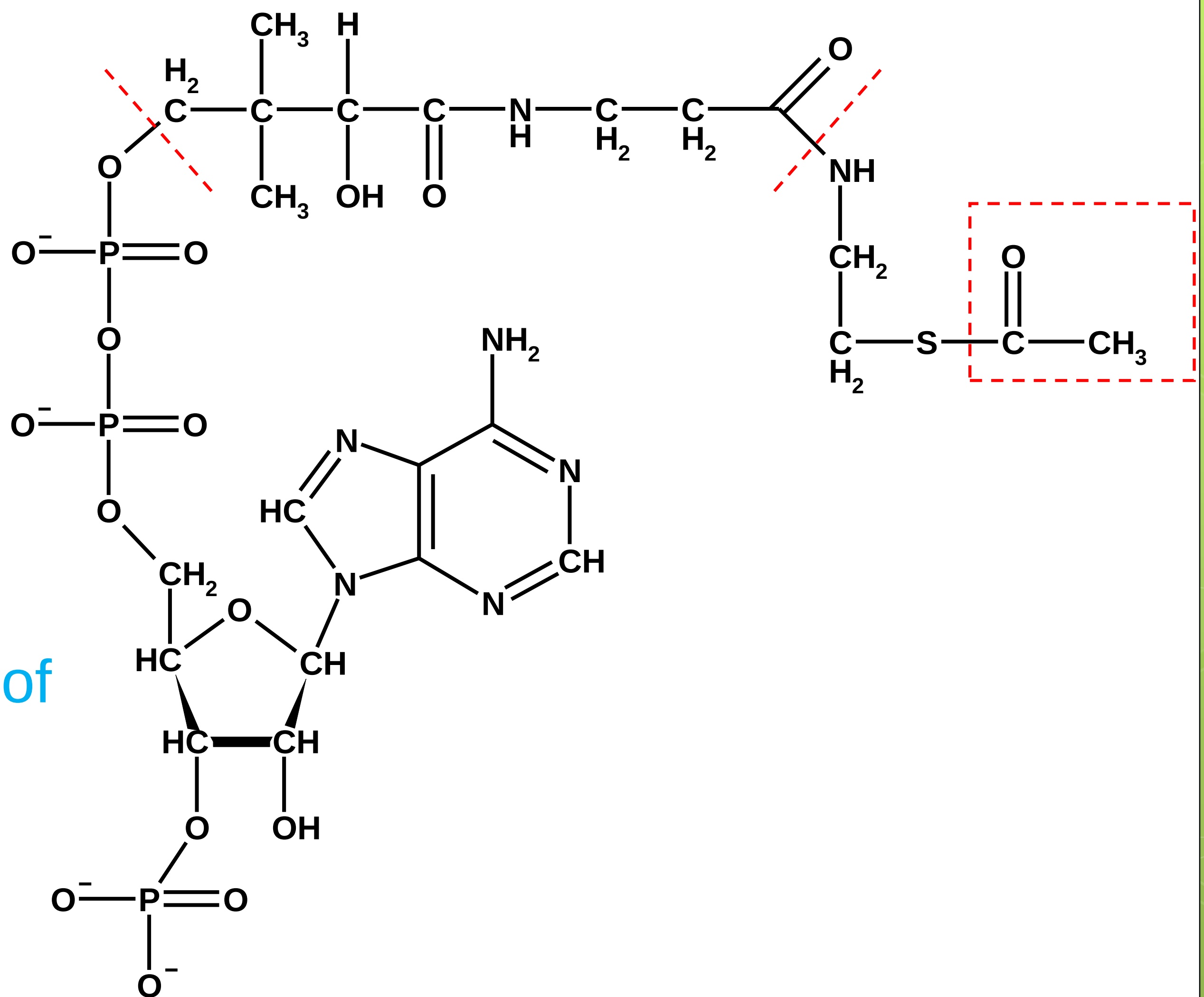
glucose + 2 ADP + 2 P_i + 2 NAD → 2 pyruvate + 2 ATP + 2 NADH + 2 H^+ + 2 H_2O

Digestion is depolymerization

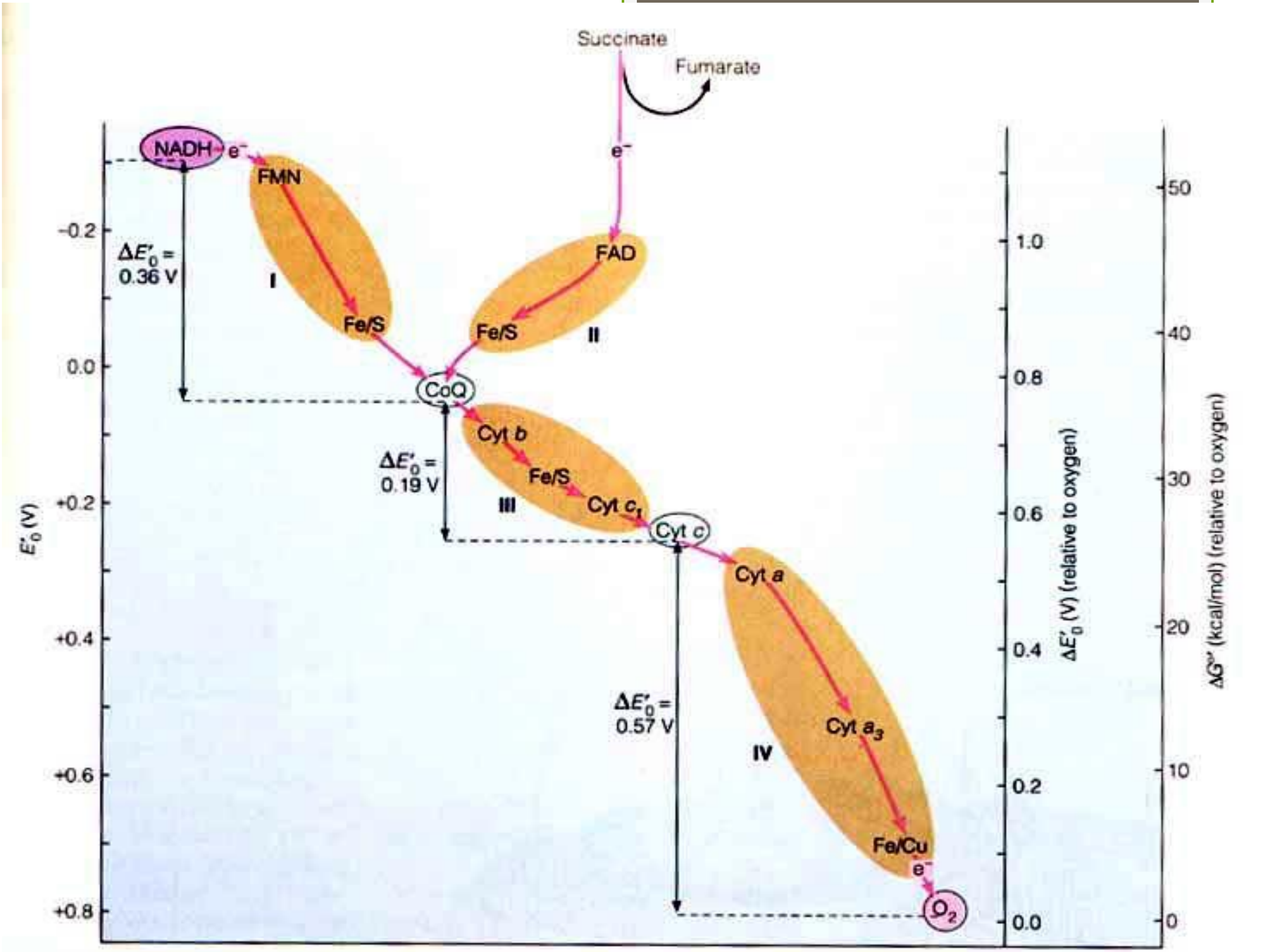
Carbohydrates	→	**Sugars**	→	$CO_2 + H_2O$
Fat	→	**Fatty acids, glycerol**	→	$CO_2 + H_2O$
Protein	→	**Amino acids**	→	$CO_2 + H_2O$
			↘	Urea, sulfate

Convergent and divergent metabolic pathways





The structure of Acetyl-CoA



Succinate
Fumarate
NADH
e⁻
FMN
Fe/S
I
e⁻
FAD
Fe/S
II
CoQ
Cyt b
Fe/S
Cyt c_1
III
Cyt c
Cyt a
Cyt a_3
Fe/Cu
IV
e⁻
O_2
$\Delta E'_0$ = 0.36 V
$\Delta E'_0$ = 0.19 V
$\Delta E'_0$ = 0.57 V
E'_0 (V)
-0.2
0.0
+0.2
+0.4
+0.6
+0.8
$\Delta E'_0$ (V) (relative to oxygen)
1.0
0.8
0.6
0.4
0.2
0.0
$\Delta G^{\circ\prime}$ (kcal/mol) (relative to oxygen)
50
40
30
20
10
0