Metabolism

- **Catabolism:**

  Breaking down of molecules

  – Food contains three nutrients that are used as energy sources

  – These nutrients can be broken down into smaller molecules

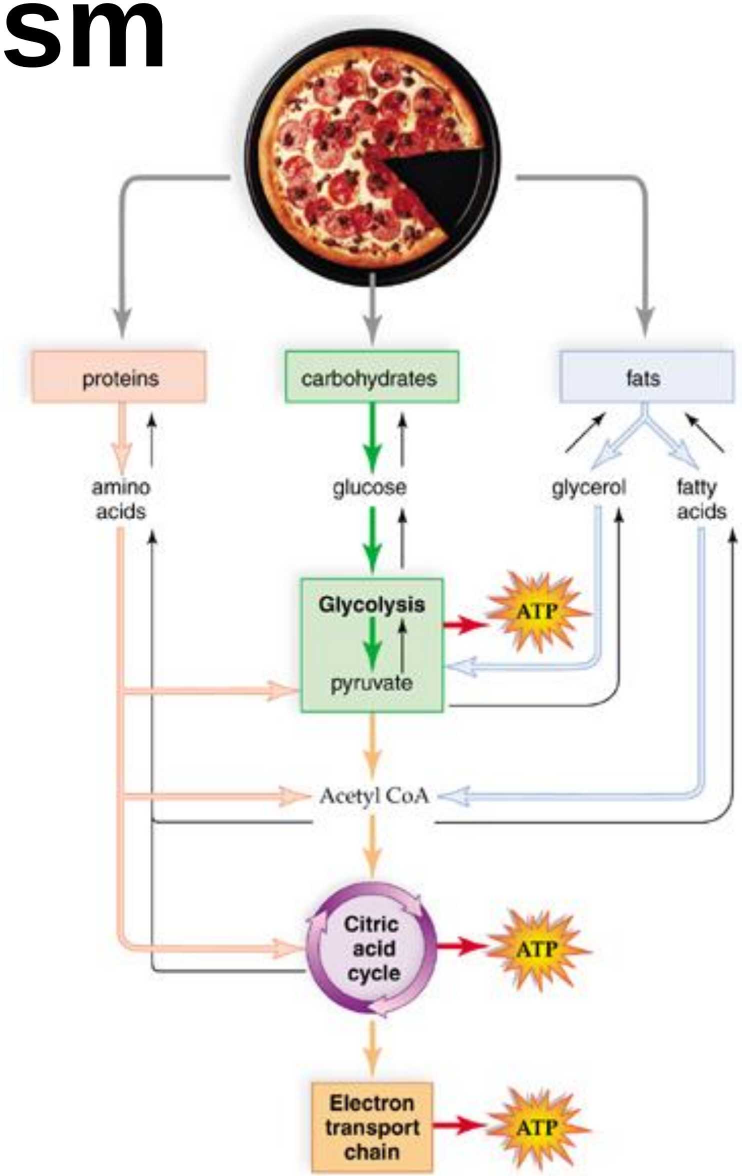
    - Carbohydrates Glucose
    - Fats Glycerol and Fatty Acids
    - Proteins Amino Acids

- **Anabolism:**

  Building up of molecules

  – Many of the building blocks of larger molecules come directly from our food.

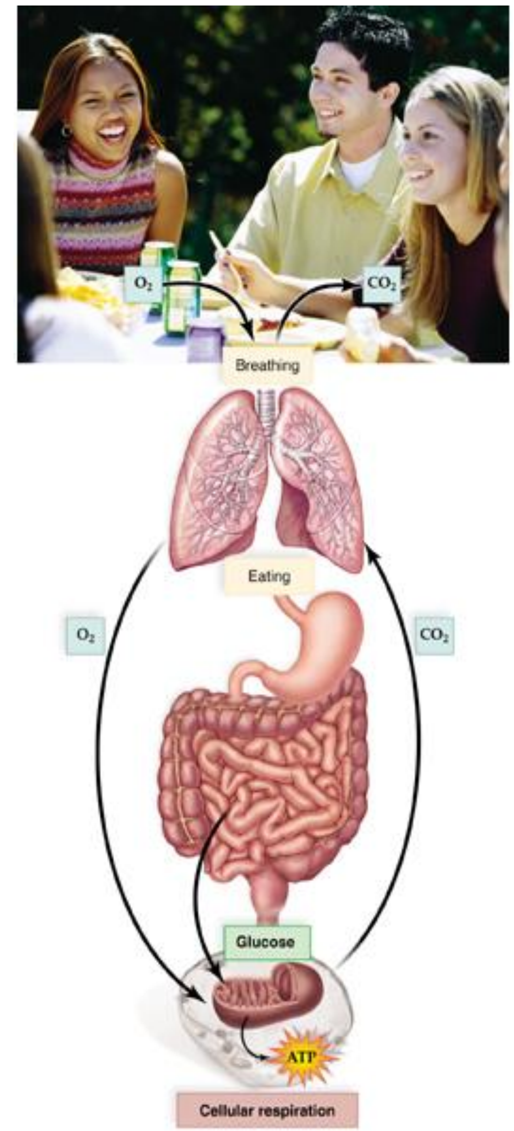
    - Glucose Glycogen
    - Amino Acids Proteins



(ATP is the energy currency used by these reactions)

Metabolism

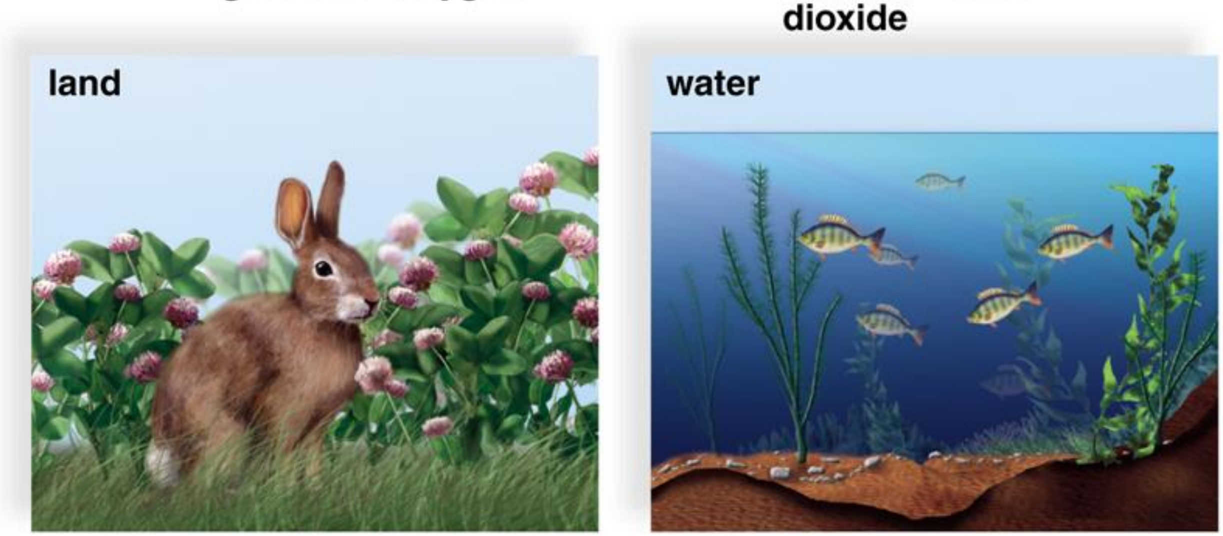
- **Cellular Respiration**
  - Release of energy from glucose (usually) coupled to ATP synthesis
  - An aerobic process that requires O_2 and releases CO_2



ADP + P → ATP

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

glucose **oxygen** **carbon dioxide** **water**

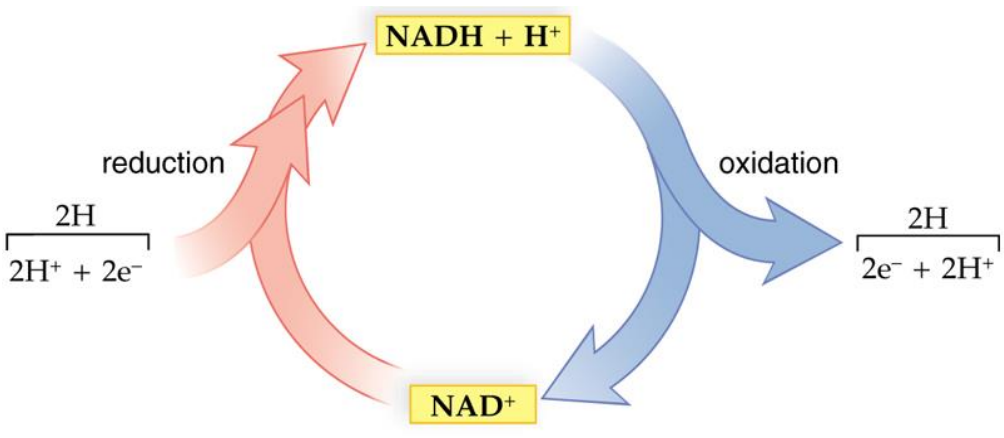


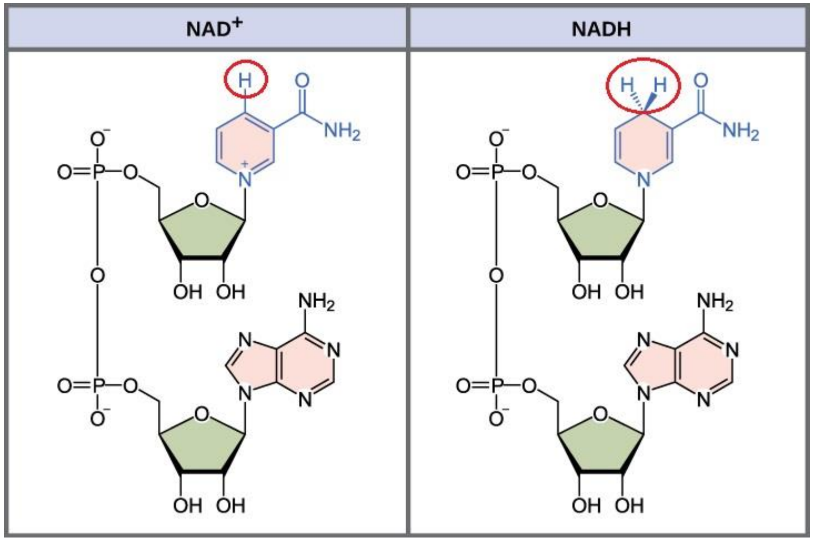
Breakdown of glucose results in 36 or 38 ATP molecules

Overview of Cellular Respiration

- **NAD$^+$ and FAD**
  - Two co-enzymes of oxidation and reduction that are active during cellular respiration
  - They carry electrons from the cytoplasm or the mitochondrial matrix and carry them to the cristae of the mitochondria
  - NAD$^+$ and FAD each carry two electrons and two hydrogen atoms

The NAD$^+$ Cycle

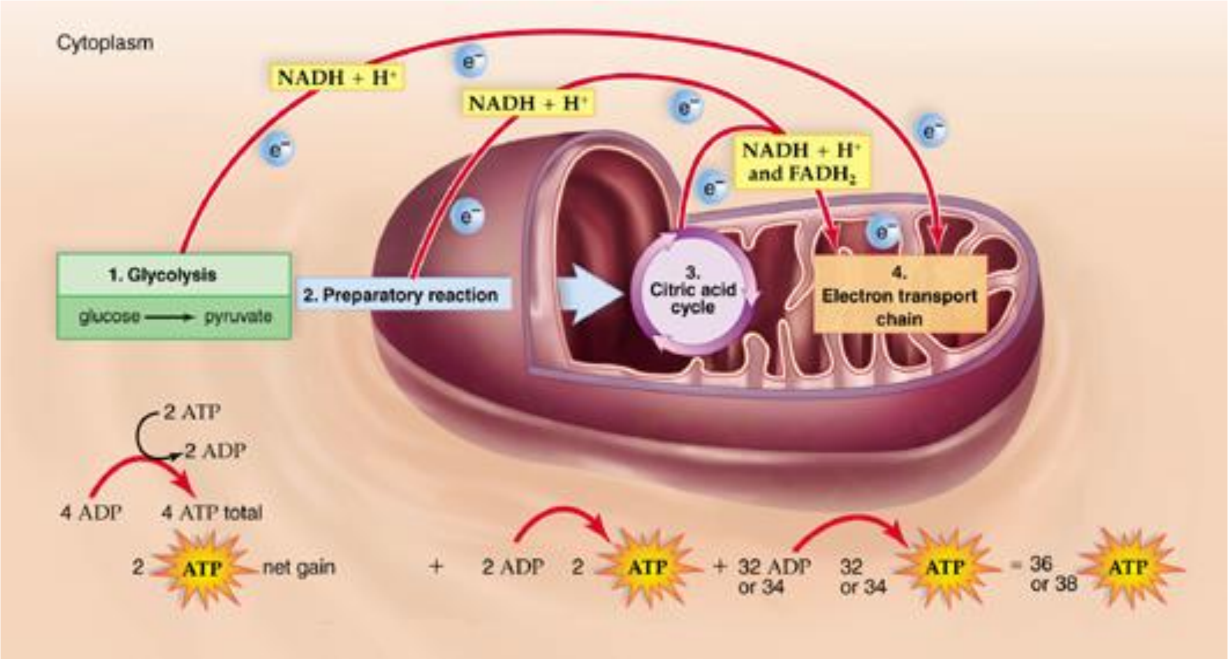




Phases of Cellular Respiration

- Glycolysis
- Preparatory Reaction
- Citric Acid Cycle
- Electron Transport Chain
- **We will simplify: Glycolysis, Krebs cycle, electron transport**

Phases of Glucose Breakdown

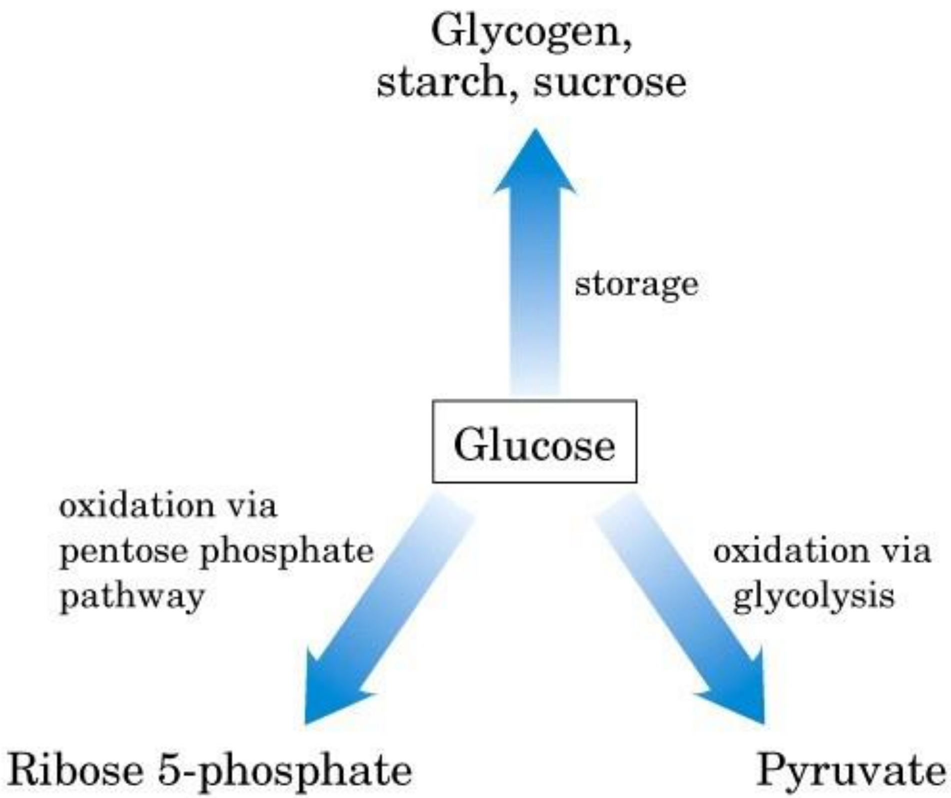


Fate of glucose in living systems

Glucose + $6O_2$ = $6CO_2$ + $6H_2O$ δG_o= -2840 kJ/mol

Glucose + $2NAD_+$ = 2Pyruvate + 2NADH + $2H_+$ δGo = -146 kJ/mol

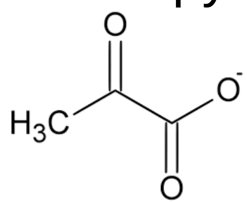
- **5.2% of total free energy that can be released by glucose is released in glycolysis.**



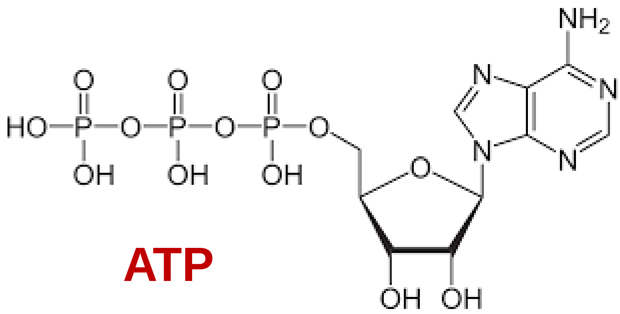
Glycolysis

Glykys = Sweet, Lysis = splitting

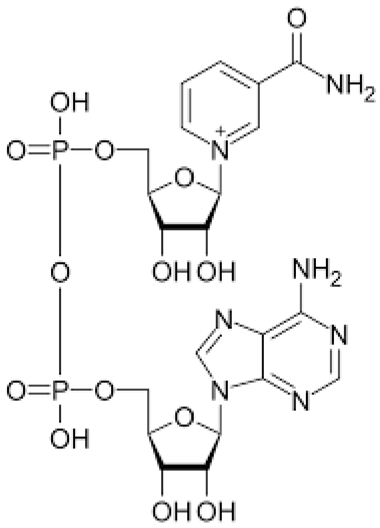
❖ During this process one molecule of glucose (6 carbon molecule) is degraded into two molecules of pyruvate (three carbon molecule).



❖ Free energy released in this process is stored as 2 molecules of ATP, and 2 molecules of NADH.



ATP



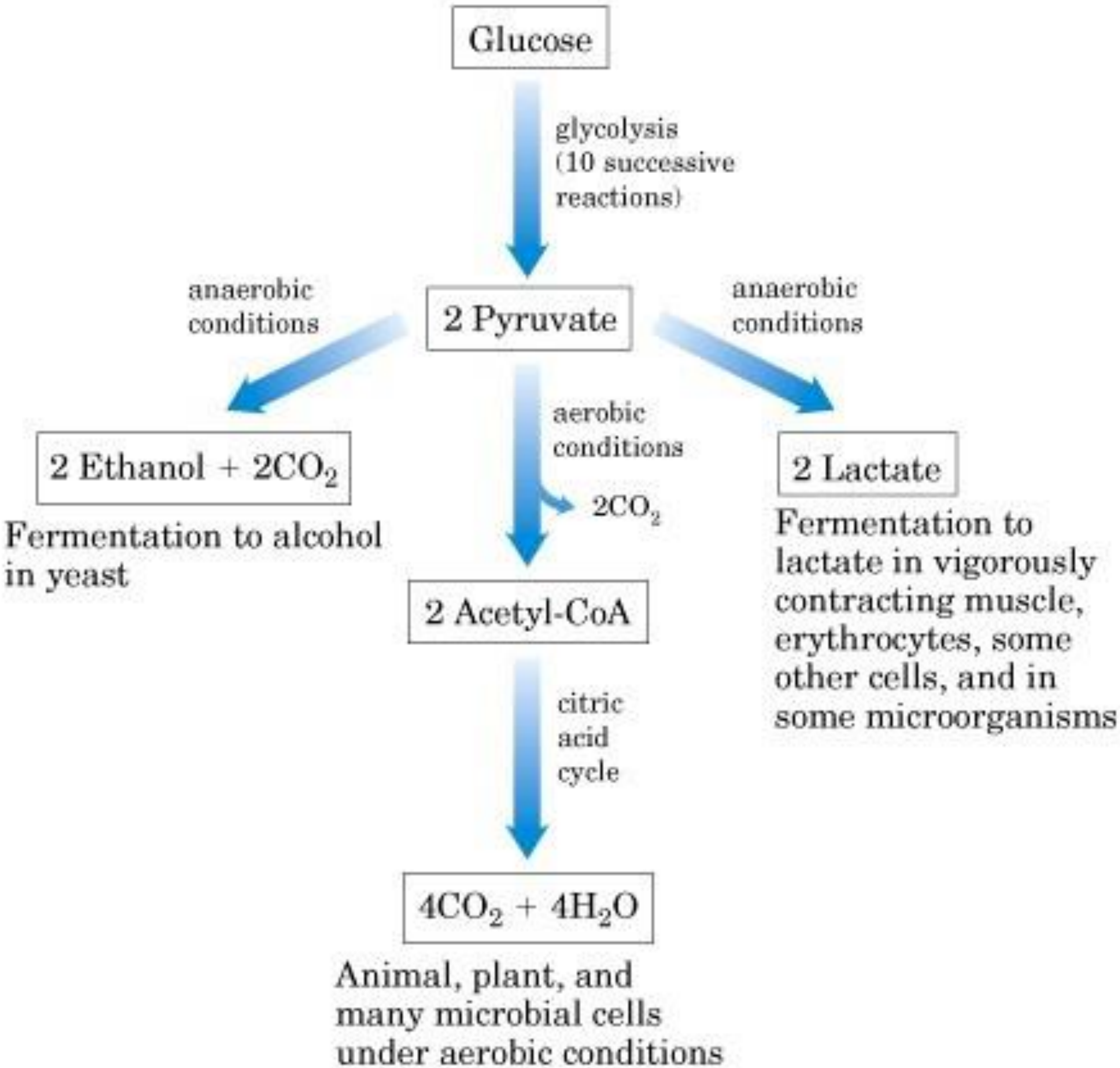
NADH

Glucose + 2NAD+ = 2Pyruvate + 2NADH + 2H+ δG° = **-146** kJ/mol

2ADP + 2Pi = 2ATP + 2H2O δG° = 2X(30.5 kJ/mol) = **61** kJ/mol

δG° (overall) = -146+61 = **-85** kJ/mol

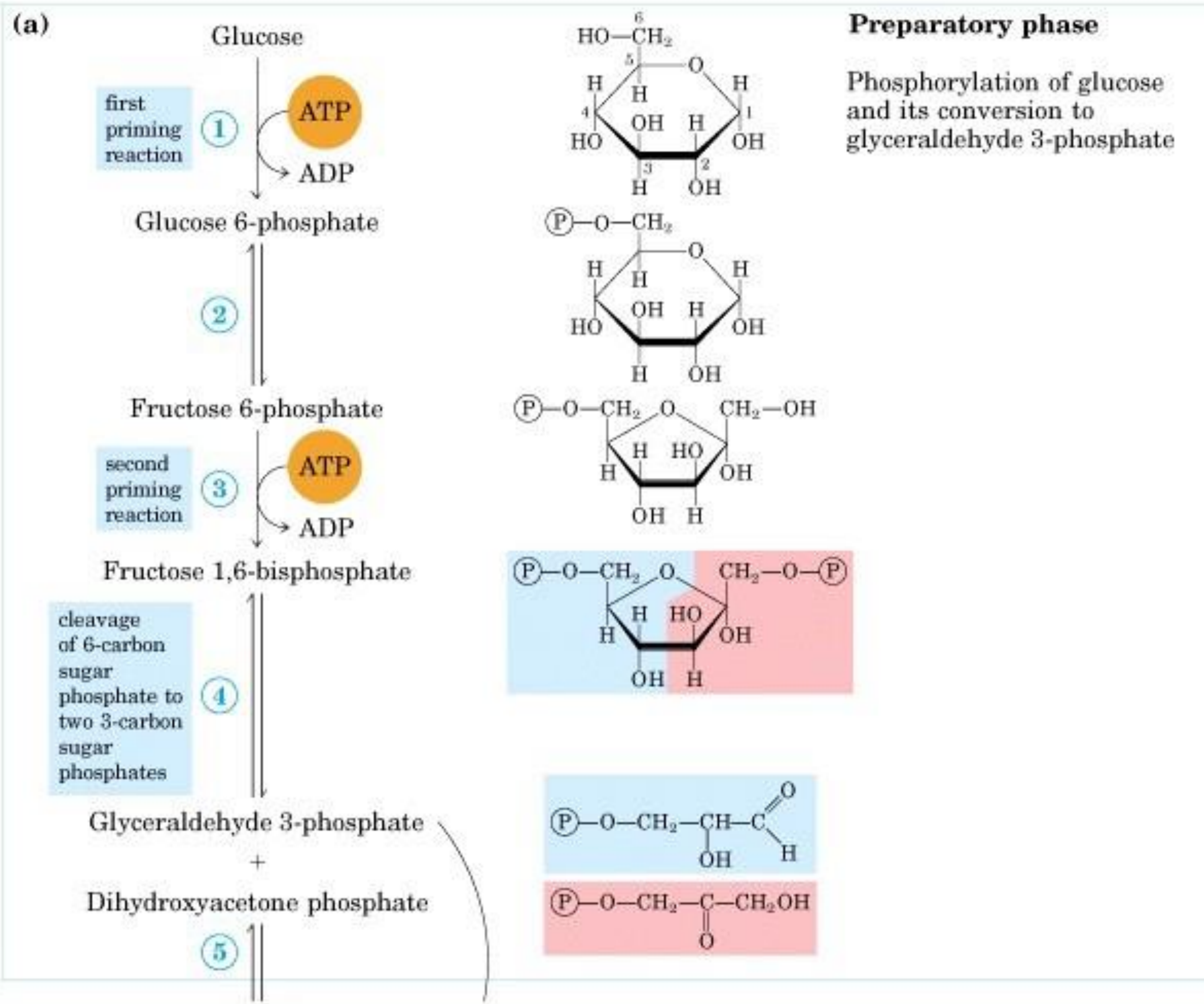
❖ In standard condition glycolysis is an exergonic reaction which tends to be irreversible because of negative δG°.

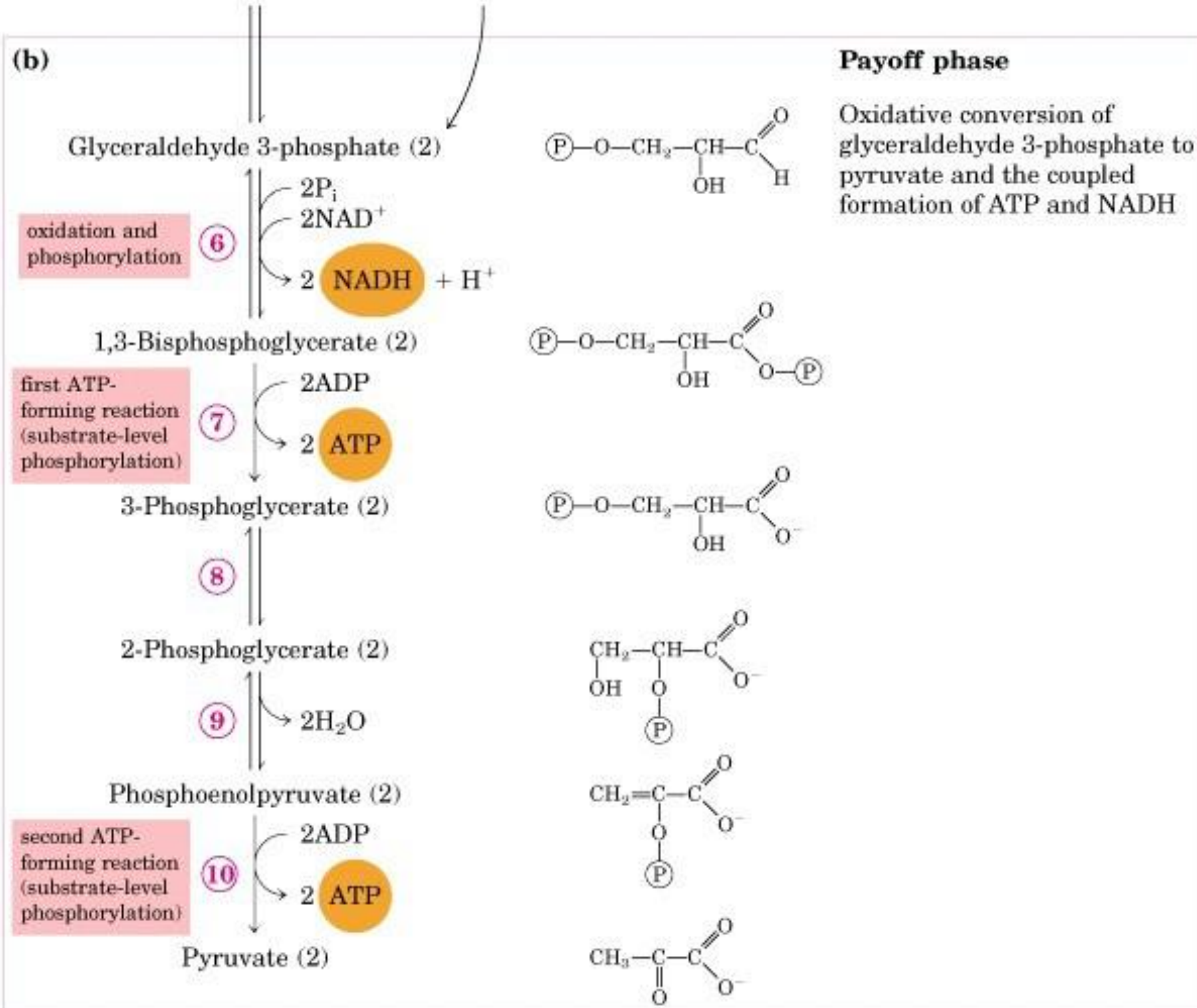

Glucose
glycolysis (10 successive reactions)
anaerobic conditions
2 Pyruvate
anaerobic conditions
aerobic conditions
$2 \text{Ethanol} + 2CO_2$
$2CO_2$
2 Lactate
Fermentation to alcohol in yeast
Fermentation to lactate in vigorously contracting muscle, erythrocytes, some other cells, and in some microorganisms
2 Acetyl-CoA
citric acid cycle
$4CO_2 + 4H_2O$
Animal, plant, and many microbial cells under aerobic conditions

Steps of Glycolysis

- **Preparatory Reaction**
  - Stage 1: (Reactions 1-5)
  - A preparatory stage in which glucose is phosphorylated,
  - Converted to fructose
  - It is again phosphorylated and cleaved into two molecules of glyceraldehyde-3-phosphate.
  - In this phase there is an investment of two molecules of ATP.

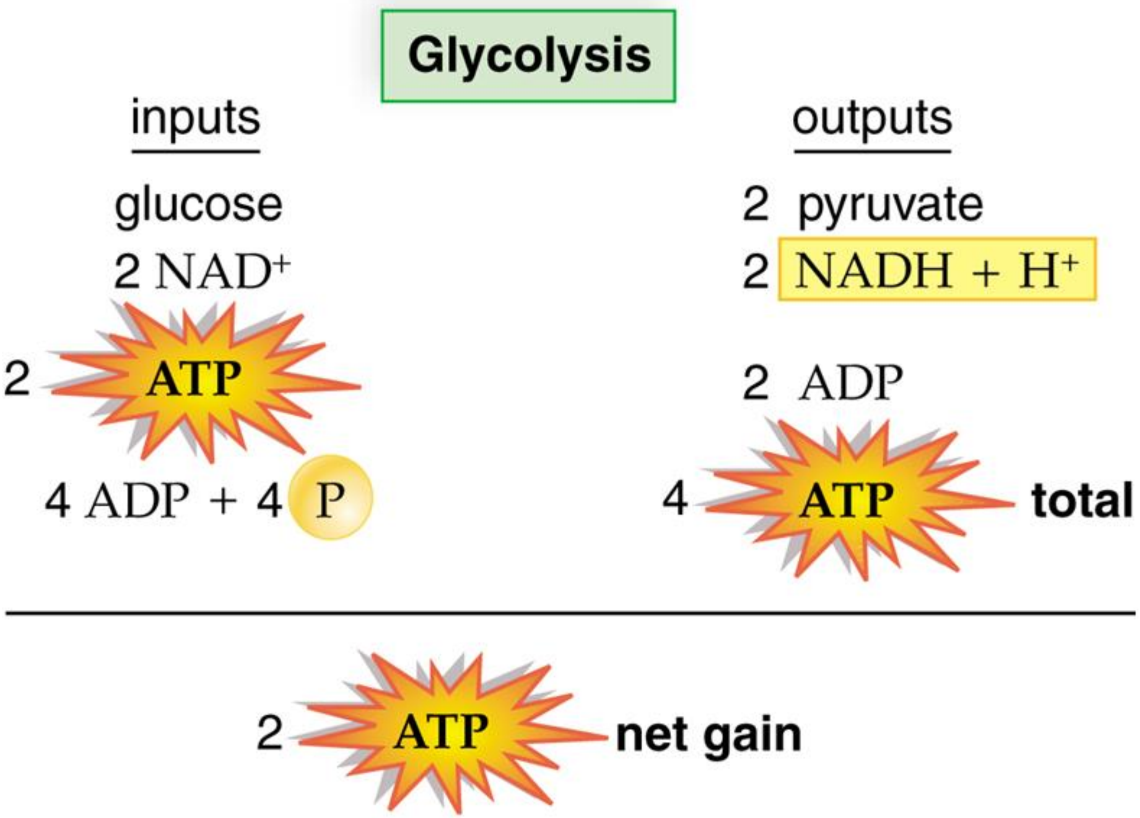
- **Payoff phase**
  - Stage 2: (Reactions 6-10)
  - The two molecules of glyceraldehyde-3-phosphate are converted to pyruvate.
  - Concomitant generation of four ATP molecules and two molecules of NADH.
  - Thus, there is a net gain of two ATP molecules per molecule of Glucose in glycolysis.

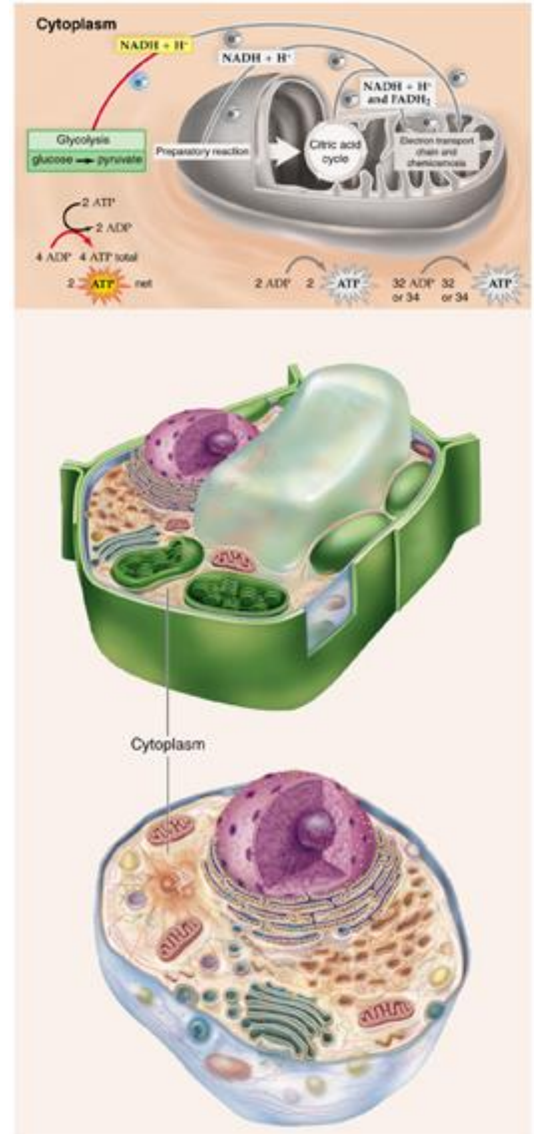

(a)
Preparatory phase
Phosphorylation of glucose and its conversion to glyceraldehyde 3-phosphate
Glucose
first priming reaction
1
ATP
ADP
Glucose 6-phosphate
2
Fructose 6-phosphate
second priming reaction
3
ATP
ADP
Fructose 1,6-bisphosphate
cleavage of 6-carbon sugar phosphate to two 3-carbon sugar phosphates
4
Glyceraldehyde 3-phosphate
+
Dihydroxyacetone phosphate
5



(b)
Payoff phase
Oxidative conversion of glyceraldehyde 3-phosphate to pyruvate and the coupled formation of ATP and NADH
Glyceraldehyde 3-phosphate (2)
2Pi
2NAD+
oxidation and phosphorylation
6
2 NADH + H+
1,3-Bisphosphoglycerate (2)
first ATP-forming reaction (substrate-level phosphorylation)
7
2ADP
2 ATP
3-Phosphoglycerate (2)
8
2-Phosphoglycerate (2)
9
2H2O
Phosphoenolpyruvate (2)
second ATP-forming reaction (substrate-level phosphorylation)
10
2ADP
2 ATP
Pyruvate (2)

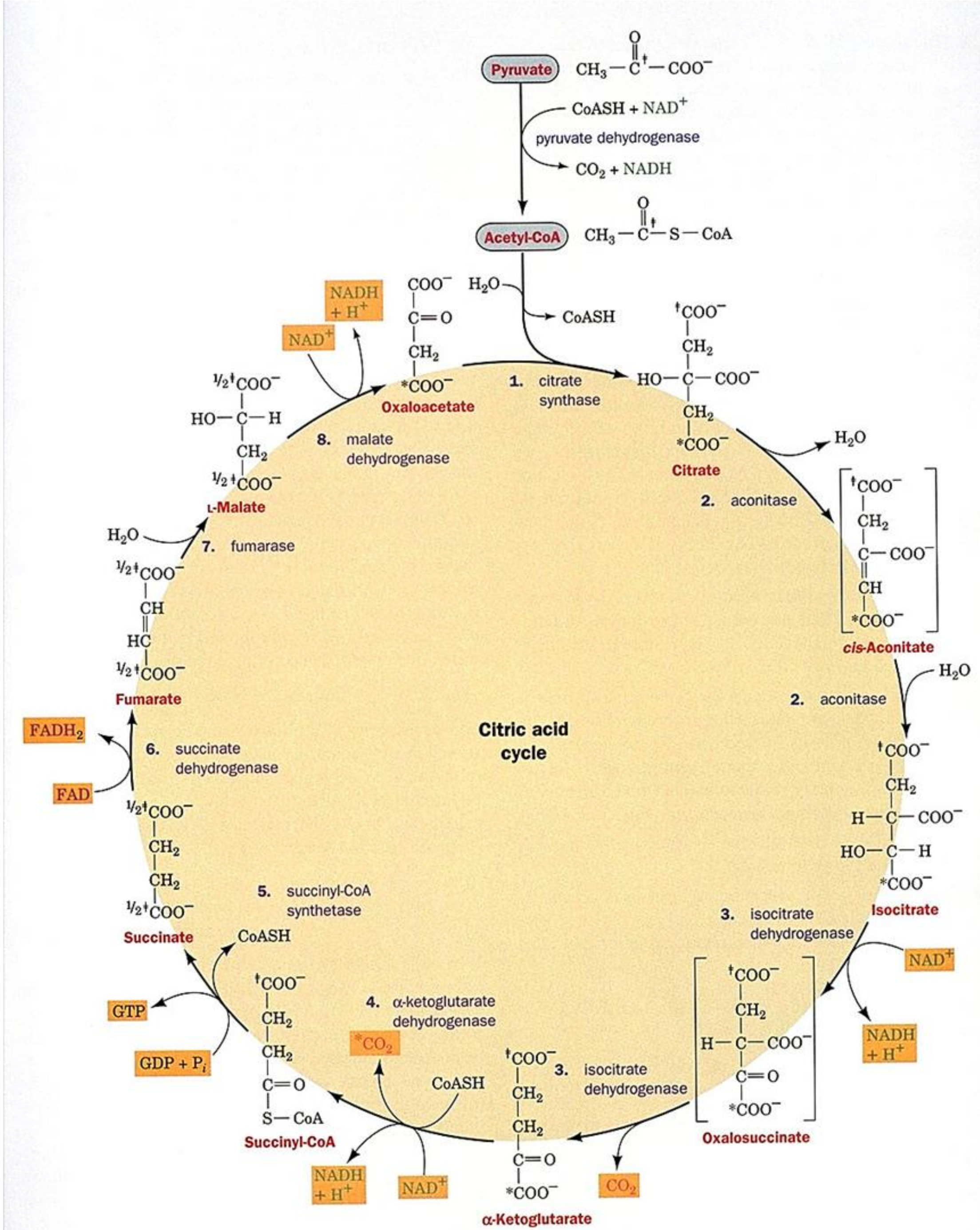
Glycolysis: Inputs and Outputs





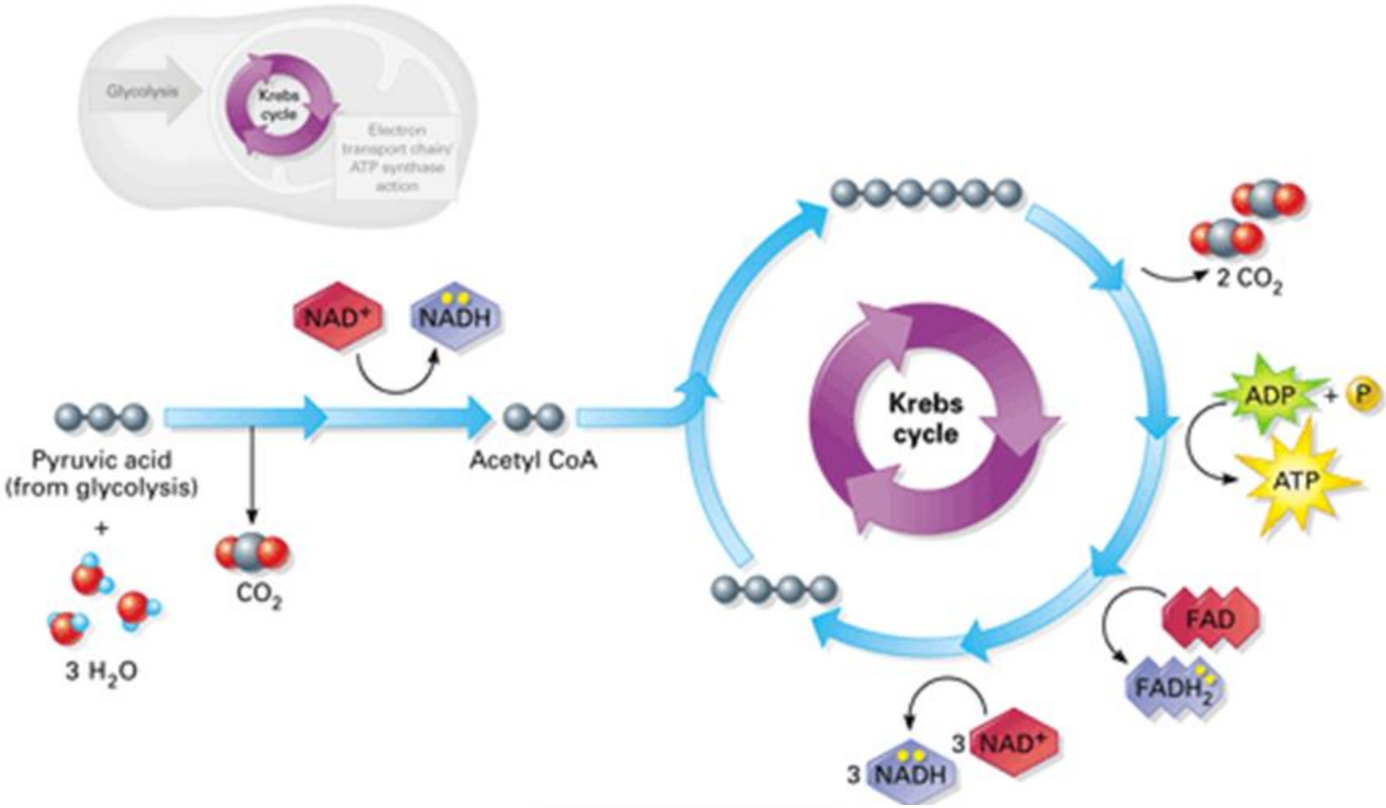
The Krebs/ Citric Acid Cycle

- **Location:** In the Mitochondrial Matrix
- **Main Goal:**
  - To Break down pyruvate (pyruvic acid) into carbon dioxide and Acetyl Co-A and release more energy
  - The acetyl group is formed in stage II of metabolism from carbohydrate and amino acid metabolism
  - Acetyl CoA is converted to citric acid and enters the cycle
  - Citric acid cycle turns twice because 2 acetyl CoA's are produced per glucose
  - 1GTP (ATP in bacteria) and 1 $FADH_2$ is produced during one turn of the cycle
  - 3 NADH are produced during one turn of the cycle
  - NADH and $FADH_2$ energize electron transport and oxidative phosphorylation
  - Overall, eight reactions make up the Krebs cycle



Pyruvate
CoASH + NAD+
pyruvate dehydrogenase
CO2 + NADH
Acetyl-CoA
H2O
CoASH
Citric acid cycle
1. citrate synthase
Citrate
H2O
2. aconitase
cis-Aconitate
H2O
2. aconitase
Isocitrate
3. isocitrate dehydrogenase
NAD+
NADH + H+
Oxalosuccinate
CO2
3. isocitrate dehydrogenase
α-Ketoglutarate
4. α-ketoglutarate dehydrogenase
*CO2
CoASH
NAD+
NADH + H+
Succinyl-CoA
5. succinyl-CoA synthetase
CoASH
GTP
GDP + Pi
Succinate
6. succinate dehydrogenase
FADH2
FAD
Fumarate
H2O
7. fumarase
L-Malate
8. malate dehydrogenase
NAD+
NADH + H+
Oxaloacetate

Citric Acid Cycle: Inputs and Outputs

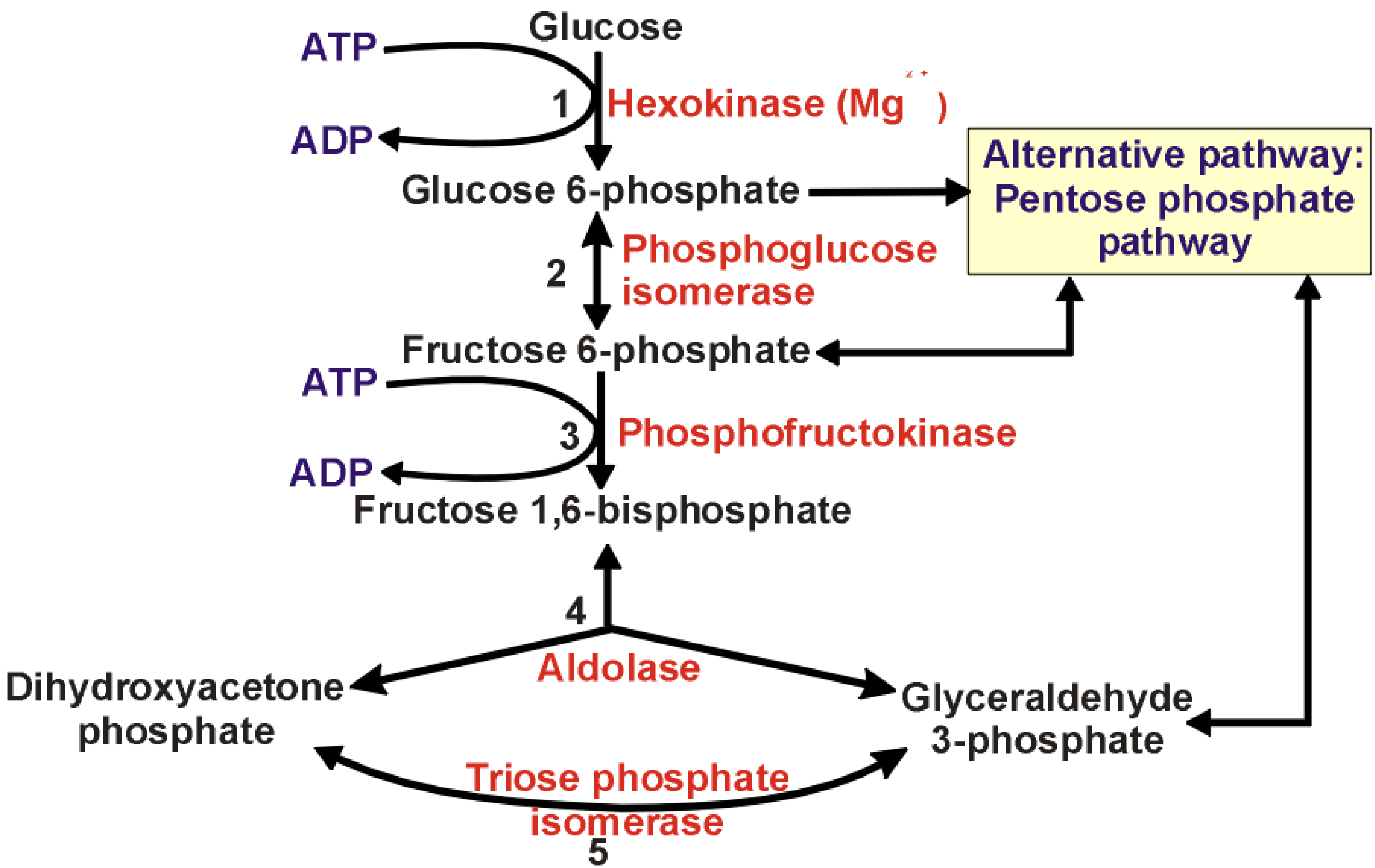


Citric acid cycle

inputs	outputs
2 acetyl groups	4 CO_2
6 NAD^+	6 $NADH + H^+$
2 FAD	2 $FADH_2$
2 ADP + 2 P	2 ATP

Pentose Phosphate Pathway

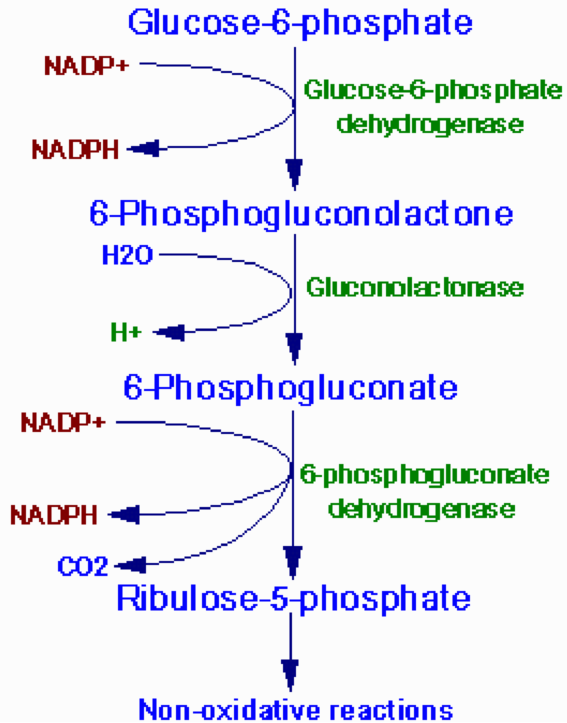
It's a shunt

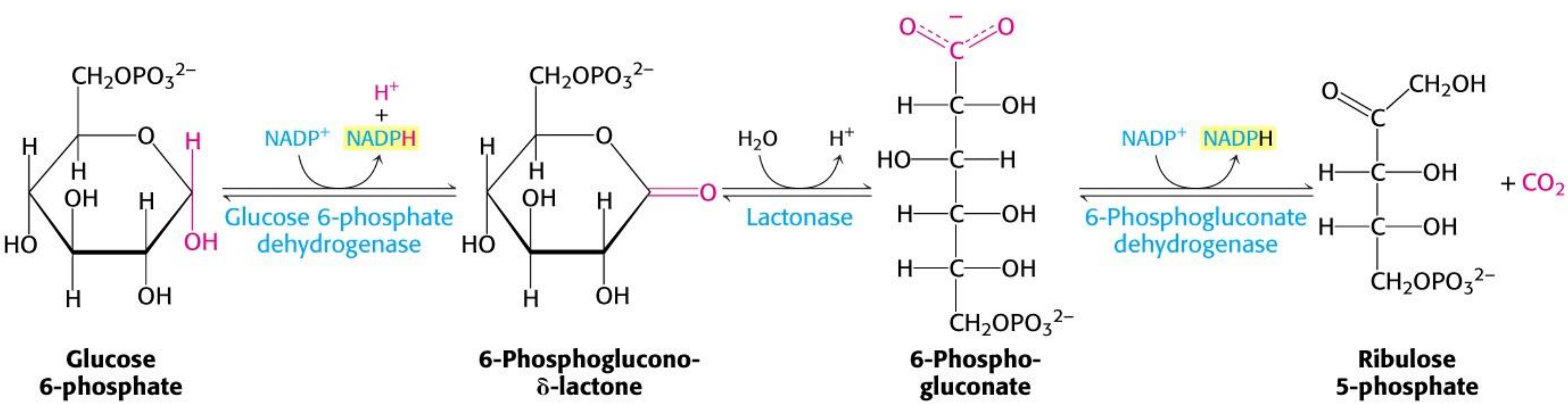


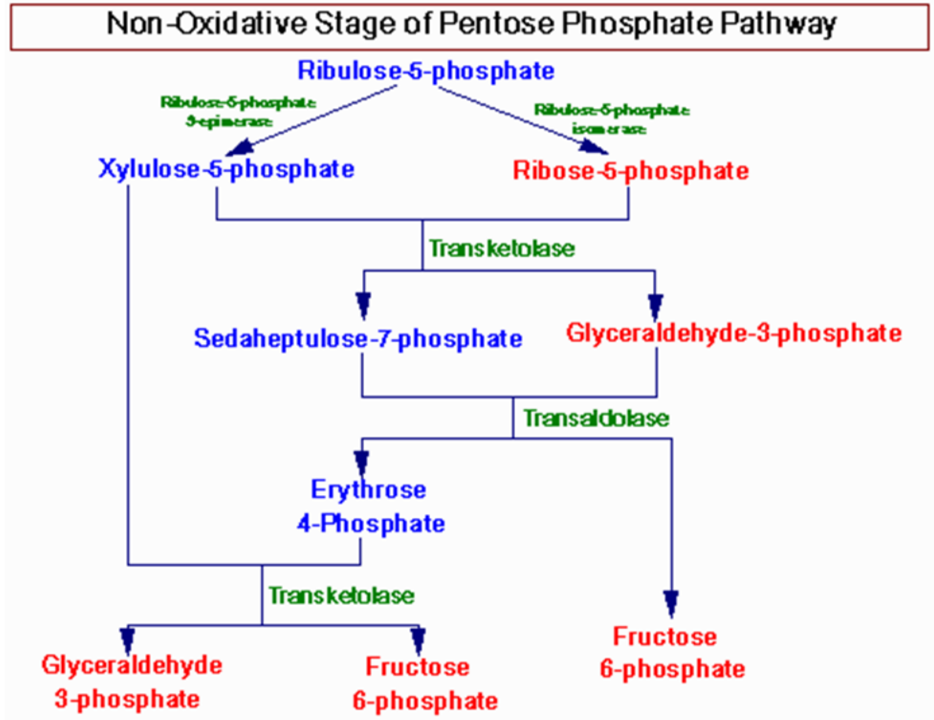
Tissues with active pentose phosphate pathways

Tissue	Function
Adrenal gland	Steroid synthesis
Liver	Fatty acid and cholesterol synthesis
Testes	Steroid synthesis
Adipose tissue	Fatty acid synthesis
Ovary	Steroid synthesis
Mammary gland	Fatty acid synthesis
Red blood cells	Maintenance of reduced glutathione

Oxidative Stage of Pentose Phosphate Pathway







Regulation of the Pentose Pathway

- Glucose 6-phosphate DH is the regulatory enzyme.
- NADPH is a potent competitive inhibitor of the enzyme.
- Usually the ratio $NADPH/NADP^+$ is high so the enzyme is inhibited.
- But, with increased demand for NADPH, the ratio decreases, and enzyme activity is stimulated.
- The reactions of the non-oxidative portion of the pentose pathway are readily reversible.
- The concentrations of the products and reactants can shift depending on the metabolic needs of a particular cell or tissue.