AL-FARABI KAZAKH NATIONAL UNIVERSITY
FACULTY OF BIOLOGY AND BIOTECHNOLOGY
DEPARTMENT OF BIOTECHNOLOGY

Lecture 3

Carbohydrates of Physiological Significance. Glycolysis & the Oxidation of Pyruvate.

PhD, Acting Associate
Professor, Doktyrbay Gulina

Lecture Plan

1. Physiologically importantcarbohydrates and their functions in the human body
2. Glucose as the main metabolic fuel and overview of carbohydrate metabolism
3. Glycolysis: definition, location, phases and key reactions (energy investment and payoff)
4. ATP and NADH production and regulation of glycolysis
5. Fate of pyruvate: aerobic and anaerobic pathways
6. Oxidation of pyruvate to acetyl-CoA and role of pyruvate dehydrogenase complex
7. Energetic significance of pyruvate oxidation
8. Integration of glycolysis with cellular respiration
9. Physiological and clinical significance of carbohydrate metabolism
10. Summary, key concepts, and student tasks/questions

Learning objectives

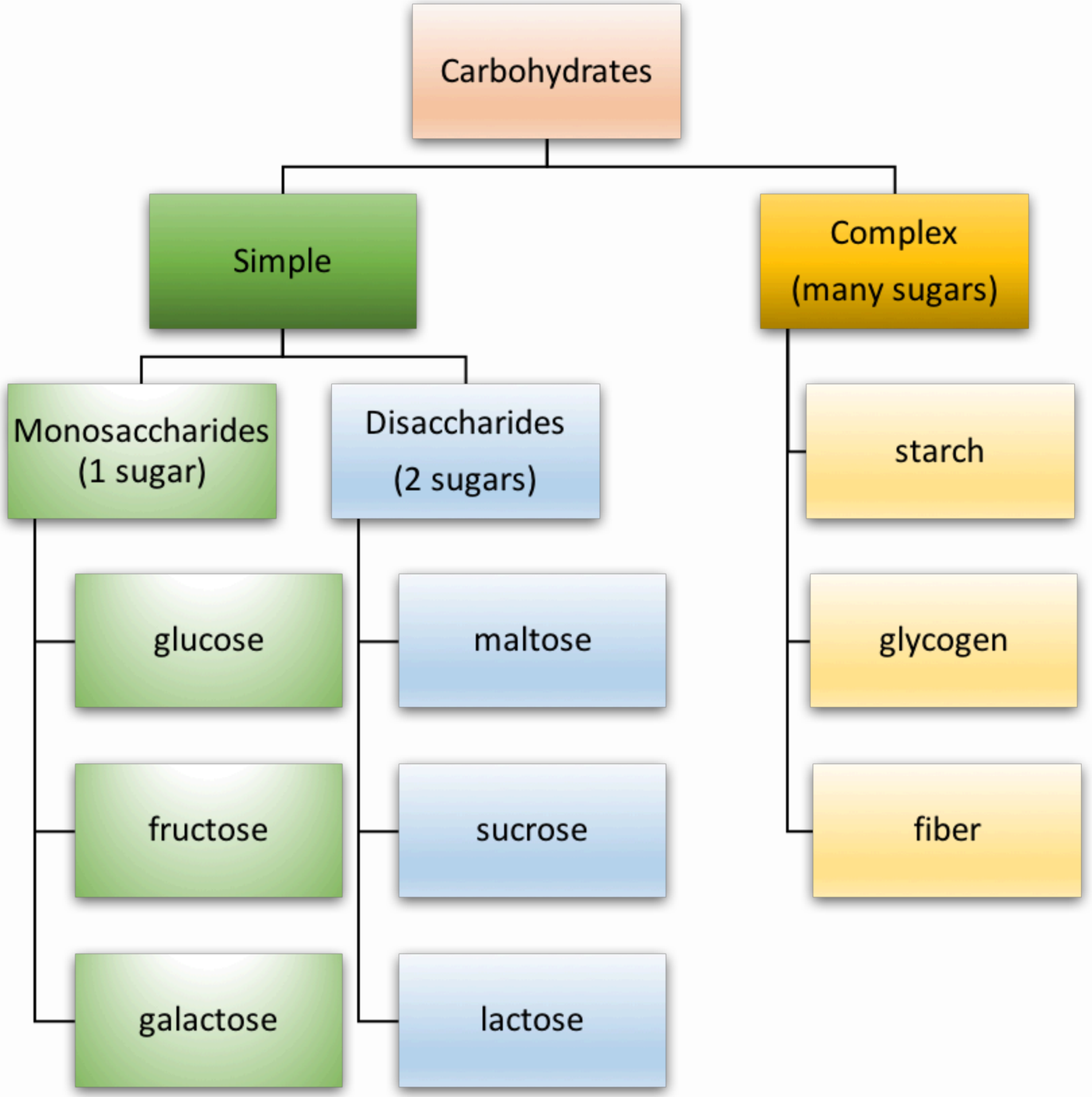
Bytheend of the lecture, studentsshould be able to:

- Identify key physiologically important carbohydratesand describe their main functions
- Explain glucose as a major energy source in the human body
- Define glycolysis and indicate its cellular location
- Outline the main stages of glycolysis and name its key substrates and products
- Explain the formation of ATP and NADH during glycolysis and state the net yield per glucose molecule
- Identify the key regulatory enzymes of glycolysis
- Describe the fate of pyruvate under aerobic and anaerobic conditions
- Explain the conversion of pyruvate to acetyl-CoA and describe the pyruvate dehydrogenase complex
- List the products of pyruvate oxidation
- Explain the relationship between glycolysis, the citric acid cycle, and cellular respiration
- Relate glycolysis to physiological conditions such as exercise and hypoxia

Carbohydrates are organic molecules composed mainly of carbon, hydrogen and oxygen human

In physiology, the most important carbohydrates include **glucose, fructose, galactose, lactose, sucrose and glycogen**.

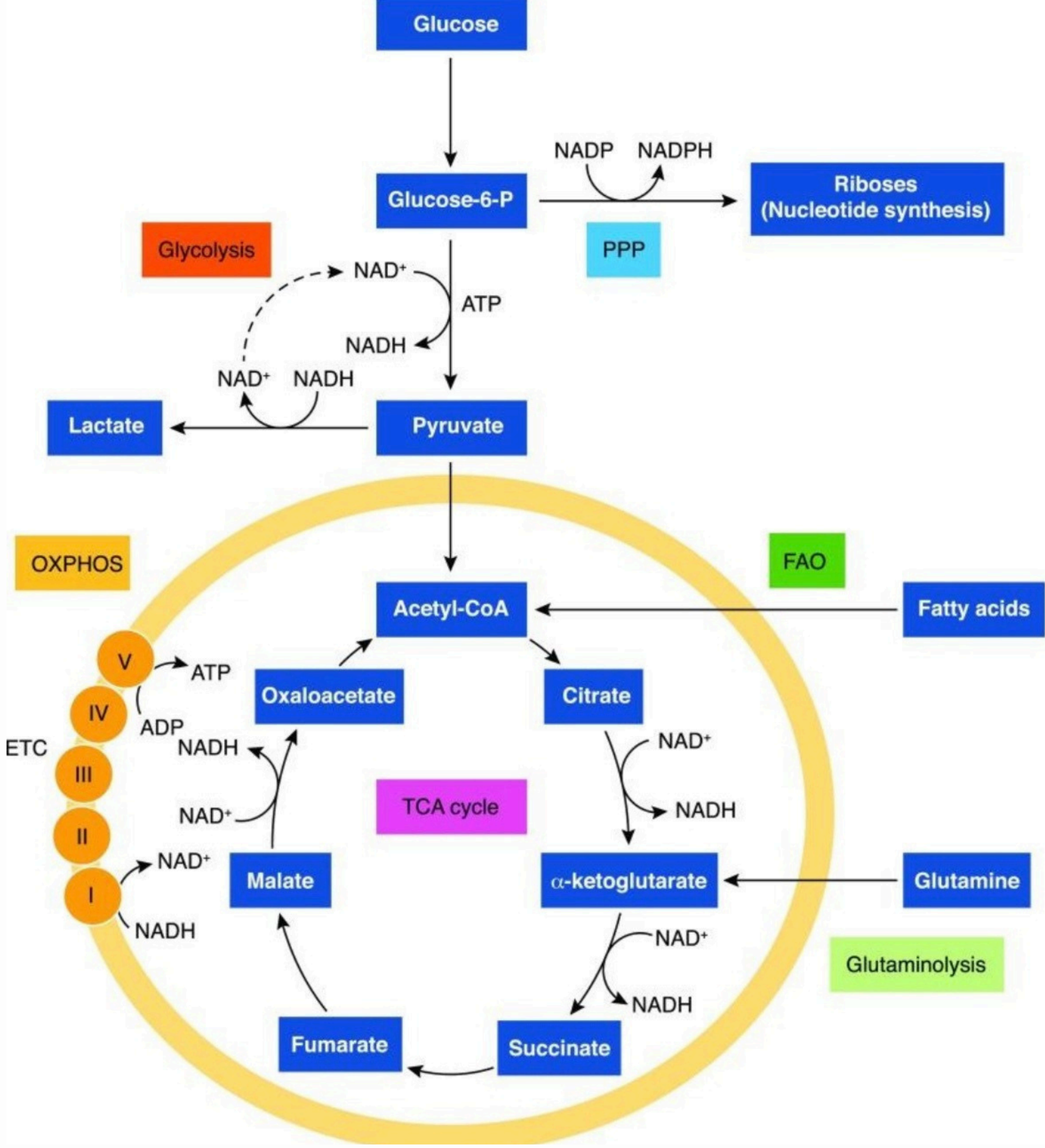
Among them, **glucose has a central role in energy metabolism** because it can be rapidly converted into ATP through glycolysis and subsequent oxidative pathways.



Physiological functions of carbohydrates

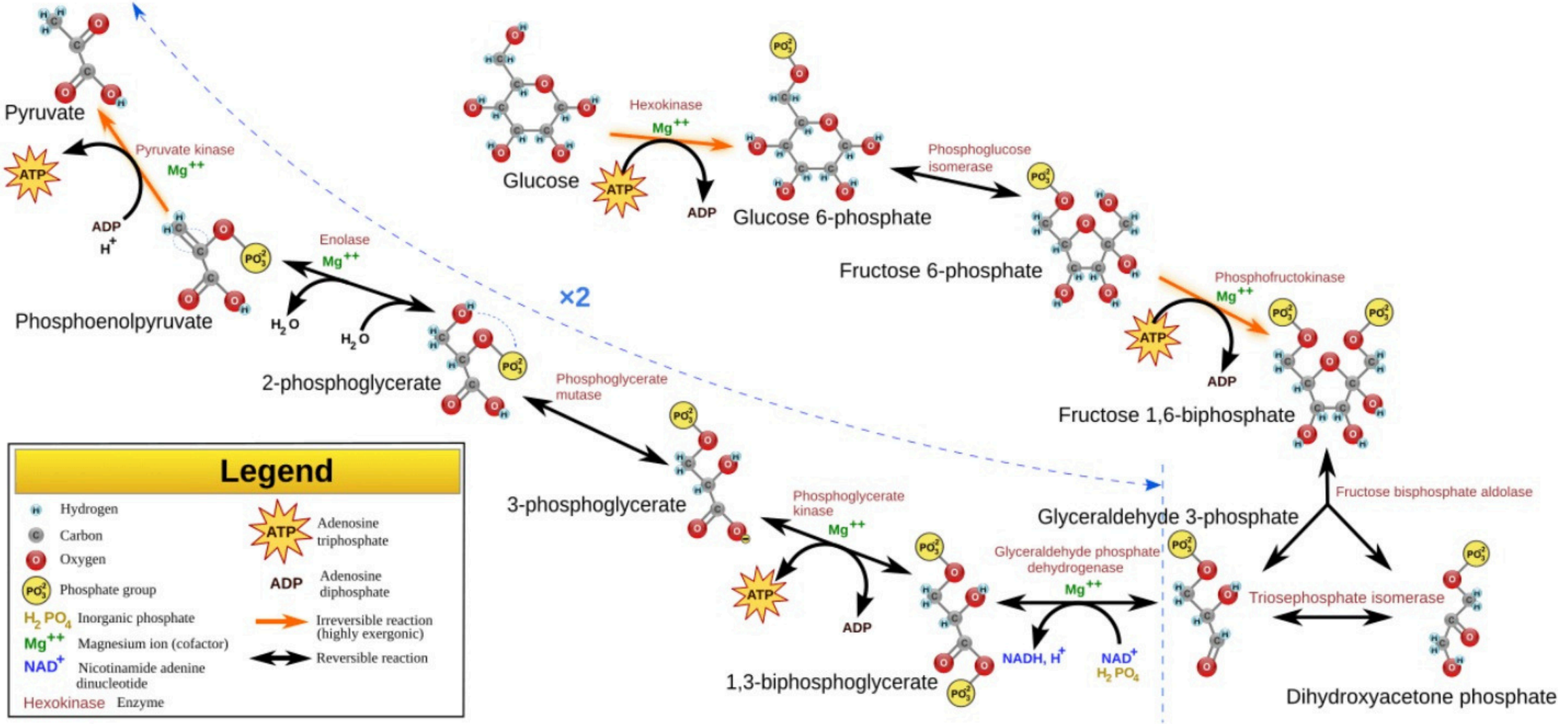
Energy source	Glucose is an important fuel for ATP production.
Energy storage	Excess glucose is stored primarily as **glycogen** in the liver and skeletal muscles.
Structural function	Carbohydrate-containing molecules contribute to the structure of glycoproteins, glycolipids and extracellular components.
Metabolic precursors	Carbohydrate intermediates are used for the synthesis of amino acids, lipids, nucleotides and other molecules.
Maintenance of blood glucose	The regulation of glucose concentration in the blood is essential for metabolic homeostasis.

Glucose is particularly important because it can be metabolized by many tissues and can generate ATP rapidly. General glucose metabolism:



Glycolysis is a 10-step metabolic pathway that converts glucose into 2 pyruvate, producing 2 ATP and 2 NADH per glucose.

$$Glucose + 2\ NAD^+ + 2\ ADP + 2\ Pi \rightarrow 2\ Pyruvate + 2\ NADH + 2\ H^+ + 2\ ATP + 2\ H_2O$$



Glycolysis

Glycolysis is a metabolic pathway in which one molecule of glucose is converted into two molecules of pyruvate.

Location: cytosol

Starting molecule: Glucose

Final product: 2 Pyruvate

Main energy products:

- 2 ATP net
- 2 NADH

3 functional stages of glycolysis

Stage 1 – Energy Investment

Glucose is phosphorylated and activated.

Stage 2 – Cleavage

The six-carbon molecule is split into two three-carbon molecules.

Stage 3 – Energy Payoff

The three-carbon molecules are converted into pyruvate, producing ATP and NADH.

Energy InvestmentPhase (Reactions 1–3)

Reaction 1 of Glycolysis
Glucose → Glucose-6-phosphate
Enzyme: Hexokinase
ATP → ADP
Purpose:

- traps glucose inside the cell;
- activates glucose for further metabolism.

Reaction 2 of Glycolysis
Glucose-6-phosphate → Fructose-6-phosphate
Enzyme: Phosphoglucose isomerase
This is an isomerization reaction.
The structure of the six-carbon sugar is rearranged to prepare it for the next phosphorylation

Reaction 3 of Glycolysis
Fructose-6-phosphate →
Fructose-1,6-bisphosphate
Enzyme: Phosphofructokinase-1 (PFK-1)
ATP→ADP
This is a major regulatory step of glycolysis.
At the end of Stage 1:
2 ATP have been consumed.

Cleavage of the six-carbon molecule

Reaction 4

Fructose 1 ,6-bisphosphate

↓

Glyceraldehyde-3-phosphate (G3P)

+

Dihydroxyacetone phosphate (DHAP)

Enzyme: Aldolase

Reaction 5

DHAP → G3P

Enzyme:Triose phosphate isomerase

Result: 1 glucose → 2 G3P

From this point onward, every subsequent reaction of glycolysis occurs twice per glucose molecule.

Energy Payoff Phase

Reaction 6: Oxidation of G3P
G3P → 1,3-Bisphosphoglycerate
Enzyme: Glyceraldehyde-3-phosphate dehydrogenase
NAD^+ → NADH
Because there are 2 G3P molecules:
2 NADH are produced.

Reaction 7: First ATP-Producing Reaction 1,3-Bisphosphoglycerate → 3-Phosphoglycerate
Enzyme: Phosphoglycerate kinase
ADP → ATP
Because the reaction occurs twice:
2 ATP are produced.
This is substrate-level phosphorylation.

Reaction 8
3-Phosphoglycerate → 2-Phosphoglycerate Enzyme: Phosphoglycerate mutase

Reaction 9
2-Phosphoglycerate → Phosphoenolpyruvate (PEP)
Enzyme: Enolase
These reactions prepare the molecule for the final ATP-producing

Reaction 10 of Glycolysis
Phosphoenolpyruvate → Pyruvate
Enzyme: Pyruvate kinase
ADP → ATP
Because two PEP molecules are converted: 2 ATP are produced.
And finally: 2 Pyruvate are formed.

Summary of glycolysis:

1 Glucose → 2 Pyruvate

Energy balance:

ATP consumed: 2

ATP produced: 4

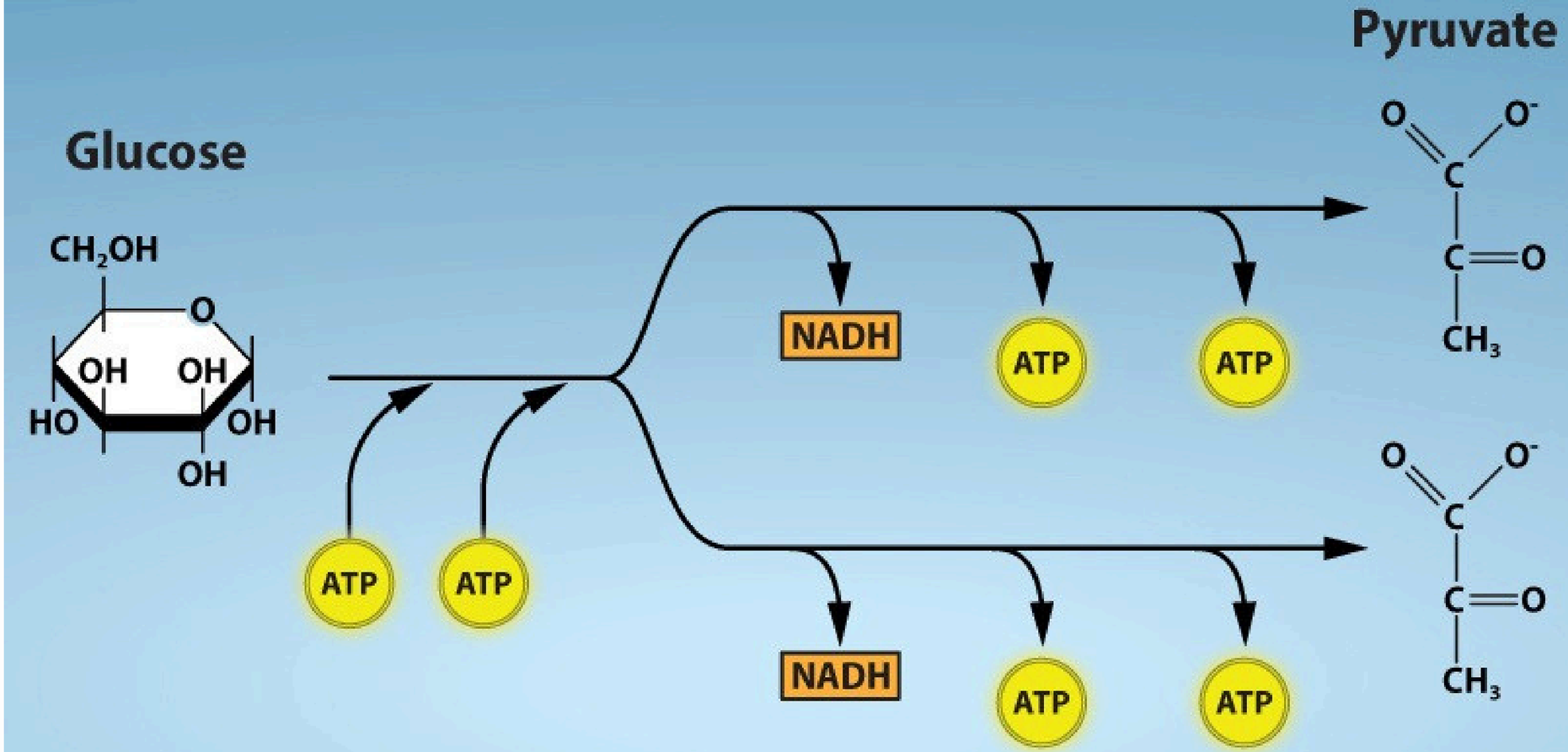
Net ATP: 2

NADH produced: 2

Overall:

$$\text{Glucose} + 2\ NAD^+ + 2\ ADP + 2\ Pi \rightarrow 2\ \text{Pyruvate} + 2\ NADH + 2\ ATP + 2\ H_2O$$

Summary of Glycolysis



Net products: 2 pyruvate molecules + 2 NADH + 2 ATP

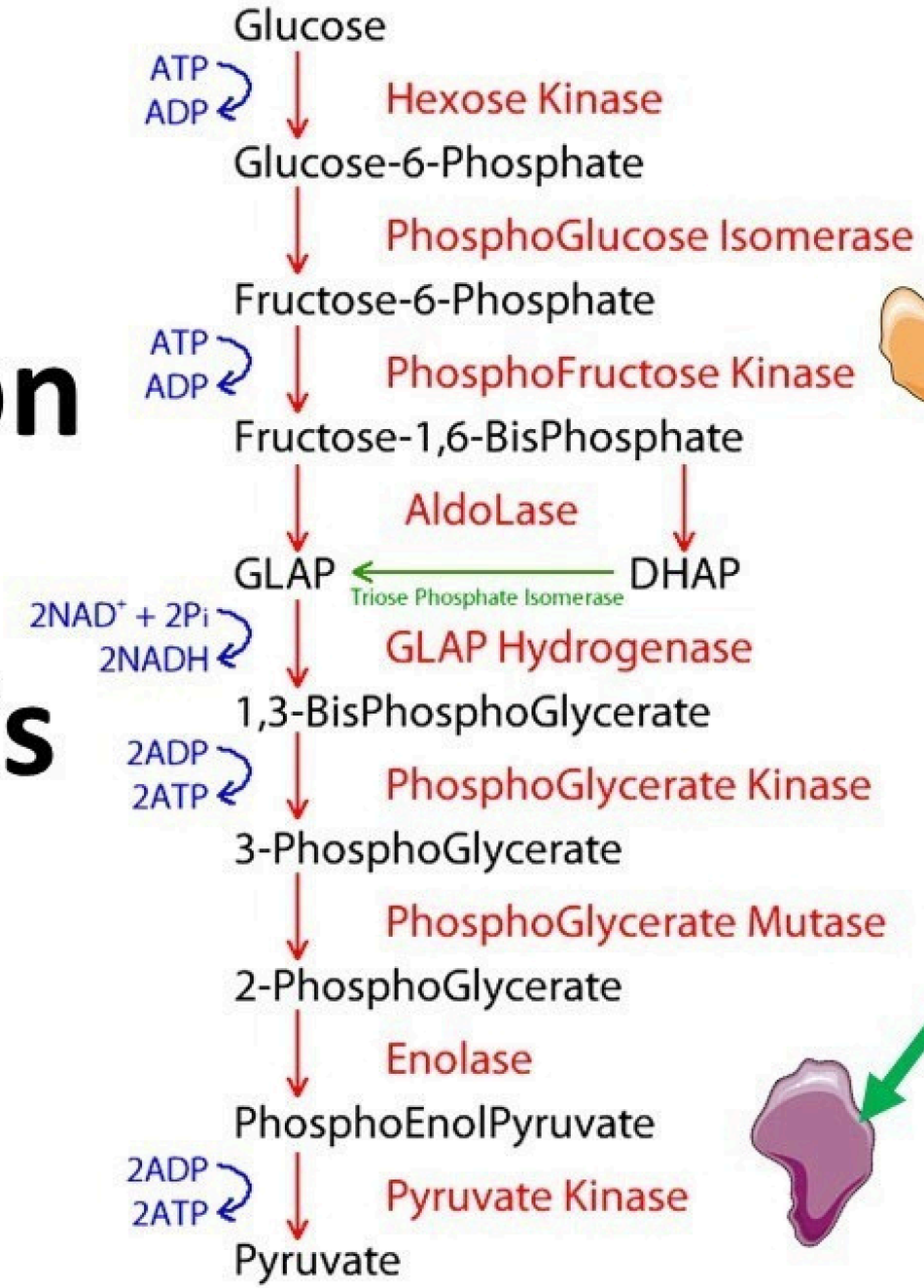
Regulation of glycolysis

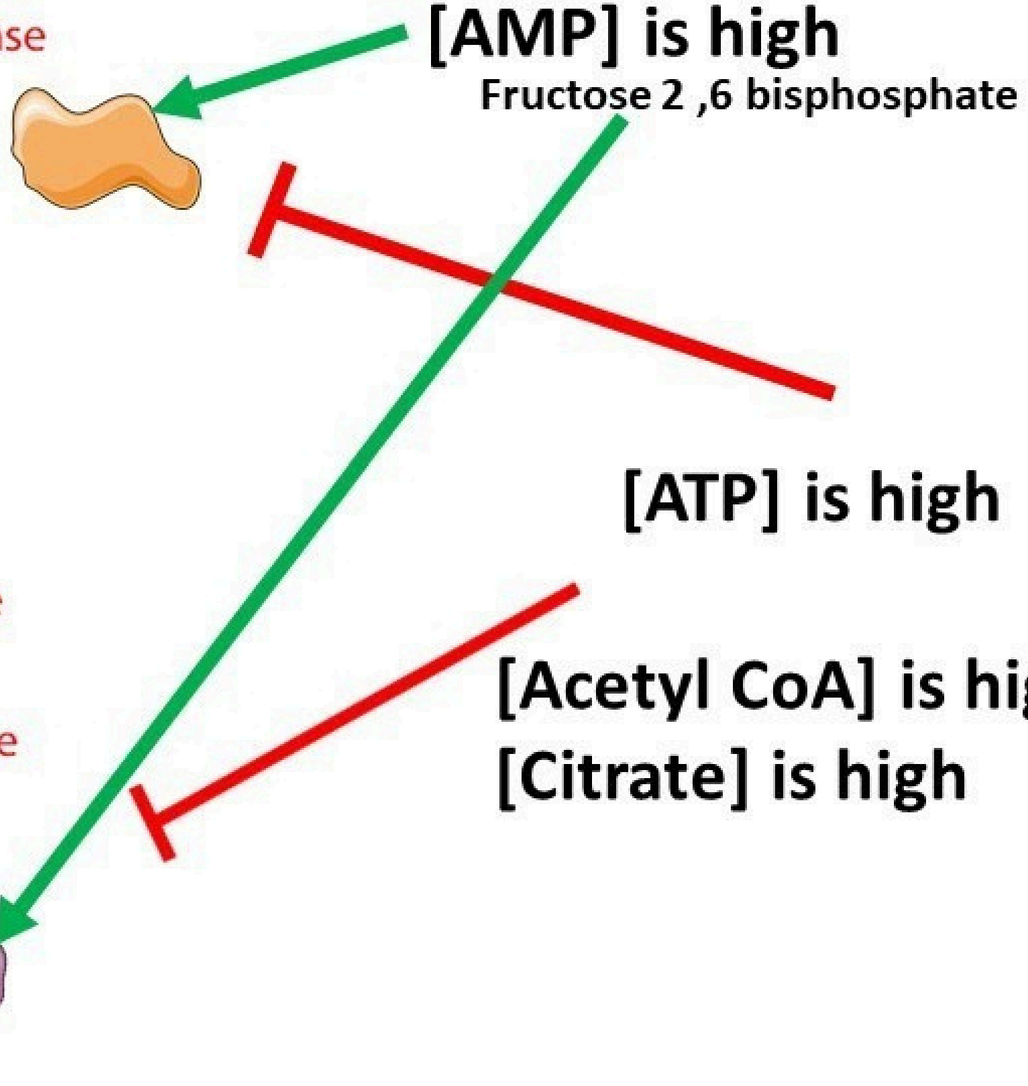
Regulation of glycolysis is the process by which the cell controls the rate of glucose breakdown according to its energy requirements.
The activity of glycolysis changes depending on the metabolic state of the cell.
When the cell has a high energy supply, glycolysis is generally decreased.
When the cell requires more ATP, glycolysis is stimulated.
The main regulatory points of glycolysis are controlled by three enzymes:

- Hexokinase / Glucokinase
- Phosphofructokinase-1 (PFK-1)
- Pyruvate kinase

Among them, PFK-1 is the major rate-limiting enzyme of glycolysis.

Regulation of Glycolysis





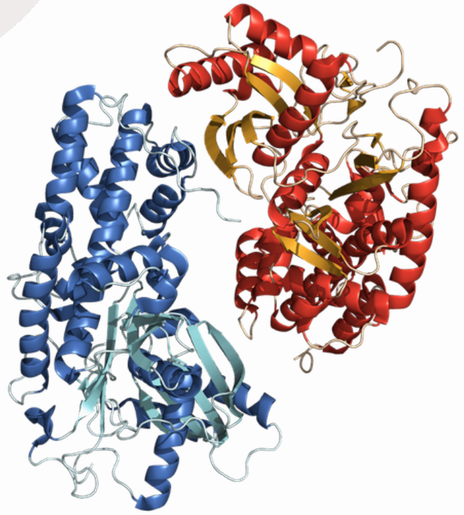
Why is glycolysis regulated?

Thecell must maintainabalancebetweenATP production andenergydemand.
If ATP production isalreadysufficient,there is noneed to continuously break down glucose at a high rate.
If ATP levels decrease, glycolysis is stimulated to provide additional energy.
Therefore, glycolysis is regulated according to:

- ATP concentration
- ADP and AMP concentration
- $NADH/NAD^+$ ratio
- availability of glucose
- hormonal signals
- metabolic needs of the tissue

Key principle:
High energy availability → glycolysis decreases
High energy demand → glycolysis increases

Hexokinase



Its main functions are:

- phosphorylating glucose;
- trapping glucose inside the cell;
- preparing glucose for further metabolism.

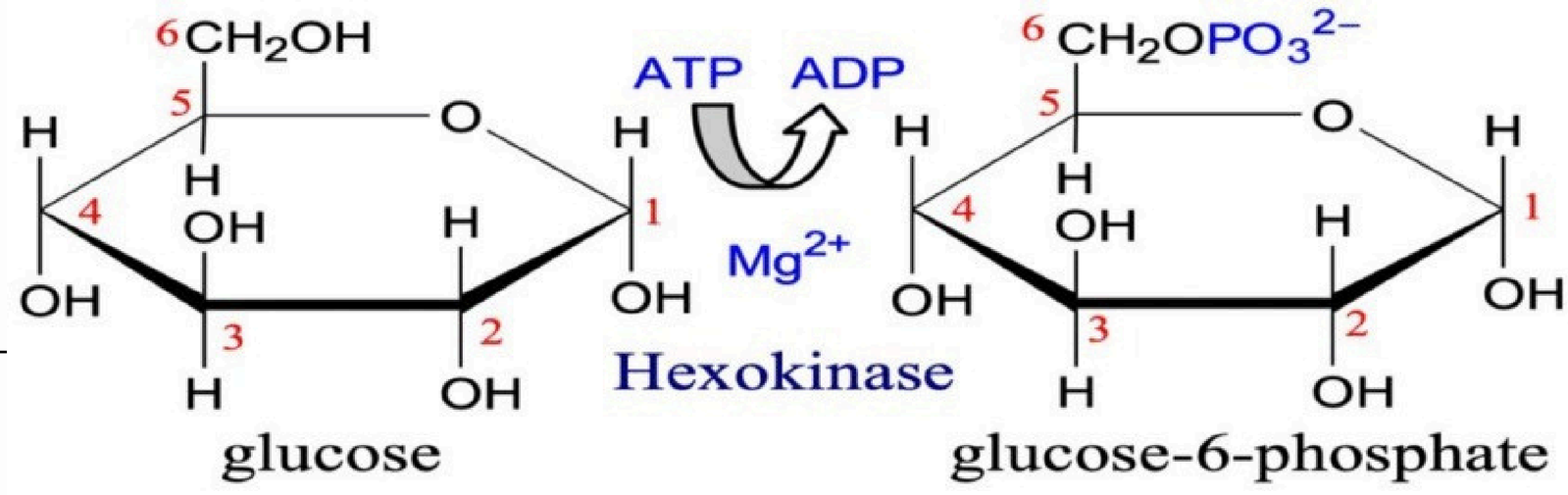
Hexokinase has a high affinity for glucose, meaning that it can function effectively even when glucose concentration is relatively low.

Hexokinase is present in most tissues.

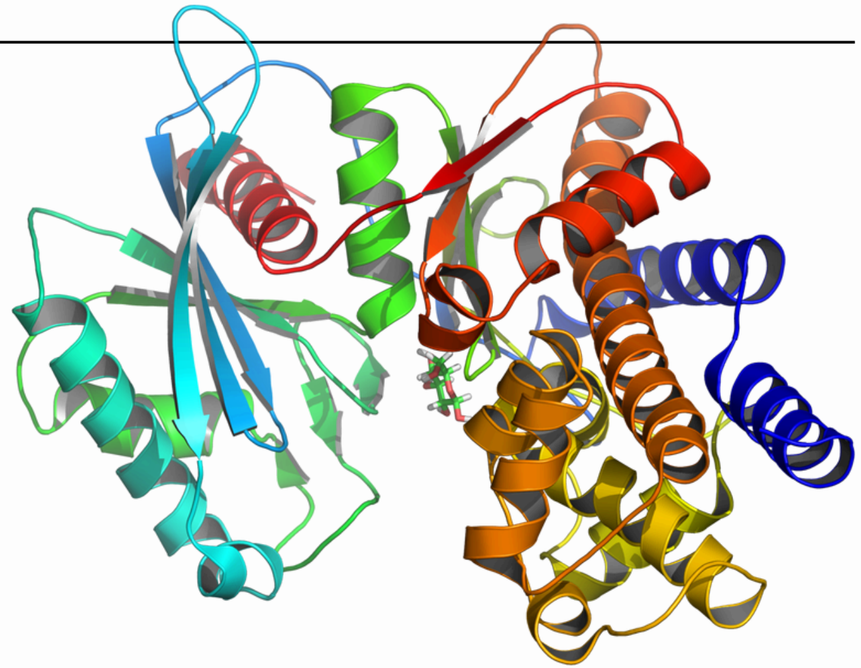
Reaction:

Glucose → Glucose-6-phosphate

Hexokinase catalyzes the first step of glycolysis.



Glucokinase



Glucokinase performs the same reaction:

Glucose → Glucose-6-phosphate

However, it is mainly found in:

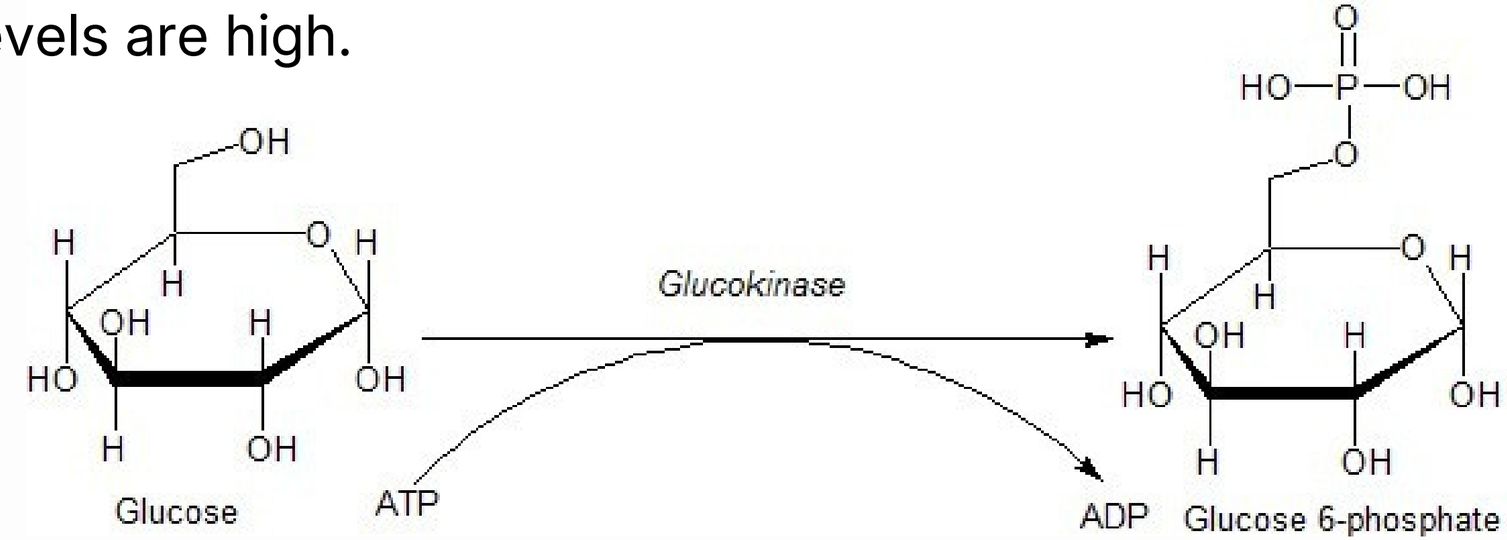
- **liver**
- **pancreatic β-cells**

Glucokinase has a lower affinity for glucose than hexokinase and becomes more active when blood glucose levels are high.

Key difference:

Hexokinase → most tissues

Glucokinase → liver and pancreatic β-cells



Phosphofructokinase-1 (PFK-1)

Reaction:

Fructose-6-phosphate → Fructose-1,6-bisphosphate

PFK-1 catalyzes the third reaction of glycolysis and is the major rate-limiting enzyme of the pathway.

This reaction requires:

ATP → ADP

PFK-1 acts as an important metabolic “control point.”

PFK-1 is inhibited by:

- High ATP
- High citrate

These signals indicate that the cell already has sufficient energy.

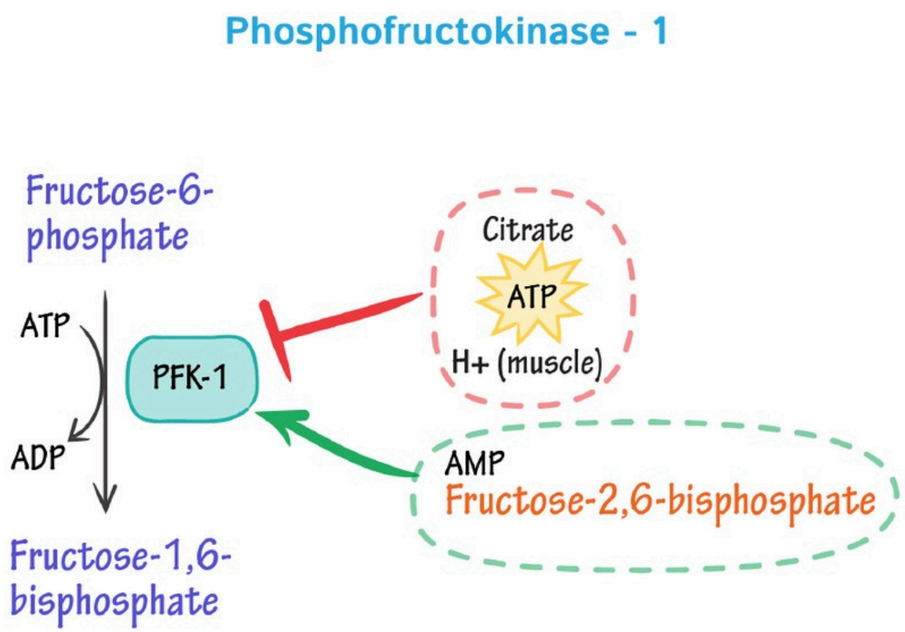
PFK-1 is activated by AMP and ADP

These molecules increase when cellular energy levels are low.

Key concept:

Low energy → PFK-1 activated → glycolysis increases

High energy → PFK-1 inhibited → glycolysis decreases



Pyruvate Kinase

Reaction:

Phosphoenolpyruvate(PEP)→ Pyruvate

Pyruvate kinase catalyzes the final reaction of glycolysis.

During this reaction:

ADP → ATP

Therefore, pyruvate kinase is responsible for the production of the second pair of ATP molecules during the energy payoff phase.

Pyruvate kinase activity is regulated according to the energy requirements of the cell.

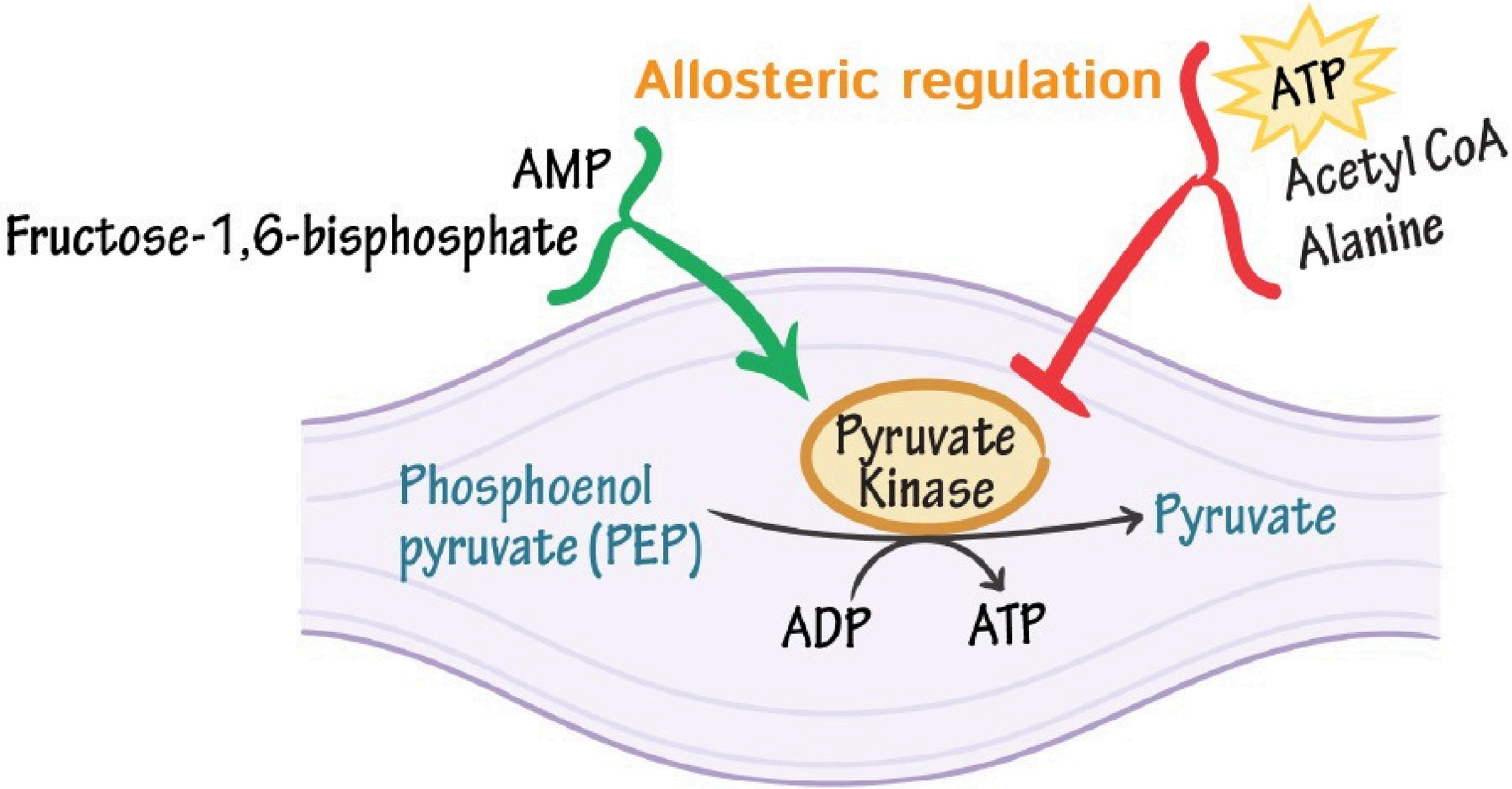
High ATP levels:

Pyruvate kinase activity decreases

Increased glycolytic demand:

Pyruvate kinase activity increases

The final product of this reaction is pyruvate, which represents an important metabolic branch point.


Allosteric regulation
ATP
AMP
Fructose-1,6-bisphosphate
Acetyl CoA
Alanine
Pyruvate Kinase
Phosphoenol pyruvate (PEP)
Pyruvate
ADP
ATP

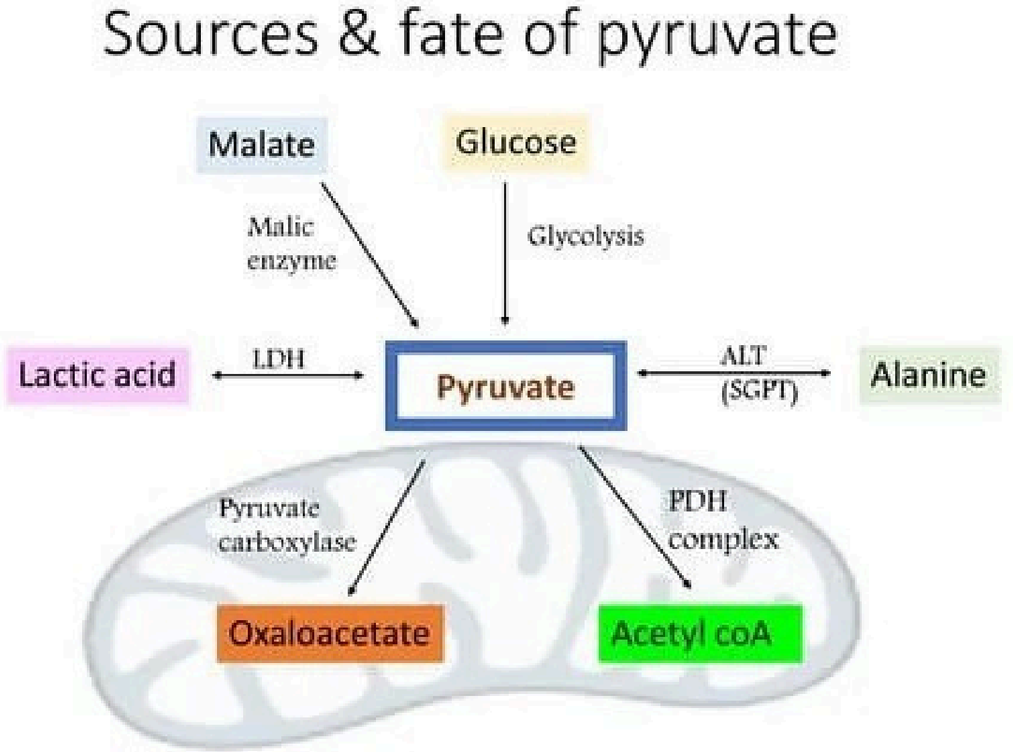
Enzyme	Reaction	Main role
Hexokinase / Glucokinase	Glucose-> Glucose-6-phosphate	Traps and activates glucose
PFK-1	Fructose-6-phosphate → Fructose-1,6-bisphosphate	Major control point of glycolysis
Pyruvate kinase	PEP ->Pyruvate	Final step and ATP production

Hexokinase → starts glycolysis
PFK-1 → controls glycolysis
Pyruvate kinase → finishes glycolysis

Fate of pyruvate

At the end of glycolysis, one molecule of glucose has been converted into two molecules of pyruvate.
Pyruvate is a metabolic branch point, meaning that it can follow different pathways depending on the conditions of the cell.

Under aerobic conditions:
Pyruvate → Acetyl-CoA
The acetyl-CoA then enters the **Citric Acid Cycle**.
Under anaerobic or oxygen-limited conditions:
Pyruvate → Lactate
Therefore, the fate of pyruvate determines how the products of glycolysis are further metabolized.



Pyruvate Oxidation

Pyruvate oxidation is the metabolic process in which pyruvate is converted into acetyl-CoA before entering the citric acid cycle.
It is also called **Oxidative decarboxylation of pyruvate**
The process occurs in the Mitochondrial matrix
and is catalyzed by the **Pyruvate Dehydrogenase Complex (PDC)**

Pyruvate produced during glycolysis cannot directly enter the citric acid cycle.
It must first be converted into acetyl-CoA.
Therefore:
Glycolysis → Pyruvate → Pyruvate oxidation → Acetyl-CoA → Citric Acid Cycle

The main purpose of pyruvate oxidation is to:

1. Produce Acetyl-CoA

Acetyl-CoA enters the citric acid cycle.

2. Produce NADH

NADH carries high-energy electrons to the **electron transport chain**, where they can contribute to ATP production.

3. Release CO_2

One carbon is removed from pyruvate and released as carbon dioxide.

Pyruvate oxidation connects glycolysis with aerobic cellular respiration.

How does Pyruvate become Acetyl-CoA?

Step 1 – Decarboxylation
One carbon is removed from pyruvate.
Pyruvate (3C) → 2-carbon fragment + CO_2

Step 2 – Oxidation
The remaining two-carbon fragment is oxidized.
The released electrons are transferred to:
NAD^+ → NADH

Step 3 – Formation of Acetyl-CoA
The two-carbon acetyl group is transferred to Coenzyme A (CoA).

Final product: **Acetyl-CoA**

The conversion of pyruvate into acetyl-CoA is catalyzed by a large multienzyme complex called the:
Pyruvate Dehydrogenase Complex (PDC)
The complex contains three enzyme components:
E1 Pyruvate dehydrogenase
→ removes CO_2 from pyruvate
E2 Dihydrolipoyl transacetylase
→ transfers the acetyl group to CoA
E3 Dihydrolipoyl dehydrogenase
→ transfers electrons to NAD^+ and regenerates the complex

The Pyruvate Dehydrogenase Complex requires five important cofactors:

Important connection:

Vitamin B1 → TPP

Vitamin B5 → CoA

This is one reason why vitamin deficiencies can affect energy metabolism.

Cofactor	Role
TPP	Helps with decarboxylation
Lipoamide	Transfers the acetyl group and electrons
CoA	Accepts the acetyl group
FAD	Participates in electron transfer
NAD+	Accepts electrons to form NADH

Task for students

Answer the following questions:

1. What is glycolysis?
2. Where does glycolysis occur?
3. What is the starting substrate of glycolysis?
4. What are the final products of glycolysis?
5. What are the three functional stages of glycolysis?
6. How many ATP molecules are consumed during glycolysis?
7. How many ATP molecules are produced?
8. What is the net ATP yield?
9. How many NADH molecules are produced?
10. Why does each reaction after the cleavage of fructose 1,6-bisphosphate occur twice per glucose molecule?

Conclusion

Glycolysis occursinthecytosol. Each glucose molecule yields two pyruvate, two net ATP and two NADH.

Hexokinase or glucokinase, PFK-1 and pyruvate kinase regulate glycolysis according to cellular energy demand.

Lactate formation regenerates NAD+ and allows glycolysis to continue when mitochondrial oxidation is limited.

In the mitochondrial matrix, the pyruvate dehydrogenase complex converts each pyruvate into acetyl-CoA, producing one NADH and one CO2.

Acetyl-CoA enters the citric acid cycle, linking glycolysis to further oxidation and ATP production.

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