# TEACHING MATERIAL ON

# Botany

# (Department of School of Science)

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LECTURE CLASS NOTE ON **GLYCOLYSIS: THE FIRST STAGE OF CELLULAR RESPIRATION BY DR KAMAL KANT PATRA**

## Introduction

Glycolysis is the first and one of the most fundamental stages of cellular respiration. It is a sequence of chemical reactions that break down a molecule of glucose (a six-carbon sugar) into two molecules of pyruvate (a three-carbon compound). This process occurs in the cytoplasm of both prokaryotic and eukaryotic cells and does not require oxygen, making it an anaerobic process.

Glycolysis is not only the starting point for both aerobic and anaerobic respiration but also plays a critical role in providing energy in cells under varying environmental conditions. Understanding glycolysis is essential as it serves as the foundation for further metabolic pathways, including the Citric Acid Cycle (in aerobic respiration) and fermentation (in anaerobic respiration).

## Overview of Glycolysis

- **Location**: Cytoplasm (of both prokaryotic and eukaryotic cells).
- **Oxygen Requirement**: None (anaerobic).
- **End Products**:
    - **2 molecules of pyruvate** (which can be further metabolized aerobically or anaerobically).
    - **2 molecules of NADH** (which are used in other stages of cellular respiration).
    - **Net gain of 2 ATP molecules** (from 1 glucose molecule).

Glycolysis consists of 10 enzymatically controlled steps and can be divided into two phases: the **Energy Investment Phase** and the **Energy Payoff Phase**.

## Phases of Glycolysis

**1. Energy Investment Phase (Steps 1-5)**

In this phase, the cell invests energy (in the form of ATP) to initiate the breakdown of glucose.

1. **Step 1: Phosphorylation of Glucose**
   - **Enzyme**: Hexokinase (or Glucokinase in liver cells).
   - **Reaction**: Glucose ($C_6$) is phosphorylated by ATP to form **glucose-6-phosphate (G6P)**.
   - **ATP Used**: 1 ATP.
   - **Purpose**: This phosphorylation traps glucose inside the cell and prepares it for further breakdown.
2. **Step 2: Isomerization of Glucose-6-Phosphate**
   - **Enzyme**: Phosphoglucose isomerase.
   - **Reaction**: Glucose-6-phosphate is converted to its isomer, **fructose-6-phosphate (F6P)**.
   - **Purpose**: Converts the aldose (glucose) into a ketose (fructose), preparing for further modifications.
3. **Step 3: Second Phosphorylation**
   - **Enzyme**: Phosphofructokinase-1 (PFK-1).
   - **Reaction**: Fructose-6-phosphate is phosphorylated by ATP to form **fructose-1,6-bisphosphate (F1,6BP)**.
   - **ATP Used**: 1 ATP.
   - **Purpose**: This is a crucial regulatory step in glycolysis, and PFK-1 is considered the rate-limiting enzyme. It commits the glucose molecule to continue through glycolysis.
4. **Step 4: Cleavage of Fructose-1,6-bisphosphate**
   - **Enzyme**: Aldolase.
   - **Reaction**: Fructose-1,6-bisphosphate is split into two three-carbon molecules: **glyceraldehyde-3-phosphate (G3P)** and **dihydroxyacetone phosphate (DHAP)**.
   - **Purpose**: Cleaves the six-carbon molecule into two three-carbon molecules, which will later be converted into G3P.
5. **Step 5: Interconversion of DHAP and G3P**

    - **Enzyme**: Triose phosphate isomerase.
    - **Reaction**: Dihydroxyacetone phosphate (DHAP) is converted into **glyceraldehyde-3-phosphate (G3P)**.
    - **Purpose**: Ensures that only one molecule, G3P, proceeds through the remainder of glycolysis.

At the end of the energy investment phase, **2 molecules of G3P** are formed, and **2 ATPs have been consumed** (1 ATP in Step 1 and 1 ATP in Step 3).

**2. Energy Payoff Phase (Steps 6-10)**

In this phase, energy is generated in the form of ATP and NADH.

6. **Step 6: Oxidation and Phosphorylation of G3P**
    - **Enzyme**: Glyceraldehyde-3-phosphate dehydrogenase (GAPDH).
    - **Reaction**: Glyceraldehyde-3-phosphate is oxidized by $NAD^+$ and inorganic phosphate (Pi) to form **1,3-bisphosphoglycerate (1,3-BPG)**.
    - **NADH Produced**: 1 NADH per molecule of G3P.
    - **Purpose**: This step generates NADH, which will later be used in the electron transport chain (if oxygen is present).
7. **Step 7: ATP Generation**
    - **Enzyme**: Phosphoglycerate kinase.
    - **Reaction**: 1,3-bisphosphoglycerate donates a high-energy phosphate group to ADP, forming **ATP** and **3-phosphoglycerate (3PG)**.
    - **ATP Produced**: 1 ATP per molecule of G3P (2 ATP total, as there are two G3P molecules).
    - **Purpose**: This step results in the generation of ATP, which is essential for cellular energy.
8. **Step 8: Conversion of 3PG to 2PG**
    - **Enzyme**: Phosphoglycerate mutase.
    - **Reaction**: 3-phosphoglycerate is converted to **2-phosphoglycerate (2PG)**.
    - **Purpose**: Prepares the substrate for the next step, which will involve dehydration.

9. **Step 9: Dehydration of 2PG to Form PEP**
   - **Enzyme**: Enolase.
   - **Reaction**: 2-phosphoglycerate is dehydrated to form **phosphoenolpyruvate (PEP)**.
   - **Purpose**: Generates a high-energy intermediate, phosphoenolpyruvate.
10. **Step 10: ATP Generation and Pyruvate Formation**
    - **Enzyme**: Pyruvate kinase.
    - **Reaction**: Phosphoenolpyruvate (PEP) donates its phosphate group to ADP, forming **ATP** and **pyruvate**.
    - **ATP Produced**: 1 ATP per molecule of PEP (2 ATP total).
    - **End Product**: 2 molecules of pyruvate, 2 ATP (net gain), and 2 NADH (from Step 6).

At the end of the energy payoff phase, **2 molecules of pyruvate** are produced from the original glucose molecule, along with a net gain of **2 ATP molecules** and **2 NADH molecules**.

**Summary of Glycolysis**

- **Glucose ($C_6H_{12}O_6$)** is broken down into **2 pyruvate** molecules.
- **Energy Output**:
  - **Net Gain of 2 ATP** (from 4 ATP produced and 2 ATP consumed).
  - **2 NADH molecules** (which can be used in oxidative phosphorylation to produce more ATP, if oxygen is available).
- **No oxygen is required**, making glycolysis an **anaerobic** process.
- The end product, **pyruvate**, can enter the **mitochondria** for further processing in aerobic respiration (through the citric acid cycle) or undergo fermentation in the absence of oxygen.

**Importance of Glycolysis**

1. **Energy Production**: Glycolysis is the first step in cellular energy production, providing cells with quick ATP in both aerobic and anaerobic conditions.

2. **Metabolic Flexibility**: The products of glycolysis, including pyruvate and NADH, are crucial intermediates in several metabolic pathways, including fermentation (in the absence of oxygen) and the citric acid cycle (in the presence of oxygen).
3. **Evolutionary Significance**: Glycolysis is an ancient pathway found in nearly all living organisms, indicating its fundamental role in metabolism.

**Regulation of Glycolysis**

The rate of glycolysis is tightly regulated, primarily by three key enzymes:

1. **Hexokinase** (Step 1): Inhibited by its product, glucose-6-phosphate, preventing the excessive accumulation of glucose-6-phosphate.
2. **Phosphofructokinase-1 (PFK-1)** (Step 3): The rate-limiting enzyme of glycolysis, regulated by various factors such as ATP (which inhibits PFK-1) and AMP (which activates it).
3. **Pyruvate Kinase** (Step 10): Regulated by ATP, fructose-1,6-bisphosphate, and other metabolites.

**Conclusion**

Glycolysis is the first step in cellular respiration and an essential metabolic pathway. It provides energy in the form of ATP and NADH, generates pyruvate for further energy production in both aerobic and anaerobic conditions, and serves as the foundation for other metabolic pathways. Understanding glycolysis is critical for comprehending energy metabolism in cells and organisms.