Glycolysis

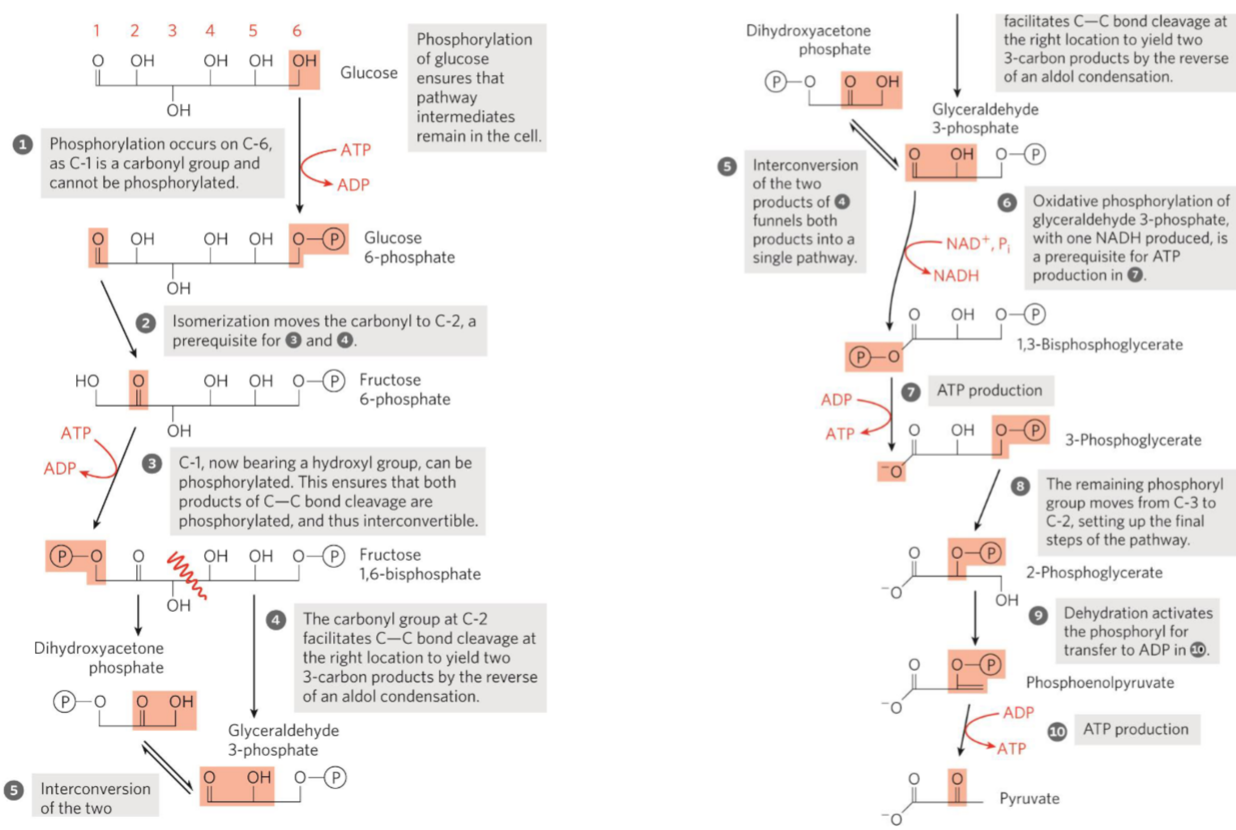
- The process of converting one molecule of glucose into two molecules of pyruvate
- Occurs in the cytoplasm of cells
- Net reaction:

$$\text{Glucose} + 2\ \text{NAD}^{+} + 2\ \text{Pi} \rightarrow 2\ \text{Pyruvate} + 2\ \text{NADH} + 2\ \text{ATP} + 2\ \text{H}_2\text{O}$$

Glycolysis

- is the first step in cellular respiration
- generates ATP and NADH for energy
- provides intermediates for other metabolic pathways
- does not require oxygen

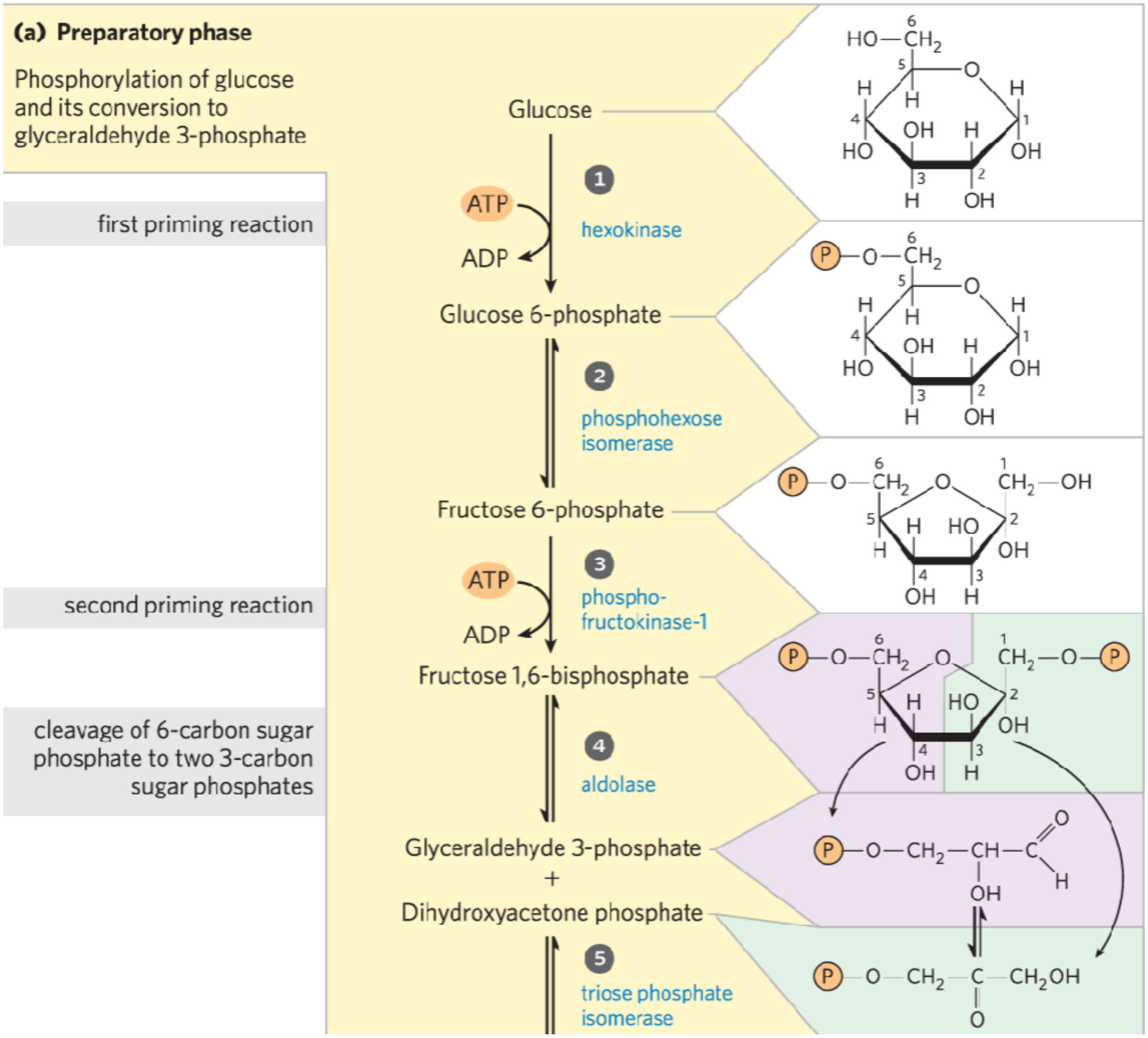
The Chemical Logic of the Glycolytic Pathway



Stage I: Preparatory Phase / Energy Investment

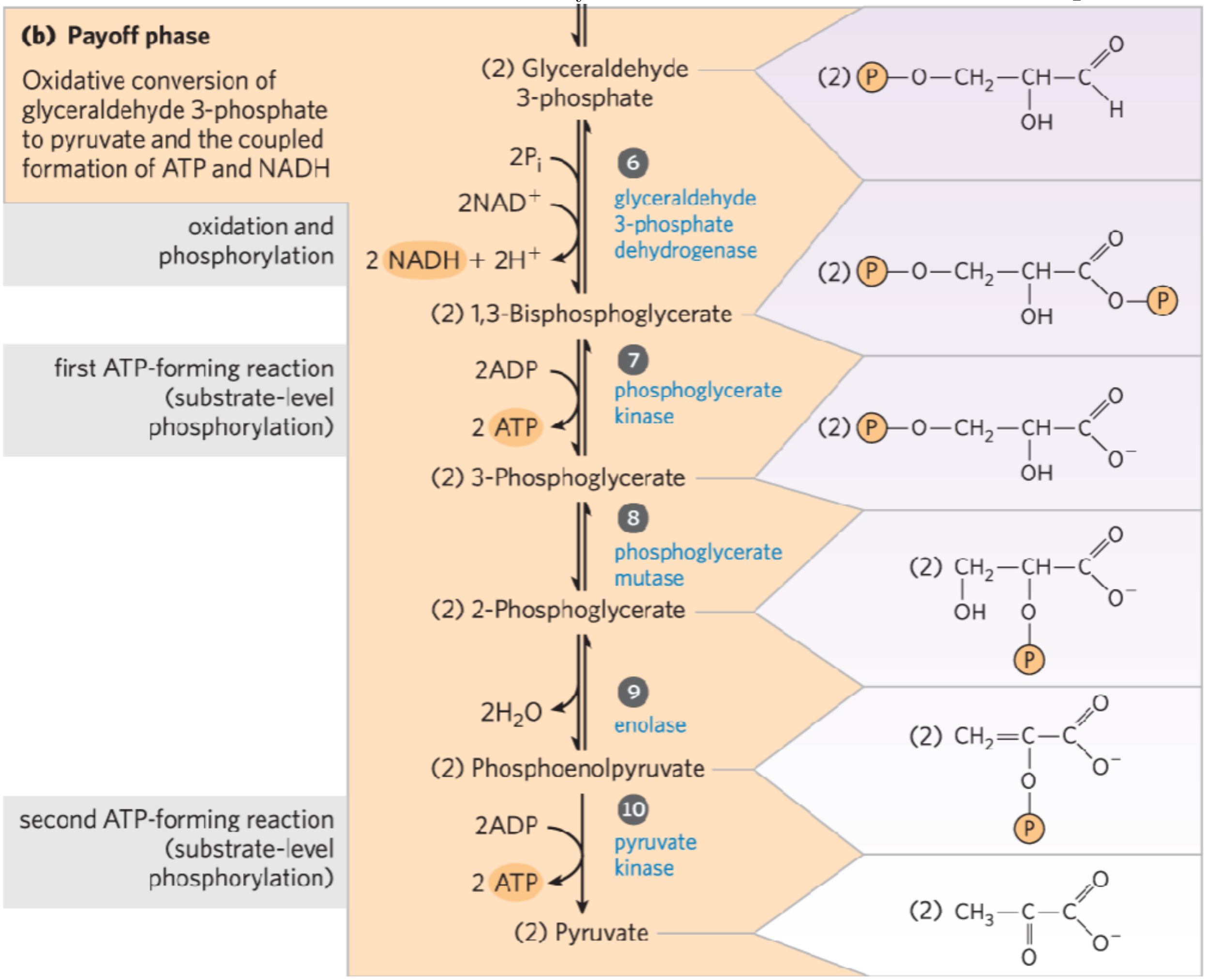
$$\text{Glucose} + 2\ \text{ATP} \rightarrow 2\ \text{G3P} + 2\ \text{ADP}$$

- G3P = Glyceraldehyde 3-Phosphate



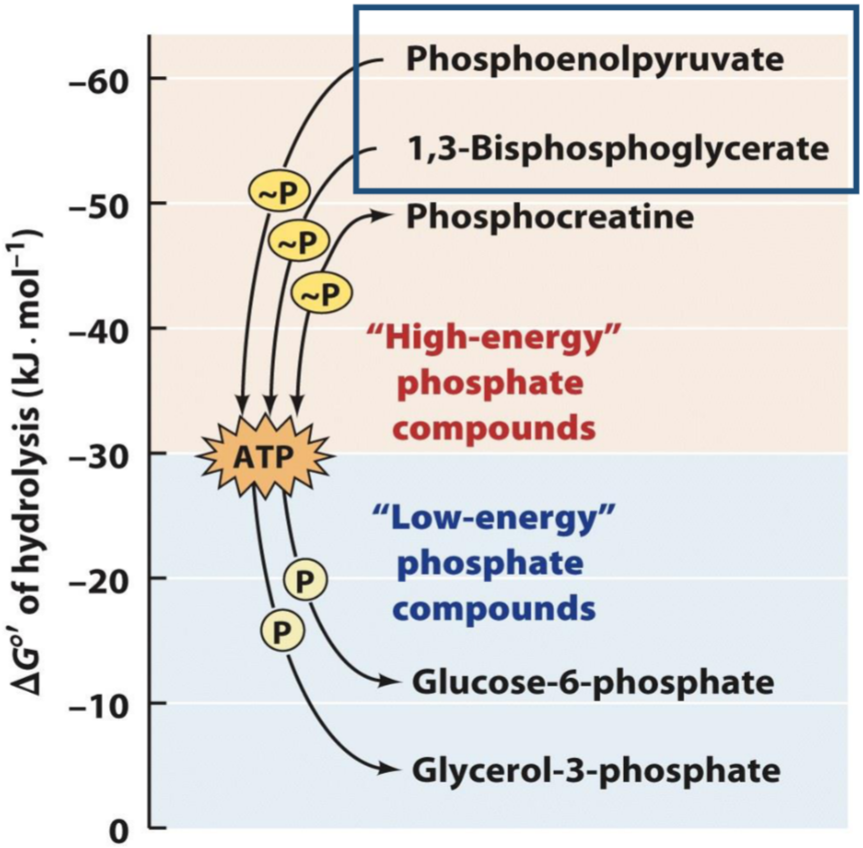
Stage II: Payoff Phase

$$2\ \text{G3P} + 2\ \text{NAD}^+ + 4\ \text{ADP} + 2\ \text{Pi} \rightarrow 2\ \text{Pyruvate} + 2\ \text{NADH} + 2\ \text{H}^+ + 4\ \text{ATP} + 2\ \text{H}_2\text{O}$$



- **Substrate-level phosphorylation** is a type of **ATP (or GTP) synthesis** that occurs when a phosphate group is directly transferred from a **high-energy phosphorylated compound** to **ADP (or GDP)** to form ATP (or GTP). This process does **not** require oxygen or the electron transport chain.

High-energy phosphate compounds



- These are high-energy phosphate compounds, and therefore capable of substrate-level phosphorylation
  - Substrate-level phosphorylation is an oxygen-independent mechanism for ATP synthesis that relies on direct phosphate transfer from high-energy compounds, making it essential for both aerobic and anaerobic energy metabolism
- Compounds with Δ G$^{\circ\prime}$ more negative than ATP ($\sim$ -30.5 kJ/mol) can transfer phosphate groups to form ATP through **substrate-level phosphorylation**
- Compounds with Δ G$^{\circ\prime}$ less negative than ATP cannot phosphorylate ADP to ATP and typically require ATP for phosphorylation.

Metabolites like glucose are often activated with a high-energy group before their catabolism. Glycolysis is a nearly universal 10-step metabolic pathway for producing ATP by the oxidation of glucose. In this process, two molecules of ATP are invested to activate glucose, but the products of the pathway include four ATP, as well as NADH (**a form of reducing power**) and the triose pyruvate, which can be metabolized further in other pathways

ATP and NADH Formation Coupled to Glycolysis

- the overall equation for glycolysis is:

$$\text{glucose} + 2\ \text{NAD}^{+} + 2\ \text{ADP} + 2\ \text{Pi} \rightarrow 2\ \text{pyruvate} + 2\ \text{NADH} + 2\ \text{H}^{+} + 2\ \text{ATP} + 2\ \text{H}_2\text{O}$$

- the reduction of NAD^{+}proceeds by the enzymatic transfer of a hydride ion (**:**H^{-}) from the aldehyde group of glyceraldehyde 3-phosphate (G3P) to the nicotinamide ring of NAD^{+}, yielding NADH

Noteworthy Chemical Transformations of Glycolysis

Three noteworthy chemical transformations:

1. degradation of the carbon skeleton of glucose to yield **pyruvate**
2. **phosphorylation of ADP to ATP** by compounds with high phosphoryl group transfer potential, formed during glycolysis
3. transfer of a hydride ion to NAD^+, forming **NADH**

Resolving the Equation of Glycolysis into Two Processes

- The conversion of glucose to pyruvate is exergonic:

$$\text{glucose} + 2\ \text{NAD}^+ \rightarrow 2\ \text{pyruvate} + 2\ \text{NADH} + 2\ \text{H}^+$$
$$\Delta G_1'^{\circ} = \text{-146 kJ/mol}$$

- The formation of ATP from ADP and Pi is endergonic:

$$2\ \text{ADP} + 2\ \text{Pi} \rightarrow 2\ \text{ATP} + 2\ \text{H}_2\text{O}\Delta G_2'^{\circ} = 2(30.5\ \text{kJ/mol}) = 61.0\ \text{kJ/mol}$$

The Standard Free-Energy Change of Glycolysis, $\Delta G'^{\circ}_{\mathbf{Sum}}$

- The sum of the two processes gives the overall standard free-energy change of glycolysis, $\Delta G'^{\circ}_{\text{Sum}}$:

$$\begin{aligned}\Delta G'^{\circ}_{\text{Sum}} &= \Delta G_1'^{\circ} + \Delta G_2'^{\circ} \\ &= -146\text{kJ/mol} + 61.0\text{kJ/mol} \\ &= -85\text{kJ/mol}\end{aligned}$$

- **under standard and cellular conditions, glycolysis is essentially irreversible**

Energy Remaining in Pyruvate

- energy stored in pyruvate can be extracted by:
  - **aerobic processes:**
    - oxidative reactions in the citric acid cycle (TCA cycle)
    - oxidative phosphorylation
  - **anaerobic processes:**
    - reduction to lactate
    - reduction to ethanol
- pyruvate can provide the carbon skeleton for alanine synthesis or fatty acid synthesis