CHAPTER 19: GLYCOlySIS

Glycolysis: From the greek word “glykys,” meaning “sweet” and “lysis” meaning “splitting”

- A sequence of enzyme-catalyzed reactions that convert a molecule of glucose into two molecules of pyruvate (a three-carbon compound) with the production of some ATP and NADH
History of Glycolysis

- 1897: Hans and Eduard Buchner discovered that sucrose is fermented into alcohol by yeast extract
- 1860: Louis Pasteur discovered fermentation
- 1905: Arthur Harden and William Young isolated a key component of glycolysis (fructose 1, 6- bisphosphosphate)
- 1940’s: Elucidation of the complete glycolytic pathway by Embden, Meyerhor, Neuberg, Parnas, Warburg, Gerty Cori, and Carl Cori
Key structures

\[ \text{CH}_2\text{OH} \quad \text{C} = \text{O} \quad \text{CH}_2\text{OH} \quad \text{dihydroxyacetone} \]

\[ \begin{array}{c}
\text{O} \\
\text{C} \\
\text{H} \\
\text{H} - \text{C} - \text{OH}
\end{array} \quad \text{glyceraldehyde} \]

\[ \begin{array}{c}
\text{O} \\
\text{C} \\
\text{O}^- \\
\text{H} \\
\text{H} - \text{C} - \text{OH}
\end{array} \quad \text{glycerate} \]

\[ \begin{array}{c}
\text{O} \\
\text{C} \\
\text{O}^- \\
\text{C} = \text{O} \\
\text{CH}_3
\end{array} \quad \text{pyruvate} \]
Key reactions

**Phosphoryl transfer**

\[ R-\text{OH} + \text{ATP} \xrightarrow{\text{Kinase}} R-\text{O}^\text{P} \text{P}^- + \text{ADP} + H^+ \]

**Phosphoryl shift**

\[ \text{OH} \quad \xrightarrow{\text{Mutase}} \quad \text{OR} \]

\[ \text{R-C-CH}_2\text{OH} \quad \xrightarrow{\text{CH}_2\text{OH}} \quad \text{R-C-CH}_2\text{PO}_4^- \]

**Isomerization**

\[ \text{CH}_2\text{OH} \quad \xrightarrow{\text{Isomerase}} \quad \text{C} \]

\[ \text{R-C-O} \quad \xrightarrow{\text{Isomerase}} \quad \text{R-C-H} \]

**Dehydration**

\[ \text{H} \quad \xrightarrow{\text{Dehydratase}} \quad \text{H} \]

\[ \text{H-C-OH} \quad \xrightarrow{\text{Dehydratase}} \quad \text{H-C} + \text{H}_2\text{O} \]

**Aldol cleavage**

\[ \text{HO-C-H} \quad \xrightarrow{\text{Aldolase}} \quad \text{HO-C-H} + \text{C=O} \]

\[ \text{R-C-O} \quad \xrightarrow{\text{Aldolase}} \quad \text{R-C-O} + \text{R'-C=O} \]

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Reaction types, page 485

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1. **Phosphorylation of glucose**

   \[ \text{Glucose} + \text{ATP} \xrightarrow{\text{Hexokinase}} \text{Glucose 6-phosphate} \]

   \[ \Delta G^\circ = -4.0 \text{ kcal/mol} \]

2. **Conversion of glucose-6-phosphate to fructose 6-phosphate**

   \[ \text{Glucose 6-phosphate} \xrightarrow{\text{Phosphogluco isomerase}} \text{Fructose 6-phosphate} \]

   \[ \Delta G^\circ = +0.4 \text{ kcal/mol} \]

3. **Phosphorylation of fructose 6-phosphate**

   \[ \text{Fructose 6-phosphate} + \text{ATP} \xrightarrow{\text{Phosphofructokinase}} \text{Fructose 1,6-bisphosphate} \]

   \[ \Delta G^\circ = -3.4 \text{ kcal/mol} \]

*Assorted figures from pages 486 and 487*

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4. Cleavage of fructose 1,6-bisphosphate

\[
\text{Fructose 1,6-bisphosphate} \xlongequal{\text{Aldolase}} \text{Dihydroxyacetone phosphate} + \text{Glyceraldehyde 3-phosphate}
\]

\[\Delta G'' = +5.7 \text{ kcal/mol}\]
6. Oxidation of glyceraldehyde 3-phosphate

\[
\begin{align*}
\text{Glyceraldehyde 3-phosphate} & \quad + \quad \text{NAD}^+ \quad + \quad \text{P}_i \\
\text{Glyceraldehyde 3-phosphate dehydrogenase} & \rightarrow \quad \text{1,3-Bisphosphoglycerate} (1,3-BPG)
\end{align*}
\]

\[\Delta G^\circ = +1.5 \text{ Kcal/mol}\]

7. Phosphoryl transfer from 1,3-bisphosphoglycerate to ADP

\[
\begin{align*}
\text{1,3-Bisphosphoglycerate} & \quad + \quad \text{ADP} \\
\text{Phosphoglycerate kinase} & \rightarrow \quad \text{3-Phosphoglycerate} + \text{ATP}
\end{align*}
\]

\[\Delta G^\circ = -4.5 \text{ Kcal/mol}\]
5. Interconversion of the triose phosphates

\[ \text{Dihydroxyacetone phosphate} \quad \xrightleftharpoons{\text{Triose phosphate isomerase}} \quad \text{Glyceraldehyde 3-phosphate} \]

\( \Delta G^\circ = +1.8 \text{ kcal/mol} \)

8. Conversion of 3-phosphoglycerate to 2-phosphoglycerate

\[ \text{3-Phosphoglycerate} \quad \xrightleftharpoons{\text{Phosphoglycerate mutase}} \quad \text{2-Phosphoglycerate} \]

\( \Delta G^\circ = +1.1 \text{ kcal/mol} \)

9. Dehydration of 2-phosphoglycerate to phosphoenolpyruvate

\[ \text{2-Phosphoglycerate} \quad \xrightarrow{\text{Enolase}} \quad \text{Phosphoenolpyruvate} \]

\( \Delta G^\circ = +0.4 \text{ kcal/mol} \)

10. Transfer of the \( \sim P \) group to ADP

\[ \text{Phosphoenolpyruvate} \quad \xrightarrow{\text{Pyruvate kinase}} \quad \text{Pyruvate} \]

\( \Delta G^\circ = -7.5 \text{ kcal/mol} \)

Glycolytic reactions, pages 488, 489

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T-55
The net reaction in the transformation of glucose into pyruvate is

\[
\text{Glucose} + 2 \text{P}_i + 2 \text{ADP} + 2 \text{NAD}^+ \rightarrow 2 \text{pyruvate} + 2 \text{ATP} + 2 \text{NADH} + 2 \text{H}^+ + 2 \text{H}_2\text{O}
\]

Table 19-1

Consumption and generation of ATP in glycolysis

<table>
<thead>
<tr>
<th>Reaction</th>
<th>ATP change per glucose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose → glucose 6-phosphate</td>
<td>-1</td>
</tr>
<tr>
<td>Fructose 6-phosphate → fructose 1,6-bisphosphate</td>
<td>-1</td>
</tr>
<tr>
<td>2 1,3-Bisphosphoglycerate → 2 3-phosphoglycerate</td>
<td>+2</td>
</tr>
<tr>
<td>2 Phosphoenolpyruvate → 2 pyruvate</td>
<td>+2</td>
</tr>
<tr>
<td>Net</td>
<td>+2</td>
</tr>
</tbody>
</table>
Reactions of glycolysis

<table>
<thead>
<tr>
<th>Step</th>
<th>Reaction</th>
<th>Enzyme</th>
<th>Type*</th>
<th>ΔG°</th>
<th>ΔG</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Glucose + ATP → glucose 6-phosphate + ADP + H⁺</td>
<td>Hexokinase</td>
<td>a</td>
<td>-4.0</td>
<td>-8.0</td>
</tr>
<tr>
<td>2</td>
<td>Glucose 6-phosphate ⇌ fructose 6-phosphate</td>
<td>Phosphogluucose isomerase</td>
<td>c</td>
<td>+0.4</td>
<td>-0.6</td>
</tr>
<tr>
<td>3</td>
<td>Fructose 6-phosphate + ATP → fructose 1,6-bisphosphate + ADP + H⁺</td>
<td>Phosphofructokinase</td>
<td>a</td>
<td>-3.4</td>
<td>-5.3</td>
</tr>
<tr>
<td>4</td>
<td>Fructose 1,6-bisphosphate → dihydroxyacetone phosphate + glyceraldehyde</td>
<td>Aldolase</td>
<td>e</td>
<td>+5.7</td>
<td>-0.3</td>
</tr>
<tr>
<td></td>
<td>3-phosphate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Dihydroxyacetone phosphate → glyceraldehyde</td>
<td>Triose phosphate isomerase</td>
<td>c</td>
<td>+1.8</td>
<td>+0.6</td>
</tr>
<tr>
<td></td>
<td>3-phosphate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Glyceraldehyde 3-phosphate + P_i + NAD⁺ → 1,3-bisphosphoglycerate + NADH + H⁺</td>
<td>Glyceraldehyde 3-phosphate dehydrogenase</td>
<td>f</td>
<td>+1.5</td>
<td>-0.4</td>
</tr>
<tr>
<td>7</td>
<td>1,3-Bisphosphoglycerate + ADP → 3-phosphoglycerate + ATP</td>
<td>Phosphoglycerate kinase</td>
<td>a</td>
<td>-4.5</td>
<td>+0.3</td>
</tr>
<tr>
<td>8</td>
<td>3-Phosphoglycerate → 2-phosphoglycerate</td>
<td>Phosphoglyceratmutase</td>
<td>b</td>
<td>+1.1</td>
<td>+0.2</td>
</tr>
<tr>
<td>9</td>
<td>2-Phosphoglycerate → phosphoenolpyruvate + H₂O</td>
<td>Enolase</td>
<td>d</td>
<td>+0.4</td>
<td>-0.8</td>
</tr>
<tr>
<td>10</td>
<td>Phosphoenolpyruvate + ADP + H⁺ → pyruvate + ATP</td>
<td>Pyruvate kinase</td>
<td>a</td>
<td>-7.5</td>
<td>-4.0</td>
</tr>
</tbody>
</table>

*Reaction type: (a) phosphoryl transfer; (b) phosphoryl shift; (c) isomerization; (d) dehydration; (e) aldol cleavage; (f) phosphorylation coupled to oxidation.

Note: ΔG° and ΔG are expressed in kcal/mol. ΔG, the actual free-energy change, has been calculated from ΔG° and known concentrations of reactants under typical physiologic conditions. Glycolysis can proceed only if the ΔG values of all reactions are negative. The small positive ΔG values of three of the above reactions indicate that the concentrations of metabolites in vivo in cells undergoing glycolysis are not precisely known.
Galactokinase

Galactose + ATP $\rightarrow$ galactose 1-phosphate + ADP + H⁺

\[ \begin{align*}
\text{Galactose 1-phosphate} & \quad \text{UDP-glucose} \\
\quad \quad & \quad \text{UDP-galactose} \quad \text{Glucose 1-phosphate}
\end{align*} \]

The sum of the reaction:

Galactose + ATP $\rightarrow$ glucose 1-phosphate + ADP + H⁺