ENZYMES AND CELLULAR METABOLISM OF GLUCOSE BY GLYCOLYSIS
Characteristics of Enzymes

• Function: Biological catalysts
• Almost all enzymes are proteins
• Speed up chemical reactions by reducing activation energy
• Do not themselves become part of the reaction
• Do not catalyze reactions that would not take place anyway
• Are very specific in the reactions they catalyze
Enzymes: Organic Catalysts

• Liver catalase (*the enzyme*)
  
  – $\text{H}_2\text{O}_2$ (*the substrate*)
    
    • is an oxidizing agent that is extremely toxic to cells
  
  – Neutralized by an enzyme, catalase, present in many tissues
Enzyme-Substrate Complex

- Lock and key model
  - Active site is the specific shape (perfect fit) to accommodate the substrate
Induced Fit Model

- Substrate induces a shape change in the active site that creates the “perfect fit”
Coenzymes/Cofactors

- **Coenzymes** are organic molecules that are required by certain enzymes to carry out catalysis
  - *Coenzymes* bind to the active site

- **Cofactors** are often classified as inorganic substances that are required for, or increase the rate of, catalysis
  - Do not bind to the active site
  - Some enzymes require multiple cofactors
Coenzymes
Organic Molecules

<table>
<thead>
<tr>
<th>Coenzyme</th>
<th>Transfers or Coenzyme for</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAD⁺</td>
<td>electrons (2e⁻)</td>
</tr>
<tr>
<td>NADP</td>
<td>electron</td>
</tr>
<tr>
<td>FAD</td>
<td>electrons (2e⁻)</td>
</tr>
<tr>
<td>CoA</td>
<td>acyl group (CH₃-C=O)</td>
</tr>
<tr>
<td>CoQ</td>
<td>electrons</td>
</tr>
<tr>
<td>Thiamine (vitamin B1)</td>
<td>Aldehydes (CHO)</td>
</tr>
<tr>
<td>Pyridoxine (vitamin B6)</td>
<td>amino groups (NH₂)</td>
</tr>
<tr>
<td>Biotin (vitamin B7)</td>
<td>carbon dioxide (CO₂)</td>
</tr>
<tr>
<td>Vitamin B12</td>
<td>alkyl groups (hydrocarbons)</td>
</tr>
</tbody>
</table>
# Cofactors

## Metal Ions as Cofactors

<table>
<thead>
<tr>
<th>Cofactor</th>
<th>Enzyme or Protein Cofactor for</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zn(^{2+})</td>
<td>Carbonic anhydrase</td>
</tr>
<tr>
<td>Zn(^{2+})</td>
<td>Alcohol dehydrogenase</td>
</tr>
<tr>
<td>Fe(^{3+}), Fe(^{2+})</td>
<td>Cytochromes, hemoglobin</td>
</tr>
<tr>
<td>Fe(^{3+}), Fe(^{2+})</td>
<td>Ferridoxin</td>
</tr>
<tr>
<td>Cu(^{2+}), Cu(^{+})</td>
<td>Cytochrome oxidase</td>
</tr>
<tr>
<td>K(^{+}), Mg(^{2+})</td>
<td>Pyruvate phosphokinase</td>
</tr>
<tr>
<td>Ca(^{2+})</td>
<td>Na(^{+}) channel gating</td>
</tr>
</tbody>
</table>
Reaction Rate

• Rate of enzyme-catalyzed reactions measured by the rate substrates are converted to products

• Factors influencing rate:
  – Temperature
  – pH
  – [cofactors and coenzyme]
  – [enzyme and substrate]
  – Stimulatory and inhibitory effects of products of enzyme action
Effect of Temperature

- Rate of reaction increases as temperature increases.
- Reaction rate plateaus, slightly above body temperature (37°C).
- Reaction rate decreases as temperature increases.
- Enzymes denature at high temperatures.
Effect of pH

- Each enzyme exhibits peak activity at narrow pH range (pH optimum).
- pH optimum reflects the pH of the body fluid in which the enzyme is found.
- If pH changes outside of optimal range, the reaction rate will decrease.
- Why?
Effect of [Substrate]

- At a specific [enzyme], rate of product formation increases as the [substrate] increases
- Plateau of maximum velocity occurs when enzyme is saturated
- Additional [substrate] does not increase reaction rate
Regulating Enzyme Activity

Activation and Inhibition

**Allosteric Modulation**
- Binds to an allosteric site
- A substance that regulates protein activity (*enhances*)
- Helps to stabilize functional conformation
- Regulates enzymes, receptors, transporters

**Covalent Modulation**
- Proteins are activated or inhibited by a molecule being attached to or removed from the protein
- Catalyzed by another enzyme
- Common group that acts as a modifier is phosphate
  - $\text{PO}_4^-$
Regulating Enzyme Activity

*Activation and Inhibition*

**Denaturation**
- Permanent changes to the protein which renders the protein non-functional
- Can be caused by
  - Temperature extremes
  - pH extremes

**End Product Inhibition**
- The product of a metabolic pathway inhibits the first enzyme in that pathway

All of these involve a change in the conformation of the enzyme!
Endergonic and Exergonic Reactions

- **Endergonic**
  - Energy in
  - Products must contain more free energy than reactants

- **Exergonic:**
  - Energy out
  - Convert molecules with more free energy to molecules with less
  - Release energy in the form of heat (measured in calories)
Formation of ATP

- Formation of ATP requires the input of energy
- This energy is released when ATP hydrolyzed to ADP and $p_i$
  - 7 Kcal
- ATP is the universal energy transfer molecule of the cell
Oxidation-Reduction Reactions

- Reduced = substance gains electrons
- Oxidized = substance loses electrons
- Redox reactions are coupled
- Usually involves the transfer of $2\text{H}^+$ rather than free electrons

Remember....
Electrons have to come from somewhere and go somewhere!
Metabolic Pathways

Sequence of enzymatic reactions that begins with initial substrate, progresses through intermediates and ends with a final product.
Cellular Respiration

- **Glycolysis:**
  - occurs in the cytosol

- **Krebs cycle:**
  - occurs in the matrix of the mitochondria

- **ETS:**
  - occurs on the cristae of the mitochondria

![Cellular Respiration Diagram](image-url)
Glycolysis

- Although fats, proteins, and carbohydrates can be used by the body as an energy source, glycolysis operates **only** on carbohydrates.

- Glycolysis is an **anaerobic** process.

- During glycolysis:
  - Glucose is broken down to two molecules of pyruvic acid (pyruvate).
  - Energy carrier molecules are reduced, producing ATP and NADH + H⁺.
Glycolysis