**Enzymes**

Catalysts for Biochemical Reactions

- Enzymes bring reactants together in the proper orientation for reaction to occur.
- Enzymes speed up the reaction by stabilizing the transition state.
- Reaction proceeds via a different mechanism in the presence of the enzyme.

**Enzymes and the Arrhenius Equation**

\[ k = A e^{-\frac{E_a}{RT}} \]

Enzymes lower the activation energy by allowing the reaction to proceed via a different mechanism.

**Enzymes**

**Reaction Mechanisms**

Uncatalyzed Reaction

\[ S \rightarrow P \]

Catalyzed Reaction

\[ E + S \rightleftharpoons ES \]

\[ ES \rightarrow P + E \]

Key:
- S = substrate
- E = enzyme
- ES = enzyme-substrate complex
- P = product

**Substrate Binding**

The Active Site

Enzymes bind the substrate (reactants) in the active site. This is a cleft that is lined with an array of polar, non-polar, and charged amino acids arranged in such a way as to interact favorably, and selectively, with the substrate.

- Acetylcholinesterase
- HIV Protease

**Enzyme Activity**

The Native Structure

Enzymes fold into a specific shape called the native structure. If the enzyme is unfolded from this structure (denatured), it no longer functions as a catalyst. The native structure is held together largely by a combination of non-covalent interactions (H-bonding, charge-charge, dispersion, etc.). If the pH or temperature conditions change from the optimal ones, these interactions are disturbed and the enzyme will denature and no longer act as a catalyst.
Case Study

Acetylcholinesterase

• Essential for nerve transmission at neuromuscular junctions (nerve-muscle connections)
• Removes excess acetylcholine (neurotransmitter) from synapse allowing neuron to reload and fire next nerve impulse.
• Target of nerve agents (Sarin, Tabun, Soman, etc)

Acetylcholine

A Neurotransmitter

Acetylcholine is a neurotransmitter, a chemical messenger that propagates the nerve impulse across a synapse (gap between neurons).

Nerve Transmission

Resting State

Acetylcholine (ACh) diffuses across the synapse. When ACh binds to receptors on the other side of the synapse, it triggers changes in ion concentration that result in an electrical impulse. This signal is passed on to the next nerve and the process repeats itself down the line.

Receptors

Acetylcholinesterase (AChE) clears the excess ACh out of the synapse by hydolytic cleavage. When the synaptic ACh concentration is reduced, acetylcholine diffuses away from the receptors (Le Chatelier’s principle).

Acetylcholinesterase plays a major role in the nerve transmission process. The excess ACh present in the synapse must be removed so that the nerve cell is ready for the next nerve impulse.

Reaction Catalyzed by Acetylcholinesterase

Reverse of Condensation Reaction

Acetylcholinesterase

Catalytic Triad

Histidine 440
Serine 200
Glutamate 199

These three amino acids, the catalytic triad, are located at the active site and play a crucial role in catalysis.
Nerve Agents

Nerve agents work by reacting with the OH group of the active-site serine that is required for catalytic activity. This disables (inhibits) the enzyme.

\[
\begin{align*}
\text{Sarin} & : CH_3CH_2OCH_2CH_2OCH_2CH_2OCH_3 \\
\text{Soman} & : CH_3CH_2OCH_2CH_2OCH_2CH_2OCH_3 \\
\text{VX} & : CH_3CH_2OCH_2CH_2OCH_2CH_2OCH_3
\end{align*}
\]

Exercises

1. Draw the Lewis structure of the dipeptide Val-Ser. (Hint: The structures of these amino acids appear on the "Examples of Amino Acids" slide in this presentation.)

2. The amino acid valine has a hydrocarbon side chain. In the native (folded) structure of a water-soluble protein, would you expect to find the majority of the valines on the exterior of the protein or in the interior. Explain your answer.

3. Which terms of the Arrhenius Equation are favorably affected by the action of enzymes?

4. A chemist measures the rate of an enzyme-catalyzed reaction as a function of temperature and obtains a relationship such as that shown in the plot below. Provide an explanation. Is this the relationship between rate and temperature that is found for reactions that do not involve enzymes?