EC 6 Ligases joining to molecule together at the expense of an high-energy (th

Ligases catalyze the formation of C–C, C–S, C–O, and C–N bonds. The energy for these reactions is always supplied by ATP hydrolysis. Other common names for ligases include *synthetases*, because they are used to synthesize new molecules.

$$A + B + ATP \longrightarrow A-B + ADP$$

Example

Carboxylases — Use CO_2 as a substrate.

Biochemical nomenclature distinguishes synthetases from synthases. *Synthases* catalyze condensation reactions in which no nucleoside triphosphate (ATP and GTP) is required as an energy source. *Synthetases* catalyze condensations that *do* use nucleoside triphosphate as a source of energy for the synthetic reaction. A synthase is a lyase and does not require any energy, whereas a synthetase is a ligase and thus requires energy.

1.12.2 What enzyme does?

A chemical reaction between two substances occurs only when an atom, ion, or molecule of one collides with an atom, ion, or molecule of the other. Only a fraction of the total collisions result in a reaction, because usually only a small percentage of the molecules interacting have the minimum amount of kinetic energy that a molecule must possess for it to react. When the reactants collide, they may form an intermediate product whose chemical energy is higher than the combined chemical energy of the reactants. In order for this transition state in the reaction to be achieved, some energy must enter into the reaction other than the chemical energy of the reactants. The transition state is the one with the highest free energy. The difference in free energy between the transition state and the reactants is called the *Gibbs free energy of activation* or simply the *activation energy*.

An enzyme lowers the activation energy of a reaction, thereby increasing the fraction of molecules that have enough energy to attain the transition state and making the reaction go faster in both directions. However, the catalyst does not change the relative energies of the initial and final states. The free energy of reaction, $\Delta G°$, remains unchanged in the presence of a catalyst, so the relative amounts of reactants and products at equilibrium are unchanged. In other words, a catalyst does not influence the position of equilibrium. It only increases the rate of a reaction by lowering the activation energy.

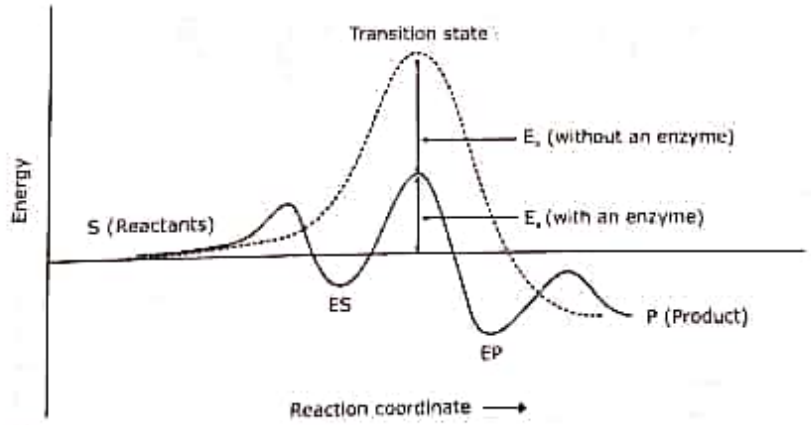
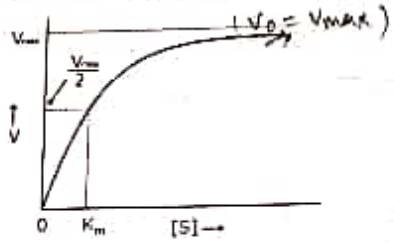


Figure 1.88 Energy profile of a simple enzyme-catalyzed reaction. The non-enzyme catalyzed reaction proceeds via a higher energy transition state and hence the reaction has a higher activation energy than the enzyme catalyzed reaction.

In this equation k_1 is the rate constant for the formation of the [illegible] E, and the substrate, S; k_{-1} is the rate constant for the reverse reaction, dissociation of the ES complex to free enzyme and substrate; and k_2 is the rate constant for the conversion of the ES complex to product P and the subsequent release of product from the enzyme.

According to Michaelis-Menten approach, when the rate (also called the velocity) of an enzyme catalyzed reaction is measured at varying substrate concentrations, the rate depends on the substrate concentrations [S]. At a relatively low concentration of substrate, initial velocity (V) increases almost linearly with an increase in a substrate concentration. The reaction reaches a maximum velocity (V_{max}) with an increase in substrate concentration and it doesn't increase any further by increasing the concentration of substrate.



The hyperbolic relationship between initial velocity (V) and substrate concentration [S] of an enzyme catalyzed reaction.

Concentration of substrate at which reaction velocity reaches half its maximum velocity is called **Michaelis constant** (K_m). It is the ratio of constants $(k_{-1} + k_2)/k_1$. The K_m is expressed as mole of substrate per litre. Lower value of K_m describes the greater affinity of the enzymes for the substrate.

$$K_m = \frac{k_{-1} + k_2}{k_1}$$

Michaelis and Menten put forward a mathematical equation to establish the mathematical relationship among the quantities [E], [S], V_{max} and K_m.

$$V = \frac{V_{max}\,[S]}{K_m + [S]}$$

1. When $[S] << K_m$, then $V \propto [S]$
2. When $[S] >> K_m$, then $V = V_{max}$
3. When $[S] = K_m$, then $V = \frac{V_{max}}{2}$