Homework #1 - SOLUTIONS

How do maximum rate of an enzyme reaction (v_m) and half-velocity constant (K_M) change by “product inhibition”?

(50 points)

Hints:

1) Assume that the product (P) reversibly binds to the enzyme-substrate complex (ES) but not to the free enzyme (E).

2) Assume pseudo-steady state for the concentration of the enzyme-substrate-product complex (ESP).

Solution)

Reaction for product inhibition:

$$ES + P \underset{k_{-5}}{\overset{k_5}{\rightleftarrows}} ESP$$

As [ESP] does not change over time

$$k_5 [ES][P] = k_{-5} [ESP]$$

Finding solution

$$[ESP] = \frac{1}{K_P}[ES][P], \ \textit{where} \ K_P = \frac{k_{-5}}{k_5}$$

When we derived Michaelis-Menten equation, we got

$$[E] = K_M \frac{[ES]}{[S]}$$

From enzyme mass balance,

$$[E]_{total} = [E] + [ES] + [ESP] = K_M \frac{[ES]}{[S]} + [ES] + \frac{1}{K_P}[ES][P]$$

The rate of enzyme reaction under product inhibition:

$$v = v_m \frac{[ES]}{[E]_{total}} = v_m \frac{[ES]}{K_M \frac{[ES]}{[S]} + [ES] + \frac{1}{K_P}[ES][P]}$$

$$= v_m \frac{[S]}{K_M + \left(1 + \frac{[P]}{K_P}\right)[S]} = v_m{}^* \frac{[S]}{K_M{}^* + [S]}$$

$$\text{where } v_m{}^* = \left(1 + \frac{[P]}{K_P}\right)^{-1} v_m \text{ and } K_M{}^* = \left(1 + \frac{[P]}{K_P}\right)^{-1} K_M$$

Therefore, both v_m and K_M decreases