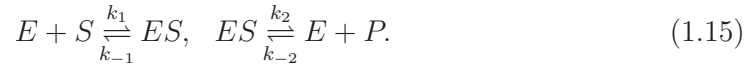


Homework # 4 (Due Friday, Nov. 4)

1. Let us consider a reversible enzyme reaction with enzyme molecule E at a much much lower concentration than that of substrate and product molecules, S and P , according to Michaelis-Menten kinetics:



(a) Following the law of mass action to write the system of ODEs for the concentrations of S , E , ES , and P at time t , denoted as $s(t)$, $e(t)$, $c(t)$, and $p(t)$, respectively.

(b) If we assume that the concentration of ES reaches a steady state rapidly, i.e., we can write $\frac{dc(t)}{dt} = 0$. while $s(t)$ and $p(t)$ are still changing with time, show that the rate of product formation

$$\frac{dp(t)}{dt} = -\frac{ds(t)}{dt} = \frac{\frac{V_{max}^+}{K_{MS}} - \frac{V_{max}^-}{K_{MP}}}{1 + \frac{s}{K_{MS}} + \frac{p}{K_{MP}}}. \quad (1.16)$$

Give the parameters K_{MS} , K_{MP} , V_{max}^+ and V_{max}^- in terms of the k 's.

(c) Using the fact that the concentration of E is much much smaller than that of S and P , justify the assumption in (b): $\frac{dc}{dt} = 0$.

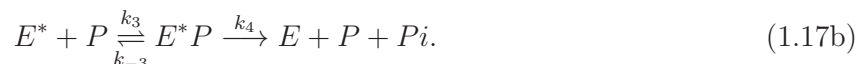
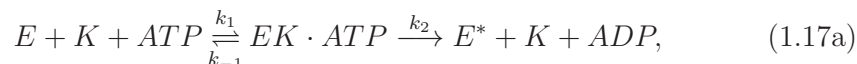
2. Let us again consider the enzyme reaction kinetics in Eq. 1.15. However, this time we assume $k_{-2} = 0$. We further assume there is only a single enzyme molecule, in a sea of substrate molecules S with concentration s . Since there is only a single E molecule, the concentration of S , s can be treated as a constant over time.

(a) Write the chemical master equation for the stochastic enzyme reaction with single enzyme molecule and fixed S concentration. In other words, the number of E is either zero or one; and correspondingly the number of ES is either one or zero.

(b) The enzyme E has only two possible states: E or ES . Solve the steady state probabilities for the single enzyme in the E state and in the ES state.

(c) The enzyme is continuously going through the kinetic cycle of combining with an S to form an ES , dropping a P and free itself, and then combining with another S to form an ES again, etc. Compute what is the mean steady state rate of increasing P ? Compare your result with Eq. 1.16.

3. Let us consider the phosphorylation and dephosphorylation reactions catalyzed by corresponding enzymes called kinase (K) and phosphatase (P),



ATP, ADP, and Pi are called adenosine triphosphate, adenosine diphosphate, and inorganic phosphate respectively. A complete phosphorylation-dephosphorylation cycle yield one ATP hydrolysis $ATP \rightleftharpoons ADP + Pi$. We shall again assume that the concentrations of ATP, ADP, and Pi are all sustained and constant. That means their concentrations are treated as constants.

(a) Following the theory of Michaelis-Menten kinetics, the two enzymatic reactions in (1.17a) and (1.17b) each has its own K_M and V_{max} . Let them be K_1 and V_1 and K_2 and V_2 , respectively. Show that

$$\frac{d[E^*]}{dt} = \frac{V_1[E]}{K_1 + [E]} - \frac{V_2[E^*]}{K_2 + [E^*]}, \quad (1.18)$$

in which $[E] + [E^*] = E_T$ is the total amount of substrates E and E^* , neglecting the very small amount of $EK \cdot ATP$ and E^*P complexes.

(b) Find the steady state fraction of phosphorylated protein $f = [E^*]/E_T$.

(c) $f = [E^*]/E_T$ is a function of $\hat{K}_1 = K_1/E_T$, $\hat{K}_2 = K_2/E_T$ and $\theta = V_1/V_2$. What is

$$\lim_{\hat{K}_1, \hat{K}_2 \rightarrow 0} f(\theta, \hat{K}_1, \hat{K}_2) = ?$$