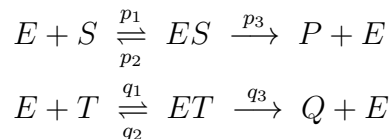


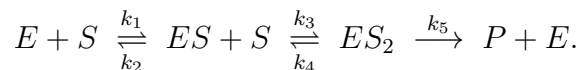
Read: Chapter 2.3: Modeling biochemical reactions with differential equations, by R. Robeva, and N. Yildirim. pages 40–46.

1. Consider the reactions where two substrates S and T compete for binding to an enzyme E to produce two different products P and Q :



Assume that each reaction follows the Michaelis-Menten kinetics. Also, assume that the initial enzyme concentration is $E_0 = [E] + [ES] + [ET]$.

- (a) Derive rate equations for P and Q in this system in terms of $[ES]$ and $[ET]$. That is, determine $d[P]/dt$ and $d[Q]/dt$.
 - (b) Derive rate equations for ES and ET .
 - (c) Assume that the enzyme-substrate complexes reach equilibrium quickly: $d[ES]/dt \approx 0$ and $d[ET]/dt \approx 0$. Solve for $[E]$ in each of these equations.
 - (d) Equate the two expressions for $[E]$ from Part (c) and solve for $[ET]$.
 - (e) Solve for $[ES]$ by plugging your answers to Parts (c) and (d) into $E_0 = [E] + [ES] + [ET]$. You should not have $[E]$ or $[ET]$ in your final answer.
 - (f) Plug this into the original ODE for $d[P]/dt$.
 - (g) Repeat the previous three steps but solve for $[ES]$ instead of $[ET]$.
 - (h) Explain the effects of the competition occurring.
2. The Hill equation is an approximation for multi-molecule binding and it assumes simultaneous binding of n -molecules of a substrate S to the enzyme E . Suppose that two molecules of the substrate S are undergoing a reaction with an enzyme in an ordered manner as follows:



Assume that the reaction follows the Michaelis-Menten kinetics and that the initial enzyme concentration is $E_0 = [E] + [ES] + [ES_2]$.

- (a) Derive rate equations for P , ES , and ES_2 . Be *very* careful with the $ES \xrightarrow{k_2} E + S$ reaction when deriving the equation for $[ES]$.
- (b) Assume that $d[ES_2]/dt \approx 0$ and solve for $[ES]$.
- (c) Assume that $d[ES]/dt \approx 0$. Plug your answer to Part (b) into this and solve for $[E]$.
- (d) Plug your expressions for $[E]$ and $[ES]$ back into $E_0 = [E] + [ES] + [ES_2]$ and solve for $[ES_2]$.
- (e) Derive an ODE for $[P]$ of the form $d[P]/dt = f([S])$.

(f) Compare your answer to Part (d) to the Hill equation with Hill coefficient $n = 2$:

$$\frac{d[P]}{dt} = \frac{V_{\max}[S]^2}{K_m + [S]^2}.$$

When do these two equations become roughly the same?