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:

$$E + S \underset{p_2}{\overset{p_1}{\rightleftharpoons}} ES \xrightarrow{p_3} P + E$$
$$E + T \underset{q_2}{\overset{q_1}{\rightleftharpoons}} ET \xrightarrow{q_3} Q + E$$

Assume that each reaction follows the Michaelis-Menten kinetics. Also, assume that 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 occuring.

2. The Hill equation is an approximation for multi-molecule binding and it assumes simultaneous binding of n-moecules 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:

$$E + S \underset{k_2}{\overset{k_1}{\rightleftharpoons}} ES + S \underset{k_4}{\overset{k_3}{\rightleftharpoons}} ES_2 \xrightarrow{k_5} P + E.$$

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?