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CAAM 588
Homework – Chemmical Kinetics

In this homework, we explored there models of chemical kinetics that influence the signaling networks in the brain: Michaelis-Menten (MM) Model for enzyme reactions, reduced MM model and the model for Calcium dependent plasticity (CaDP).

The MM model follows the simple rule:

$$S + E \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} C \xrightarrow{k_2} P + E$$

whre S is the substrate, E is the enzyme, C is the enzyme + substrate complex, P is the reaction product, and ki are reaction rate constants. Differential equations for the rate of change of reaction constituents can be constructed as follows:

$$\begin{aligned} \frac{d}{dt}s(t) &= -k_1 s(t)(e_T - c(t)) + k_{-1}c(t) \\ \frac{d}{dt}c(t) &= -k_{-1}c(t) + k_1 s(t)(e_T - c(t)) - k_2 c(t) \\ \frac{d}{dt}p(t) &= k_2 c(t). \end{aligned}$$

Here, et is the total enzyme concentration, which is C – S. Below, are simulations modeling the temporal dynamics of the system. We compare the concentration outcomes of S, C, and P for different parameters to determine how the rates and initial concentrations of substrate and enzyme influence how the reaction plays out. Figure 1 a) shows the dynamics of a normal system, with a large fast forward reaction rates k1 and k2, slow backward rate k-1, and an initial concentration of substrate that is large relative to that of th enzyme. Figure 1 b) shows the effect of increasing the initial enzyme concentration to the point where it equals that of the substrate, in this case, the reaction progresses very quickly and it will run out of substrate very soon. However, if in the same scenario the forward reaction rate k1 is very slow, than the reation will play out slowly, even if enzyme concentraiton is high.

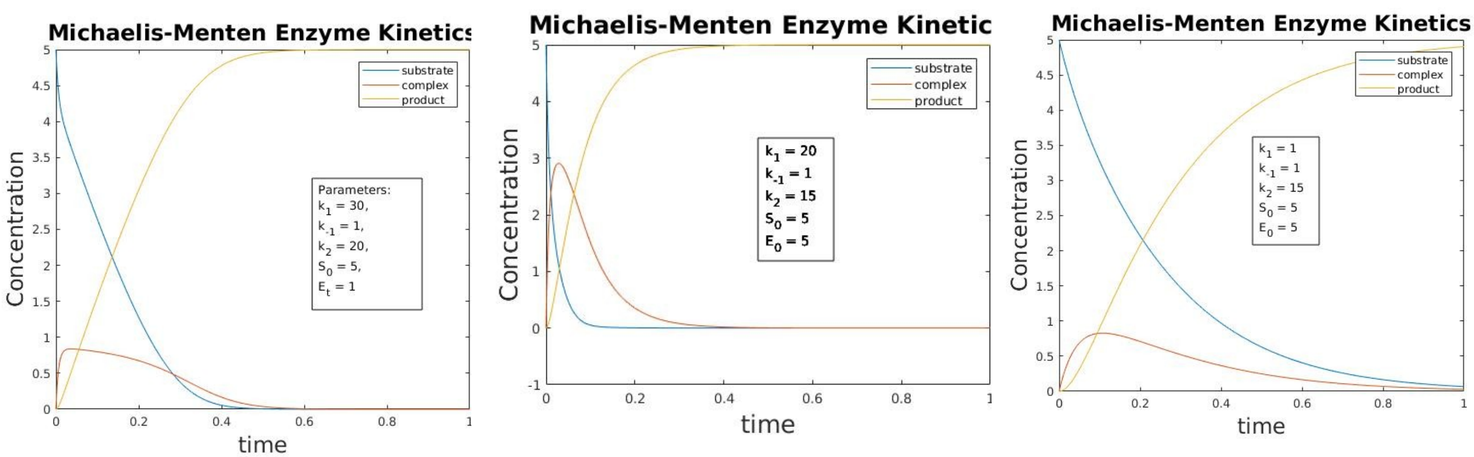


Figure 1: a) b) c)

In the quasi-steady state, the dc/ct = 0. Using, this assumption, a reduced MM model can be constructed which only tracks how the substrate is being converted into product. It is summarized by the following equation:

$$\text{rate of } S \rightarrow P = \frac{k_2 k_1 e_T s}{k_{-1} + k_2 + k_1 s}$$

We model the dynamics of the reduced MM model and compare it to the full MM model, as shown in Figure 2. Figure 2 a) shows the dynamics for a typical system, and Figure 2 b) shows the dynamics for a system where the concentration of substrate is hight compared to that of the enzyme. In both cases, in both cases, the reduced model does a good job at approximation. However, some coefficient values make the reduced model a better approximation than others. These dynamics are consistent with the quasi static state approximation.

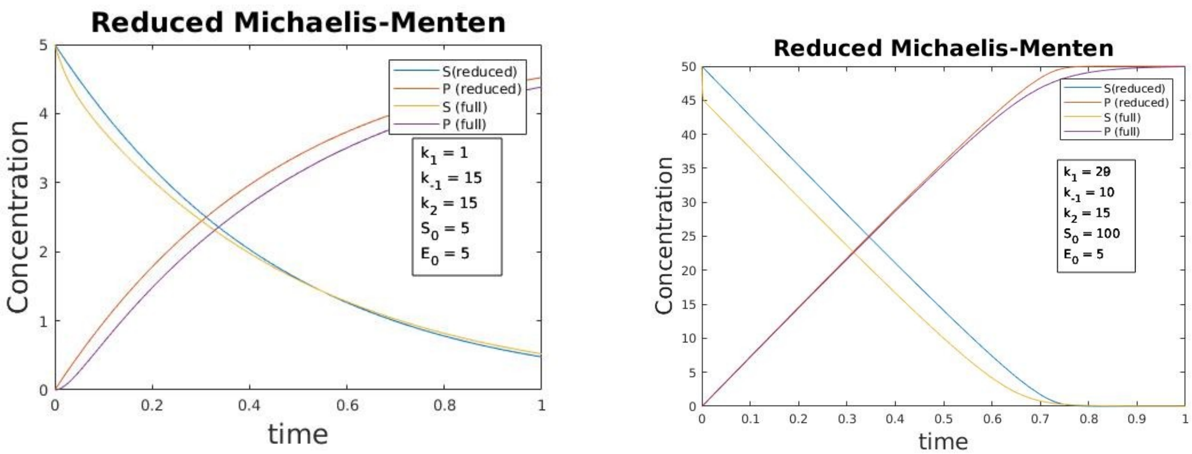


Figure 2: a) b)

Lastly, we looked at the Ca-dependent plasticity model, best summarized by:

$$\frac{dw_i}{dt} = \eta([\mathrm{Ca}]_i)(\Omega([\mathrm{Ca}]_i) - w_i)$$

where omega is the function of Ca concentration at a synapse, and has the form:

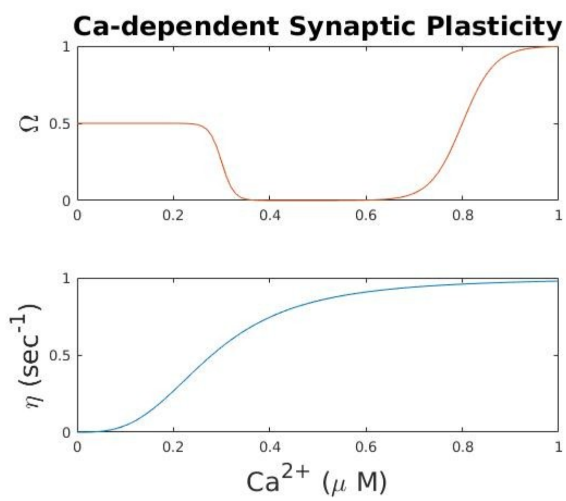
$$\Omega(x) = \alpha_o - \alpha_0 \mathrm{sig}(x - \alpha_1, \beta_1) + \mathrm{sig}(x - \alpha_2, \beta_2)$$

and eta is the calcium dependendent learning rate, of the form:

$$\eta(x) = p_1 \frac{(x + p_4)^{p_3}}{(x + p_4)^{p_3} + (p_2)^{p_3}}$$

The following parameters were simulate the model:

Figure 3.



a0 = 0.5;
a1 = .3;
a2 = .8;
b1 = 80;
b2 = 30;
p1 = 1;
p2 = 0.28;
p3 = 3;
p4 = 0.00001;

Figure 3 shows how omega and eta change with Ca ion concentration. The rate of convergence of omega to the maximum LTD and minimum LTP depends on the parameters a1 and a2. If a1 is large with respect to a2, the rate of convergence for LTD is larger. On the other hand, if a2 > a1, the rate of convergence of LTP is larger. In the scenario above, I a1 > a2, so the rate of convergence for LTP is faster.