NANYANG TECHNOLOGICAL UNIVERSITY SINGAPORE

Enzyme Kinetics

HU Xin Wen, Elisa
huxinwen23@163.com
Application Report for Msc Biomedical Data Science

Enzymes are catalysts that help convert molecules that we will call substrates into other molecules that we will products. They themselves are not changed by the reaction. Within cells, enzymes are typically proteins. They can speed up biological reactions, sometimes by up to millions of times. They are also regulated by a very complex set of positive and negative feedback systems. Computational biologists are painstakingly mapping out this complex set of reactions. In this problem, we will model and simulate a simplified enzyme reaction.

An enzyme E converts the substrate S into the product P through a two-step process. First, E forms a complex with S to form an intermediate species ES in a reversible manner at the forward rate k_1 and reverse rate k_2. The intermediate ES then breaks down into the product P at a rate k_3, thereby releasing E. Schematically, we write

$$E + S \underset{k_2}{\overset{k_1}{\rightleftharpoons}} ES \overset{k_3}{\rightarrow} E + P$$

1 Problem 1 Solution

Based on the loss of mass function, the rate of chages of four species can be written as:

$$\begin{aligned} \frac{d[E]}{dt} &= k_2[ES] + k_3[ES] - k_1[E][S] \\ \frac{d[S]}{dt} &= k_2[ES] - k_1[E][S] \\ \frac{d[ES]}{dt} &= k_1[E][S] - k_2[ES] - k_3[ES] \\ \frac{d[P]}{dt} &= k_3[ES] \end{aligned} \tag{1}$$

2 Problem 2 Solution

Through simulate the kinetics of a chemical reaction by implement the fourth order Runge-Kutta method, we can get the concentration of each objects at unit of time.

By the mathematical function derived in Problem 1 (E.q. 1), we can see that since enzyme will not directly take part in the reaction, in other words, the total concentration of the enzyme will not be consumed. So the total concentration of enzyme E_T will not change, and $E(t) = E_T - ES(t)$. Rewritten ES as c, then we can simplify the equation set into:

$$\begin{aligned} \frac{d[s(t)]}{dt} &= k_2[c(t)] - k_1[e_T - c(t)][s(t)] \\ \frac{d[c(t)]}{dt} &= k_1[e_T - c(t)][s(t)] - k_3[c(t)] - k_2[c(t)] \\ \frac{d[P]}{dt} &= k_3[c(t)] \end{aligned} \tag{2}$$

Algorithm 1 Fourth Order Runge-Kutta method

Input: RungeKutta4f, g, h, n, s_0, c_0 Fourth order Runge-Kutta method for solving a system of ODEs
f: function handle for the derivative of the substrate concentration
g: function handle for the derivative of the intermediate species concentration
h: step size for the simulation
n: number of steps in the simulation
s_0: initial substrate concentration
c_0: initial intermediate species concentration
Initialize lists to store the solution
$t \leftarrow []$
$s \leftarrow [s_0]$
$c \leftarrow [c_0]$
for $k \leftarrow 0$ ***to*** $n - 1$ **do**
end
Loop through each time step
Calculate the four intermediate estimates of s and c
$z_0 \leftarrow h * f(t[k], s[k], c[k])$
l_0

In the simulation process, we first assume the reaction will last for 1 minute and the time step will be 0.01. Then we got the result in the following Figure 1:

We can see that the reaction has already stop at 30s, hence, we cut down the result to 0.01 in order to get further information. The final result is shown in the following Figure 2:

From the figure we can see:

1. Within the first few seconds, the reaction takes place very violently. The concentration of enzyme and substrate decreases rapidly. The concentration and intermediate species and product increases rapidly.

2. Within 10 seconds, the reaction slows down, the concentration of the reaction substrate S decreases and the concentration of the product P increases. The enzyme concentration gradually returns to its initial concentration and the concentration of the intermediate decreases to 0.

3. From 10 to 20 seconds, the reaction gradually stops, resulting in a concentration of approximately 0 um of substrate S, 10 μm of product P, 1 μm of enzyme and 0 μm of intermediate species.

3 Problem 3 Solution

Since the velocity V is the rate of change of product P in the enzymatic reaction, we can define V as (c denotes the intermediate species ES):

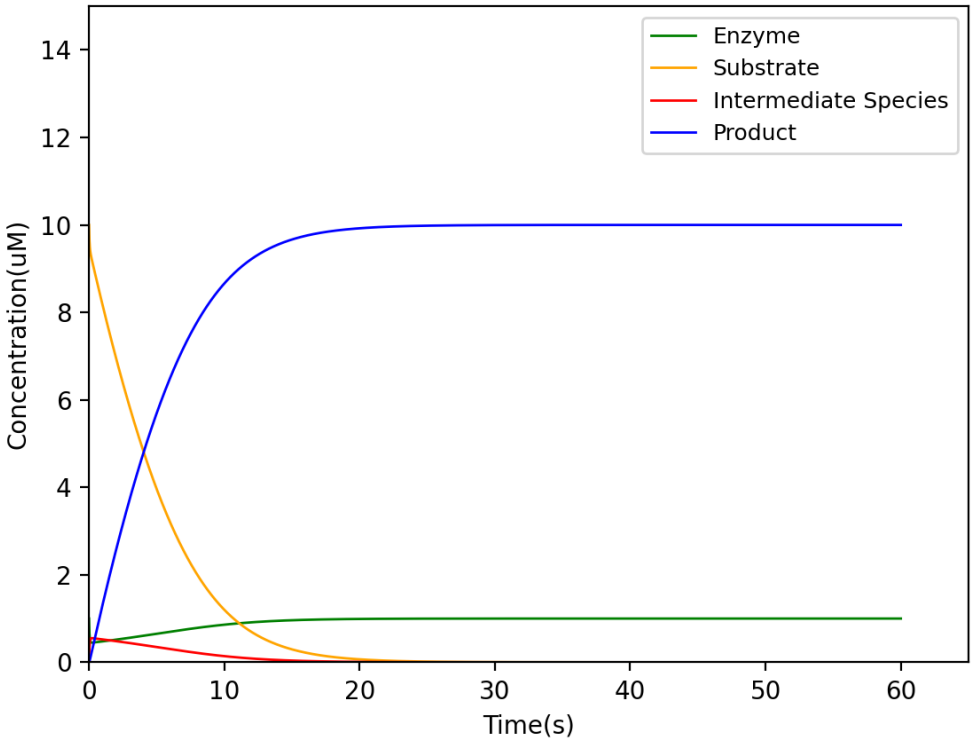

Figura 1: Time-Concentration Plot in 60s with time-step = 0.01

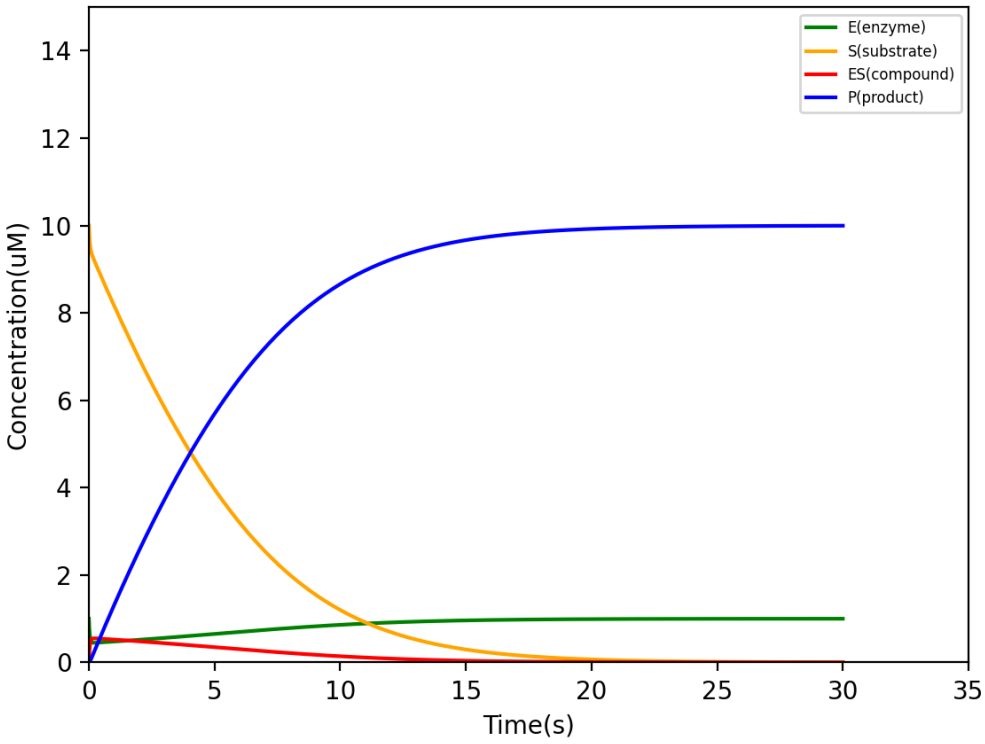

Figura 2: Time-Concentration Plot in 30s with time-step = 0.001

$$V = \frac{d[P]}{dt} = k_3[c(t)] \tag{3}$$

Since the function start from the original point, the function can also been seen as a differential function of V and S. Hence, we can plot the the function of the concentration of the substrate by:

$$\begin{aligned} \frac{d[V]}{dS} &= \frac{d[k_3 c(t)]}{dS} \\ &= \frac{k_3 d[c(t)]}{dS} \end{aligned} \tag{4}$$

From E.q.1:

$$\frac{d[ES]}{dt} = k_1[E][S] - k_2[ES] - k_3[ES]$$

So E.q.4 can written as:

$$\begin{aligned} \frac{d[V]}{dS} &= k_3 \frac{d[c(t)]}{dt}\frac{dt}{dS} \\ &= \frac{k_3[k_1 c(t) - k_2 c(t) - k_3 c(t)}{-k_1 c(t) + k2c(t)} \end{aligned} \tag{5}$$

Coding by Python, we an obtain the following Figure 3. Form it, we can see that:

1. The velocity V increases approximately linearly when the concentrations of S are very small, approximately at the interval of [0, 4]μm.

2. When the concentration is larger that 4μm, the change of rate of P start to grow in exponential level.

3. The change rate of P reach the peak at about 9μm of concentration of S. So the maximum value of velocity is approximately 1.4 μm

Hence, the maximum value of velocity is approximately $V_m = 1.4$ at concentration of $S = 9\mu m$.

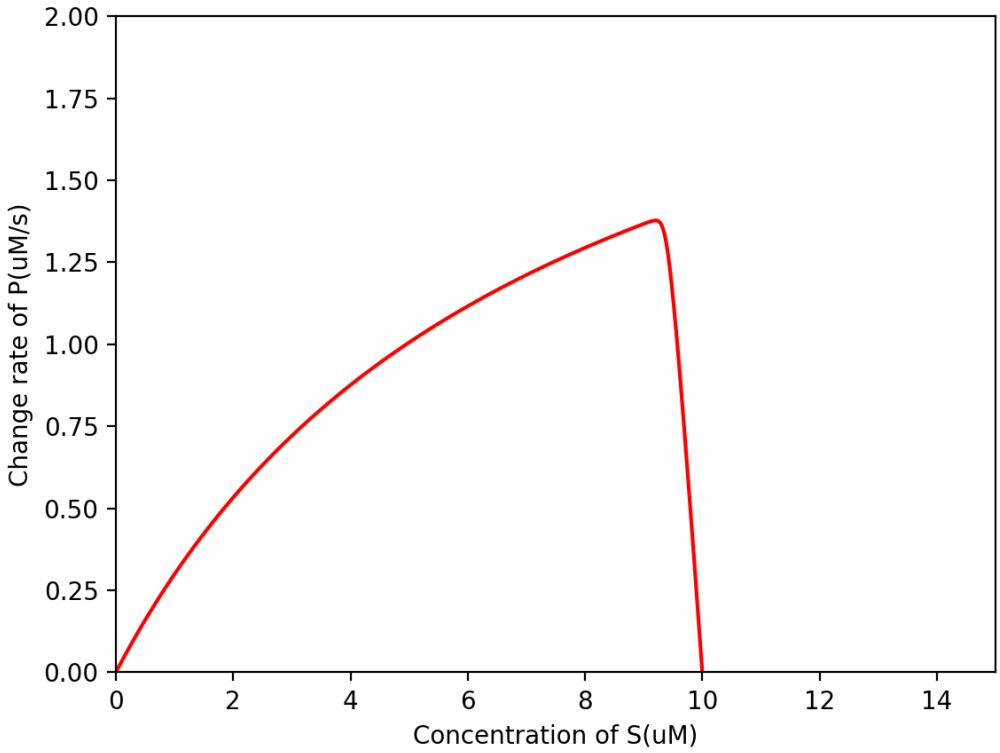

Figura 3: Velocity-Concentration(S) Plot

Referências

[1] J. Keener, J. Sneyd. (1998). Mathematical Physiology, *Springer*

[2] J. Salgado course on Biochemistry at University of Valencia.

[3] J. P.S. Thiagarajan lecture on *Reaction kinetics* at National University of Singapore.