College of the Redwoods
Math 55, Differential Equations

Michaelis-Menten Enzyme Kinetics

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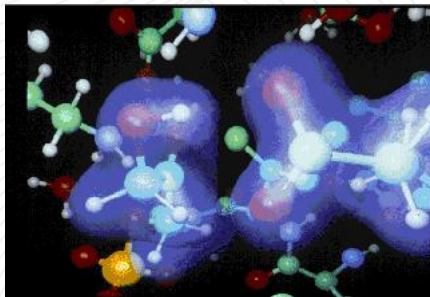fadedgator@yahoo.com

Introduction

Figure 1: Triophosphate Enzyme

What is Enzyme Kinetics?

- Kinetics is the study of rates of chemical reactions

- Enzymes are little molecular machines that carry out reactions in cells

- Enzyme kinetics is the study of rates of chemical reactions that involve enzymes

Michaelis-Menten Equation

- The Michaelis-Menten Equation is a differential equation used to model the rate at which enzymatic reactions occur

- This model allows scientist to predict how fast a reaction will take place based on the concentrations of the chemicals being reacted.
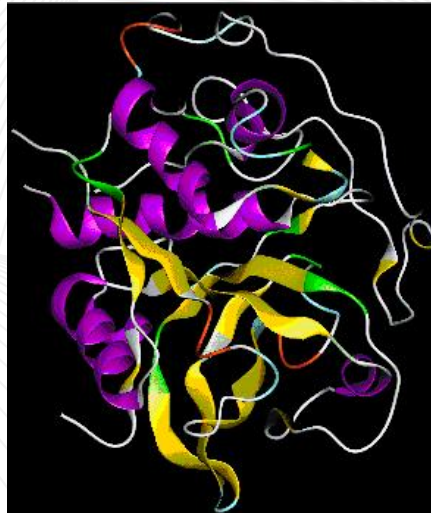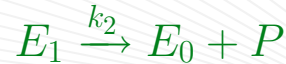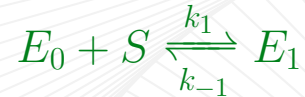

Figure 2: A Model of an Enzyme

Typical Enzymatic Reactions

$$E_0 + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} E_1$$

$$E_1 \xrightarrow{k_2} E_0 + P$$

S	the concentration of the substrate (the unreacted molecules)
P	the concentration of product (the reacted molecules)
E_0	the concentration of the unoccupied enzymes
E_1	the concentration of occupied enzymes.
$k_1,\ k_{-1},\ k_2$	the rate constants

Conditions for Michaelis-Menten Modelling

- In order to model an enzymatic reaction, some conditions must be maintained:

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  - Each enzyme can act on only one other molecule at a time
  - The enzyme must remain unchanged during the course of the reaction.
  - The concentration of substrate must be much higher than the concentration of enzyme

Rate Equations

$$E_0 + S \mathrel{\mathop{\rightleftharpoons}^{k_1}_{k_{-1}}} E_1 \qquad (1)$$

$$E_1 \xrightarrow{k_2} E_0 + P \qquad (2)$$

- The rate at which reaction (1) occurs is derived as follows:

  - The number of possible contacts between S and E_0 is directly proportional to SE_0.

  - The number of successful contacts over a certain amount of time is proportional to the number of possible contacts.

  - Thus, the rate of reaction is directly proportional to SE_0:

  $$\text{Rate}_1 = k_1 S E_0.$$

  where k_1 is the rate constant.

$$E_0 + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} E_1 \tag{1}$$

$$E_1 \overset{k_2}{\longrightarrow} E_0 + P \tag{2}$$

- The rate at which the reverse of reaction (1) occurs is derived as follows:

  - A certain proportion of E_1 will release S over a certain amount of time before the reaction is carried out.

  - The rate of the reverse reaction is directly proportional to E_1:

  $$\text{Rate}_{-1} = k_{-1}E_1$$

  where k_{-1} is the rate constant.

$$E_0 + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} E_1 \tag{1}$$

$$E_1 \xrightarrow{k_2} E_0 + P \tag{2}$$

- The rate at which reaction (2) occurs is derived as follows:

  − A certain proportion of E_1 will produce P over a certain amount of time.

  − The rate of production of P is directly proportional to E_1:

  $$\text{Rate}_2 = k_2 E_1$$

  where k_2 is the rate constant.

Specific Rates of Reactions for each Compound

$$E_0 + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} E_1 \tag{1}$$

$$E_1 \xrightarrow{k_2} E_0 + P \tag{2}$$

$$\text{Rate}_1 = k_1 S E_0, \quad \text{Rate}_{-1} = k_{-1} E_1, \quad \text{and} \quad \text{Rate}_2 = k_2 E_1$$

The rate equations associated with each reaction determines the rate of change of S, E_0, E_1, and P. Realizing this, we can write the following:

$$\begin{aligned}
\frac{dS}{dt} &= -\text{Rate}_1 + \text{Rate}_{-1} \\
&= -k_1 S E_0 + k_{-1} E_1
\end{aligned}$$

Specific Rates of Reactions for each Compound

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$$\frac{dE_0}{dt} = -\text{Rate}_1 + \text{Rate}_{-1} + \text{Rate}_2$$

$$= -k_1 S E_0 + k_{-1} E_1 + k_2 E_1$$

Specific Rates of Reactions for each Compound

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$$\frac{dE_1}{dt} = \text{Rate}_1 - \text{Rate}_{-1} - \text{Rate}_2$$

$$= k_1 S E_0 - k_{-1} E_1 - k_2 E_1$$

Specific Rates of Reactions for each Compound

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The rate equations associated with each reaction determines the rate of change of S, E_0, E_1, and P. Realizing this, we can write the following:

$$\frac{dP}{dt} = \text{Rate}_2$$
$$= k_2 E_1$$

Thus the system of differential equations modelling the process is:

$$\frac{dS}{dt} = -k_1 S E_0 + k_{-1} E_1$$

$$\frac{dE_0}{dt} = -k_1 S E_0 + k_{-1} E_1 + k_2 E_1$$

$$\frac{dE_1}{dt} = k_1 S E_0 - k_{-1} E_1 - k_2 E_1$$

$$\frac{dP}{dt} = k_2 E_1$$

The rate constants can be difficult or impossible to determine. For the purpose of seeing the behavior of the system, we give them the the values $k_1 = 10$, $k_{-1} = 1$, and $k_2 = 5$, with initial conditions $S = 1.0$ and an $E_0 = 0.08$.

Substrate/ Enzyme Reaction Model
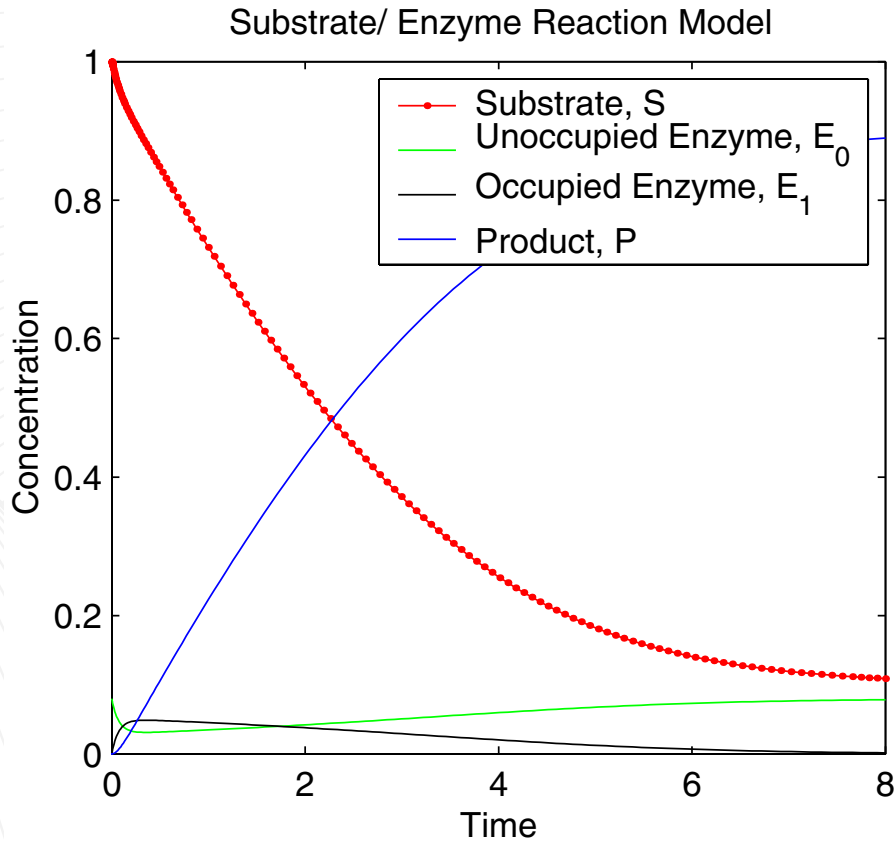
Reducing the Four Equations to Two

By adding equations and doing some algebraic manipulation, we find that

$$\frac{dS}{dt} = -k_1 S E_T + (k_{-1} + k_1 S)E_1$$
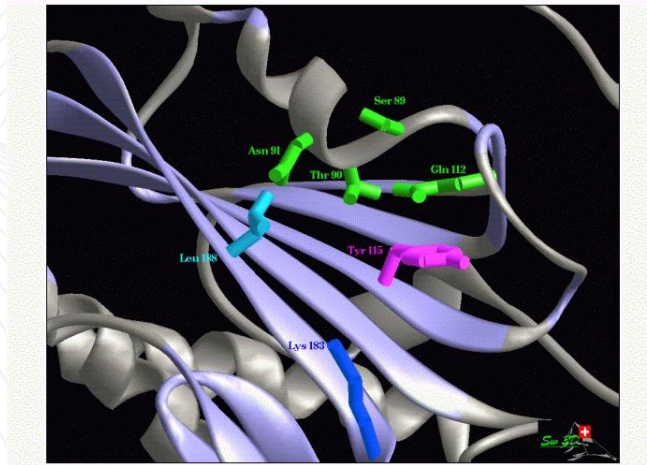
$$\frac{dE_1}{dt} = k_1 S E_T - (k_1 S + k_{-1} + k_2)E_1$$

Figure 3: A model of an enzyme

The Quasi-Steady-State Assumption

As long as $E_T \ll S$ then we can assume that $dE_1/dt \approx 0$.

$$\frac{dS}{dt} = -k_1 S E_T + (k_{-1} + k_1 S) E_1$$
$$0 \approx k_1 S E_T - (k_1 S + k_{-1} + k_2) E_1$$

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Solve dE_1/dt for E_1

$$E_1 = \frac{k_1 S E_T}{(k_{-1} + k_2 + k_1 S)}$$

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Solve dE_1/dt for E_1

$$E_1 = \frac{k_1 S E_T}{(k_{-1} + k_2 + k_1 S)}$$

Plug this into dS/dt and evaluate various steps to obtain

$$\frac{dS}{dt} = -\frac{V_{max} S}{K_M + S} \qquad \text{where } V_{max} = k_2 E_T \text{ and } K_M = \frac{k_{-1} + k_2}{k_1}.$$

$$\frac{dS}{dt} = -\frac{V_{max}S}{K_M + S} \qquad \text{where } V_{max} = k_2 E_T \text{ and } K_M = \frac{k_{-1} + k_2}{k_1}.$$

This is the Michealis-Menten enzyme equation.

- This one equation replaces the system for the modelling the substrate rate equation.

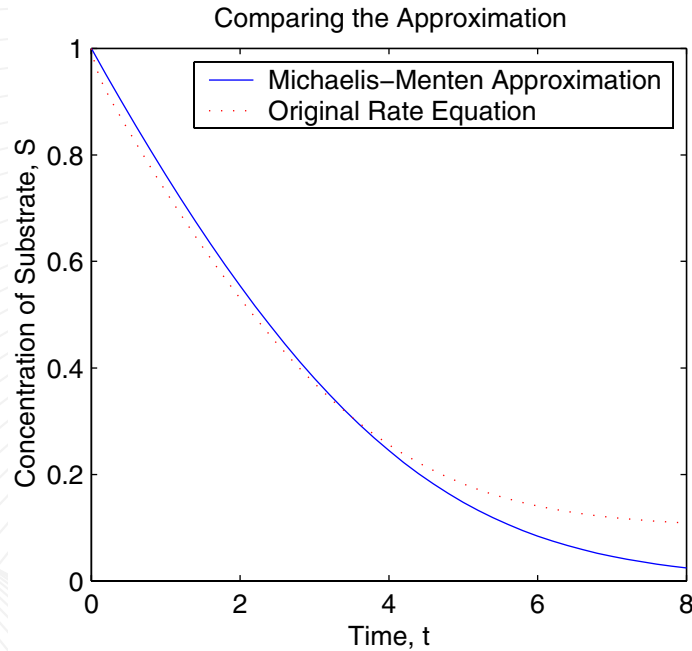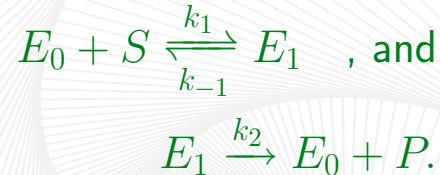- There are only two parameters, and they can both be determined experimentally.

Figure 4: The solutions for the Michaelis-Menten Equation and the Original dS/dt.

Summary

- The overall process of converting a substrate to a product is given by the following two reactions:

$$E_0 + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} E_1 \quad , \text{ and}$$

$$E_1 \xrightarrow{k_2} E_0 + P.$$

- These reactions give rise to a system of differential equations:

$$\frac{dS}{dt} = -k_1 S E_0 + k_{-1} E_1$$

$$\frac{dE_0}{dt} = -k_1 S E_0 + k_{-1} E_1 + k_2 E_1$$

$$\frac{dE_1}{dt} = k_1 S E_0 - k_{-1} E_1 - k_2 E_1$$

$$\frac{dP}{dt} = k_2 E_1.$$

- By manipulating these equations we can derive the Michaelis-Menten equation for dS/dt.

$$\frac{dS}{dt} = -\frac{V_{max}S}{K_M + S} \qquad \text{where } V_{max} = k_2 E_T \text{ and } K_M = \frac{k_{-1} + k_2}{k_1}.$$
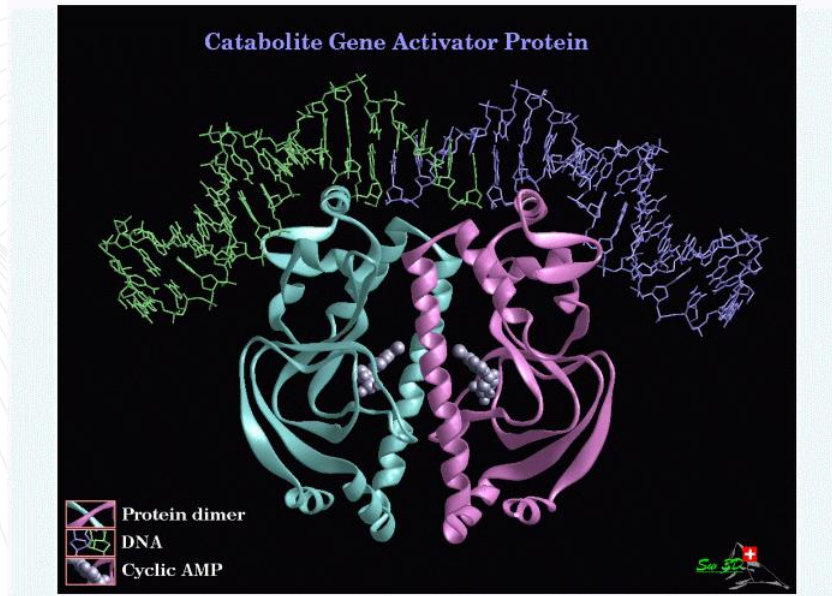
Figure 5: A model of an enzyme

References

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