Enzyme Kinetics

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Abstract

This paper consists of a mathematical derivation of the Michaelis-Menten equation, which models the rate of reaction of certain enzymatic reactions. From the kinetics of these reactions, we derive a system of four rate equations, one for each molecular compound involved, and then we make the steady-state assumption and do some algebraic manipulations to reduce the system to a single differential equation, the Michaelis-Menten equation. We show that the approximation produces fairly accurate results, and we do some some dimensional analysis to provide a more precise meaning of the approximation. Also, we explore the behavior of the model and discuss methods of determining the parameters K_{M} and $V_{\max}$.

1. Introduction

Many biological systems depend on enzymes to catalyze their chemical reactions. A simple model of an enzymatic reaction involves an enzyme binding to a substrate and causing it to react into a new product molecule. Often the exact mechanisms involved are not well understood and can involve very complicated pathways with multiple enzymes and other catalysts involved. It can be very important for scientists to be able to predict how much reacting will be done over a certain amount of time or what concentration of a certain compound would be required to have it react at a specified rate. So in the year 1913, two scientists by the names of Michaelis and Menton derived a way of modelling certain types of enzymatic reactions.

1.1. Conditions

To begin with our explanation of Michaelis-Menton enzyme kinetics, it is important to understand that it only applies when certain conditions are satisfied:

- Temperature, ionic strength, pH, and other physical conditions which affect the rate of reaction must remain constant.
- Each enzyme can act on only one other molecule at a time.
- The enzyme itself must be unchanged through the process.
- The concentration of enzyme must be much higher than the concentration of molecules they act upon

The above conditions are not unreasonable and are satisfied in many situations, both artificially in test tubes and in living systems.

1.2. Notation

We use the following system of notation throughout our paper. To keep it simple we drop the customary brackets used in representing concentrations.

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}, and k_2	rate constants

2. The Rate Equations of Enzymatic Reactions

Throughout all branches of science, rates are studied extensively–from the rate of change in the position of an object to rate of change in a population. In chemistry, rates of reaction are very important and

the study of them is called chemical kinetics. Interestingly, chemical rate equations are derived in a similar way as those of populations, and in fact we referred to the predator-prey model of an ordinary differential equations book to explain how the rate of change of chemical concentrations works.

2.1. General Rates

To derive the Michaelis-Menton equation, we first simplify the overall process into two well-defined steps, which we refer to as reactions (1a) and (1b). The first involves a substrate molecule binding to an enzyme and forming an enzyme-substrate complex, or as we will call it, an occupied enzyme.

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

For this reaction to occur successfully, an enzyme and a substrate molecule must collide with each other at just the right angle and velocity. Assuming that the enzyme and substrate are randomly distributed throughout a solution, the total number of successful contacts over any given time period will be proportional to the total possible number of contacts SE_0. Thus the rate of the reaction would also be proportional to the total possible number of contacts.

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

After an enzyme successfully binds to a substrate, it sometimes releases its hold before acting on the substrate to transform it into the product molecule. This reverse reaction occurs to a certain proportion of the occupied enzymes over any given time period. Thus the rate is proportional to the occupied enzyme concentration. This reaction is really just the opposite of the first reaction, and so the rate constant is notated as k_{-1}.

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

The second reaction is where the product comes in. For the product to be formed, an occupied enzyme must act upon its bound substrate and then release it back into solution as product. This reaction is irreversible.

$$E_1 \xrightarrow{k_2} E_0 + P \tag{1b}$$

For any given time period, a certain proportion of the occupied enzymes will complete this reaction, and so the rate will be proportional to the total concentration of occupied enzyme.

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

2.2. The Specific Rates of Reaction for Each Compound

In our chemical reactions there are four separate chemical compounds. To describe the overall process, the individual rates of change of concentration for each compound must be determined. Of course these rates depend on the rates of reaction which we just derived.

The substrate concentration will decrease as the first reaction proceeds but will also increase as the first reaction reverses itself:

$$\begin{aligned} \frac{dS}{dt} &= -\text{Rate}_1 + \text{Rate}_{-1} \\ &= -k_1 S E_0 + k_{-1} E_1 \end{aligned} \tag{2a}$$

The unoccupied enzyme concentration changes at a similar rate as that of the substrate except that it also increases as the second reaction proceeds.

$$\begin{aligned} \frac{dE_0}{dt} &= -\text{Rate}_1 + \text{Rate}_{-1} + \text{Rate}_2 \\ &= -k_1 S E_0 + k_{-1} E_1 + k_2 E_1 \end{aligned} \tag{2b}$$

The rate of change of the occupied enzyme is also made up of three individual rates. The rate that the first reaction proceeds contributes to it, the rate that the first reaction reverses decreases it, and the rate of the second reaction decreases it. As would be expected, the rates of occupied and unoccupied enzymes are the opposites of each other; since for every occupied enzyme formed, an unoccupied enzyme is lost.

$$\begin{aligned} \frac{dE_1}{dt} &= \text{Rate}_1 - \text{Rate}_{-1} - \text{Rate}_2 \\ &= k_1 S E_0 - k_{-1} E_1 - k_2 E_1 \end{aligned} \tag{2c}$$

Since the product only appears in the second equation, its rate is the same as that of the second reaction:

$$\begin{aligned}\frac{dP}{dt} &= \text{Rate}_2 \\ &= k_2 E_1 \end{aligned} \tag{2d}$$

For the purpose of qualitative analysis, we let $k_1 = 10$, $k_{-1} = 1$, and $k_2 = 5$. Using a numerical solver, we obtain the following plot of the solutions to the system of equations (2a-d) modelling the enzyme/substrate reaction. See Figure 1.

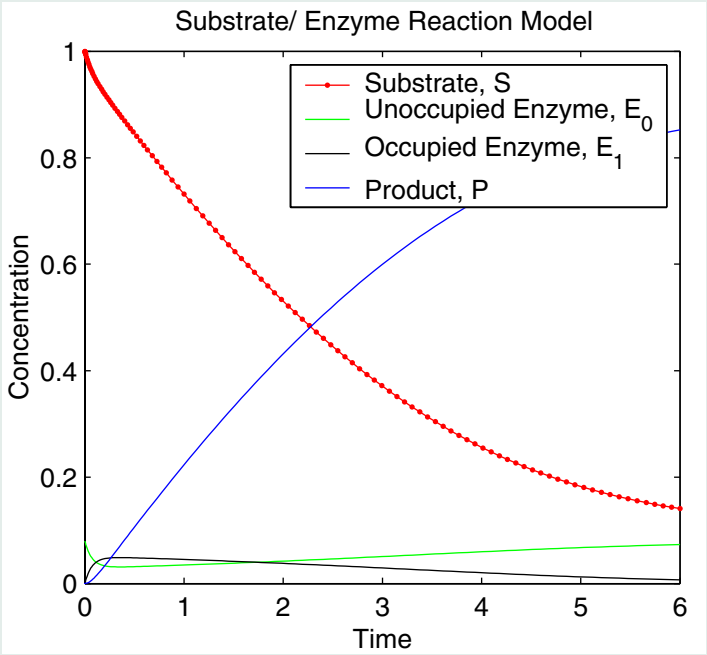

Figure 1: Plot of S, E_0, E_1, and P

Giving the rate constants arbitrary values is all well and good for a qualitative analysis of the solution's behavior. However, to actually determine these values for a real life situation would be difficult or impossible. Part of why the Michaelis-Menton equation is so useful is that it has only two parameters, both of which are easily determined.

2.3. Reducing the Four Rate Equations into Two

By adding rate equations (2b) and (2c) we get

$$\begin{aligned}\frac{dE_0}{dt} + \frac{dE_1}{dt} &= k_1 S E_0 - k_{-1} E_1 + k_2 E_1 - k_1 S E_0 + k_{-1} E_1 + k_2 E_1 \\ \frac{dE_0}{dt} + \frac{dE_1}{dt} &= 0. \end{aligned} \tag{3a}$$

Since the change of E_0 combined with the change of E_1 is 0, this implies that the total enzyme concentration remains constant.

$$E_0 + E_1 = E_T. \tag{3b}$$

Where E_T is the total concentration of both occupied and unoccupied enzyme. This would be expected since the concentration of enzyme does not change. The only thing that is seemingly changing is the concentration of the occupied and unoccupied enzymes.

By equation (3b) we can write

$$E_0 = E_T - E_1. \tag{3c}$$

Substituting (3c) into equation (2a) results in the following equation for dS/dt:

$$\begin{aligned}\frac{dS}{dt} &= -k_1 S E_0 + k_{-1} E_1 \\ &= -k_1 S(E_T - E_1) + k_{-1} E_1 \\ &= -k_1 S E_T + k_1 S E_1 + k_{-1} E_1 \\ &= -k_1 S E_T + (k_{-1} + k_1 S) E_1. \end{aligned} \tag{4a}$$

By making the same substitution for equation (2c), the following equation is derived for dE_1/dt:

$$\begin{aligned}\frac{dE_1}{dt} &= k_1S(E_T - E_1) - k_{-1}E_1 - k_2E_1 \\ &= k_1SE_T - (k_1SE_1 + k_{-1}E_1 + k_2E_1) \\ &= k_1SE_T - (k_1S + k_{-1} + k_2)E_1. \end{aligned} \tag{4b}$$

2.4. The Quasi-Steady-State Assumption

Before proceeding further with the mathematical manipulating of the equations, there is an important assumption to make. First remember that we are modelling a situation where we have enzymes and substrate suspended together in solution and the concentration of substrate is much greater than the concentration of enzyme. Thus, shortly after the enzyme and substrate are mixed together, the concentration of unoccupied enzyme will reach its maximum value. Then the enzyme will take on new substrate at approximately the same rate as the product is released. In other words the rate of change of occupied enzyme concentration is so small it can be approximated to equal zero. It is important to note however that it is just an approximation. In actuality, it is very slightly negative because as the substrate concentration decreases, the number of successful collisions between enzyme and substrate also will decrease, however slowly. With this assumption in mind, we rewrite equations (4a) and (4b)

$$\frac{dS}{dt} = -k_1SE_T + (k_{-1} + k_1S)E_1 \tag{5a}$$

$$0 \approx k_1SE_T - (k_1S + k_{-1} + k_2)E_1. \tag{5b}$$

Making this assumption hugely changes the nature of the problem. Now instead of having a system of differential equations, we have a single equation and an algebraic expression. As already mentioned, this makes the equations suspect for time near the start, and all we have given is a physical argument as to why it works at all. However, a more rigourously mathematical explanation is given under the section "Dimensional Analysis."

2.5. Combining Everything into the Michaelis-Menton Equation

Solving equation (5b) for E_1 yields

$$E_1 = \frac{k_1SE_T}{(k_{-1} + k_2 + k_1S)}.$$

Plug this result into equation (5a):

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

Distrubuting through and simplifying produces

$$\begin{aligned} &= -k_1 S E_T + \frac{(k_1 k_{-1} S E_T + k_1^2 S^2 E_T)}{k_{-1} + k_2 + k_1 S} \\ &= \frac{-k_1 S E_T (k_{-1} + k_2 + k_1 S) + (k_1 k_{-1} S E_T + k_1^2 S^2 E_T)}{(k_{-1} + k_2 + k_1 S)} \\ &= \frac{-k_1 k_{-1} S E_T - k_1 k_2 S E_T - k_1^2 S^2 E_T + k_1 k_{-1} S E_T + k_1^2 S^2 E_T}{(k_{-1} + k_2 + k_1 S)}. \end{aligned}$$

At this point it might seem as if we have a mess on our hands, but if you look closely, some nice cancellation is about to occur.

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

By dividing top and bottom by k_1, we get

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

Finally, simplify everything, and we have the Michaelis-Menten equation:

$$\frac{dS}{dt} = -\frac{V_{\max} S}{K_{\mathrm{M}} + S} \qquad \text{where } V_{\max} = k_2 E_T \text{ and } K_{\mathrm{M}} = \frac{k_{-1} + k_2}{k_1}. \tag{5c}$$

Notice that this one differential equation takes the place of the system of equations (2a-d) in modelling the substrate rate equation. There are now only two parameters, the Michaelis-Menton constant K_{M} and the maximum velocity $V_{\max}$, both of which can be determined experimentally.

Comparing the solution of this new equation for dS/dt with the original equation for dS/dt (equation 2a), shows that there is only a slight difference in the two models as long as the time span is not too extreme. See Figure 2.

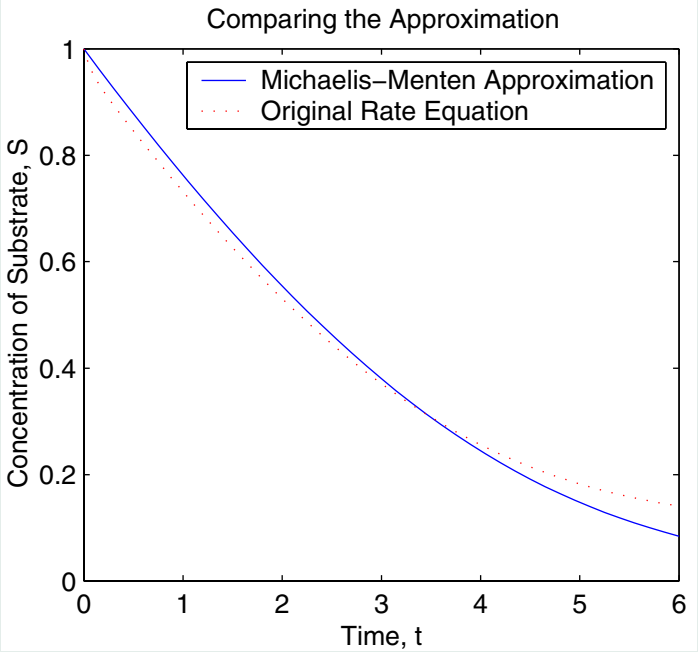

Figure 2: Comparing the Michaelis-Menton Approximation with the Derived Rate Equation.

As time goes on, an error begins to develop. This can be explained by the fact that the Michaelis-Menten equation does not take into account the fact that the occupied enzyme concentration gradually decreases, and thus it overestimates the amount of substrate that is reacted.

2.6. Behavior of dS/dt

To simplify the notation, we write dS/dt as V from here on.

It is interesting to note that there is no explicit mention of the total concentration of enzyme in the equation, which may seem strange. However, $V_{\max}$ depends on E_T, the total concentration of occupied and unoccupied enzyme, so an increase in E_T will increase $V_{\max}$, and thus increase V. Also, increasing the substrate concentration will increase the amount of contacts between substrate and enzyme so that the reaction will proceed faster. This is seen from the equation by taking the derivative with respect to S.

$$\begin{aligned}\frac{dV}{dS} &= -\frac{(K_{\mathrm{M}}+S)V_{\max}-V_{\max}S}{(K_{\mathrm{M}}+S)^2}\\ &= -\frac{K_{\mathrm{M}}V_{\max}}{(K_{\mathrm{M}}+S)^2}\end{aligned}$$

Since the derivative is negative, V will become increasingly negative if the substrate concentration is increased. The rate of reaction can only go so fast however, before a point is reached where the enzyme is working at its maximum capacity. Then if the substrate concentration were to be increased further the rate of reaction will not change. This is the maximum velocity, $V_{\max}$. This can be seen from the Michaelis-Menton equation if we let the substrate concentration become very large (take the limit as $S \to \infty$):

$$\begin{aligned}\lim_{S\to\infty} V &= \lim_{S\to\infty} -\frac{V_{\max}S}{K_{\mathrm{M}}+S}\\ &= \lim_{S\to\infty} -\frac{\frac{1}{S}(V_{\max}S)}{\frac{1}{S}(K_{\mathrm{M}}+S)}\\ &= \lim_{S\to\infty} -\frac{V_{\max}}{\frac{K_{\mathrm{M}}}{S}+1}\\ &= -\frac{V_{\max}}{0+1}\\ &= -V_{\max}\end{aligned}$$

2.7. Determining V_{max} and K_M

By doing a relatively simple experiment, one can get sample data for V and S. The values of $V_{\max}$ and K_M can be roughly approximated right from a plot of V vs S, without any calculations necessary. $V_{\max}$ is the value that V approaches asymptotically. Finding K_M, however, is a little more subtle. It turns out that $S = K_M$ at the point that $V = V_{\max}/2$. So by drawing a line from $V_{\max}/2$ over to the curve and finding the value of S directly beneath we have K_M. See Figure 3. This can be seen from the equation by replacing V with $V_{\max}/2$:

$$\frac{1}{2}V_{\max} = -\frac{V_{\max}S}{K_M + S}$$
$$K_M + S = \frac{-V_{\max}S}{\frac{1}{2}V_{\max}}$$
$$K_M = S$$

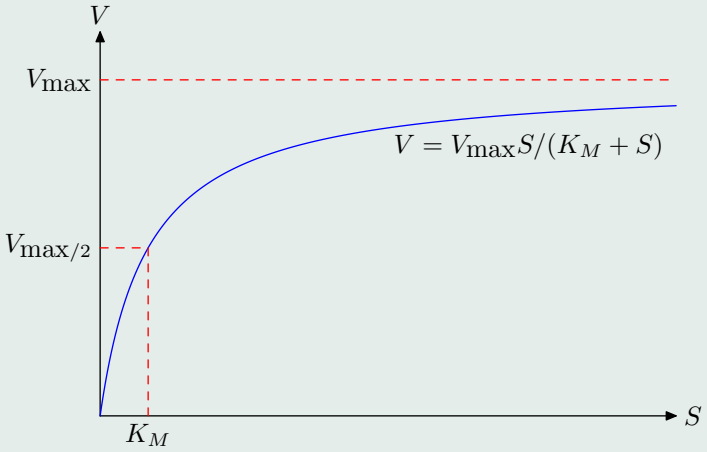

Figure 3: Substrate Concentration vs. Rate of Reaction

V approaches $V_{\max}$ very slowly so that it is extremely difficult to get experimental data that clearly

shows what the value $V_{\max}$ is, and consequently what K_{M} is. Hans Lineweaver and Dean Burk discovered a better way of plotting the data which makes it possible to get these values more accurately. Their method is called the Lineweaver-Burk or double reciprocal plot. It is derived by plotting $1/V$ versus $1/S$. See Figure 4:

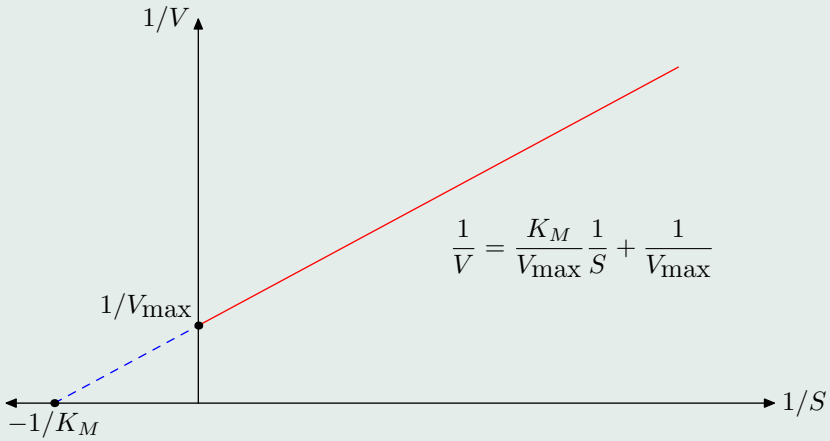

Figure 4: Inverse Substrate Concentration vs. Inverse Rate of Reaction

To understand how it works, invert both sides of the Michaelis-Menton equation:

$$\begin{aligned}\frac{1}{V} &= \frac{1}{\frac{V_{\max}S}{K_{\mathrm{M}}+S}} \\ &= \frac{K_{\mathrm{M}}+S}{V_{\max}S} \\ &= \frac{K_{\mathrm{M}}}{V_{\max}S} + \frac{S}{V_{\max}S} \\ &= \frac{K_{\mathrm{M}}}{V_{\max}}\frac{1}{S} + \frac{1}{V_{\max}}\end{aligned}$$

This equation gives a linear relationship between $1/V$ and $1/S$. The slope is equal to $K_{\mathrm{M}}/V_{\max}$, where the y intercept is equal to $1/V_{\max}$, and the x intercept is equal to $-1/K_{\mathrm{M}}$. There are some problems

with the Lineweaver-Burk plot though. To find the x and y intercepts, the line must be extrapolated to negative and infinite concentrations. In doing so, errors will arise. However, this method gives fairly accurate results, without any complicated calculations. There are other ways of analyzing the data that are more complicated but give more precise results, such as the Eadie-Hofstee equation, the Hanes-Woolf equation and the Eisenthal and Cornish-Bowden equation.

3. Dimensional Analysis

As previously mentioned, the steady state assumption used in deriving the Michaelis-Menten equation does not apply at the moment the enzyme and substrate first come in contact and immediately following. During this time, the enzyme must go from being completely unoccupied to reaching its maximum occupancy. Clearly the rate of change of the unoccupied enzyme concentration cannot be approximated to equal zero. To better explain the behavior of the rates requires that we simplify the equations using dimensional analysis.

To derive the Michaelis-Menton equation, we used two rate equations (4a,b) one for substrate and one for occupied enzyme concentration:

$$\frac{dS}{dt} = -k_1 E_T S + (k_{-1} + k_1 S) E_1 \tag{4a}$$

$$\frac{dE_1}{dt} = k_1 E_T S - (k_{-1} + k_2 + k_1 S) E_1 \tag{4b}$$

Before proceeding with dimensional analysis, it is important to understand that the variables and parameters of the rate equations come from experimental measurements, usually in conventional units. However the choice of units is completely arbitrary. For example, the substrate concentration could be given in any of the following ways:

$$\begin{aligned} S &= 100 \quad \mu M \\ &= 1 \times 10^{-4} M \\ &= x \quad m \\ &= y \quad \text{ppm} \\ &= S^* \hat{S}. \end{aligned}$$

In other words, the original variable can be written many ways, but they all are in the form of $S^*\hat{S}$, where S^* is simply a variable with no dimensions and depends on the scale being used, and $\hat{S}$ is a constant that carries the physical dimensions. The three variables in our equations can be written then as follows:

$$S = S^*\hat{S}$$
$$E_1 = E_1^*\hat{E}_1$$
$$t = t^*\tau$$

The first step in changing the rate equations into dimensionless form is to substitute in the above expressions into equations (4a) and (4b).

$$\frac{d(S^*\hat{S})}{d(t^*\tau)} = -k_1 E_T S^*\hat{S} + (k_{-1} + k_1 S^*\hat{S})E_1^*\hat{E}_1$$
$$\frac{d(E_1^*\hat{E}_1)}{d(t^*\tau)} = k_1 E_T S^*\hat{S} - (k_{-1} + k_2 + k_1 S^*\hat{S})E_1^*\hat{E}_1$$

Since $\hat{S}$, $\hat{E}_1$, and τ are constants, they can be pulled out in front of the differential.

$$\frac{\hat{S}}{\tau}\frac{dS^*}{dt^*} = -k_1 r S^*\hat{S} + (k_{-1} + k_1 S^*\hat{S})E_1^*\hat{E}_1 \quad (7a)$$
$$\frac{\hat{E}_1}{\tau}\frac{dE_1^*}{dt^*} = k_1 E_T S^*\hat{S} - (k_{-1} + k_2 + k_1 S^*\hat{S})E_1^*\hat{E}_1 \quad (7b)$$

Let us first focus on equation (7a). Multiplying both sides by $\tau/\hat{S}$ eliminates the constants on the LHS.

$$\begin{aligned}\frac{\tau}{\hat{S}}\frac{\hat{S}}{\tau}\frac{dS^*}{dt^*} &= \frac{\tau}{\hat{S}}[-k_1 r S^*\hat{S} + (k_{-1} + k_1 S^*\hat{S})E_1^*\hat{E}_1] \\ &= \frac{\tau}{\hat{S}}(-k_1 r S^*\hat{S}) + \frac{\tilde{\tau}}{\hat{S}}(k_{-1} + k_1 S^*\hat{S})E_1^*\hat{E}_1 \\ &= -k_1\tau r S^* + (\frac{k_{-1}\tau}{\hat{S}} + k_1\tau S^*)E_1^*\hat{E}_1\end{aligned}$$

Thus,

$$\frac{dS^*}{dt^*} = -k_1 E_T S^* \tau + \left(\frac{k_{-1}\tau}{\hat{S}} + k_1 S^* \tau \right) E_1^* \hat{E}_1 \tag{8a}$$

Now we turn our attention to equation (7b) and free the LHS of constants

$$\frac{\hat{E}_1}{\tau} \frac{dE_1^*}{dt^*} = k_1 E_T S^* \hat{S} - (k_{-1} + k_2 + k_1 S^* \hat{S}) E_1^* \hat{E}_1$$

Multiplying both sides by $\tau/\hat{E}_1$ eliminates the constants from the LHS.

$$\begin{aligned} \frac{\tau}{\hat{E}_1} \frac{\hat{E}_1}{\tau} \frac{dE_1^*}{dt^*} &= \frac{\tau}{\hat{E}_1} [k_1 E_T S^* \hat{S} - (k_{-1} + k_2 + k_1 S^* \hat{S}) E_1^* \hat{E}_1] \\ \frac{dE_1^*}{dt^*} &= \frac{\tau}{\hat{E}_1} (k_1 E_T S^* \hat{S}) - \frac{\tau}{\hat{E}_1} (k_{-1} + k_2 + k_1 S^* \hat{S}) E_1^* \hat{E}_1 \\ &= \frac{\tau}{\hat{E}_1} (k_1 E_T S^* \hat{S}) - ((k_{-1} + k_2)\tau + k_1 S^* \tau) E_1^* \end{aligned}$$

Thus,

$$\frac{dE_1^*}{dt^*} = \frac{k_1 E_T S^* \hat{S} \tau}{\hat{E}_1} - ((k_{-1} + k_2)\tau + k_1 S^* \hat{S} \tau) E_1^*. \tag{8b}$$

Equations (8a) and (8b) will be referred to several times from here on as we choose certain scalings for τ, $\hat{S}$, and $\hat{E}_1$.

3.1. Scaling time with $\tau = 1/k_1 E_T$

Notice that $\hat{S}$, $\hat{E}_1$, and τ are unspecified constants, and can be set to equal anything and the scalar multiples S^*, E_1^*, and t^* will just adjust accordingly. By choosing the following values, several parameters cancel out and the equations become much simpler:

$$\tau = \frac{1}{k_1 E_T} \qquad \hat{E}_1 = E_T \qquad \hat{S} = S_0$$

Next we will use these scales in equations (8a) and (8b). The scaling for equation (8a) is as follows:

$$\begin{aligned}\frac{dS^*}{dt^*} &= -k_1 E_T S^* \tau + \left(\frac{k_{-1}\tau}{\hat{S}} + k_1 S^* \tau\right) E_1^* \hat{E}_1 \\ &= -\frac{k_1 E_T S^*}{k_1 E_T} + \left(\frac{k_{-1}}{k_1 E_T S_0} + \frac{k_1 S^*}{k_1 E_T}\right) E_1^* E_T\end{aligned}$$

Thus, by distributing the E_1^*, we obtain

$$\frac{dS^*}{dt^*} = -S^* + \left(\frac{k_{-1}}{k_1 S_0} + S^*\right) E_1^*. \tag{9a}$$

We now turn our attention to equation (8b) and applying a similar derivation.

$$\begin{aligned}\frac{dE_1^*}{dt^*} &= \frac{k_1 E_T S^* \hat{S}\tau}{\hat{E}_1} - ((k_{-1} + k_2)\tau + k_1 S^* \hat{S}\tau) E_1^* \\ &= \frac{k_1 E_T S^* S_0}{k_1 E_T^2} - \left(\frac{k_{-1} + k_2}{k_1 E_T} + \frac{k_1 S^* S_0}{k_1 E_T}\right) E_1^*\end{aligned}$$

By factoring out a S_0/E_T from the second term, we find

$$\frac{dE_1^*}{dt^*} = \frac{S_0}{E_T} S^* - \frac{S_0}{E_T}\left(\frac{k_{-1} + k_2}{k_1 S_0} + S^*\right) E_1^*. \tag{9b}$$

To further simplify things, the remaining constants can be combined together into new constants:

$$\epsilon = \frac{E_T}{S_0} \qquad \kappa = \frac{k_{-1} + k_2}{k_1 S_0} \qquad \lambda = \frac{k_2}{k_1 S_0}$$

We now evaluate equation (9a) and (9b) using these scalars of combined constants. We first evaluate equation (9a).

$$\begin{aligned}\frac{dS^*}{dt^*} &= -S^* + \left(\frac{k_{-1}}{k_1 S_0} + S^*\right) E_1^* \\ &= -S^* + (\kappa - \lambda + S^*) E_1^*\end{aligned}$$

Next we evaluate equation (9b).

$$\begin{aligned}\frac{dE_1^*}{dt^*} &= \frac{S_0}{E_T} S^* - \frac{S_0}{E_T}\left(\frac{k_{-1} + k_2}{k_1 S_0} + S^*\right) E_1^* \\ &= \frac{S^*}{\epsilon} - \frac{E_1^*}{\epsilon}(\kappa + S^*) \\ &= \frac{1}{\epsilon}\left[S^* - E_1^*(\kappa + S^*)\right]\end{aligned}$$

Multiplying both sides by ϵ,

$$\epsilon \frac{dE_1^*}{dt^*} = S^* - (\kappa + S^*) E_1^*$$

Now the equations are completely dimensionless, and the number of parameters has been reduced from five to three. Most importantly however, note that $\epsilon\, dS^*/dt^* \approx 0$. This is because we defined ϵ to equal E_T/S_0, and one of the conditions specified at the beginning of this paper is that $S_0 \gg E_T$. So dimensional analysis shows that with time scales on the order of $\tau = 1/(k_1 E_T)$, the process of a substrate being acted upon by an enzyme can indeed be modelled by a differential equation coupled with an algebraic equation:

$$\begin{aligned}\frac{dS^*}{dt^*} &= -S^* + (\kappa - \lambda + S^*) E_1^* \\ 0 &= S^* - (\kappa + S^*) E_1^*\end{aligned}$$

From here we could solve for E_1^* and plug it into the equation for dS^*/dt^*, much like we did in deriving the Michaelis-Menton equation. However, our intent is just to show that the quasi-steady-state approximation is justified mathematically, not just through physical arguments.

4. Conclusion

Since enzymatic reactions are so important to biological chemical reactions, it is of great interest to be able to model them. By use of the study of chemical kinetics, it is possible derive rate equations for the steps involved in an enzymatic reaction. These rate equations are differential equations and can be used to model the concentrations of each compound in the system. However, this system of differential equations is hard to determine experimentally because of the difficulty of determining the rate constants. By use of the Quasi-Steady-State Assumption, we can turn our system of differential equations into the Michaelis-Menten enzyme equation. Many benefits stem from this transition. One benefit is the fact that it is now easy to determine the constants related to the enzyme equations. However, how do we know the Quasi-Steady-State Assumption is valid? It seems reasonable from a physical argument. By use of dimensional analysis, we can give a more rigorous mathematical argument for the Quasi-Steady-State Assumption. The Michaelis-Menten enzyme equation is very important in the study of cellular systems by allowing a model that can be easily derived through experimentation.

References

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