

Section 9.5

Rates of Chemical Reactions

Stoichiometric rules are not sufficient to determine the equilibrium position of a reversible chemical reaction; but adding reaction rate principles makes the calculation possible. Primarily, rate equations were designed to foretell the speed of specific reactions, and, in this capacity, they predict an exponentially decaying speed, as reactants are consumed, characterized by the reaction's rate constant. But in fact, the equilibrium position of a reversible reaction is reached when the rate of formation equals the rate of dissociation. Therefore equilibrium positions, as well as reaction rates, are determined by a combination of the forward and reverse rate constants.

Irreversible (uni-directional) reactions are limited by the first reactant to be exhausted.

Consider the irreversible bimolecular reaction



in which one molecule each of reactants A and B chemically combine to make one molecule each of products X and Y . It follows that the rate of disappearance of reactants equals the rate of appearance of products. The *Conservation of Mass* principle takes the form

$$\frac{dX}{dt} = \frac{dY}{dt} = -\frac{dA}{dt} = -\frac{dB}{dt}.$$

If M_0 denotes the initial number of molecules of species M , by integrating each member of this chain of equalities from time 0 to time t , we get

$$X(t) - X_0 = Y(t) - Y_0 = -A(t) + A_0 = -B(t) + B_0. \quad (9.5.2)$$

Equation (9.5.2) gives the amount of each species in terms of the others, so if any one of them is known, then they all are. But in order to know the amount of any one of them, we must know how fast the reaction occurs. This is answered by the *Law of Mass Action* (due to Lotka): The rate of at which two or more chemical species simultaneously combine is proportional to the product of their concentrations. Letting $[M]$ denote the concentration of species M , the mass action principle states that the rate at which product is formed is equal to

$$k[A][B] \quad (9.5.3)$$

where the constant of proportionality k is characteristic of the reaction.

So far our considerations have been completely general, but now we must make some assumptions about where the reaction is occurring. We suppose this to occur in a closed reaction vessel, such as a beaker with a fixed amount of water. In this case, concentration is the number of molecules divided by, for all species, the same fixed volume of medium.¹² We allow the possibility that one or more of the products, X or Y , be insoluble and precipitate out of solution. This is one of the main reasons that a bimolecular reaction may be irreversible. For such an insoluble species, "concentration" means the ratio of its number of molecules over the volume of the medium, even though it is not dissolved. While a product may precipitate out without disturbing the reaction, the reactants must remain dissolved. We now use the notation $m(t)$, to mean this extended notion of concentration of species M .

Combining the mass action principle with equation (9.5.2) we get

$$\begin{aligned} \frac{dx}{dt} &= kab \\ &= k(a_0 + x_0 - x)(b_0 + x_0 - x) \end{aligned} \quad (9.5.4)$$

with initial value $x(0) = x_0$. The stationary points of equation (9.5.4) are given by setting the right-hand side to zero and solving to get (see Section 2.4)

$$x = a_0 + x_0, \quad \text{or} \quad x = b_0 + x_0. \quad (9.5.5)$$

The first of these says that the amount of X will be its original amount plus an amount equal to the original amount of A . In other words, A will be exhausted. The second equation says the reaction stops when B is exhausted.

Suppose, just for argument, that $a_0 < b_0$. Then also $a_0 + x_0 < b_0 + x_0$. While $x(t) < a_0 + x_0$, the right-hand side of equation (9.5.4) is positive, therefore the derivative is positive, so x increases. This continues until x asymptotically

¹²By contrast, for an open reaction vessel, such as the heart or a chemostat, the concentrations are determined by that of the inflowing reactants.

reaches $a_0 + x_0$, whereupon the reaction stops. The progression of the reaction as a function of time is found by solving equation (9.5.4) which is variables separable:

$$\frac{dx}{(a_0 + x_0 - x)(b_0 + x_0 - x)} = k dt.$$

Note the similarity of this equation to the Lotka–Voterra system of Section 4.4. The left-hand side can be written as the sum of simpler fractions

$$\begin{aligned} \frac{1}{(a_0 + x_0 - x)(b_0 + x_0 - x)} &= \frac{1}{b_0 - a_0} \frac{1}{a_0 + x_0 - x} \\ &\quad - \frac{1}{b_0 - a_0} \frac{1}{b_0 + x_0 - x}. \end{aligned}$$

Thus equation (9.5.4) may be rewritten as

$$\left[\frac{1}{a_0 + x_0 - x} - \frac{1}{b_0 + x_0 - x} \right] dx = (b_0 - a_0)k dt.$$

Integrating gives the solution

$$\begin{aligned} -\ln(a_0 + x_0 - x) + \ln(b_0 + x_0 - x) &= (b_0 - a_0)kt + q \\ \ln\left(\frac{b_0 + x_0 - x}{a_0 + x_0 - x}\right) &= (b_0 - a_0)kt + q, \end{aligned}$$

where q is the constant of integration. Now this may be solved for in terms of x ,

$$x = \frac{(a_0 + x_0)Qe^{(b_0 - a_0)kt} - (b_0 + x_0)}{Qe^{(b_0 - a_0)kt} - 1}, \quad (9.5.6)$$

where $Q = e^q$ is a constant. This equation is graphed in Figure 9.5.1. For the purpose of drawing the figure, we choose the constants, solve the resulting differential equation and draw its graph as follows:

```
> k:=1; a0:=2; b0:=3; x0:=1/2;
> dsolve({diff(x(t),t)=k*(a0+x0-x(t))*(b0+x0-x(t)),x(0)=x0}, {x(t)});
> simplify(");
> x:=unapply(rhs("),t);
> plot([t,x(t),t=0..4],t=-1..3,tickmarks=[3,3],labels=['t','x(t)]);
```

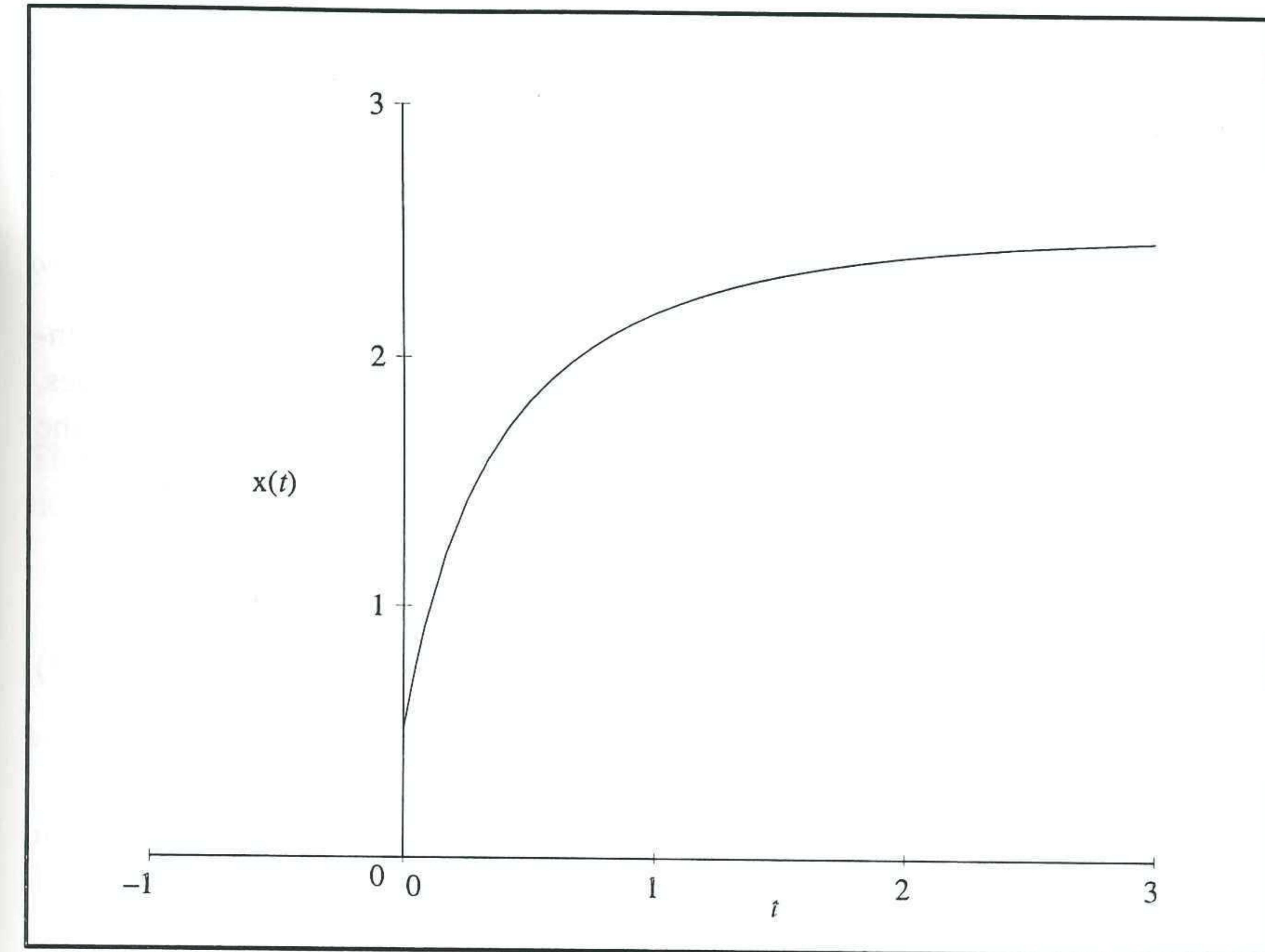


Figure 9.5.1 A typical solution to equation (9.5.4).

The result is

$$x(t) = \frac{1}{2} \frac{-15 + 14e^{-t}}{-3 + 2e^{-t}}.$$

Example: Suppose 2 moles of silver nitrate (AgNO_3) are mixed with 3 moles of hydrochloric acid (HCl). A white precipitate, silver chloride, is formed, and the reaction tends to completion,



From above, asymptotically, the reaction stops when the 2 moles of silver nitrate have reacted, leaving 2 moles of silver chloride precipitate and 1 mole of hydrochloric acid unreacted.

Kinetics for reversible reactions work the same way.

Now assume reaction (9.5.1) is reversible



with the reverse reaction also being bimolecular. This time there is a backward rate constant, k_{-1} as well as a forward one, k_1 . From the mass action principle applied to the reverse reaction, we have

$$\text{rate of conversion of } X + Y = k_{-1}[X][Y].$$

Under normal circumstances, the forward and backward reactions take place independently of each other and consequently the net rate of change of any species, say X , is just the sum of the effects of each reaction separately. It follows that the net rate of change in X is given by

$$\begin{aligned} \frac{dx}{dt} &= (\text{conversion rate of } A+B) - (\text{conversion rate of } X+Y) \\ &= k_1[A][B] - k_{-1}[X][Y], \\ &= k_1(a_0 + x_0 - x)(b_0 + x_0 - x) - k_{-1}x(y_0 - x_0 + x), \end{aligned} \quad (9.5.8)$$

where equation (9.5.2) has been used in the last line. Circumstances under which the forward and backward reactions are not independent include precipitation of one of the species, as we have seen above. Another occurs when one of the reactions is highly exothermic. In that case, conditions of the reaction radically change, such as the temperature.

The analysis of equation (9.5.8) goes very much like that of equation (9.5.4). The stationary points are given as the solutions of the $\frac{dx}{dt} = 0$ equation

$$\begin{aligned} 0 &= k_1(a_0 + x_0 - x)(b_0 + x_0 - x) - k_{-1}x(y_0 - x_0 + x) \\ &= (k_1 - k_{-1})x^2 - (k_1(a_0 + b_0 + 2x_0) + k_{-1}(y_0 - x_0))x \\ &\quad + k_1(a_0 + x_0)(b_0 + x_0) \end{aligned} \quad (9.5.9)$$

As one can see, if $k_1 \neq k_{-1}$, this is a quadratic equation and therefore has two roots, say $x = \alpha$, and $x = \beta$, which may be found using the quadratic formula, $\frac{1}{2a}(-b \pm \sqrt{b^2 - 4ac})$. The right-hand side of equation (9.5.8) thus factors into the linear factors

$$\frac{dx}{dt} = (k_1 - k_{-1})(x - \alpha)(x - \beta). \quad (9.5.10)$$

Again, just as above, this variable separable differential equation is easily solved but the nature of the solution depends on whether the roots are real or complex, equal or distinct. To decide about that, we must examine the discriminant of the quadratic formula, $b^2 - 4ac$. By direct substitution of the coefficients from equation (9.5.9) into the discriminant and then simplifying, we get

$$b^2 - 4ac = k_1^2(a_0 - b_0)^2 + 2k_1k_{-1}(a_0 + b_0 + 2x_0)(y_0 - x_0) + k_{-1}^2(y_0 - x_0)^2. \quad (9.5.11)$$

The first and last terms are squares and so are positive (or zero). We see that, if $y_0 \geq x_0$, then the discriminant is always positive or zero and the two roots are real. Since X was an arbitrary choice, we can always arrange that $y_0 \geq x_0$, so we assume this is so.

Unless the initial concentrations are equal, $a_0 = b_0$ and $y_0 = x_0$, the roots will be distinct. We assume without loss of generality that

$$\alpha < \beta. \quad (9.5.12)$$

Then, in a similar way to the derivation of equation (9.5.6), the solution of equation (9.5.10) is

$$\ln\left(\frac{x - \beta}{x - \alpha}\right) = (\beta - \alpha)(k_1 - k_{-1})t + q,$$

where q is the constant of integration. This may be solved in terms of x ,

$$x = \frac{\beta - Qe^{rt}}{1 - Qe^{rt}} \quad (9.5.13)$$

where Q is a constant and

$$r = (\beta - \alpha)(k_1 - k_{-1}).$$

If the discriminant is zero, then $\beta = \alpha$ and in that case the solution is

$$\frac{-1}{x - \alpha} = (k_1 - k_{-1})t + q,$$

or

$$x = \alpha - \frac{1}{(k_1 - k_{-1})t + q}$$

where q is again the constant of integration.

Exercises

- Suppose that $A + B \rightarrow C$, that the initial concentrations of A , B , and C are $1/2$, $1/3$, and 0 , respectively, and that the rate constant is k .
 - Show that this leads to the differential equation in $z(t) = [C(t)]$ given by

$$z' = k \left(\frac{1}{2} - z \right) \left(\frac{1}{3} - z \right), \quad z(0) = 0.$$

- Solve this equation.

c. Show that the corresponding equation for $x(t) = [A(t)]$ is

$$x' = kx \left(\frac{1}{6} - x \right), \quad x(0) = \frac{1}{2}.$$

- d. Solve this equation. Show by adding the solutions x and z that the sum is constant.
e. At what time is 90% of the steady state concentration of C achieved?
f. Suppose that k is increased 10%. Now rework part e.
2. Suppose that $A + B \leftrightarrow C + D$ is a reversible reaction, the initial concentrations of A and B are $4/10$ and $5/10$, respectively, and that the initial concentrations of C and D are 0 . Take $k_1 = 10$ and $k_{-1} = 5/2$.
a. Show that this leads to the differential equation

$$y' = 10(0.4 - y)(0.5 - y) - \frac{5y^2}{2}, \quad y(0) = 0.$$

- b. What is the equilibrium level of $[C]$? Draw two graphs, one where $k_{-1} = 5/2$ and one where $k_{-1} = 5/4$.

Section 9.6

Enzyme Kinetics

Enzymes serve to catalyze reactions in living systems, enabling complex chemical transformations to occur at moderate temperatures, many times faster than their uncatalyzed counterparts. Proteins, serving as the catalysts, are first used and then regenerated in a multi-step process. Overall, the simplest enzyme-catalyzed reactions transform the enzyme's specific substrate into product, possibly with the release of a by-product. Referred to as enzyme saturation, these reactions are typically rate limited by the amount of enzyme itself. The degree to which saturation occurs relative to substrate concentration is quantified by the Michaelis–Menten constant of the enzyme-substrate pair.

Enzyme catalyzed reactions are normally rate-limited by enzyme saturation.

The importance of enzyme catalyzed reactions along with a general description of the biochemical principles of enzyme catalysis was given in Section 9.4. Here we will consider an enzyme, E , which acts on a single substrate, S , and converts it to an alternate form which is regarded as the product P . The enzyme performs this function by temporarily forming an enzyme-substrate complex, C , which then decomposes into product plus enzyme:



The regenerated enzyme is then available to repeat the process.¹³ Here we will work through the mathematics of enzyme kinetics. The general principles of chemical kinetics discussed in the previous section apply to enzyme kinetics as well. However, due to the typically small amount of enzyme compared to substrate, the conversion rate of substrate to product is limited when the enzyme becomes *saturated* with substrate as enzyme-substrate complex.

As in the previous section, we let m denote the concentration of species M . The forward and reverse rate constants for the first reaction will be denoted k_1 and k_{-1} respectively while the rate constant for the second will be taken as k_2 . The rate equations corresponding to the reactions (9.6.1) are¹⁴

$$\begin{aligned} \frac{dc}{dt} &= k_1 es - k_{-1} c - k_2 c \\ \frac{ds}{dt} &= -k_1 es + k_{-1} c \\ \frac{de}{dt} &= -k_1 es + k_{-1} c + k_2 c \\ \frac{dp}{dt} &= k_2 c. \end{aligned} \quad (9.6.2)$$

Note that complex C is both formed and decomposed by the first reaction and decomposed by the second. Similarly, enzyme E is decomposed and formed by the first reaction and formed by the second. The first three equations are independent of the formation of product P , and so, for the present, we can ignore the last equation. As before, we denote by subscript 0 the initial concentrations of the various reactants. In particular, e_0 is the initial, and therefore total, amount of enzyme since it is neither created nor destroyed in the process.

By adding the first and third equation of system (9.6.2) we get

$$\frac{dc}{dt} + \frac{de}{dt} = 0.$$

Integrating this and using the initial condition that $c_0 = 0$, we get

$$e = e_0 - c. \quad (9.6.3)$$

We may use this to eliminate e from system (9.6.2) and get the following reduced system:

$$\begin{aligned} \frac{dc}{dt} &= k_1 s(e_0 - c) - (k_{-1} + k_2)c \\ \frac{ds}{dt} &= -k_1 s(e_0 - c) + k_{-1}c. \end{aligned} \quad (9.6.4)$$

¹³Compare this scheme to Figure 9.4.3. $S+E$ constitutes the initial state, C is the transition state and $P+E$ is the final state.

¹⁴The units of k_1 are different than those of k_{-1} and k_2 since the former is a bimolecular constant while the latter are uni-molecular.

In Figure 9.6.1 we show some solutions of this system of differential equation.

For the purpose of drawing the figure, we take the constants to be

```
> k1:=1/10; km1:=1/10; k2:=1/10; e0:=4/10; (km1+k2)/k1;
```

The equations are non-linear and cannot be solved in closed form. Consequently we use numerical methods to draw these graphs. It should be observed that the level S, graphed as $s(t)$, drops continuously toward zero. Also, the intermediate substrate C, graphed as $c(t)$, starts at zero, rises to a positive level, and gradually settles back to zero. In the exercises we establish that this behavior is to be expected.

```
> with(plots): with(DEtools):
> enz:=[diff(c(t),t)=k1*s(t)*(e0-c(t))-(km1+k2)*c(t),
       diff(s(t),t)=-k1*s(t)*(e0-c(t)) + km1*c(t)];
> J:=DEplot2(enz,[c,s],0..100,[0,0,8/10],stepsize=1,
   scene=[t,s],labels=['t', ' ']);
> K:=DEplot2(enz,[c,s],0..100,[0,0,8/10],stepsize=1,
   scene=[t,c],labels=['t', ' ']);
> L:=textplot({[75,0.3,'s(t)'],[60,0.1,'c(t)']});
> display({J,K,L});
```

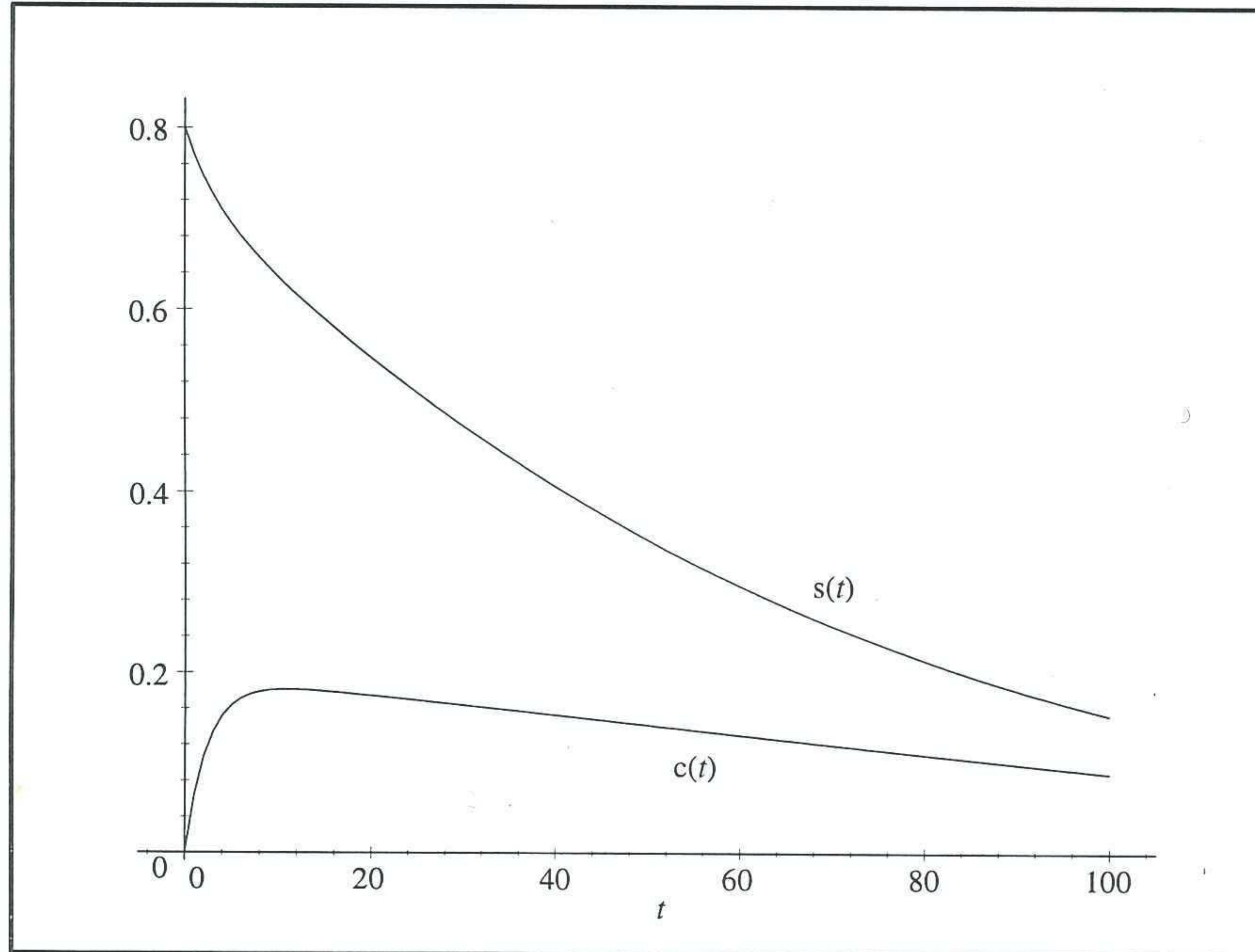


Figure 9.6.1 Solutions for Equation (9.6.2)

In the exercises we provide techniques to draw what may be a more interesting graph: Figure 9.6.2. In particular, we draw graphs of $s(t)$, $p(t)$, and $e(t)$. The first two of these are, in fact, the most interesting as they demonstrate how much of S is left and how much of P has been formed. The addition of a graph for $e(t)$ illustrates that during the intermediate phase, some of the enzyme is tied up in the enzyme-substrate complex, but as the reaction approaches equilibrium, the value of $e(t)$ returns to its original value.

From Figure 9.6.1, notice that the concentration of complex rises to a relatively invariant (“effective”) level which we denote as c_{Eff} . This is found by setting $\frac{dc}{dt} = 0$ in system (9.6.4) and solving for c ,

$$0 = k_1 s(e_0 - c) - (k_{-1} + k_2)c$$

or

$$s(e_0 - c) = \frac{k_{-1} + k_2}{k_1}c.$$

The combination k_M of rate constants

$$k_M = \frac{k_{-1} + k_2}{k_1} \quad (9.6.5)$$

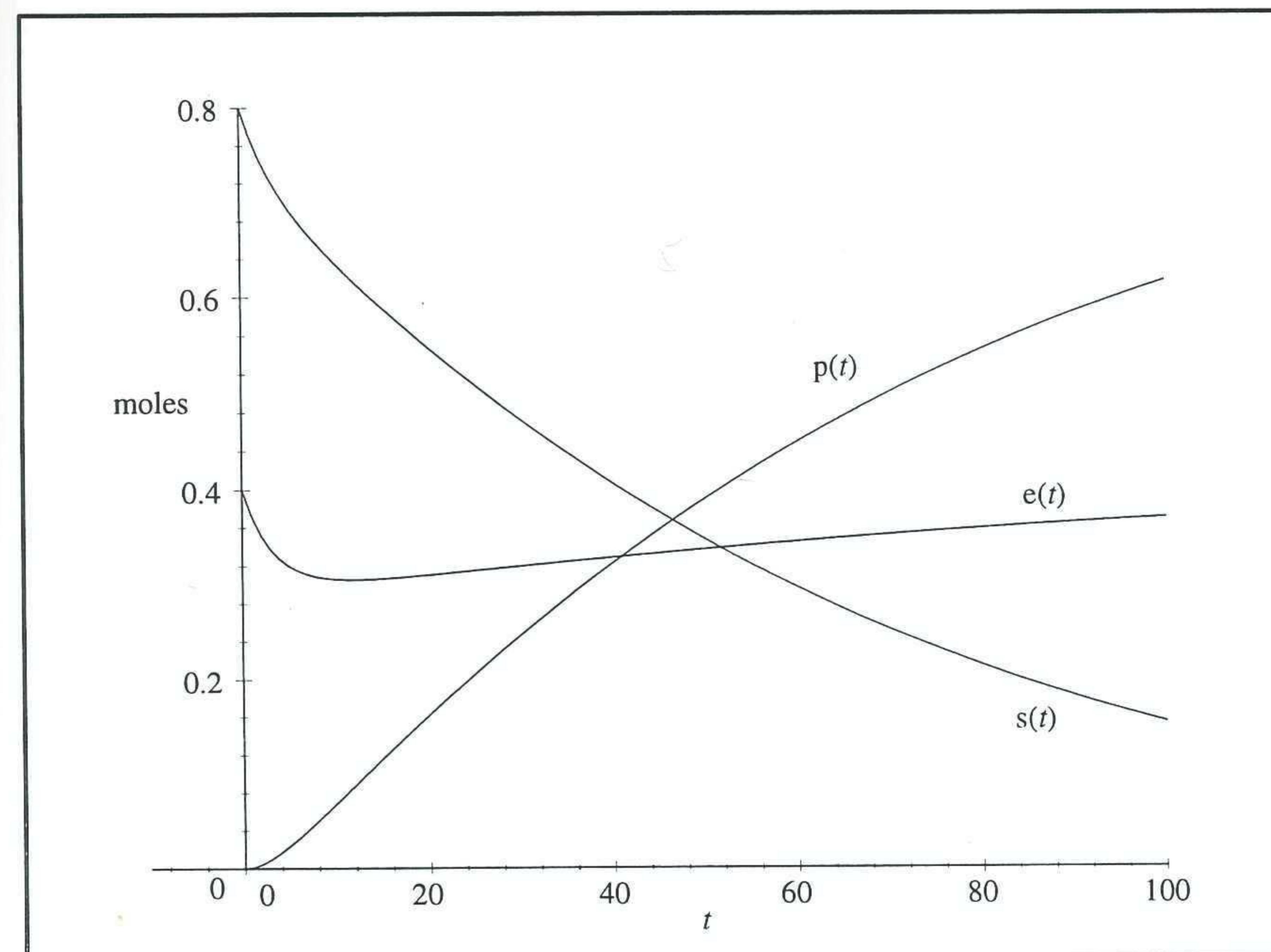


Figure 9.6.2 Solutions for Equation (9.6.1)

is known as the *Michaelis–Menten constant*; it has units moles per liter. Solving for c above we get

$$c = \frac{se_0}{k_M + s}, \quad (9.6.6)$$

which is seen to depend on the amounts of substrate S . But if s is much larger than k_M , then the denominator of equation (9.6.6) is approximately just s and we find the invariant level of complex to be

$$c_{\text{Eff}} \approx e_0. \quad (9.6.7)$$

Thus, most of the enzyme is tied up in enzyme-substrate complex.

By the *velocity* v of the reaction we mean the rate, $\frac{dp}{dt}$, at which product is formed. From equation (9.6.2), this is equal to $k_2 c$. When the concentration of substrate is large, we may use c_{Eff} as the concentration of complex and derive the maximum reaction velocity

$$v_{\max} = k_2 e_0. \quad (9.6.8)$$

Likewise, from equations (9.6.6) and (9.6.8), the initial reaction velocity, v_0 , is given by

$$\begin{aligned} v_0 &= \left. \frac{dp}{dt} \right|_{t=0} = k_2 \frac{se_0}{k_M + s} \\ &= \frac{v_{\max}s}{k_M + s}. \end{aligned} \quad (9.6.9)$$

In this, s is the initial substrate concentration, $s = [S]_0$. Equation (9.6.9) is the *Michaelis–Menten equation*, the rate equation for a one-substrate, enzyme-catalyzed reaction. Its graph is shown in Figure 9.6.3.

The value of k_M for an enzyme can be experimentally found from Figure 9.6.3. At low substrate concentrations $k_M + s \approx k_M$ and so the graph approximates the line $v_0 = (v_{\max}/k_M)s$ near $s = 0$. On the other hand, at high substrate concentrations the reaction rate approaches v_{\max} asymptotically because, at these concentrations, the reaction is essentially independent of substrate concentration. By experimentally measuring the initial reaction rate for various substrate concentrations, a sketch of the graph can be made. Working from the graph, the substrate level which gives $\frac{1}{2}v_{\max}$ initial velocity is the value of k_M , seen as follows.

```
> fcn:=s->vmax*s/(kM+s); vmax:=10: kM:=15:
> crv:=plot([x,fcn(x),x=0..150],x=-20..160,y=-1..12,tickmarks=[0,0]):
> asy:=plot(10,0..150,tickmarks=[0,0]):
> midline:=plot(5,0..15.3,tickmarks=[0,0]):
> vertline:=plot([15.3,y,y=0..5],tickmarks=[0,0]):
> a:=0: A:=0.0: b:=13: B:=13*vmax/kM:
> slope:=x->A*(x-b)+(B*(x-a))/(b-a):
> slopline:=plot(slope,a..b):
> txt1:=textplot({[130.5,10.3,'-vmax-],[-10.5,5,'1/2 vmax']}),align=LEFT):
> txt4:=textplot({[b+14,B+0.5,'slope = vmax/kM']}):
> txt5:=textplot({[15.3,-0.3,'-kM-']}),align=BELLOW):
> with(plots):
> display({crv,asy,midline,vertline,slopline,txt1,txt4,txt5});
```

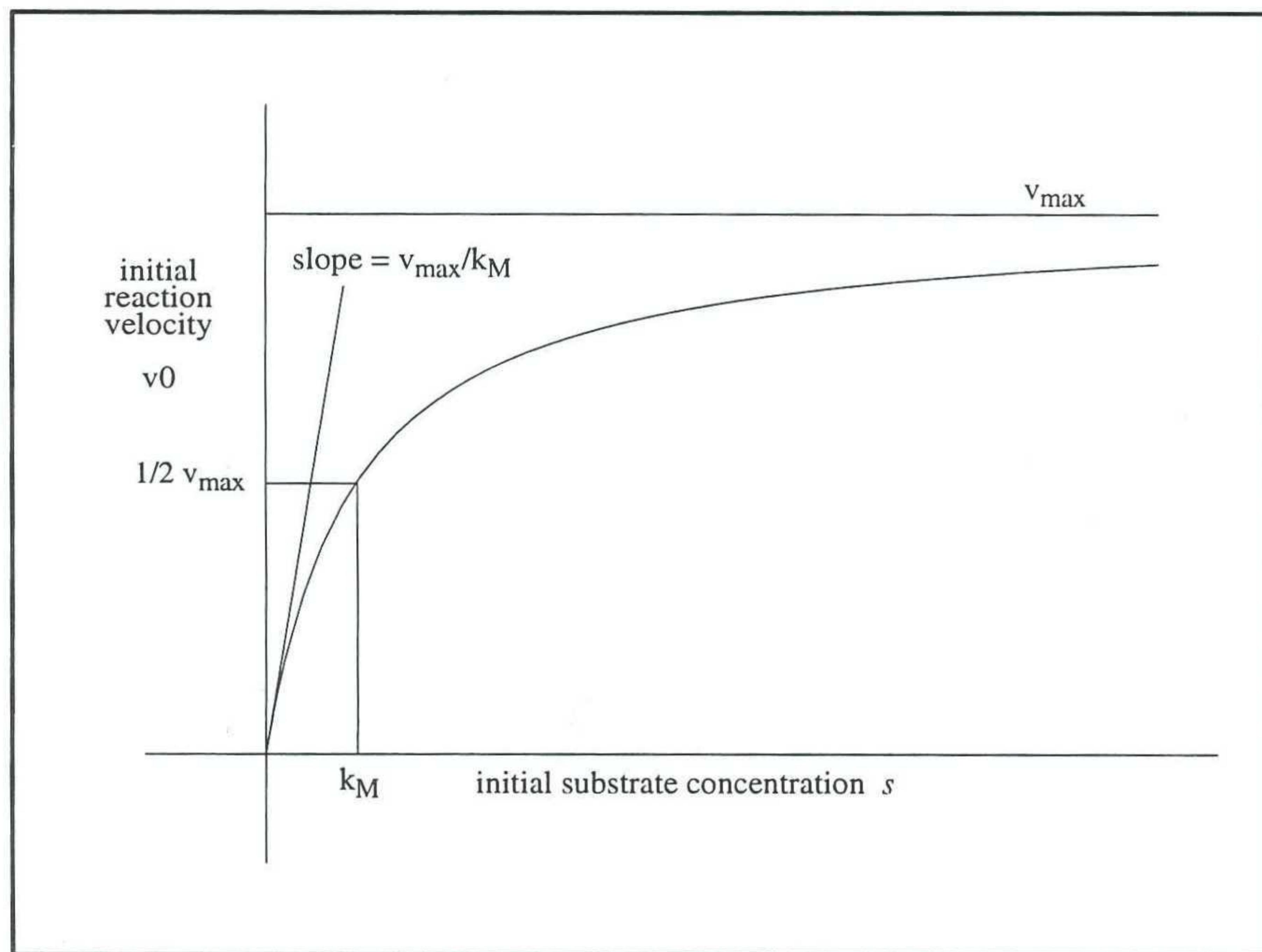


Figure 9.6.3 Michaelis-Menten plot

From equation (9.6.9) with $v_0 = v_{\max}/2$,

$$\frac{1}{2}v_{\max} = \frac{v_{\max}s}{k_M + s},$$

and, solving for k_M gives

$$k_M = s.$$

Thus, we interpret k_M as the substrate concentration at which the reaction rate is half maximal. By inverting the Michaelis–Menten equation (9.6.9) we get

$$\begin{aligned}\frac{1}{v_0} &= \frac{k_M + s}{v_{\max}s} \\ &= \frac{k_M}{v_{\max}} \frac{1}{s} + \frac{1}{v_{\max}}.\end{aligned}\tag{9.6.10}$$

This is the *Lineweaver–Burk equation* and shows that a least squares fit may be made to the *double-reciprocal plot* of $\frac{1}{v_0}$ vs $\frac{1}{s}$. This has the advantage of allowing an accurate determination of v_{\max} .

Another transform of the Michaelis–Menten equation that allows the use of least squares is obtained from equation (9.6.10) by multiplying both sides by $v_0 v_{\max}$; this yields

$$v_0 = -k_M \frac{v_0}{s} + v_{\max}.\tag{9.6.11}$$

A plot of v_0 against $v_0/[S]$ is called the *Eadie–Hofstee plot*; it allows the determination of k_M as its slope and v_{\max} as its intercept.