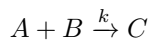


## Law of Mass Action

The Law of Mass Action states that the rate of product accumulation is proportional to the concentration of the reactants. Consider again the following reaction.



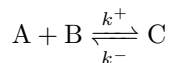
The LOMA then provides the following equation.

$$\frac{d}{dt}[C] = k[A][B]$$

## Steady-state analysis

Steady-state analysis is helpful only for small systems. However, discussing the related theory will be helpful for analyses later on.

Recall the following two-way reaction.



At equilibrium, the concentration of reactants and products do not change. In mathematical terms, the derivatives (velocity) of the concentrations is 0.

$$\frac{d}{dt}[A] = 0$$

Hence, at equilibrium we can solve for  $[C]$  as follows.

$$\begin{aligned}\frac{d}{dt}[A] &= 0 \\ k^- [C] - k^+ [A][B] &= 0 \\ k^- [C] &= k^+ [A][B] \\ [C] &= \frac{k^+}{k^-} [A][B]\end{aligned}$$

If we assume that the reaction is the only reaction in the system, we have

$$\begin{aligned}[A] + [C] &= A_0 = [A]_{t=0} \\ [C] &= \frac{k^+}{k^-} (A_0 - [C])[B] \\ [C] + \frac{k^+}{k^-} [C][B] &= \frac{k^+}{k^-} A_0 [B] \\ [C] \left(1 + \frac{k^+}{k^-} [B]\right) &= \frac{k^+}{k^-} A_0 [B] \\ [C] &= \frac{\frac{k^+}{k^-} A_0 [B]}{1 + \frac{k^+}{k^-} [B]} = \frac{A_0 [B]}{\frac{k^-}{k^+} + [B]}\end{aligned}$$

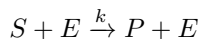
### Remark

The quantity  $\frac{k^-}{k^+} = K_0$  is called the dissociation constant, and its inverse  $\frac{k^+}{k^-}$  is called the equilibrium constant.

## Enzyme kinetics

How do we model enzymatic reactions? This section will use the following abbreviations:  $S$  for substrate,  $E$  for enzyme,  $P$  for product,  $V$  for velocity of reaction, and  $C$  for complex (substrate + enzyme).

## First attempt



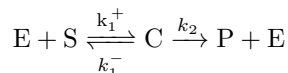
with the solution

$$\frac{d}{dt}[P] = k[S][E]$$

The problem with this approach is that according to the Law of Mass Action,  $V$  should be linear in terms of  $[S]$ , whereas empirical evidence showed a logarithmic relationship.

## Second attempt: Michaelis-Menton

Michaelis and Menton added an additional step in the reaction with a chemical intermediate: a complex of the substrate and enzyme.



Let  $x = [X]$  for all of the symbols defined in this section.

$$\begin{aligned}\frac{ds}{dt} &= k_1^- c - k_1^+ es \\ \frac{de}{dt} &= k_1^- c + k_2 c - k_1^+ es = c(k_1^- + k_2) - k_1^+ es \\ \frac{dc}{dt} &= k_1^+ es - k_1^- c - k_2 c = k_1^+ es - c(k_1^- + k_2)\end{aligned}$$

We see that  $\frac{de}{dt}$  and  $\frac{dc}{dt}$  have opposite and equal values, so  $\frac{de}{dt} + \frac{dc}{dt} = 0$ . This makes chemical sense, since in a closed system, there is a constant amount of enzyme, and that enzyme is either bound or in complex with the substrate.

From this, we have  $\frac{d}{dt}(e + c) = 0$ , which implies that the quantity  $e + c$  is a constant value (derivative of a constant is 0). Let  $e + c = e_0$ . From this relationship, we have  $e = e_0 - c$ , which allows us to remove a term from our system of equations. This concept will be very helpful in the future as we work with very large interaction networks.

We are interested in computing  $V = \frac{dp}{dt} = k_2 c$  in terms of  $s$ . Michaelis and Menton introduced the equilibrium approximation when saturated with substrate:  $\frac{ds}{dt} \approx 0$ . From this we derive the following.

$$\begin{aligned}0 &= \frac{ds}{dt} = k_1^- c - k_1^+ es \\ k_1^+ es &= k_1^- c \\ c &= \frac{k_1^+}{k_1^-} es\end{aligned}$$

We know that  $e + c = e_0 \rightarrow e = e_0 - c$ , so we derive the following.

$$\begin{aligned}c &= \frac{k_1^+}{k_1^-} es \\ c &= \frac{k_1^+}{k_1^-} (e_0 - c)s \\ c &= \frac{e_0 s}{K_0 + s}\end{aligned}$$

Therefore, we have

$$V = \frac{dp}{dt} = k_2 c = \frac{k_2 e_0 s}{K_0 + s} = \frac{V_{max} \cdot s}{K_0 + s}$$

which fits empirical data very well.