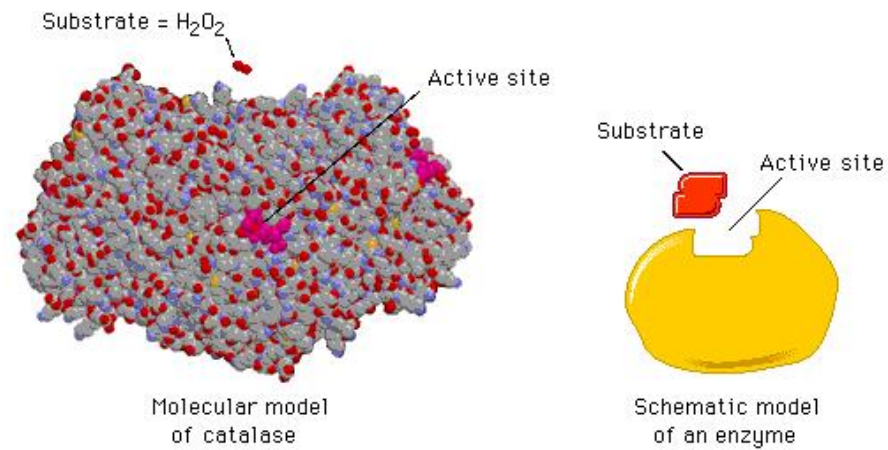
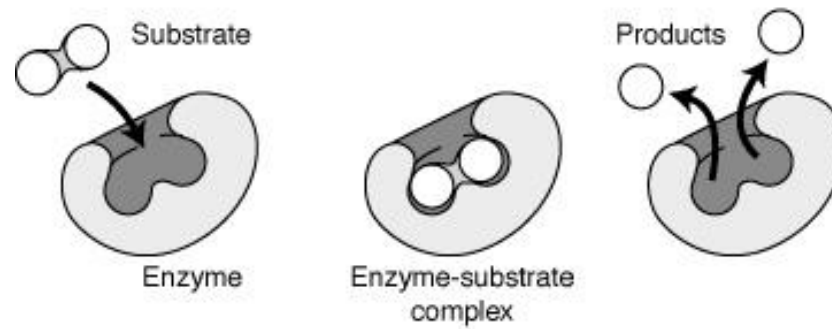


Molecular biology is one of the most important and rapidly developing areas in the life sciences, and now forms the basis of subjects such as physiology, immunology and genetics. Cellular biology is the study of cells, which make up all living creatures, and which occupy an intermediate level of biological complexity between molecules and multicellular organisms.

Biochemical kinetics concerns the concentrations of chemical substances in biological systems as functions of time. biochemical processes are often controlled by enzyme catalysts. Enzymes are proteins that catalyze (i.e. accelerate) chemical reactions. Enzymes are biochemical catalysts. In these reactions, the molecules at the beginning of the process are called substrates, and the enzyme converts these into different molecules, the products. Almost all processes in the cell need enzymes in order to occur at significant rates.

## Mechanism of enzyme activity



## Chemical reaction:

$A + B \xrightarrow{k} C$  (chemical  $A$  reacts with  $B$  to produce  $C$ )

$A(t)$ ,  $B(t)$ ,  $C(t)$ : concentration of chemicals,  $k$  reaction rate

$$\frac{dC}{dt} = kAB, \quad \frac{dA}{dt} = \frac{dB}{dt} = -kAB$$

two-direction reactions:  $A + B \rightleftharpoons_{k_-}^{k_+} C$ ,  $\frac{dC}{dt} = k_+AB - k_-C$

Michaelis-Menten enzyme reaction: enzyme first forms a complex with the substrate, then breaks down to the product and the enzyme. (Leonor Michaelis, Maud Menten (1913))



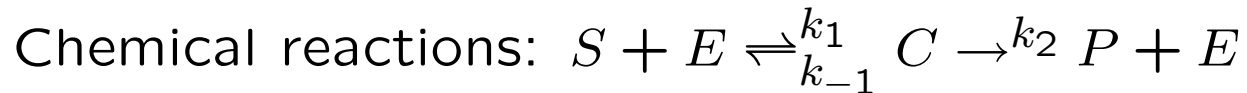
Leonor Michaelis  
1875–1949



Maud Menten  
1879–1960

$S$ : substrate molecule;  $E$ : enzyme;

$C$ : substrate-enzyme complex;  $P$ : product



Equations:

$$\begin{aligned}\frac{dS}{d\tau} &= -k_1SE + k_{-1}C \\ \frac{dE}{d\tau} &= -k_1SE + k_{-1}C + k_2C \\ \frac{dC}{d\tau} &= k_1SE - k_{-1}C - k_2C \\ \frac{dP}{d\tau} &= k_2C\end{aligned}$$

$$\frac{dE}{dt} + \frac{dC}{dt} = 0 \text{ (the total number of enzymes is a constant)}$$

Suppose that  $E + C = E_0$ , drop equations (2) and (4), we get new equation (equivalent to the old ones)

$$\frac{dS}{d\tau} = -k_1 S(E_0 - C) + k_{-1} C, \quad \frac{dC}{d\tau} = k_1 S(E_0 - C) - k_{-1} C - k_2 C$$

$$S(0) = S_0, \quad C(0) = 0.$$

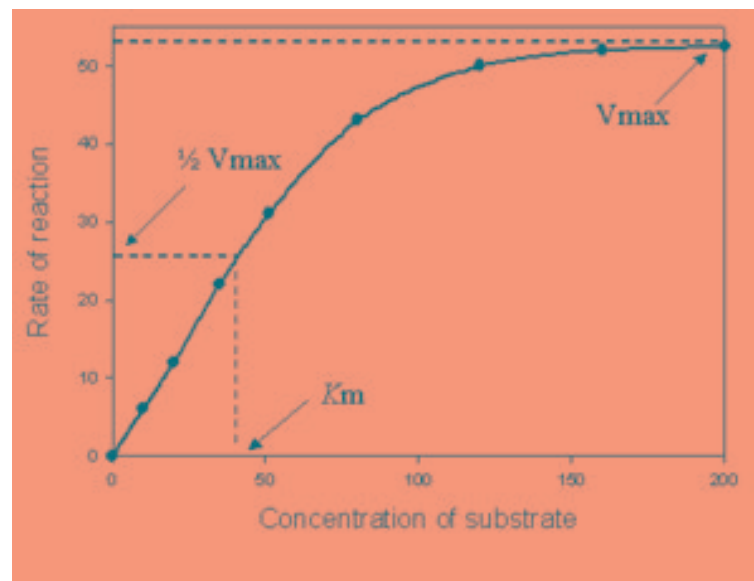
Suppose that all enzymes are always working at maximum capacity, so  $C(\tau) \approx \text{constant}$  or  $\frac{dC}{d\tau} = 0$ , then we obtain

$$C = \frac{k_1 S E_0}{k_{-1} + k_2 + k_1 S} = \frac{E_0 S}{K_m + S} \quad \text{where } K_m = \frac{k_{-1} + k_2}{k_1} \text{ is the}$$

Michaelis constant, and  $\frac{dS}{d\tau} = -\frac{V_m S}{K_m + S}$  where  $V_m = k_2 E_0$ . The

velocity of the reaction (rate product generated) is  $\frac{dP}{d\tau} = \frac{V_m S}{K_m + S}$

The maximum possible velocity is  $V_m$  if substrates are plenty, but the reaction rate slows as  $S$  is smaller.



Nondimensionalization:  $t = k_1 E_0 \tau$ ,  $s = \frac{S}{S_0}$ ,  $c = \frac{C}{E_0}$

new equations:

$$\frac{ds}{dt} = k_d c - s(1 - c)$$
$$\epsilon \frac{dc}{dt} = s(1 - c) - k_m c$$
$$s(0) = 1, \quad c(0) = 0.$$

$$\epsilon = \frac{E_0}{S_0}, k_m = \frac{k_{-1} + k_2}{k_1 S_0}, k_d = \frac{k_{-1}}{k_1 S_0}.$$

Typically  $\epsilon = \frac{E_0}{S_0}$  is very small, since the concentration of substrates is much higher than the concentration of enzymes. So  $\epsilon \simeq 0$ .

Mathematically, we can assume that

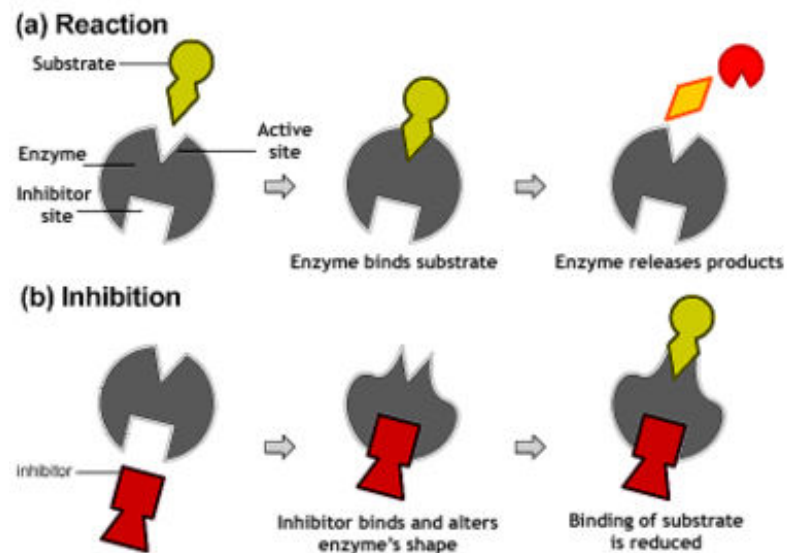
$$\begin{aligned} s(t) &= s_0(s) + \epsilon s_1(s) + \epsilon^2 s_2(s) + \dots, \\ c(s) &= c_0(s) + \epsilon c_1(s) + \epsilon^2 c_2(s) + \dots, \end{aligned}$$

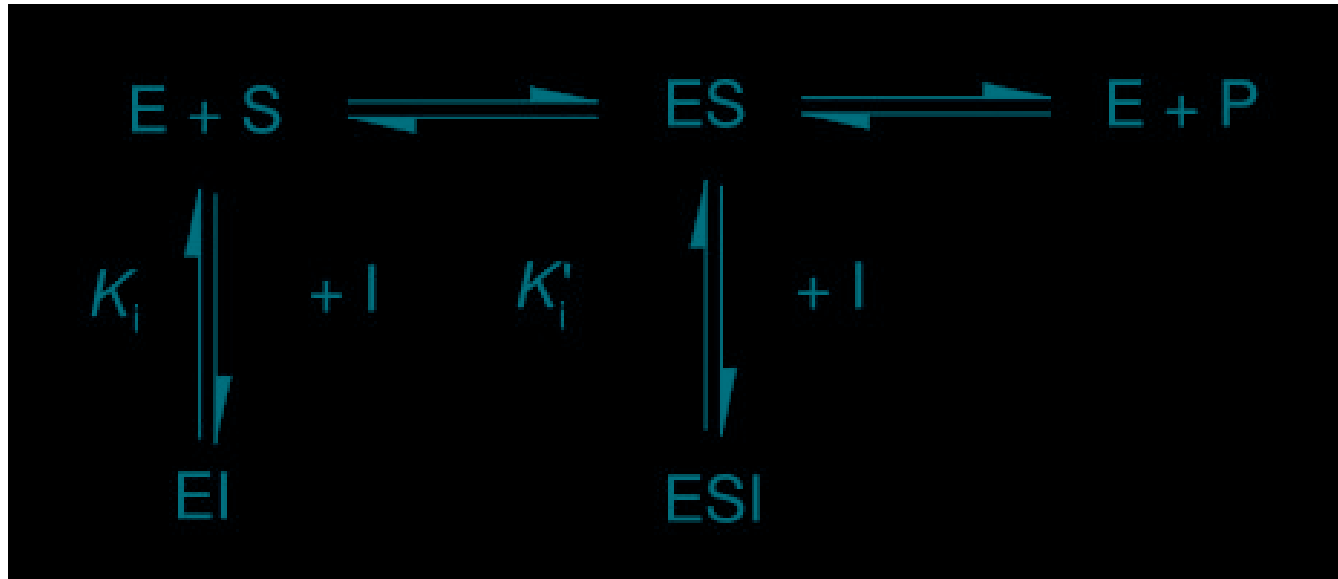
This is called **perturbation** method.  
By matching the terms, we get

$$\frac{ds_0}{dt} = k_d c_0 - s_0(1 - c_0), \quad 0 = s_0(1 - c_0) - k_m c_0$$

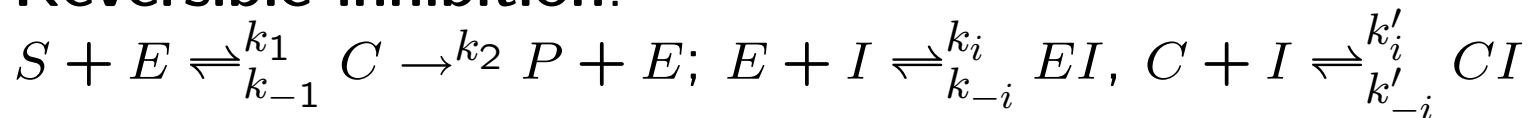
$$\text{Thus } \frac{ds_0}{dt} = -\frac{(k_m - k_d)s_0}{s_0 + k_m}, \quad c_0(t) = \frac{s_0(t)}{s_0(t) + k_m}$$

**Inhibition:** Enzyme inhibitors are molecules that bind to enzymes and decrease their activity. Since blocking an enzyme's activity can kill a pathogen or correct a metabolic imbalance. The binding of an inhibitor can stop a substrate from entering the enzyme's active site and/or hinder the enzyme from catalysing its reaction. Many drug molecules are enzyme inhibitors so their discovery and improvement is an active area of research in biochemistry and pharmacology.





**Reversible inhibition:**



Competitive inhibition:  $k'_i = 0$ , increases  $K_m$ , but not affect  $V_m$

Non-competitive inhibition:  $k_i = k'_i > 0$ : does not change  $K_m$  but decreases  $V_m$

[http://en.wikipedia.org/wiki/Enzyme\\_inhibition](http://en.wikipedia.org/wiki/Enzyme_inhibition)