

## Introduction to Kinetics

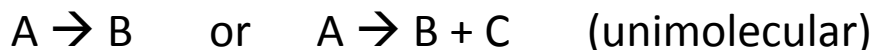
Haber–Bosch reaction:  $\text{N}_2 + 3\text{H}_2 \rightarrow 2\text{NH}_3$  (industrial ammonia production)

**Rate of reaction:** rate of change of a reagent divided by its stoichiometric coefficient

$$\text{rate} = v = (-1) \frac{d[\text{N}_2]}{dt} = (-1/3) \frac{d[\text{H}_2]}{dt} = (+1/2) \frac{d[\text{NH}_3]}{dt}$$

**Rate law:** relates concentrations to rates.

Most reactions are sequences of **elementary steps**. The Haber reaction has six steps!



For *elementary reactions only*, the rate law is:

$$v = k [\text{A}]^a [\text{B}]^b [\text{C}]^c$$

where  $k$  is a rate constant and  $a, b, c, \dots$  are the stoichiometric coefficients of each reactant A, B, C, ... .

## Introduction to Kinetics

For example,

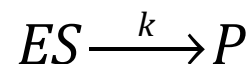
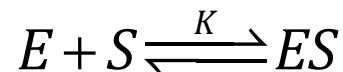


$$v = [A][B]^2$$

We say this reaction is first-order in [A], second-order in [B], and third-order overall.

If the reaction is not elementary, then the rate be more complex.

For example, this is the Michaelis–Menten scenario:



$$v = \frac{k K E_T S}{1 + K[S]}$$

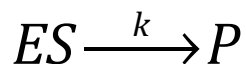
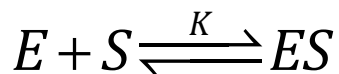
E = enzyme, S = substrate, P = product,  $E_T$  = total amount of enzyme,  $K$  = equilibrium constant,  $k$  = rate constant.

Clearly, it is not possible to assign an integer order to substrate.

## Differential vs. Integral Rate Laws

Reaction	Overall Order	Differential	Integrated
$A \rightarrow P$	first	$d[A]/dt = -k[A]$	$\ln [A] = \ln [A]_0 - kt$
$2A \rightarrow P$	second	$d[A]/dt = -k[A]^2$	$1/[A] = 1/[A]_0 + 2kt$
$A + B \rightarrow P$	second	$d[A]/dt = -k[A][B]$	$kt = 1/([B]_0 - [A]_0) * \ln( [B]_0[A]/[A]_0[B] )$

For multi-step rate laws, one can define the partial order in a reagent:



$$v = \frac{k K E_T S}{1 + K[S]}$$

If the substrate concentration is very low,  $K[S] \ll 1$ :

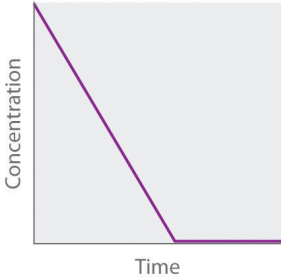
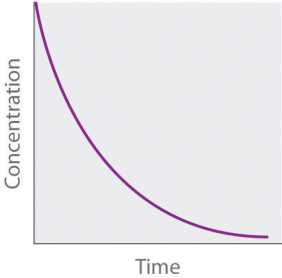
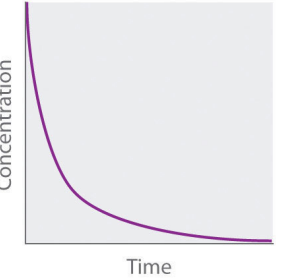
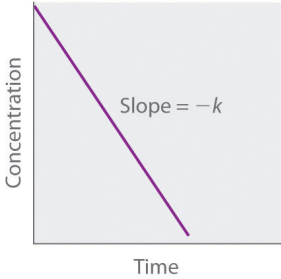

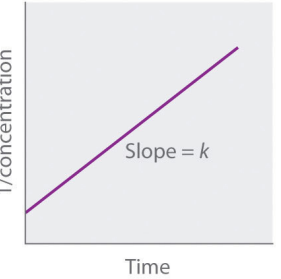
$$v = \text{constant} * [S].$$

Then the reaction is *first-order in [S]*.

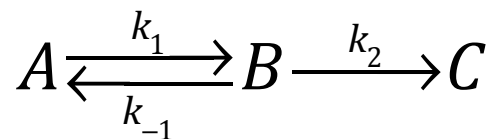
If the substrate concentration is very high,  $K[S] \gg 1$ :

$$v = \text{constant}.$$

Then, the reaction is *zero-order in [S]*:  $d[S]/dt = -\text{constant}$ ;  $[S] = [S]_0 - kt$ . (Zero-order elementary reactions are rare.)

	Zeroth Order	First Order	Second Order																								
<b>Differential rate law</b>	Rate = $-\frac{\Delta[A]}{\Delta t} = k$	Rate = $-\frac{\Delta[A]}{\Delta t} = k[A]$	Rate = $-\frac{\Delta[A]}{\Delta t} = k[A]^2$																								
<b>Concentration vs. time</b>																											
<b>Integrated rate law</b>	$[A] = [A]_0 - kt$	$[A] = [A]_0 e^{-kt}$ or $\ln[A] = \ln[A]_0 - kt$	$\frac{1}{[A]} = \frac{1}{[A]_0} + kt$																								
<b>Straight-line plot to determine rate constant</b>																											
<b>Relative rate vs. concentration</b>	<table border="1" data-bbox="627 999 879 1149"> <thead> <tr> <th>[A], M</th> <th>Rate, M/s</th> </tr> </thead> <tbody> <tr> <td>1</td> <td>1</td> </tr> <tr> <td>2</td> <td>1</td> </tr> <tr> <td>3</td> <td>1</td> </tr> </tbody> </table>	[A], M	Rate, M/s	1	1	2	1	3	1	<table border="1" data-bbox="1014 999 1265 1149"> <thead> <tr> <th>[A], M</th> <th>Rate, M/s</th> </tr> </thead> <tbody> <tr> <td>1</td> <td>1</td> </tr> <tr> <td>2</td> <td>2</td> </tr> <tr> <td>3</td> <td>3</td> </tr> </tbody> </table>	[A], M	Rate, M/s	1	1	2	2	3	3	<table border="1" data-bbox="1323 999 1574 1149"> <thead> <tr> <th>[A], M</th> <th>Rate, M/s</th> </tr> </thead> <tbody> <tr> <td>1</td> <td>1</td> </tr> <tr> <td>2</td> <td>4</td> </tr> <tr> <td>3</td> <td>9</td> </tr> </tbody> </table>	[A], M	Rate, M/s	1	1	2	4	3	9
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<b>Half-life</b>	$t_{1/2} = \frac{[A]_0}{2k}$	$t_{1/2} = \frac{0.693}{k}$	$t_{1/2} = \frac{1}{k[A]_0}$																								
<b>Units of k, rate constant</b>	M/s	1/s	M <sup>-1</sup> ·s <sup>-1</sup>																								

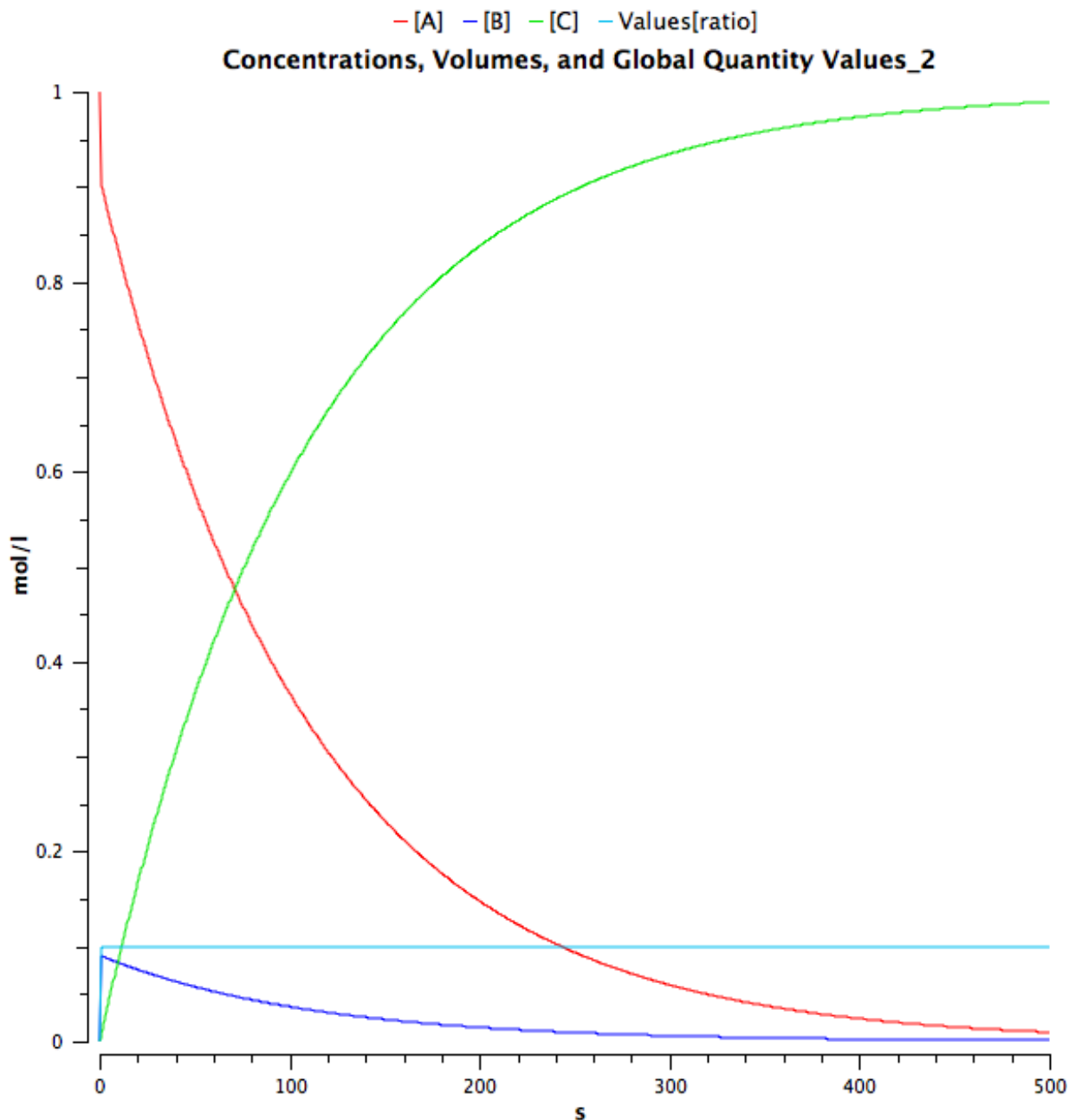
## Two-Step Rate Laws



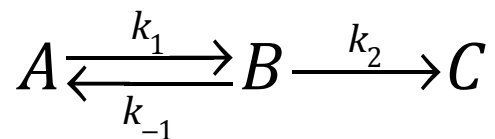
If A and B are in **pre-equilibrium**, then the ratio of  $[B]/[A]$  is maintained at  $K = k_1/k_{-1}$  throughout the reaction.

This means second step must be slow. This is a COPASI simulation for  $k_1=10 \text{ s}^{-1}$ ,  $k_{-1}=100 \text{ s}^{-1}$ , and  $k_2=0.1 \text{ s}^{-1}$ .

The cyan line shows the ratio  $[B]/[A]$  during the reaction.



## Two-Step Rate Laws



Mathematically, the approximation is

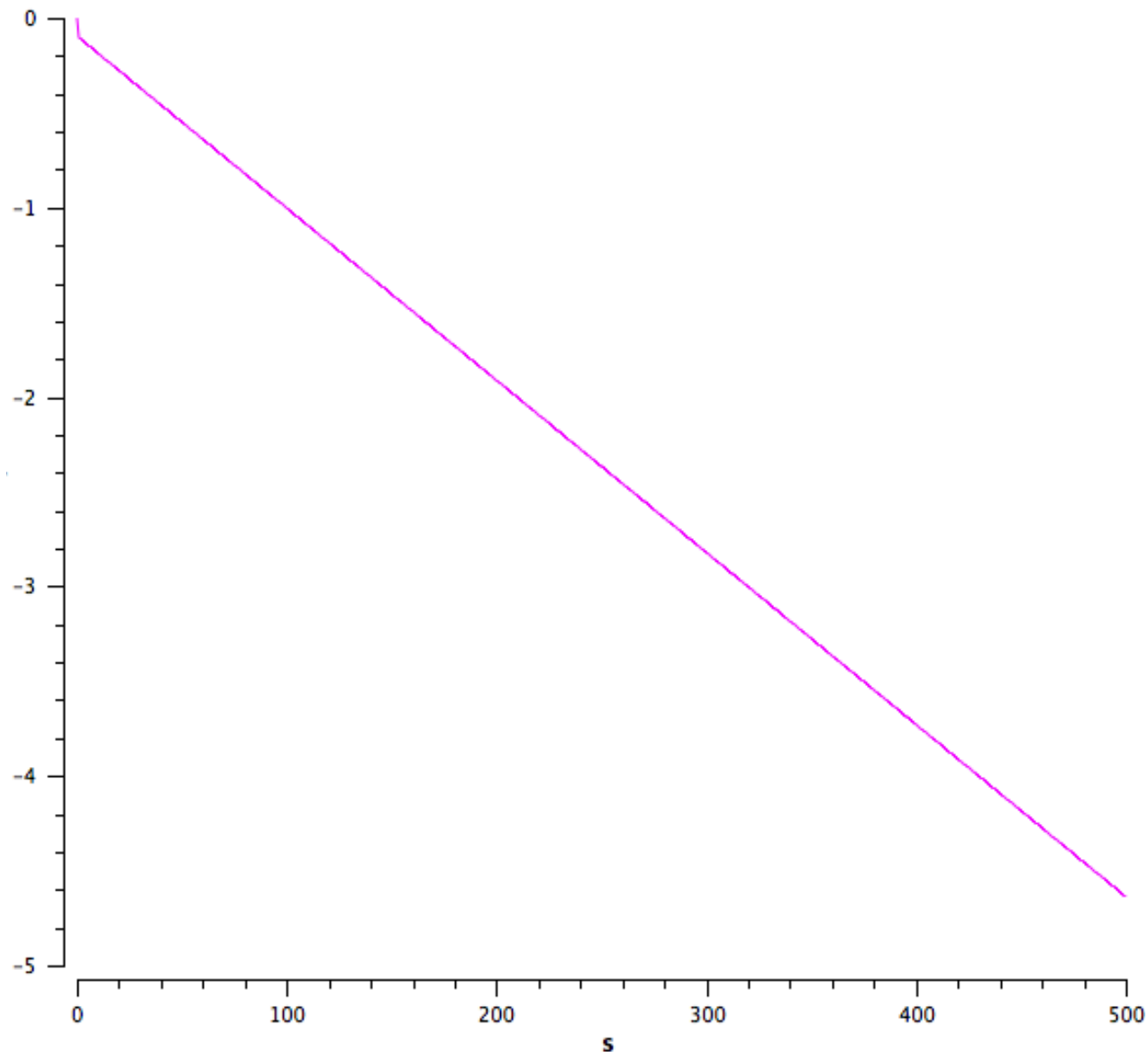
$$K = [B]/[A] = k_1/k_{-1} \\ [B] = K[A]$$

The second step is elementary, so

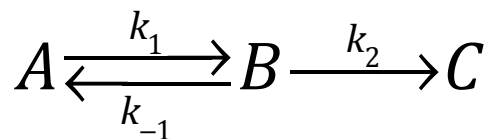
$$v = k_2[B] \\ v = k_2K[A]$$

This means that the reaction should look first-order in [A].

Left:  $\ln [A]$  vs. time.  
Slope is  $-k_2K$ .



## Two-Step Rate Laws



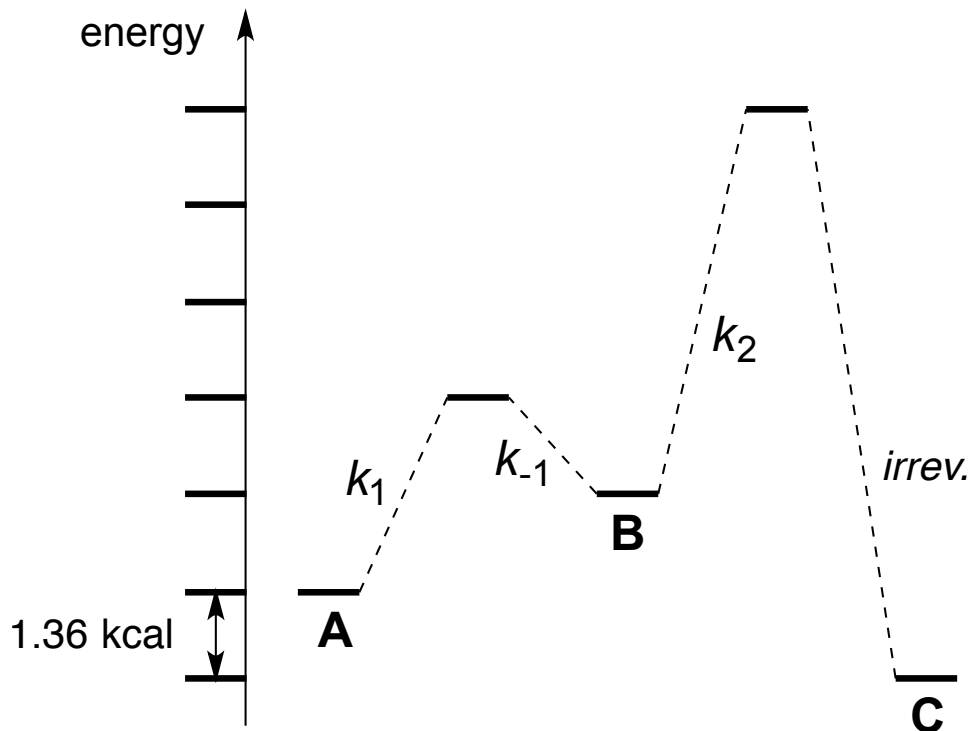
**Pre-equilibrium:**

$$k_1 = 10 \text{ s}^{-1}$$

$$k_{-1} = 100 \text{ s}^{-1}$$

$$k_2 = 0.1 \text{ s}^{-1}$$

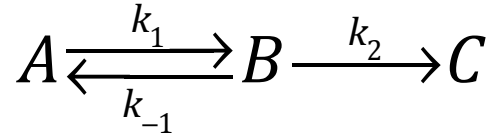
$$v = k_2 (k_1/k_{-1}) [A]$$



Each notch in the diagram represents a ten-fold difference in rate at room temperature. Smaller rates have more notches. Here, two notches represents a rate of 10 and one notch a rate of 1.

Even though the second step has the largest barrier, *there is no rate-determining step* because all of the rate constants appear in the rate.

## Two-Step Rate Laws

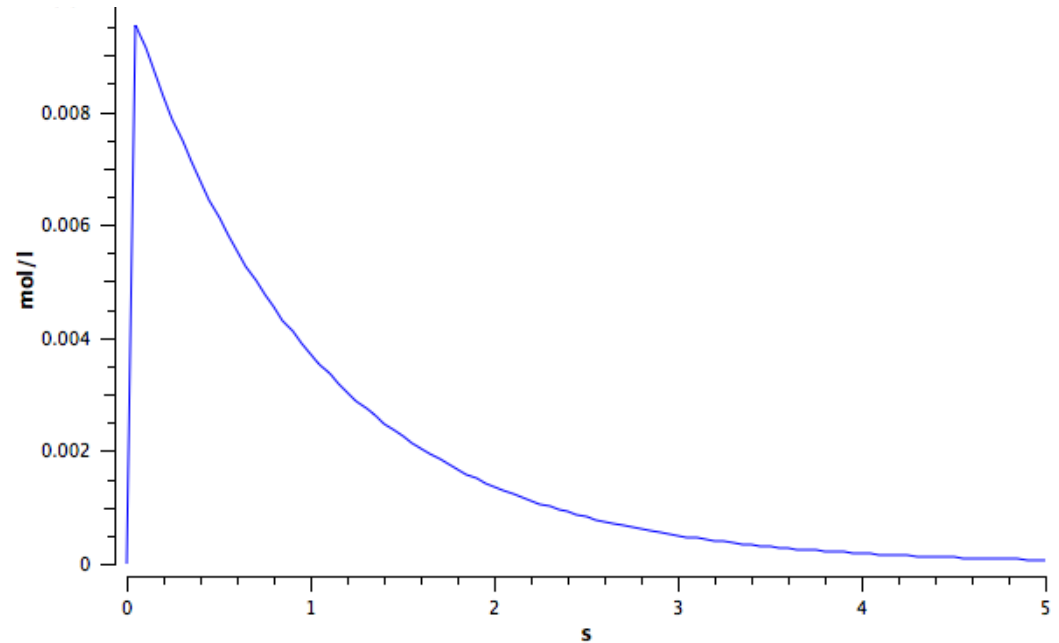
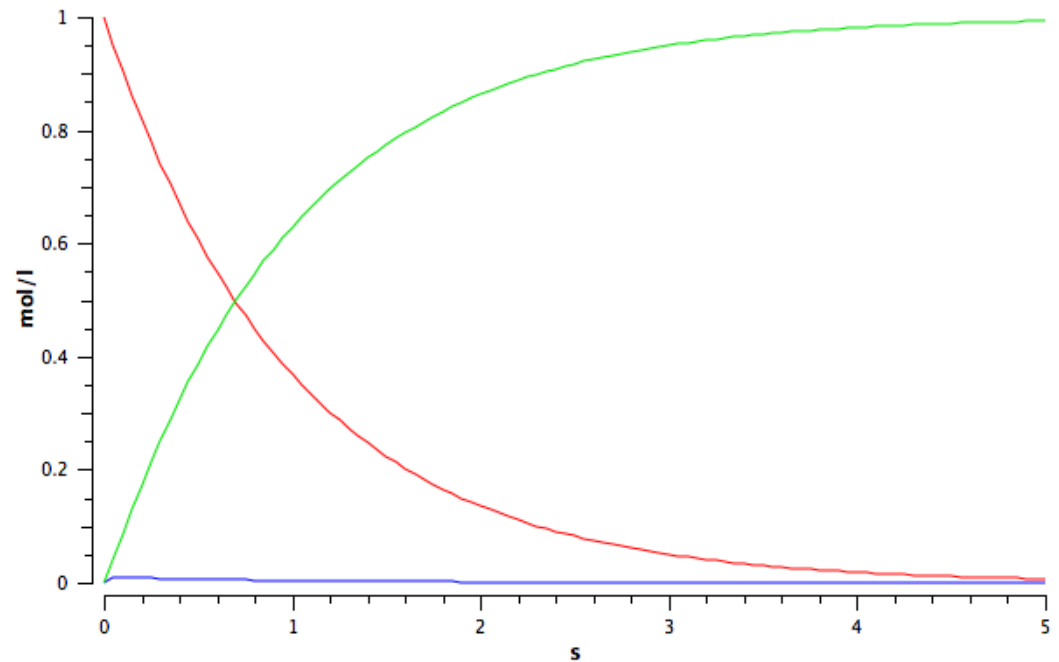


Another approximation is to say that the intermediate B is in **steady state**:

B is created and consumed at the same rate.

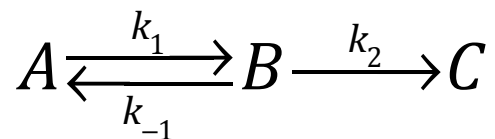
This is a COPASI simulation for  $k_1=1 \text{ s}^{-1}$ ,  $k_{-1}=0.01 \text{ s}^{-1}$ , and  $k_2=100 \text{ s}^{-1}$ .

red = A, blue = B, green = C





## Two-Step Rate Laws



$k_1=1 \text{ s}^{-1}$ ,  $k_{-1}=0.01 \text{ s}^{-1}$ , and  $k_2=100 \text{ s}^{-1}$ .

We have:

rate B formed = rate B consumed

$$k_1[A] = (k_{-1} + k_2) [B]_{SS}$$

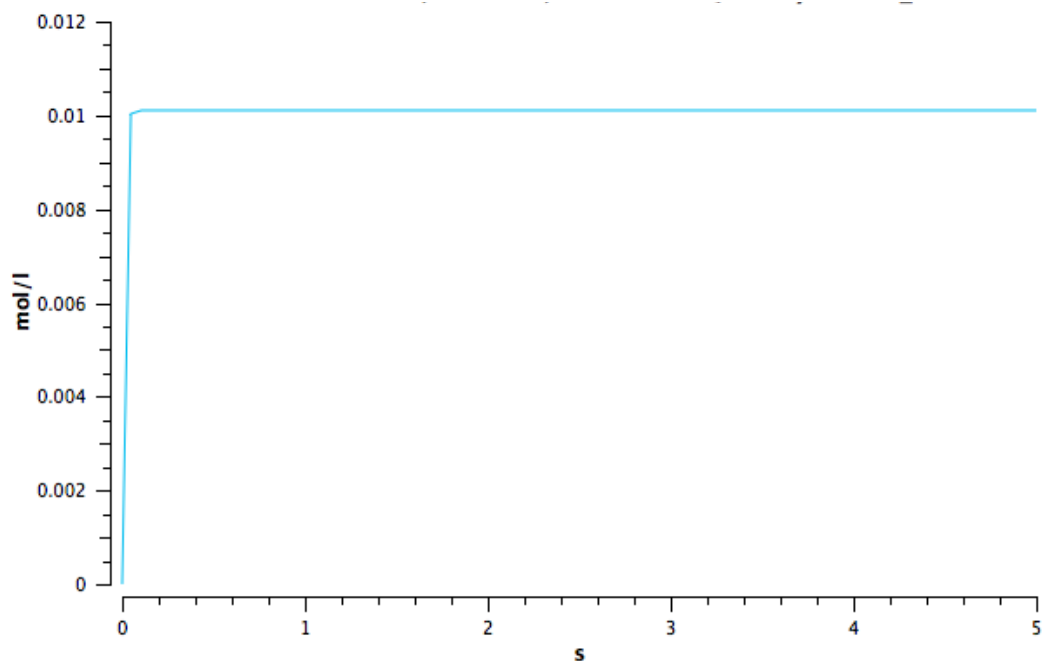
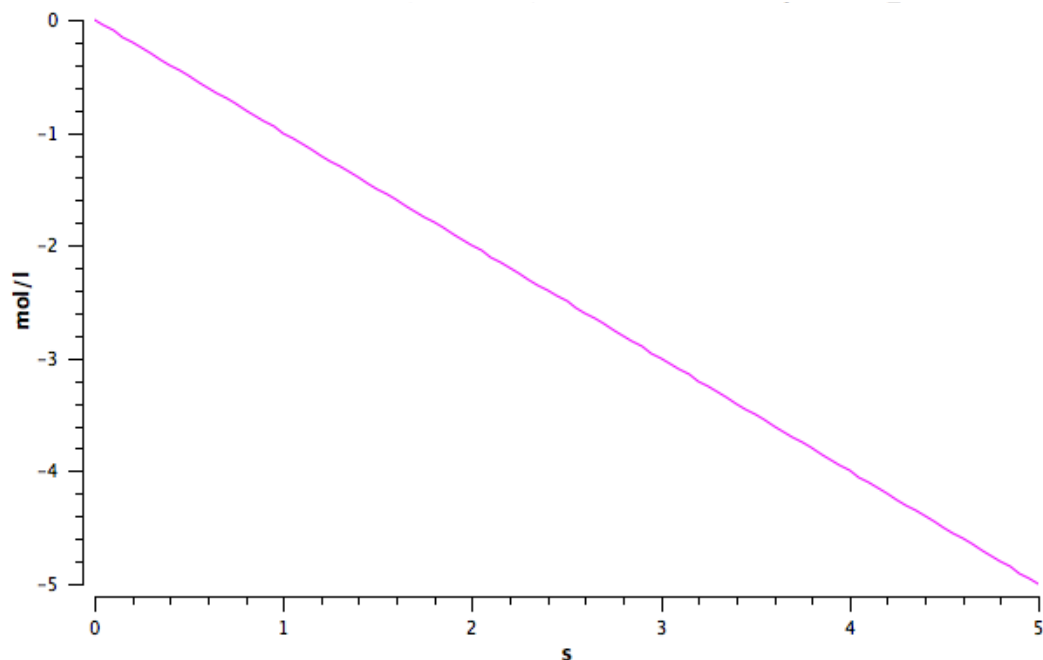
$$[B]_{SS} = k_1[A] / (k_{-1} + k_2)$$

Therefore,  $v = k_1 k_2 [A] / (k_{-1} + k_2)$ .

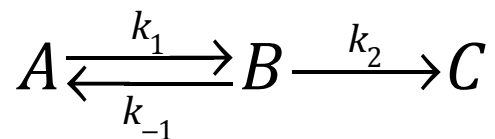
Since  $k_2 \gg k_{-1}$ ,  $v$  reduces to

$$v = k_1[A]/k_{-1},$$

which is first-order in  $[A]$  (magenta =  $\log [A]$ ). The ratio of  $[B]$  to  $[A]$  (cyan) is also maintained throughout the reaction.



## Two-Step Rate Laws



$$k_1 = 1 \text{ s}^{-1}, k_{-1} = 0.01 \text{ s}^{-1}, \text{ and } k_2 = 100 \text{ s}^{-1}.$$

The energy diagram is shown right.

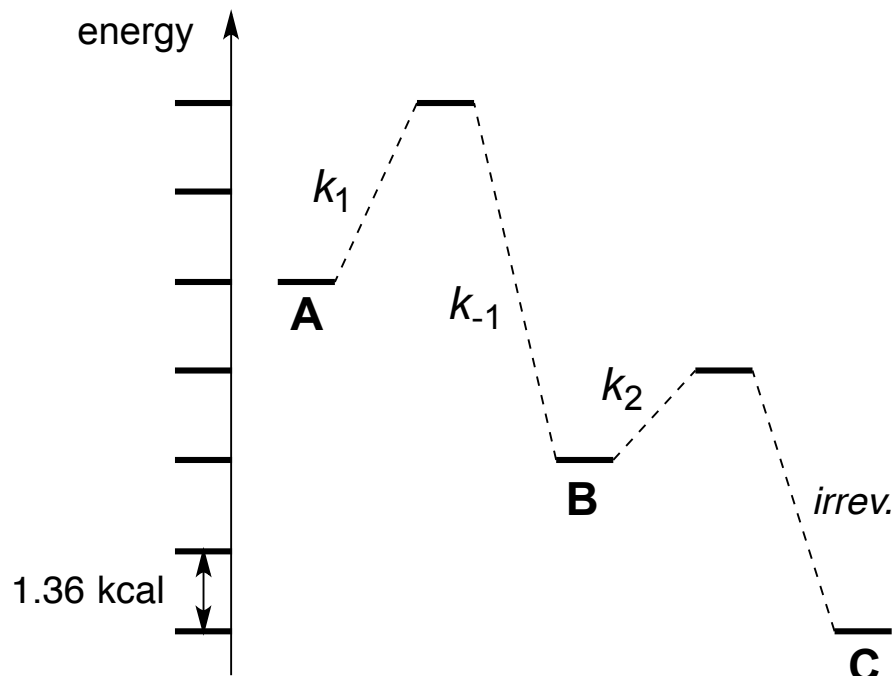
$$[B]_{SS} = k_1[A] / (k_{-1} + k_2)$$

$$[B]/[A] \approx k_1 / k_2 = 0.01$$

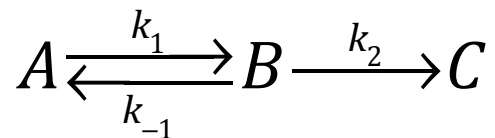
Despite the fact that the  $[B]/[A]$  ratio is maintained at 0.01 during the reaction, this is not the equilibrium ratio because of  $k_2$ .

$$v = k_1[A]/k_{-1}$$

This means the first step is rate-determining.



## Two-Step Rate Laws



If the rate constants get too close, then two-stage behavior results:

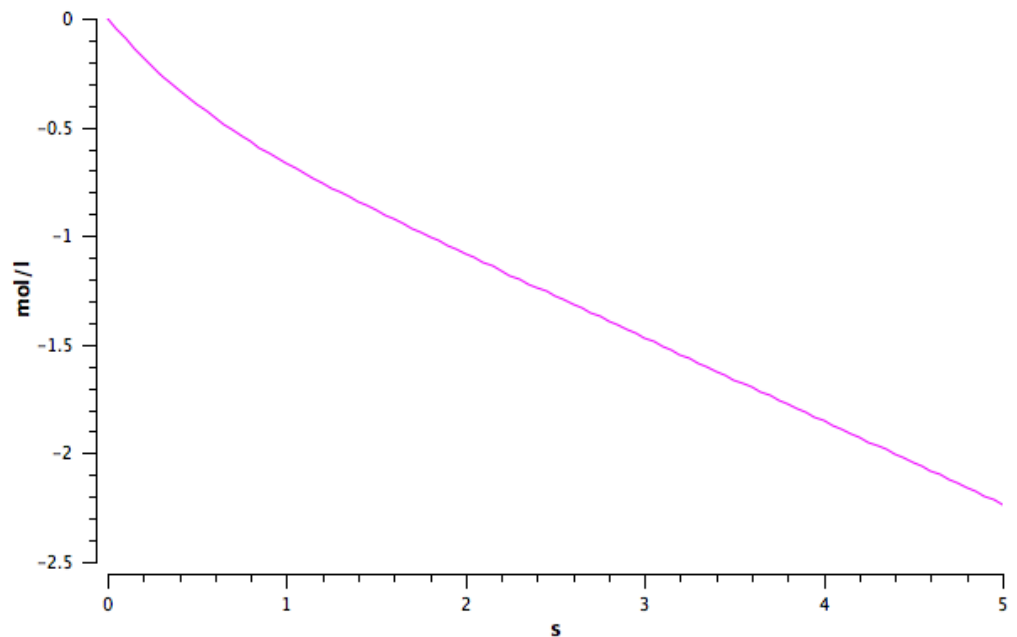
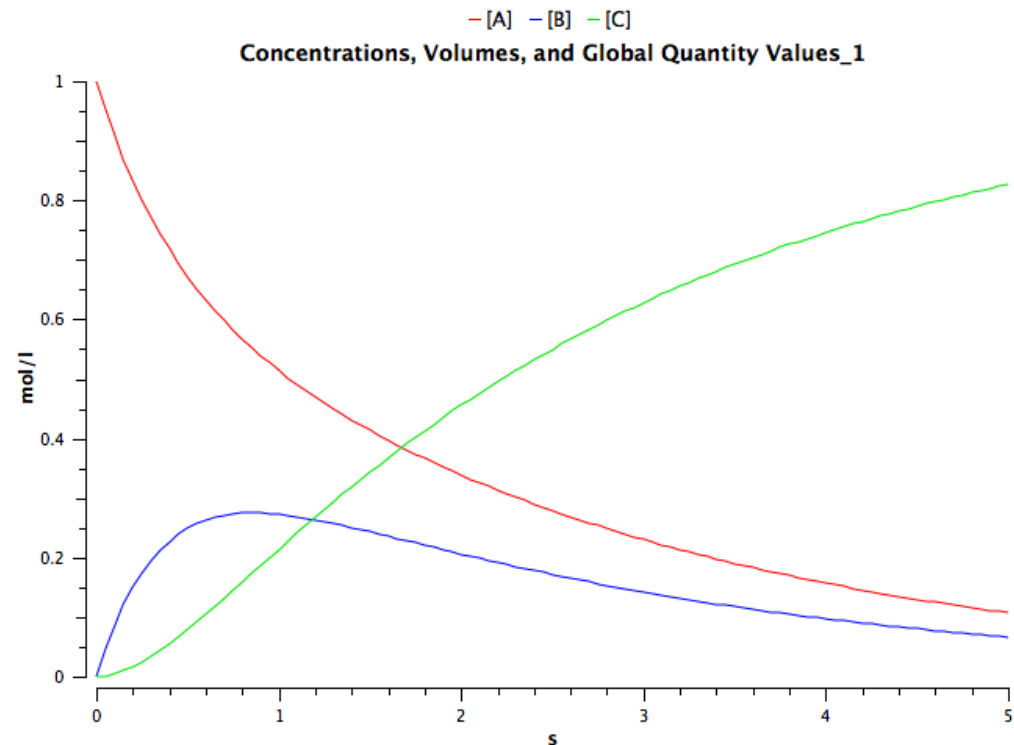
$k_1=1 \text{ s}^{-1}$ ,  $k_{-1}=1 \text{ s}^{-1}$ , and  $k_2=1 \text{ s}^{-1}$ .

This is essentially two first-order reactions superimposed.

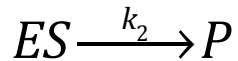
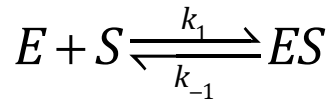
First phase: buildup of B

Second phase: formation of C

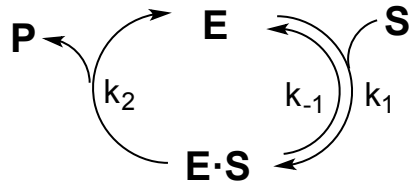
Right:  $\log [A]$  vs. time is curved.



# Catalytic Rate Laws



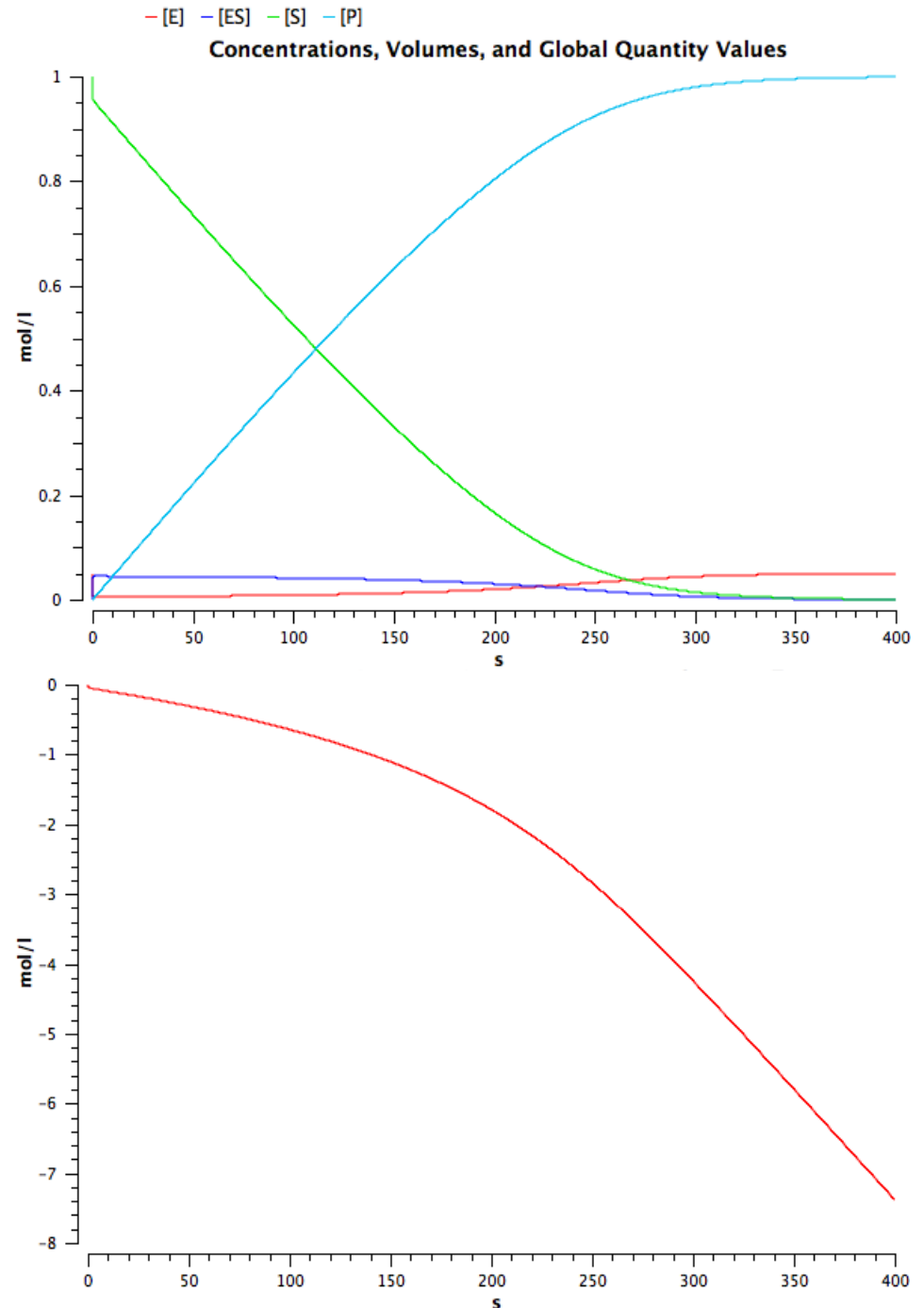
This is the Michaelis–Menten system.  
Alternatively,



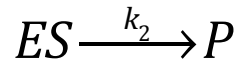
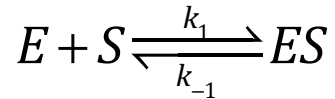
Here is a typical scenario:

$E_T = 0.05 \text{ M}$ ,  $[S]_0 = 1.0 \text{ M}$   
 $k_1 = 10 \text{ M}^{-1} \text{ s}^{-1}$ ,  $k_{-1} = 1 \text{ s}^{-1}$ , and  $k_2 = 0.1 \text{ s}^{-1}$ .

Red is  $\log [S]$ . The early reaction is zero-order in  $S$  because the enzyme is saturated. The late reaction is first-order in  $S$  because  $S$  drops and the enzyme is no longer saturated.



# Catalytic Rate Laws



**Pre-equilibrium:**  $K = k_1/k_{-1}$  is maintained.

$$K = [ES] / ([E][S])$$
$$[ES] = K[E][S]$$

$$v = k_2[ES] = k_2K[E][S]$$

[E] is not observable. In terms of total enzyme:

$$E_T = [E] + [ES]$$
$$E_T = [E] + K[E][S]$$
$$[E] = E_T / (1 + K[S])$$

This gives: 
$$v = \frac{k_2 K E_T [S]}{1 + K[S]}$$

**Steady State:**  $d[ES]/dt = 0$

$$k_1[E][S] = (k_{-1} + k_2)[ES]$$
$$[ES] = k_1[E][S] / (k_{-1} + k_2)$$

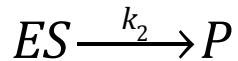
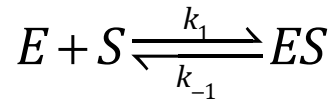
$$v = k_2[ES] = k_2k_1[E][S] / (k_{-1} + k_2)$$

[E] is not observable. In terms of total enzyme:

$$E_T = [E] + [ES]$$
$$E_T = [E] + \{ k_1[E][S] / (k_{-1} + k_2) \}$$
$$[E] = E_T (k_{-1} + k_2) / (k_{-1} + k_2 + k_1[S])$$

This gives: 
$$v = \frac{k_1 k_2 E_T [S]}{k_{-1} + k_2 + k_1[S]}$$

# Catalytic Rate Laws



**Pre-equilibrium:**  $K = k_1/k_{-1}$  is maintained.

$$v = \frac{k_2 K E_T [S]}{1 + K[S]}$$

The maximum rate will be when  $K[S] \ll 1$ .

Define:

$$v_{\max} = k_2 E_T \quad \text{and} \quad K_m = (k_{-1} + k_2) / k_1$$

$$\text{This gives: } v = \frac{v_{\max} [S]}{K_m + [S]}$$

**Steady State:**  $d[ES]/dt = 0$

$$v = \frac{k_1 k_2 E_T [S]}{k_{-1} + k_2 + k_1 [S]}$$

Maximum rate when denominator is small.

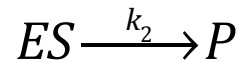
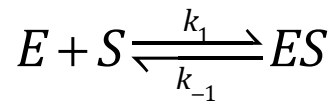
Define:

$$v_{\max} = k_2 E_T \quad \text{and} \quad K_m = (k_{-1} + k_2) / k_1$$

$$\text{This gives: } v = \frac{v_{\max} [S]}{K_m + [S]}$$

**Despite different assumptions, both rate laws have the same form.**

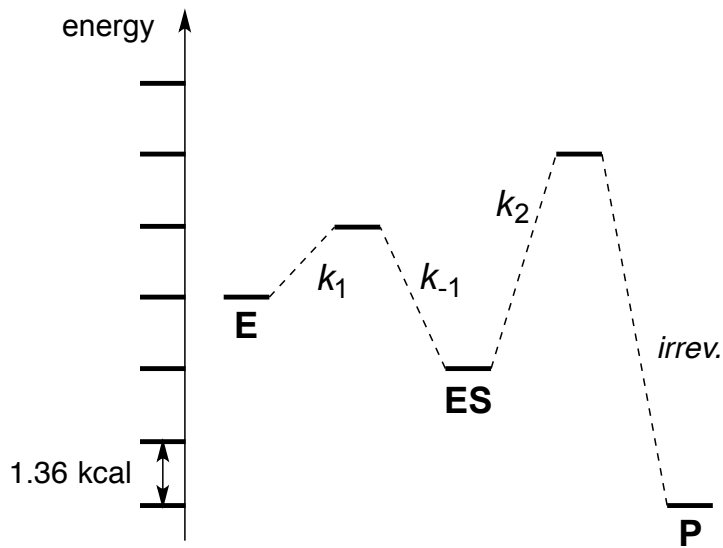
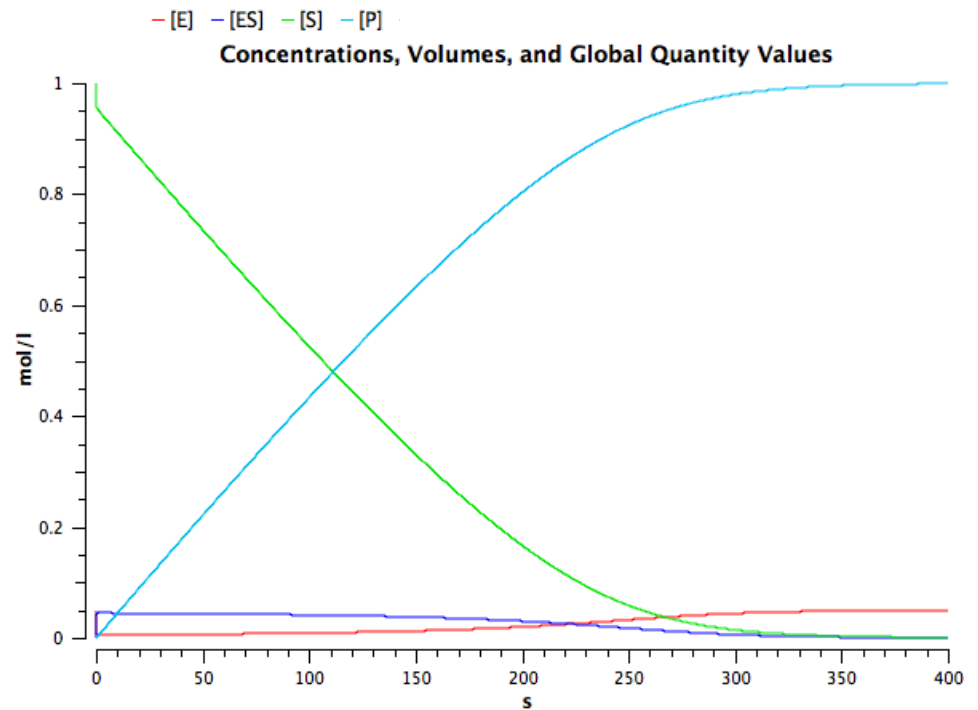
# Catalytic Rate Laws



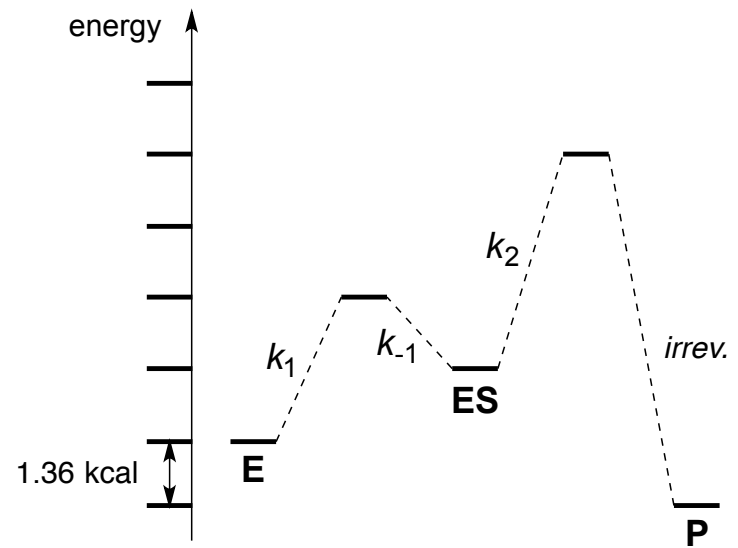
Returning to the last scenario:

$k_1=10 \text{ M}^{-1} \text{ s}^{-1}$ ,  $k_{-1}=1 \text{ s}^{-1}$ , and  $k_2=0.1 \text{ s}^{-1}$ .

The energy diagram is concentration-dependent.

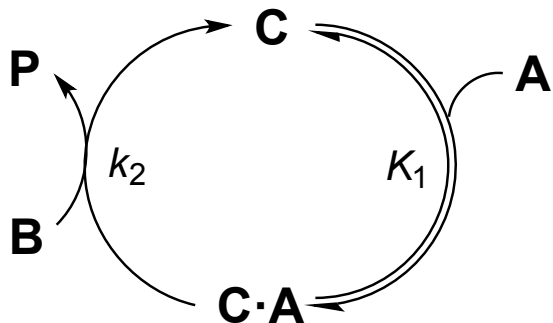


[S] = 1.0 M, enzyme is saturated



[S] = 0.01 M, enzyme is not saturated

## 1+Rate Laws



$$v = \frac{C_T [A] [B] k_2 K_1}{1 + K_1 [A]}$$

Pre-equilibrium rate laws are easy to write without derivation.

**Numerator:** All concentration, equilibrium, and rate terms going forward to product.

catalyst terms appear as total catalyst:  $C_T$

reagent terms:  $[A]$ ,  $[B]$

rate constants:  $k_2$

equilibrium constants:  $K_1$

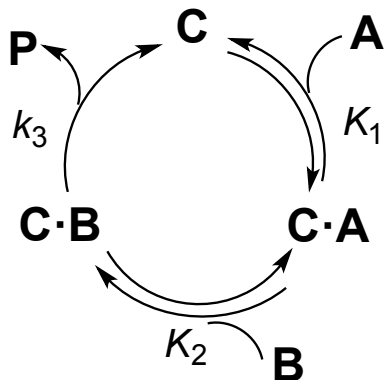
**Denominator:** All forms of catalyst.

free catalyst: 1

C•A complex:  $K_1[A]$



## 1+Rate Laws



$$v = \frac{C_T [A] [B] k_3 K_1 K_2}{1 + K_1 [A] + K_1 K_2 [A] [B]}$$

Pre-equilibrium rate laws are easy to write without derivation.

**Numerator:** All concentration, equilibrium, and rate terms going forward to product.

catalyst terms appear as total catalyst:  $C_T$

reagent terms:  $[A]$ ,  $[B]$

rate constants:  $k_3$

equilibrium constants:  $K_1$ ,  $K_2$

**Denominator:** All forms of catalyst.

free catalyst: 1

C•A complex:  $K_1 [A]$

C•A•B complex:  $K_1 K_2 [A] [B]$