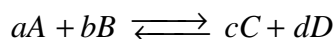


Reading Assignment: *Tinoco, Ch 7 & 8*

Chemical and Biochemical Kinetics

Chemical Equation



A, B reactants or vice versa

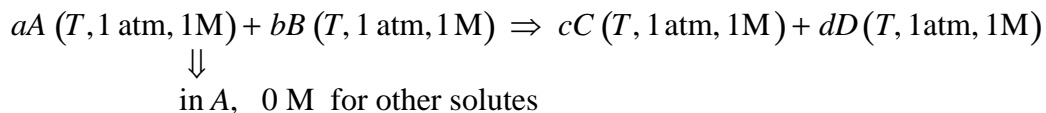
C, D products

$a, b, c, d \equiv$ stoichiometric coefficients

Chemical Equilibrium

$$\Delta G^0(T) = -RT \ln K_c = -RT \ln \left[\frac{(C)^c (D)^d}{(A)^a (B)^b} \right]_{eq}$$

where $\Delta G^0(T) \equiv$ standard free energy change for process



Departure from Chemical Equilibrium

If the system is not at equilibrium, it will approach chemical equilibrium according to a rate equation given by

$$\text{rate} = -\frac{1}{a} \frac{d[A]}{dt} = -\frac{1}{b} \frac{d[B]}{dt} = +\frac{1}{c} \frac{d[C]}{dt} = +\frac{1}{d} \frac{d[D]}{dt}$$

where the concentration derivatives < 0 if the reaction is proceeding from left to right.

In simple cases, we may write

$$\text{rate} = k_f [A]^{\alpha_f} [B]^{\beta_f} [C]^{\gamma_f} [D]^{\delta_f} - k_b [A]^{\alpha_b} [B]^{\beta_b} [C]^{\gamma_b} [D]^{\delta_b}$$

where $\alpha_f, \beta_f, \gamma_f, \delta_f, \alpha_b, \beta_b, \gamma_b, \delta_b$ are integers, half-integers, zero, and occasionally negative

If you start off with reactants, then back reaction is negligible at initial times, and

$$\text{rate} = k_f [A]^{\alpha_f} [B]^{\beta_f} [C]^{\gamma_f} [D]^{\delta_f}$$

But the second term becomes important as the reaction approaches equilibrium.

Similarly, if you start off with products, the forward reaction as written is negligible at initial times.

At Equilibrium

$$k_f [A]_{eq}^{\alpha_f} [B]_{eq}^{\beta_f} [C]_{eq}^{\gamma_f} [D]_{eq}^{\delta_f} = k_b [A]_{eq}^{\alpha_b} [B]_{eq}^{\beta_b} [C]_{eq}^{\gamma_b} [D]_{eq}^{\delta_b}$$

i.e., forward rate = reverse rate

This result, together with the result for the equilibrium quotient at chemical equilibrium, i.e.,

$$K_c = \left(\frac{[C]^c [D]^d}{[A]^a [B]^b} \right)_{eq}$$

can be used to infer the “rate law” of the reverse reaction if the “rate law” of the forward reaction is known.

Rate Laws

Rate laws are expressions showing how the observed rate depends on the concentration of reactants (and products).

Suppose the rate for the reaction $A + B \Rightarrow C$ follows the expression

$$\text{rate} = \frac{d[C]}{dt} = k [A]^\alpha [B]^\beta$$

This expression gives the rate law for the reaction.

$k \equiv$ rate constant

$\alpha \equiv$ the "order" of the reaction with respect to $[A]$

$\beta \equiv$ the "order" of the reaction with respect to $[B]$ and

$\alpha + \beta =$ total reaction order

If $\alpha = 1$, the reaction is said to be first order with respect to $[A]$

If $\alpha = 2$, the reaction is said to be second order with respect to $[A]$

If $\alpha = 3$, the reaction is said to be third order with respect to $[A]$

 etc.

Catalysts and Inhibitors

The rate law of most biochemical transformations include concentrations of molecular species that are not part of the overall chemical equation. Such species are catalysts or inhibitors, which can enhance or inhibit the reaction.

For example, in enzyme-catalyzed oxidation of isocitrate by the NAD-dependent isocitrate dehydrogenase of yeast

$$\text{rate} = k [E][S]^4 [A]^2 [N]^2 [Mg^{2+}]^2$$

where $E \equiv$ enzyme (isocitrate dehydrogenase)

$S \equiv$ substrate, i.e., isocitrate

$A \equiv$ AMP

$N \equiv$ NAD

$Mg^{2+} \equiv$ magnesium

E, A, Mg^{2+} are catalysts

total reaction order $\equiv 1 + 4 + 2 + 2 + 2 = 11$

Reaction Mechanism

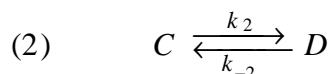
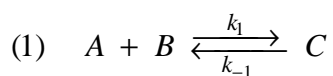
In general, a chemical reaction consists of a series of elementary steps. This series of elementary reactions that make up the overall reaction is called the reaction mechanism.

Four Important Features of a Reaction Mechanism

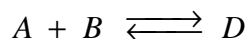
- Elementary reaction steps result from processes in a single molecule, or from reactive collisions between two or occasionally three molecules.
- No chemically stable intermediate can be detected between reactants and products in an elementary step.
- The rate law for an elementary step can be deduced from its stoichiometry assuming collision theory (unimolecular if only one molecule is involved; bimolecular if two molecules are involved, etc.).
- The sum of the elementary steps is the overall net reaction.

Example 1:

Consider a reaction that's comprised of the following elementary steps, i.e., the reaction mechanism is given by:



The net reaction or chemical equation for the overall reaction is:



The rate law for the individual elementary steps are:

$$\text{step 1} \quad \left(\frac{d[C]}{dt} \right)_1 = k_1 [A] [B] - k_{-1} [C]$$

$$\text{step 2} \quad \frac{d[D]}{dt} = k_2 [C] - k_{-2} [D]$$

Suppose step 1 is so fast that it is in rapid equilibrium and step 2 is irreversible, i.e., $k_2 \gg k_{-2}$.

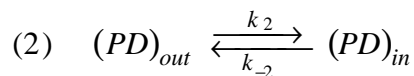
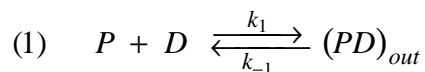
$$\text{Then } \frac{d[D]}{dt} = \text{rate} = k_2 [C] = k_2 K_1 [A][B]$$

$$\text{since } k_1 [A][B] = k_{-1} [C]$$

$$\text{or } [C] = \frac{k_1 [A][B]}{k_{-1}} = K_1 [A][B]$$

A concrete example with the above reaction mechanism:

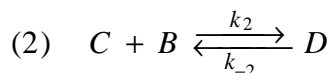
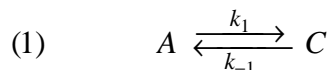
Intercalation of the drug proflavin (P) into DNA (D)



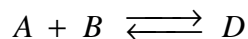
where $(PD)_{out} \equiv$ drug-DNA intermediate in which the drug is attached only loosely to the outside of the double-helix. Step 1 is bimolecular; step 2 is unimolecular.

Example 2:

Now suppose that the reaction is made up of the following elementary steps instead:



The net reaction or chemical equation for the overall reaction is:



The rate laws for the individual elementary steps are:

$$\text{step 1} \quad \left(\frac{d[C]}{dt} \right)_1 = -\frac{d[A]}{dt} = k_1 [A] - k_{-1} [C]$$

$$\text{step 2} \quad \frac{d[D]}{dt} = k_2 [C][B] - k_{-2} [D]$$

Let's Examine the Following Scenarios:

- (1) Step 1 is a fast equilibrium so that kinetics is controlled by step 2 which is slower and irreversible.

$$\text{Then } k_1 [A] = k_{-1} [C] \quad \text{or} \quad [C] = \frac{k_1}{k_{-1}} [A] = K_1 [A]$$

$$\text{and } \text{rate} \cong k_2 [C][B] = k_2 K_1 [A][B]$$

where we have assumed that $k_2 \gg k_{-2}$ (step 2 is irreversible).

Note that this scenario predicts the same rate law as the previous reaction mechanism. In practice, one can come up with several reaction mechanisms that yield the same rate law.

- (2) Step 1 is slow, but step 2 is fast and equilibrium lies toward product so that $k_2 \gg k_{-2}$.

$$\text{Then } \text{rate} = + \frac{d[D]}{dt} = - \frac{d[A]}{dt} = k_1 [A]$$

- (3) A more general scenario, where step 1 and step 2 have comparable rates. Then expect $[C]$ to be small and only slowly varying with time. That is

$$\frac{d[C]}{dt} \cong 0$$

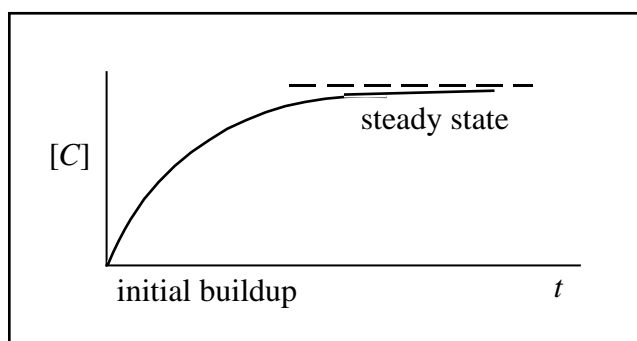


Figure 5-1

This is the so-called steady-state condition.

$$\left(\frac{d[C]}{dt}\right) = k_1[A] - k_{-1}[C] - k_2[C][B] + k_{-2}[D]$$

\downarrow
 0 if step 2 is irreversible

$$= 0 \quad \text{under steady state}$$

Solving for $[C]_{\text{steady state}}$ or $[C]_{ss}$

$$k_1[A] - k_{-1}[C]_{ss} - k_2[C]_{ss}[B] = 0$$

$$\text{or} \quad [C]_{ss} = \frac{k_1[A]}{k_{-1} + k_2[B]}$$

$$\text{Then rate} = \frac{d[D]}{dt} \cong k_2[C]_{ss}[B] = \frac{k_1k_2[A][B]}{k_{-1} + k_2[B]}$$

Examine the Limits:

(1) Step 1 is a fast equilibrium; step 2 is slower and irreversible; that is, $k_{-1} \gg k_2[B]$.

$$\begin{aligned} \text{rate} &= \frac{k_1k_2[A][B]}{k_{-1} + k_2[B]} = \frac{k_1k_2[A][B]}{k_{-1}} \\ &= K_1k_2[A][B] \end{aligned}$$

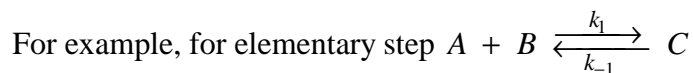
(2) Step 1 is slow and step 2 fast and irreversible; that is, $k_2[B] \gg k_{-1}$.

$$\text{rate} = \frac{k_1k_2[A][B]}{k_{-1} + k_2[B]} \cong \frac{k_1k_2[A][B]}{k_2[B]} = k_1[A]$$

which are the results expected and obtained earlier.

Note That

- (1) The equilibrium constant for an elementary step is the ratio of its forward and reverse rate constants. This result follows from the principle of microscopic reversibility and consideration of detailed balance and assumes that the rate law for an elementary step can be deduced from its stoichiometry.



The rate law for the forward reaction is:

$$-\frac{d[A]}{dt} = -\frac{d[B]}{dt} = k_1 [A][B] \quad \text{that is, it is bimolecular}$$

The rate law for the reverse reaction is:

$$-\frac{d[C]}{dt} = -k_{-1} [C] \quad \text{that is, it is unimolecular}$$

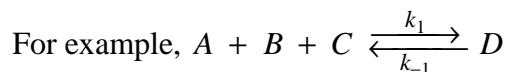
Invoking detailed balance at equilibrium:

forward rate = reverse rate

$$k_1 [A][B] = k_{-1} [C] \quad \text{at equilibrium, or}$$

$$\left(\frac{[C]}{[A][B]} \right)_{eq} = K_1 = \frac{k_1}{k_{-1}}$$

Occasionally, three molecular species participate in a reaction to give product; that is, the step is trimolecular.



- (2) The equilibrium constant for the overall reaction, K_c or $K_{overall}$ is the ratio of products of forward (k_i) and reverse (k_{-i}) rate constants for the elementary steps.

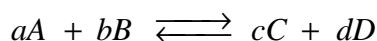
That is,

$$K_{overall} = \frac{\prod k_i}{\prod k_{-i}}$$

Detailed Balance for Overall Reaction

As mentioned earlier, the principle of microscopic reversibility and the considerations of detailed balance at chemical equilibrium are applicable to the overall reaction as well. However, here things are not so straightforward, because rate laws are not necessarily related to the stoichiometry of the overall reaction.

Return to the earlier hypothetical reaction:



$$\text{rate law for forward reaction} = k_f [A]^{\alpha_f} [B]^{\beta_f} [C]^{\gamma_f} [D]^{\delta_f}$$

$$\text{rate law for reverse reaction} = k_b [A]^{\alpha_b} [B]^{\beta_b} [C]^{\gamma_b} [D]^{\delta_b}$$

A simple scenario!

At chemical equilibrium,

$$\text{rate for forward reaction} = \text{rate for reverse reaction}$$

$$\text{or } \frac{k_f}{k_b} [A]_{eq}^{\alpha_f - \alpha_b} [B]_{eq}^{\beta_f - \beta_b} [C]_{eq}^{\gamma_f - \gamma_b} [D]_{eq}^{\delta_f - \delta_b} = 1$$

But, we also know that the following is true

$$K_c = \left(\frac{[C]^c [D]^d}{[A]^a [B]^b} \right)_{eq}$$

$$\text{or } \frac{[A]_{eq}^a [B]_{eq}^b}{[C]_{eq}^c [D]_{eq}^d} K_c = 1$$

For both equalities to hold, it is a sufficient condition that

$$\frac{k_f}{k_b} [A]_{eq}^{\alpha_f - \alpha_b} [B]_{eq}^{\beta_f - \beta_b} [C]_{eq}^{\gamma_f - \gamma_b} [D]_{eq}^{\delta_f - \delta_b} = \left(\frac{[A]_{eq}^a [B]_{eq}^b}{[C]_{eq}^c [D]_{eq}^d} K_c \right)^s$$

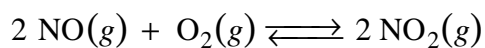
In many cases, it will turn out that s is +1 or some small integer so that a simple relation between the rates and the equilibrium expression can be obtained,

$$\text{so that } \alpha_f - \alpha_b = as$$

$$\beta_f - \beta_b = bs \quad \text{etc.}$$

$$\text{and } \frac{k_f}{k_b} = K_c^s$$

Example:



$$K_c = \left(\frac{[\text{NO}_2]^2}{[\text{NO}]^2[\text{O}_2]} \right)_{eq}$$

Given that the rate law for the reverse reaction is

$$k_b [\text{NO}_2]^2$$

you can deduce the rate law for the forward reaction.

Applying detailed balance:

$$\frac{k_f}{k_b} [\text{NO}]_{eq}^{\alpha_f - \alpha_b} [\text{O}_2]_{eq}^{\beta_f - \beta_b} [\text{NO}_2]_{eq}^{\gamma_f - \gamma_b} = \left(\frac{[\text{NO}]^2[\text{O}_2]}{[\text{NO}_2]^2} K_c \right)^s$$

where $\alpha_b = 0$

$$\beta_b = 0$$

$$\gamma_b = 2$$

Therefore $\alpha_f = 2s$

$$\beta_f = s$$

$$\gamma_f - 2 = -2s$$

Simplest solution: $s = 1$

$$\alpha_f = 2$$

$$\beta_f = 1$$

$$\gamma_f = 0$$

$$K_c = \frac{k_f}{k_b}$$

or rate law for forward reaction = $k_f [\text{NO}]^2 [\text{O}_2]^1$