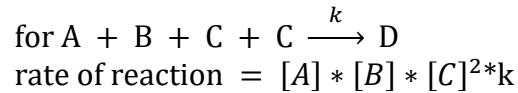


Quantitative Physiology I / Molecular and Cellular Systems, BMEN E4001x
Notes 01- Chemical Kinetics and Equilibria
Chapter 1 of Keener & Sneyd.

Law of Mass Action

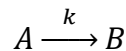


A, B, C, etc, are thus in units of concentration, while k is of units to yield conc/time.

In the following, I'll adopt K&S notation of lower case letters for species concentrations.

The number of species that appear in the rate of reaction equation is the order of the reaction.

Unimolecular reaction as a general framework – first order reaction:



A = reagent

B = product

k = rate constant, a mix of energetic and physical factors

The reaction rate for this elementary reaction is defined as the rate of conversion of A to B, which is equivalent to either the rate of loss of A or rate of generation of B.

In this simple case,

$$\frac{d[A]}{dt} = \frac{da}{dt} = -[A]k = -ak$$

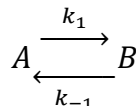
From this, we get for a starting concentration of A of $[A]_0$, or a_0 ,

$$[A](t) = [A]_0 * \exp(-kt)$$

Some considerations:

- This is not a very useful for complex biological reactions, as it is unregulated.
- However, the idea of a decay process is very important in understanding biomolecular interactions. k in this case is going to be in units of 1/time. The inverse of k is an important measure of how long it takes A to decay. When $t = 1/k$, [A] decreases 64% from the initial concentration.
- Remember that this is exponential decay. At $t = 2 * 1/k$, [A] is $1/e^2$ the original (~14%), or has dropped 86%, not $2 * 64\% = 128\%$.
- In this reaction, k has units of 1/time. This is not the case for rate constants involving interactions between different molecules (next section).

As a first level of complexity, add the reverse reaction



This reaction is first order in both forward and reverse. An isomerization reaction, for example

$$\begin{aligned}\frac{da}{dt} &= -k_1a + k_{-1}b \\ \frac{db}{dt} &= k_1a - k_{-1}b \quad \text{differential equations} \\ &\text{and} \\ a + b &= a_0 \quad \text{“conservation” equation}\end{aligned}$$

Solve, looking at expression for a, and using the conservation equation to eliminate b for now. We also introduce the temporary variable a'.

$$\frac{da}{dt} = -k_1a + k_{-1}(a_0 - a) = -(k_1 + k_{-1})a + k_{-1}a_0$$

$$a' = a - \frac{k_{-1}}{(k_1 + k_{-1})}a_0$$

(see the box a few lines down for an explanation of this step)

which leads to

$$\frac{da'}{dt} = -(k_1 + k_{-1}) \left(a' + \frac{k_{-1}}{(k_1 + k_{-1})}a_0 \right) + k_{-1}a_0 = -(k_1 + k_{-1})a'$$

or....

$$a'(t) = C \exp(-(k_1 + k_{-1})t)$$

or...

$$a(t) = C \exp(-(k_1 + k_{-1})t) + \frac{k_{-1}}{(k_1 + k_{-1})}a_0$$

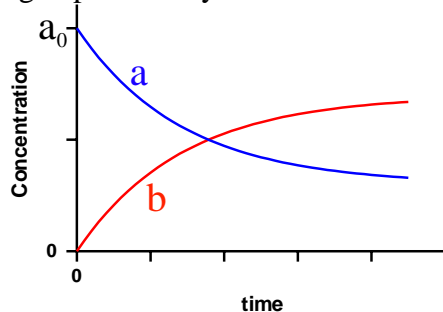
To make the assumption boundary condition that at $t=0, a=a_0$

$$a_0 = C + \frac{k_{-1}}{(k_1 + k_{-1})}a_0$$

$$(k_1 + k_{-1})a_0 = (k_1 + k_{-1})C + k_{-1}a_0$$

$$C = \frac{k_1}{(k_1 + k_{-1})}a_0$$

Let's try to draw out. We know that a graph of $[A]$ vs. t starts at $[A]=a_0$. It also approaches something exponentially.



$$a(t = \text{long}) = \frac{k_{-1}}{(k_1 + k_{-1})} a_0$$

$$b = a_0 - a$$

$$b(t = \text{long}) = a_0 \left(1 - \frac{k_{-1}}{(k_1 + k_{-1})} \right) = a_0 \left(\frac{k_1}{(k_1 + k_{-1})} \right)$$

or.....

$$\left. \frac{b}{a} \right|_{t=\text{long}} = \frac{k_1}{k_{-1}} = K_{\text{eq}}$$

and this condition is called equilibrium.

- Note that we could have gotten here by setting $da/dt=0$ and solving, but the time element would have been lost.
- Equilibrium is the long term, and the trajectory of how we got there is the kinetics
- At equilibrium, it is not that A does not become B, and vice versa, but net changes are zero.

Change of variables.

In the derivation above for the reversible reaction $A \rightleftharpoons B$, the expression for da/dt looks similar to that for the unimolecular equation, but had the added term $+k_{-1}a_0$. If that added term could be removed, then it would look like the equation for the unimolecular reaction at the beginning of this section, with the solution being an exponential decay curve.

To get rid of that last term, the variable a was substituted with a' , which has the form

$$a' = a + C.$$

The approach is to now find a value of C that eliminates that extra term for the new variable.

Since a and a' are equal except for adding a constant,

$$\frac{da'}{dt} = \frac{da}{dt} = -(k_1 + k_{-1})a + k_{-1}a_0$$

Substituting in $a = a' - C$,

$$\frac{da'}{dt} = -(k_1 + k_{-1})(a' - C) + k_{-1}a_0.$$

Which becomes

$$\frac{da'}{dt} = -(k_1 + k_{-1})a' + (k_1 + k_{-1})C + k_{-1}a_0$$

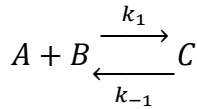
The last two terms sum to zero if

$$C = -\frac{k_{-1}}{(k_1 + k_{-1})} a_0$$

Thus, for the equation above,

$$a' = a - \frac{k_{-1}}{(k_1 + k_{-1})} a_0$$

Binding – second order reaction:



$$\begin{aligned}\frac{da}{dt} &= -abk_1 + ck_{-1} \\ \frac{db}{dt} &= -abk_1 + ck_{-1} \\ \frac{dc}{dt} &= +abk_1 - ck_{-1}\end{aligned}$$

This framework is one of the core ideas in cells signaling and molecular biology. Some examples in which it occurs:

- Protein protonation; protonation of lysines, deprotonation of aspartic acid residues. These affect protein conformation, which is the key to activity. So, in this case, A is a residue, C is a protonated residue, B is a proton (we'll come back to this concept later).
- Buffers. Reverse of protein protonation, in which we want to use salts to control presence of protons
- Enzymes. Coming up

Kinetics of this system are solvable, but rather complex; a, b, and c are interdependent. If we simplify with respect to A, a^2 terms are introduced, greatly complicating the problem.

Let's simplify by considering B constant. For example, we seek to know how much of A is bound to B (in other words, C) when B that is provided at some specific concentration.

Another way of thinking of this, assume B is at much higher concentration than A, such that the deviations of A don't modify B much.

The molecule A is thus around in two forms, A and C.

$$a + c = a_0$$

Now, substituting in $a = a_0 - c$

$$\frac{dc}{dt} = k_1((a_0 - c) \cdot b) - ck_{-1}$$

Or, rearranged:

$$\frac{dc}{dt} = -(k_1b + k_{-1})c + k_1ba_0$$

Following the isomerization reaction above, this becomes an exponential solution with time constant of $1/(k_1b + k_{-1})$. So, a bit more complicated with b showing up in the equation. Let's also look at the equilibrium condition, this time just setting the differential equation for C to zero.

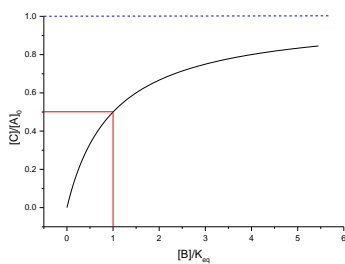
$$\frac{dc}{dt} = 0 \rightarrow -(k_1b + k_{-1})c + k_1ba_0 = 0$$

and solve for C,

$$c = a_0 \frac{b}{K_{eq} + b}; K_{eq} = \frac{k_{-1}}{k_1}$$

$$[C] = [A]_0 \frac{[B]}{K_{eq} + [B]}$$

and this looks like:



Things to note:

- $[B]/K_{eq}=1 \rightarrow [C]/[A]_0=0.5$
- K_{eq} is called equilibrium constant, note that it is different than the Mass Action reaction constant.