

## Receptor ligand binding kinetics

In the simplest case:  $A + B \leftrightarrow C$ , the system differential equation can be reduced to:

$$dC(t)/dt = k_a (A_o - C(t)) (B_o - C(t)) - k_d C(t) \quad (1)$$

Almost always, this equation (1) is resolved only in the hypothesis that  $C(t)$  remains small in front of  $A_o$  (the total concentration of receptor) which means a low receptor occupancy. This is always the case when  $B_o$  (the total concentration of ligand) is in tracer concentration.

In this case, the equation (1) becomes linear:

$$\begin{aligned} dC(t)/dt &= k_a A_o (B_o - C(t)) - k_d C(t) \\ dC(t)/dt &= k_a A_o B_o - (k_a A_o + k_d) C(t) \end{aligned}$$

and the solution is simple (assuming  $C(0) = 0$ ):

$$C(t) = k_a A_o B_o (1 - \exp(-(k_a A_o + k_d) t)) / (k_a A_o + k_d)$$

Which gives:

$$C(t) = A_o B_o (1 - \exp(-(k_a A_o + k_d)t)) / (A_o + K_d) \quad (2)$$

However, this simplification is not necessary to derive an analytical solution because the differential equation is an equation with separate variables:

$$dC(t) / (k_a (A_o - C(t)) (B_o - C(t)) - k_d C(t)) = dt$$

Factoring the denominator is performed using the solutions in the second-degree equation:

$$k_a C(t)^2 - (k_a (A_o + B_o) + k_d) C(t) + k_a A_o B_o = 0$$

By posing  $D$  (discriminant) =  $(k_a (A_o + B_o) + k_d)^2 - 4 k_a^2 A_o B_o$ , we have:

$$K_{1,2} = (k_a (A_o + B_o) + k_d) \pm D^{1/2} / 2 k_a$$

And (1) is written:

$$dC(t) / k_a (C(t) - K_1) (C(t) - K_2) = dt$$

or:

$$dC(t) (1/(C(t) - K_1) - 1/(C(t) - K_2)) = k_a (K_1 - K_2) dt$$

which integrates in a trivial way as:

$$\ln((C(t) - K_1)/(C(t) - K_2)) - k_a (K_1 - K_2) t = u$$

We notice that  $k_a (K_1 - K_2) = D^{1/2}$  and, when  $C(0) = 0$ ,  $u = \ln(K_1/K_2)$  and the solution is:

$$C(t) = K_1 K_2 (1 - \exp(D^{1/2} t)) / (K_2 - K_1 \exp(D^{1/2} t))$$

or (to show the decreasing exponential:

$$C(t) = K_1 K_2 (1 - \exp(-D^{1/2} t)) / (K_1 - K_2 \exp(-D^{1/2} t)) \quad (3)$$

We find that at the equilibrium ( $t \rightarrow \infty$ )  $C(\infty) = K_2$  (the solution  $K_1$  is obviously not suitable) and if we assume that we are far from saturation ( $K_2$  small) we find the simplified solution (2).

Surprisingly, the general solution (3) is very rarely used.