The law of mass action

The rate of a reaction should depend on the stoichiometry of the reaction identically to the equilibrium constants.

Example 1

$$\mathrm{A} + \mathrm{B} \underset{b}{\overset{f}{\rightleftharpoons}} \mathrm{C}$$

We have

$$\frac{[A][B]}{[C]} = K_{\mathrm{eq}} \qquad \frac{d[C]}{dt} = f[A][B] - b[C]$$

Example 2

$$2\,\mathrm{R} \underset{b}{\overset{f}{\rightleftharpoons}} \mathrm{R}_2$$

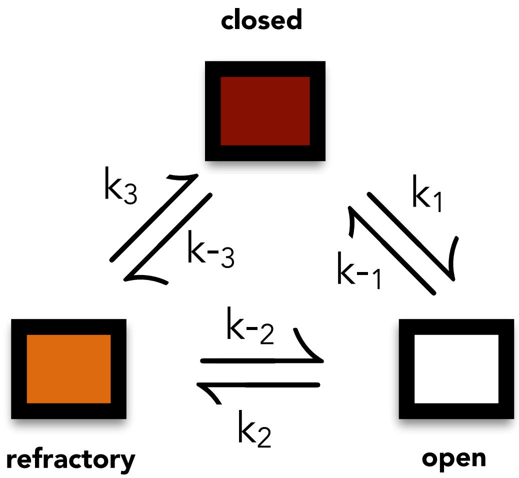
We have

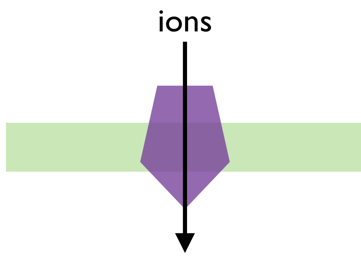
$$\frac{[R]^2}{[R_2]} = K_{\mathrm{eq}} \qquad \frac{d[R_2]}{dt} = f[R]^2 - b[R_2]$$

Rates of reactions are chosen so that the system can reach equilibrium.

Allowing reactions to go to equilibrium can restrict the values of rate constants

Ion channels often have multiple states





Detailed balance implies

$$k_1 C = k_{-1} O \quad ; \quad k_2 O = k_{-2} R \quad ; \quad k_3 R = k_{-3} C.$$

equilibrium

or

$$C = \frac{k_{-1}}{k_1} O = \frac{k_{-1}}{k_1} \cdot \frac{k_{-2}}{k_2} R = \frac{k_{-1}}{k_1} \cdot \frac{k_{-2}}{k_2} \cdot \frac{k_{-3}}{k_3} C$$

and so

$$k_1 k_2 k_3 = k_{-1} k_{-2} k_{-3}$$

if this constraint is broken, the system must use energy to bias the cycle to move in a particular direction

Hill functions

Empirical input-output relationships are often approximated as Hill functions

Hill number: determines the steepness of the response

$$y(x) = \frac{y_{\max} x^n}{K^n + x^n}$$

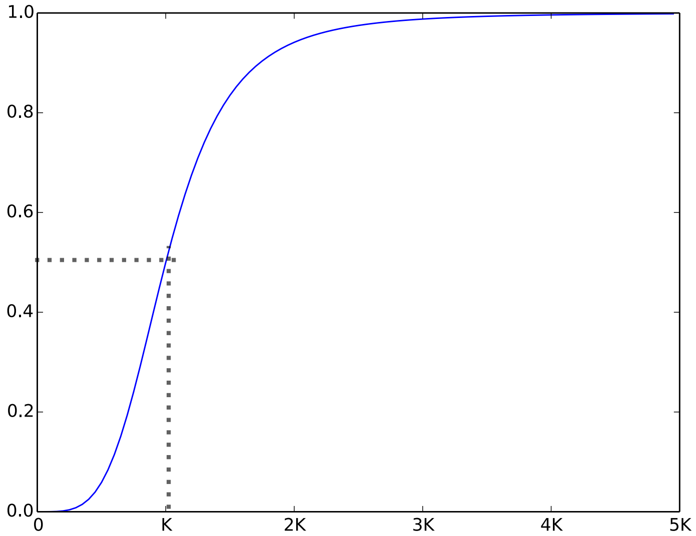
EC_{50}

$$y(x) = \frac{y_{\max} K^n}{K^n + x^n}$$

IC_{50}

output

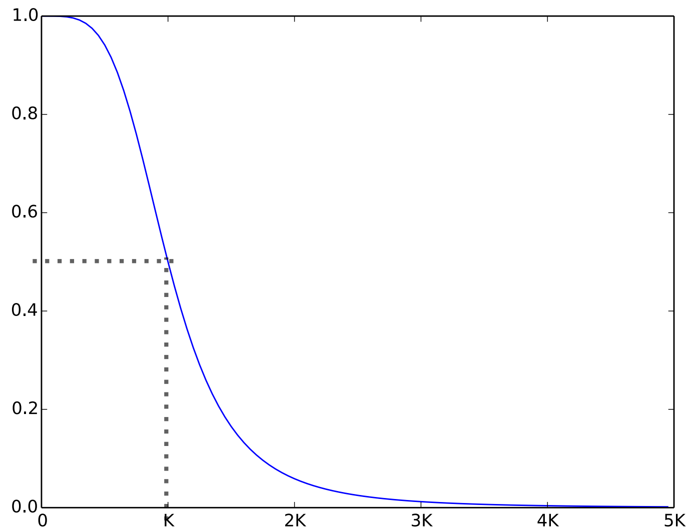
$\frac{y(x)}{y_{\max}}$



x

input

$\frac{y(x)}{y_{\max}}$



x

input

$$y(x = K) = \frac{y_{\max}}{2}$$

Sensitivity

The sensitivity of an output *s* to a quantity *p* is a measure of how much that output will change in response to a small change in *p*.

$$\Delta s \simeq \frac{ds}{dp}\Delta p$$

The relative sensitivity is a more robust measure:

$$\chi = \frac{p}{s} \times \frac{ds}{dp}$$

It is dimensionless and measures relative changes:

$$\frac{\Delta s}{s} \simeq \chi \frac{\Delta p}{p}$$

The sensitivity of a Hill function can be proportional to the Hill number

When

$$y = y_{\max} \frac{x^n}{K^n + x^n}$$

then

$$\begin{aligned} n &= 2 \frac{d \log y / y_{\max}}{d \log x} \bigg|_{x=K} \\ &= 2 \left. \chi \right|_{x=K} \end{aligned}$$

The more sensitive the response, the higher the Hill number.

Some terminology

$$y = y_{\max} \frac{x^n}{K^n + x^n}$$

n= 1: *hyperbolic* or Michaelis-Menten response

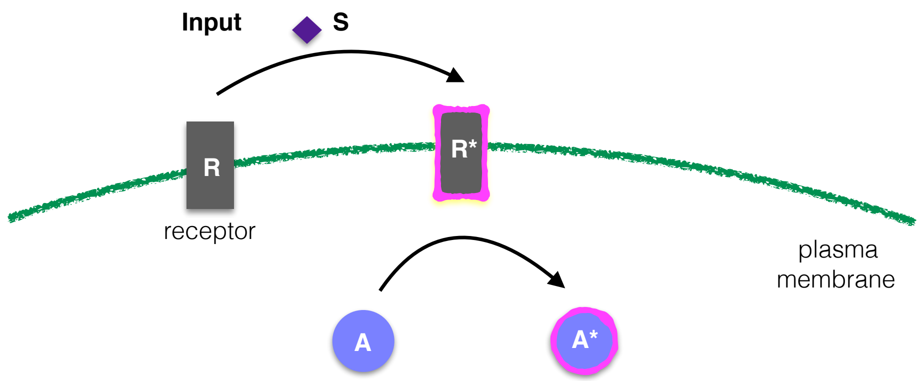
n> 1: *sigmoidal* or S-shaped response

n> 1: *ultrasensitive* response for signalling

n< 1: *subsensitive* response

n> 1: *cooperative* response for gene expression

Modelling signal transduction II



Rather than

$$[R^*] \simeq \frac{[S]R_0}{\frac{b}{f} + [S]}$$

use

$$[R^*] \simeq \frac{R_0[S]^n}{K^n + [S]^n}$$

so that

$$\frac{d[A^*]}{dt} \simeq \frac{kR_0[S]^n}{K^n + [S]^n}(A_0 - [A^*])$$

e.g. *n* molecules of S are needed to activate a receptor