Association reactions are limited by diffusion

$$f = \frac{n_A V}{t_{\mathrm{diff}} + t_{\mathrm{reac}}} < \frac{n_A V}{t_{\mathrm{diff}}}$$

$$f = \tilde{f} n_A V$$

The fastest association reaction is one where the two molecules react the instant they come together and so is determined only by diffusion

$$f_{\max} = 4\pi D a$$

from solving the diffusion equation

D: the sum of the molecules' diffusion coefficients

a: typical size of a molecule

and for molar concentrations

$$f \text{ (in M)} < f_{\max} \times n_a \times 10^3$$

n_a: 1 mole

10^3: volume in litres

Association reactions have rates less than approximately 10^9 M^{-1} s^{-1}

$$f \text{ (in M)} < f_{\max} \times n_a \times 10^3$$

$$f_{\max} = 4\pi D a$$

Assuming D is 1000 μm^2 s^{-1} (100 times faster than the typical diffusion of proteins)

$$f < 4\pi \times \overbrace{10^3 \times 10^{-12}}^{D \text{ in } \mathrm{m^2 s^{-1}}} \times \overbrace{10^{-9}}^{a} \times \overbrace{6 \times 10^{23}}^{n_a} \times \overbrace{10^3}^{\text{for } \ell}$$
$$\simeq 7.5 \times 10^9 \, \mathrm{M^{-1} s^{-1}}.$$

What is the lowest possible concentration in a bacterium?

The concentration of 1 molecule is

$$\frac{1}{n_A V}$$

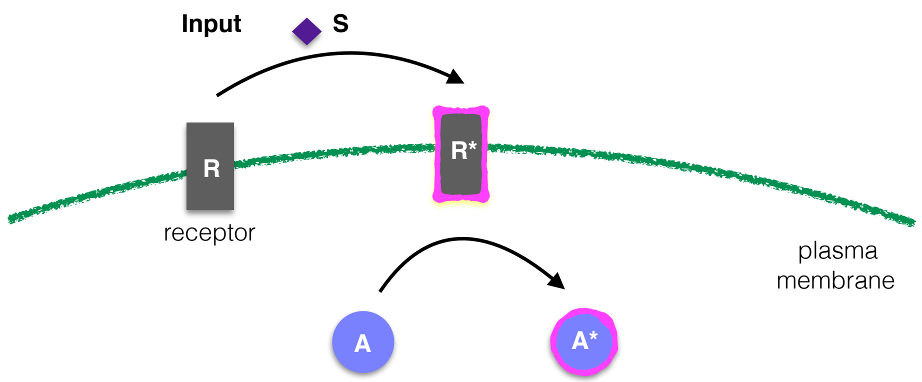
and the volume of a bacterium is 1μm³

$$\frac{1}{6 \times 10^{23} \times 10^{-18} \times 10^{3}} \simeq \frac{1}{10^{9}}$$

Avogado — volume — litres

The lowest possible concentration is 1 nM

Modelling signal transduction I.i



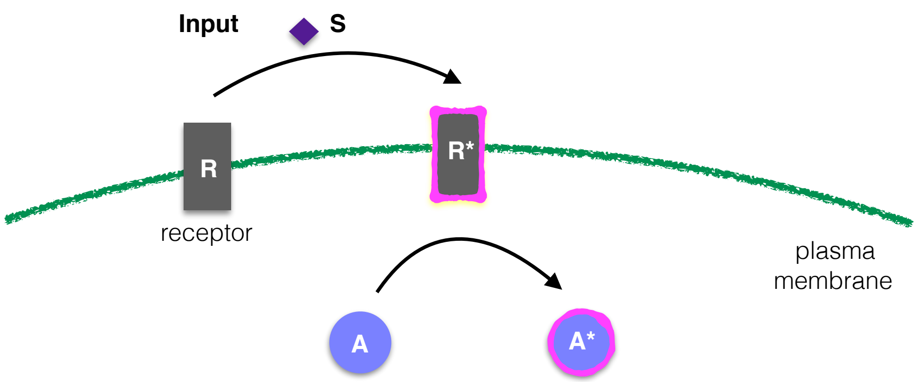
Signal (ligand) binding the receptor

$$[\mathrm{R}] + [\mathrm{S}] \underset{b}{\overset{f}{\rightleftharpoons}} [\mathrm{R}^*]$$

and activated receptors activate a downstream protein *A*

$$[\mathrm{R}^*] + [\mathrm{A}] \xrightarrow{k} [\mathrm{R}^*] + [\mathrm{A}^*]$$

Modelling signal transduction I.ii



$$[\mathrm{R}] + [\mathrm{S}] \underset{b}{\overset{f}{\rightleftharpoons}} [\mathrm{R}^*]$$

$$[\mathrm{R}^*] + [\mathrm{A}] \xrightarrow{k} [\mathrm{R}^*] + [\mathrm{A}^*]$$

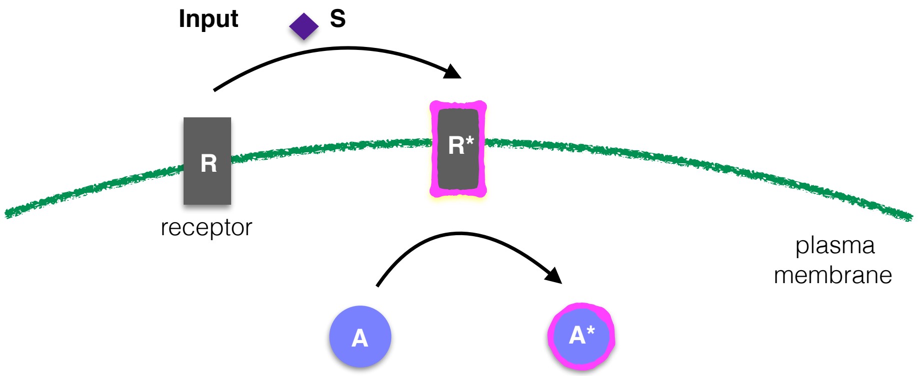
The rate equations are

$$\frac{d[S]}{dt} = -f[R][S] + b[R^*]$$
$$\frac{d[R]}{dt} = -f[R][S] + b[R^*]$$
$$\frac{d[R^*]}{dt} = f[R][S] - b[R^*]$$
$$\frac{d[A]}{dt} = -k[A][R^*]$$
$$\frac{d[A^*]}{dt} = k[A][R^*]$$

notice that the number of receptors is conserved

$$\frac{d[R]}{dt} + \frac{d[R^*]}{dt} = 0$$

Modelling signal transduction I.iii



$$[\mathrm{R}] + [\mathrm{S}] \underset{b}{\overset{f}{\rightleftharpoons}} [\mathrm{R}^*]$$

$$[\mathrm{R}^*] + [\mathrm{A}] \xrightarrow{k} [\mathrm{R}^*] + [\mathrm{A}^*]$$

We are interested in downstream effects – the rate of change of activated *A*.

Let's assume the binding of the receptor and signal is at equilibrium

$$f[R][S] \simeq b[R^*]$$

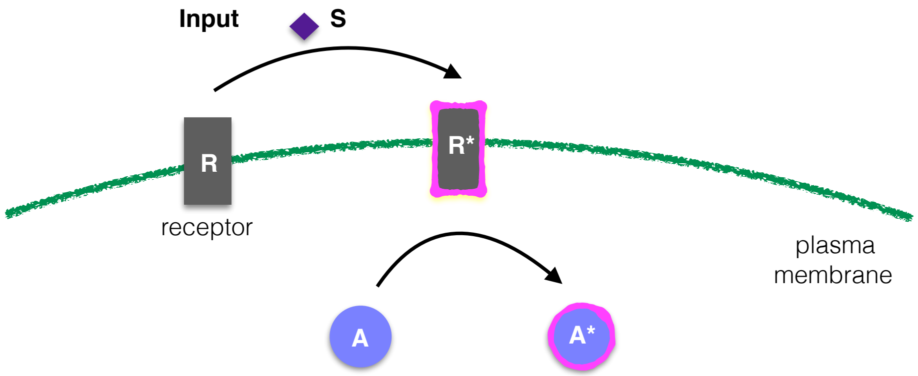
That the receptors are conserved means – for a constant R_0

$$R_0 = [R] + [R^*]$$

and so

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

Modelling signal transduction I.iv



$$[\mathrm{R}] + [\mathrm{S}] \underset{b}{\overset{f}{\rightleftharpoons}} [\mathrm{R}^*]$$

$$[\mathrm{R}^*] + [\mathrm{A}] \xrightarrow{k} [\mathrm{R}^*] + [\mathrm{A}^*]$$

We are interested in downstream effects – activated *A*

$$\frac{d[A^*]}{dt} = k[A][R^*]$$

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

and so

$$\frac{d[A^*]}{dt} \simeq \frac{k[S]R_0}{\frac{b}{f} + [S]}[A]$$

or

$$\frac{d[A^*]}{dt} \simeq \frac{k[S]R_0}{\frac{b}{f} + [S]}(A_0 - [A^*])$$

because the number of *A* molecules is also conserved