Overview

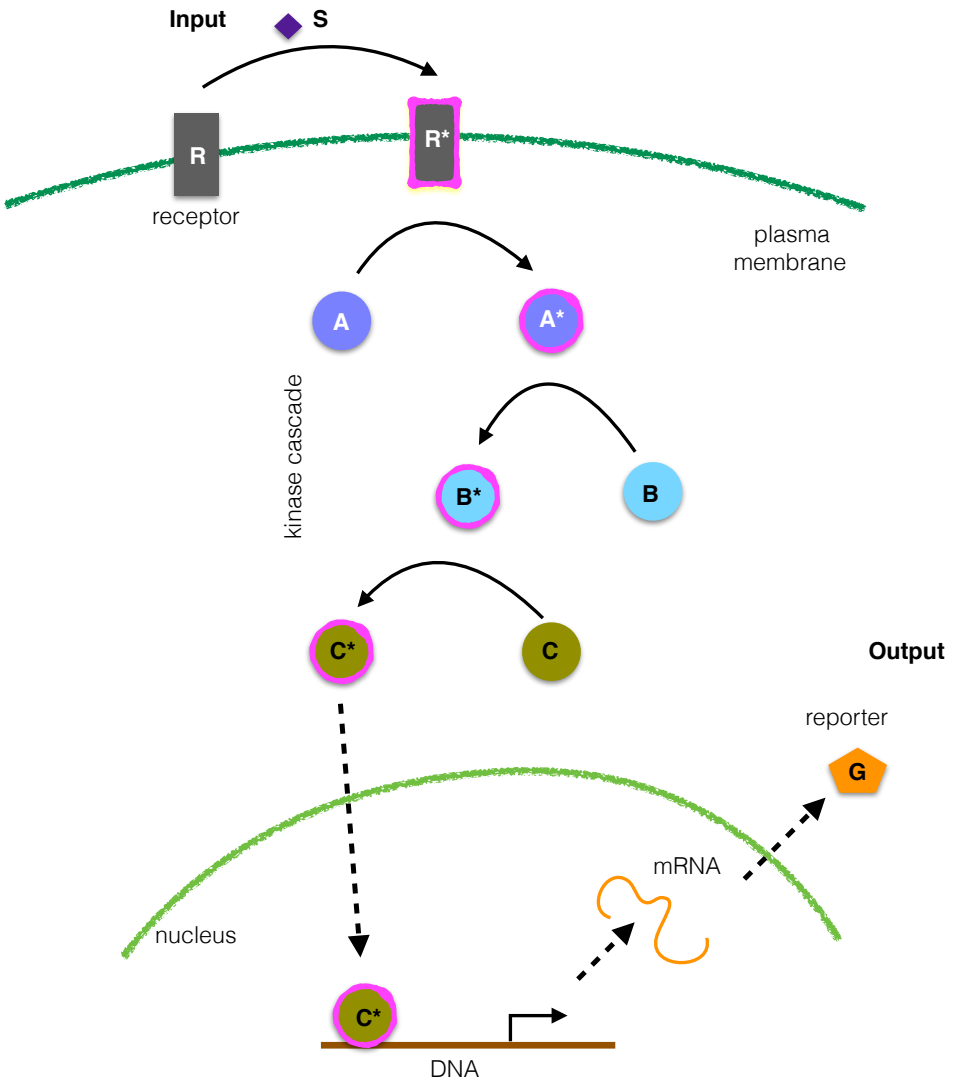
Modelling biochemical reactions

Modelling gene expression

Positive feedback and bistability

Negative feedback and oscillations

I will use a signalling pathway as an example throughout



Modelling biochemical reactions

There are two fundamental types of reactions

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

The association rate is determined by two times:

$$\text{time of reaction} = t_{\text{diff}} + t_{\text{reac}}$$

and so

$$\tilde{f} = (t_{\text{diff}} + t_{\text{reac}})^{-1}$$

The dissociation rate is determined by the lifetime of a molecule of *C*:

$$\tilde{b} = \frac{\log(2)}{\text{lifetime of } C}$$

Rate equations describe how number of molecules change with time

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

How do the numbers of molecules of, say, species *C* change with time?

$$N_C(t+dt) = N_C(t) + \tilde{f} dt N_A N_B - \tilde{b} dt N_C$$

number of pairs of *A* and *B* associating in time *dt*

number of C disassociating in time *dt*

Or

$$\frac{N_C(t+dt) - N_C(t)}{dt} = \tilde{f} N_A N_B - \tilde{b} N_C$$ and so

$$\boxed{\frac{dN_C}{dt} = \tilde{f} N_A N_B - \tilde{b} N_C}$$

Another example

$$\begin{array}{l} \mathrm{A} + \mathrm{B} \underset{\tilde{b}}{\overset{\tilde{f}}{\rightleftharpoons}} \mathrm{C} \\ \qquad\qquad \downarrow k \\ \qquad\qquad \mathrm{D} + \mathrm{E} \underset{\tilde{h}}{\overset{\tilde{g}}{\rightleftharpoons}} \mathrm{F} \end{array}$$

We now have

$$\frac{dN_C}{dt} = \tilde{f} N_A N_B - \tilde{b} N_C - k N_C$$

Each reaction that affects C has a corresponding term in the equation.
There is one positive term for the reaction that increases N_C and a negative term for each reaction that decreases N_C.

Defining concentrations

The molar concentration of C is defined as

$$[C] = \frac{N_C}{n_A V}$$

where N_C is the number of molecules of C, n_A is Avogado's number, and V is the volume of the cell in litres.

$n_A \simeq 6.02 \times 10^{23}$ 1 mole

Note that $1\ell = 10^{-3}\mathrm{m}^3$

The rate equation for concentrations

Before we had

$$\frac{dN_C}{dt} = \tilde{f} N_A N_B - \tilde{b} N_C$$

If we divide this equation by $n_A V$

$$\frac{d}{dt} \cdot \frac{N_C}{n_A V} = \tilde{f} \frac{N_A}{n_a V} \cdot \frac{N_B}{n_a V} n_a V - \tilde{b} \frac{N_C}{n_A V}$$

and so using the definition of concentration

$$\frac{d[C]}{dt} = \tilde{f} n_A V [A][B] - \tilde{b}[C]$$

$$[C] = \frac{N_C}{n_A V}$$

Defining macroscopic rates

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

then

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

Mesoscopic rates govern numbers of molecules, macroscopic rates govern concentrations

For associations, the *mesoscopic* rate depends on the cell's volume – in larger volumes, it takes longer for two molecules to associate – but the *macroscopic* rate does not

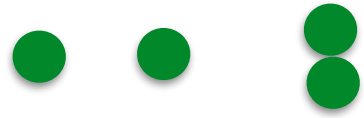
$$f = \tilde{f} n_A V$$
$$b = \tilde{b}$$

the volume terms cancel

For disassociations, the mesoscopic and macroscopic rates are the same – they are determined by the lifetime of molecules.

The difference between mesoscopic and macroscopic rates is important for running stochastic stimulations.

Dimerisation is the only tricky example



$$T + T \underset{b}{\overset{f}{\rightleftharpoons}} T_2$$

association rate: $f\,[T]^2$
disassociation rate: $b[T_2]$

An association reaction removes *two* molecules of *T*, a dissociation reaction creates *two* molecules of *T*

$$\frac{d[T]}{dt} = -2f[T]^2 + 2b[T_2]$$

An association reaction creates *one* molecule of T_2, a dissociation reaction creates *one* molecule of T_2

$$\frac{d[T_2]}{dt} = f[T]^2 - b[T_2]$$

Molecules are conserved during dimerisation

An example

$$T + T \underset{b}{\overset{f}{\rightleftharpoons}} T_2$$

time	T	T_2
	10	0
	8	1
	6	2
	8	1

each line shows the number of molecules after one reaction occurs

We have

$$\frac{d[T]}{dt} = -2f[T]^2 + 2b[T_2]$$

$$\frac{d[T_2]}{dt} = f[T]^2 - b[T_2]$$

and so

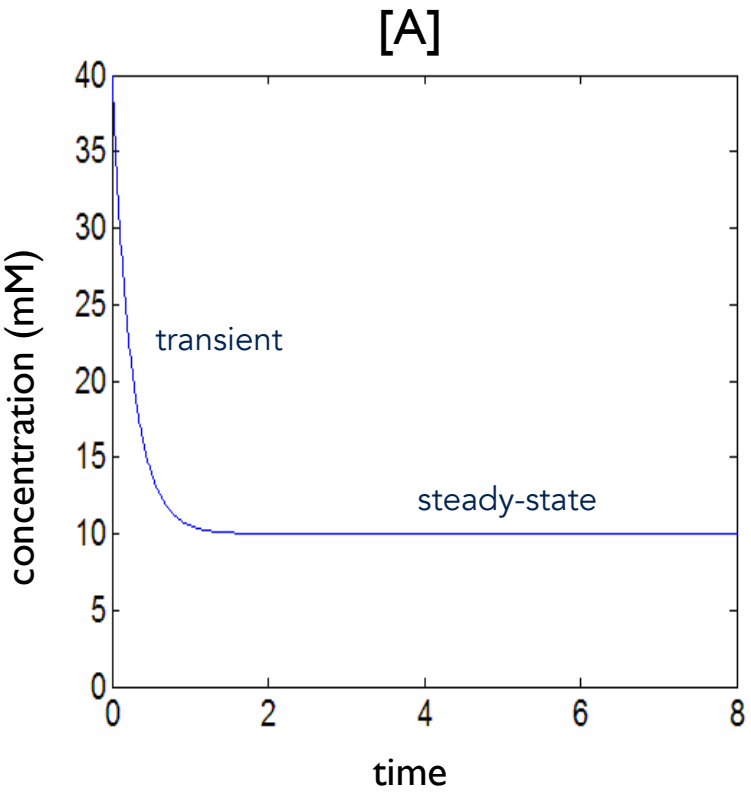
$$\frac{d[T]}{dt} + 2\frac{d[T_2]}{dt} = 0$$

implying

$$[T] + 2[T_2] = \text{constant}$$

the constant is determined by the initial numbers of monomers and dimers

A system is at *steady-state* when concentrations do not change with time – they are fixed, or steady



At steady-state $\frac{d[A]}{dt} = 0$

We will often study systems at steady-state because their behaviour is then simpler.