Modelling degradation

Modelling the degradation of a molecule that has a fixed half-life

$$\mathrm{A} \xrightarrow{k} \varnothing$$

The rate equation is

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

and so

$$[A] = [A]_0 \mathrm{e}^{-kt} \qquad \text{or} \qquad [A] = [A]_0 \cdot 2^{\frac{-kt}{\log 2}}$$

using
$\mathrm{e} = 2^{\frac{1}{\log 2}}$

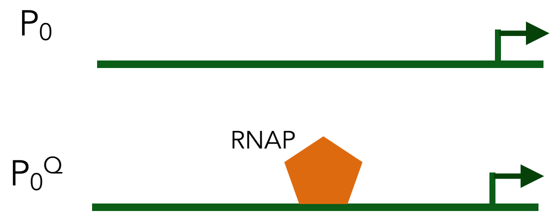
The half-life – the time taken for half the molecules to degrade – is inversely proportional to *k*

$$t_{\frac{1}{2}} = \frac{\log 2}{k}$$

Modelling gene expression

To model gene expression, we start by considering the possible states of the promoter

Constitutive (unregulated) gene expression



We assume binding of RNA polymerase, Q, to the promoter, P_0, is at equilibrium

$$P_0^Q = K_Q Q P_0 \qquad \mathrm{P}_0 + \mathrm{Q} \rightleftharpoons \mathrm{P}_0^{\mathrm{Q}}$$

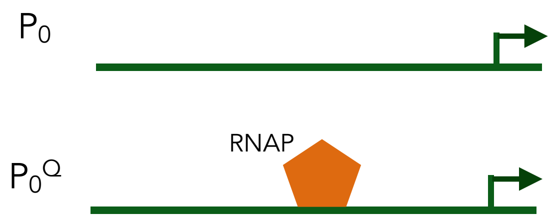
There is a fixed number, n, of promoters

$$P_0 + \overset{K_Q Q P_0}{P_0^Q} = n$$

$$P_0 = \frac{n}{1 + K_Q Q}$$

$$\boxed{P_0^Q = \frac{n K_Q Q}{1 + K_Q Q}}$$

Only the promoter state bound by RNAP initiates transcription



$$\mathrm{P_0^Q} \xrightarrow{u} \mathrm{P_0^Q} + \mathrm{M}$$
$$\mathrm{M} \xrightarrow{d_M} \varnothing$$

The rate equation for mRNA *M* is

$$\frac{dM}{dt} = uP_0^Q - d_M M$$

maximum rate of transcription (u)

reciprocal of the half-life of mRNA (d_M)

$$\frac{dM}{dt} = \frac{nuK_Q Q}{1 + K_Q Q} - d_M M$$

Translation is modelled as a first-order process

$$\mathrm{M} \xrightarrow{v} \mathrm{M} + \mathrm{P}$$
$$\mathrm{P} \xrightarrow{d_P} \varnothing$$

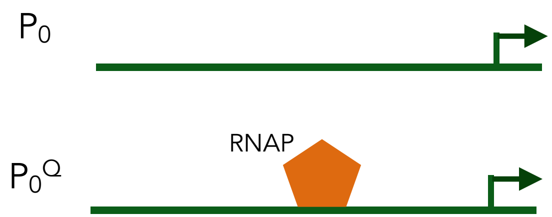
The rate equation for protein *P* is

$$\frac{dP}{dt} = vM - d_P P$$

rate of translation

reciprocal of the half-life of protein

The complete model for a constitutive promoter is then:



$$\mathrm{P}_0^{\mathrm{Q}} \xrightarrow{u} \mathrm{P}_0^{\mathrm{Q}} + \mathrm{M}$$

$$\mathrm{M} \xrightarrow{d_M} \varnothing$$

$$\mathrm{M} \xrightarrow{v} \mathrm{M} + \mathrm{P}$$

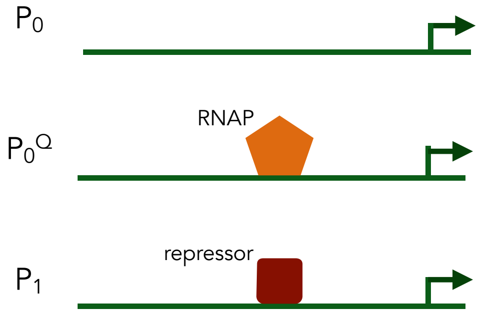
$$\mathrm{P} \xrightarrow{d_P} \varnothing$$

$$\frac{dM}{dt} = uP_0^Q - d_M M$$

$$\frac{dP}{dt} = vM - d_P P$$

$$P_0^Q = \frac{nK_Q Q}{1 + K_Q Q}$$

Modelling repression by a single repressor competing with RNA polymerase for the promoter



$$P_0 + R \rightleftharpoons P_1$$

$$P_0 + Q \rightleftharpoons P_0^Q$$

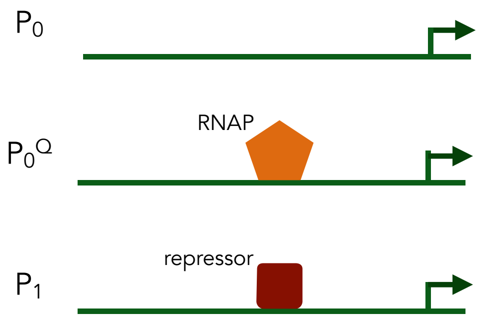
We assume that binding of all proteins at the promoter is at equilibrium

$$P_1 = K_R R P_0 \quad ; \quad P_0^Q = K_Q Q P_0$$

and that the total number of promoters is conserved

$$P_0 + P_0^Q + P_1 = n$$

The higher the number of repressors, the less RNAP binds to the promoter



$$P_1 = K_R R P_0$$

$$P_0^Q = K_Q Q P_0$$

The total number of promoters is conserved

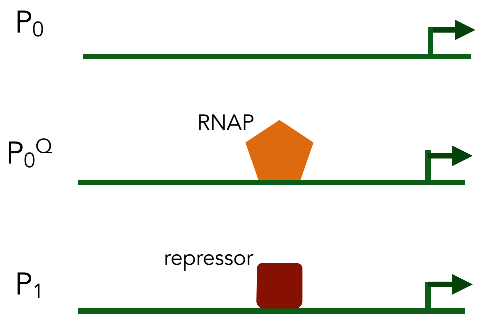
$$P_0 + K_Q Q P_0 + K_R R P_0 = n$$

and so

$$P_0 = \frac{n}{1 + K_Q Q + K_R R}$$

$$\boxed{P_0^Q = \frac{n K_Q Q}{1 + K_Q Q + K_R R}}$$

The model for gene expression from a repressed protein is then



$$\frac{dM}{dt} = \frac{nuK_Q Q}{1 + K_Q Q + K_R R} - d_M M$$

$$\frac{dP}{dt} = vM - d_P P$$

$$u_{\max} = \frac{nuK_Q Q}{1+K_Q Q}$$

$$K_1 = \frac{1+K_Q Q}{K_R}$$

If the concentration of RNAP is constant

$$\frac{dM}{dt} = u_{\max}\left[\frac{1}{1 + \frac{R}{K_1}}\right] - d_M M$$