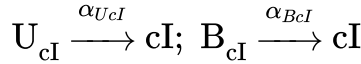
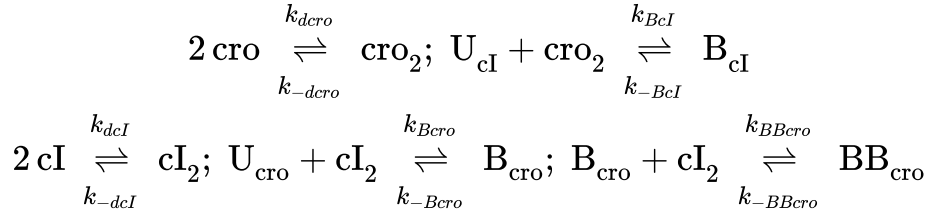


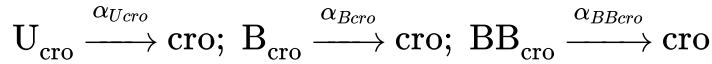
LTM Switch Derivations

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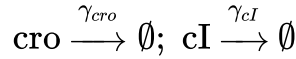
Molecular Reaction Network



where: $\alpha_{UcI} \gg \alpha_{BcI}$



where: $\alpha_{Ucro} \gg \alpha_{Bcro} \gg \alpha_{BBcro}$



QSSA Reaction Network ODEs

I outline the QSSA equations which describe the dimerization of repressors. At QSSA, $\frac{d[\text{cro}]}{dt} = \frac{d[\text{cro}_2]}{dt} = 0$. The following equations are derived from this statement:

$$\begin{aligned}
 [\text{cro}]_{tot} &= [\text{cro}] + 2[\text{cro}_2] \\
 [\text{cro}]^2 k_{dcro} &= [\text{cro}_2] k_{-dcro}; \quad [\text{cro}_2] = [\text{cro}]^2 \frac{k_{dcro}}{k_{-dcro}}
 \end{aligned}$$

$$\begin{aligned}
 [\text{cI}]_{tot} &= [\text{cI}] + 2[\text{cI}_2] \\
 [\text{cI}]^2 k_{dcI} &= [\text{cI}_2] k_{-dcI}; \quad [\text{cI}_2] = [\text{cI}]^2 \frac{k_{dcI}}{k_{-dcI}}
 \end{aligned}$$

I then describe the binding of the cro dimer to the DNA region controlling cI transcription. Our result is a member of the Generalized Hill function family.

$$[DNA_{cI}]_{tot} = [D_{cI}] = [U_{cI}] + [B_{cI}] = 1$$

$$\frac{d[U_{cI}]}{dt} = \frac{d[B_{cI}]}{dt} = 0$$

$$[U_{cI}][cro_2]k_{BcI} = [B_{cI}]k_{-BcI} = 0$$

$$= ([D_{cI}] - [U_{cI}])k_{-BcI}$$

$$[U_{cI}] = [D_{cI}] / (1 + [cro_2] \frac{k_{BcI}}{k_{-BcI}})$$

$$[U_{cI}] = \frac{1}{1 + (\frac{[cro]}{c_{cro}})^2}$$

$$\text{where } c_{cro} = (\frac{k_{-BcI}k_{-Dcro}}{k_{BcI}k_{Dcro}})^{1/2}$$

Ignoring any production from the bound states, we can now model the production of protein cI as follows:

$$[cI] = [U_{cI}]\alpha_{UcI} + [B_{cI}]\alpha_{BcI} - [cI]\gamma_{cI} = [U_{cI}]\alpha_{UcI} - [cI]\gamma_{cI}$$

$$[cI] = \frac{\alpha_{UcI}}{1 + (\frac{[cro]}{c_{cro}})^2} - [cI]\gamma_{cI}$$

We may model production of cro in a very similar manner. However, given the fact that there are two possible binding sites for cI, we must slightly modify our formulation.

$$[DNA_{cro}]_{tot} = [D_{cro}] = [U_{cro}] + [B_{cro}] + [BB_{cro}] = 1$$

$$\frac{d[U_{cro}]}{dt} = \frac{d[B_{cro}]}{dt} = \frac{d[BB_{cro}]}{dt} = 0$$

To simplify this problem, we can consider each of the two binding sites separately.

$$[U_{cro}][cI_2]k_{Bcro} = [B_{cro}]k_{-Bcro} = 0$$

$$= ([D_{cro}] - [U_{cro}])k_{-Bcro}$$

$$[U_{cro}] = [D_{cro}] / (1 + [cI_2] \frac{k_{Bcro}}{k_{-Bcro}})$$

$$[U_{cro}] = \frac{1}{1 + (\frac{[cI]}{c_{cI}})^2}$$

$$\text{where } c_{cI} = (\frac{k_{-Bcro}k_{-DcI}}{k_{Bcro}k_{DcI}})^{1/2}$$

We can then redefine our unbound state as follows, only considering production for the fully unbound state.

$$[U_{cro}] = [D_{cro}](\text{Prop Unbound Site 1})(\text{Prop Unbound Site 1})$$

$$= \left(\frac{1}{1 + \left(\frac{[cI]}{c_{cI}} \right)^2} \right) \left(\frac{1}{1 + \left(\frac{[cI]}{c_{cI}} \right)^2} \right)$$

$$= \frac{1}{\left(\left(\frac{[cI]}{c_{cI}} \right)^2 + 1 \right)^2}$$

$$[\dot{cro}] = [U_{cro}]\alpha_{Ucro} + [B_{cro}]\alpha_{Bcro} + [BB_{cro}]\alpha_{BBcro} - [cI]\gamma_{cI} = [U_{cro}]\alpha_{Ucro} - [cro]\gamma_{cro}$$

$$[\dot{cro}] = \frac{\alpha_{Ucro}}{\left(\left(\frac{[cI]}{c_{cI}} \right)^2 + 1 \right)^2} - [cro]\gamma_{cro}$$