LTM Switch Derivations

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Molecular Reaction Network

$$2\,\mathrm{cro} \underset{k_{-dcro}}{\overset{k_{dcro}}{\rightleftharpoons}} \mathrm{cro_2};\ \mathrm{U_{cI}} + \mathrm{cro_2} \underset{k_{-BcI}}{\overset{k_{BcI}}{\rightleftharpoons}} \mathrm{B_{cI}}$$

$$2\,\mathrm{cI} \underset{k_{-dcI}}{\overset{k_{dcI}}{\rightleftharpoons}} \mathrm{cI_2};\ \mathrm{U_{cro}} + \mathrm{cI_2} \underset{k_{-Bcro}}{\overset{k_{Bcro}}{\rightleftharpoons}} \mathrm{B_{cro}};\ \mathrm{B_{cro}} + \mathrm{cI_2} \underset{k_{-BBcro}}{\overset{k_{BBcro}}{\rightleftharpoons}} \mathrm{BB_{cro}}$$

$$\mathrm{U_{cI}} \xrightarrow{\alpha_{UcI}} \mathrm{cI};\ \mathrm{B_{cI}} \xrightarrow{\alpha_{BcI}} \mathrm{cI}$$

$$\text{where: } \alpha_{UcI} >> \alpha_{BcI}$$

$$\mathrm{U_{cro}} \xrightarrow{\alpha_{Ucro}} \mathrm{cro};\ \mathrm{B_{cro}} \xrightarrow{\alpha_{Bcro}} \mathrm{cro};\ \mathrm{BB_{cro}} \xrightarrow{\alpha_{BBcro}} \mathrm{cro}$$

$$\text{where: } \alpha_{Ucro} >> \alpha_{Bcro} >> \alpha_{BBcro}$$

$$\mathrm{cro} \xrightarrow{\gamma_{cro}} \emptyset;\ \mathrm{cI} \xrightarrow{\gamma_{cI}} \emptyset$$

QSSA Reaction Network ODEs

I outline the QSSA equations which describe the dimerization of repressors. At QSSA, $\frac{d[cro]}{dt} = \frac{d[cro_2]}{dt} = 0$. The following equations are derived from this statement:

$$[cro]_{tot} = [cro] + 2[cro_2]$$

$$[cro]^2 k_{dcro} = [cro_2]k_{-dcro}; \quad [cro_2] = [cro]^2 \frac{k_{dcro}}{k_{-dcro}}$$

$$[cI]_{tot} = [cI] + 2[cI]$$

$$[cI]^2 k_{dcI} = [cI_2]k_{-dcI}; \quad [cI_2] = [cI]^2 \frac{k_{dcI}}{k_{-dcI}}$$

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.

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$$[DNA_{cI}]_{tot} = [D_{cI}] = [U_{cI}] + [B_{cI}] = 1$$
$$\frac{d[U_{cI}]}{dt} = \frac{d[B_{cI}]}{dt} = 0$$
$$[U_{cI}][cro_2]k_{BcI} = [B_{cI}]k_{-BcI} = 0$$
$$= ([D_{cI}] - [U_{cI}])k_{-BcI}$$
$$[U_{cI}] = [D_{cI}]/(1 + [cro_2]\frac{k_{BcI}}{k_{-BcI}})$$
$$[U_{cI}] = \frac{1}{1 + (\frac{[cro]}{c_{cro}})^2}$$
$$\text{where } c_{cro} = (\frac{k_{-BcI}k_{-Dcro}}{k_{BcI}k_{Dcro}})^{1/2}$$

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

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

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.

$$[U_{cro}] = [D_{cro}](\text{Prop Unbound Site 1})(\text{Prop Unbound Site 1})$$
$$= (\frac{1}{1+(\frac{[cI]}{c_{cI}})^2})(\frac{1}{1+(\frac{[cI]}{c_{cI}})^2})$$
$$= \frac{1}{((\frac{[cI]}{c_{cI}})^2+1)^2}$$
$$[\dot{cro}] = [U_{cro}]\alpha_{Ucro} + [B_{cro}]\alpha_{Bcro} + [BB_{cro}]\alpha_{BBcro} - [cI]\gamma_{cI} = [U_{cro}]\alpha_{Ucro} - [cro]\gamma_{cro}$$
$$[\dot{cro}] = \frac{\alpha_{Ucro}}{((\frac{[cI]}{c_{cI}})^2+1)^2} - [cro]\gamma_{cro}$$