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Bistable switch first order feedback (mutually exclusive binding) notes

List of species:

- g_x^{00}: gene X with no protein bound
- g_x^{10}: gene X with one protein X bound
- g_x^{01}: gene X with one protein Y bound
- g_y^{00}: gene Y with no protein bound
- g_y^{10}: gene Y with one protein X bound
- g_y^{01}: gene Y with one protein Y bound
- m_x: mRNA transcribed by gene X
- m_y: mRNA transcribed by gene Y
- p_x: protein produced by gene X
- p_y: protein produced by gene Y

List of reactions:

$$
\begin{aligned}
g_x^{ij} &\xrightarrow{k_{ij}^x} g_x^{ij} + m_x & \qquad g_y^{ij} &\xrightarrow{k_{ij}^y} g_y^{ij} + m_y \\
m_x &\xrightarrow{k_p^x} m_x + p_x & \qquad m_y &\xrightarrow{k_p^y} m_y + p_y \\
m_x &\xrightarrow{d_m^x} \varnothing & \qquad m_y &\xrightarrow{d_m^y} \varnothing \\
p_x &\xrightarrow{d_p^x} \varnothing & \qquad p_y &\xrightarrow{d_p^y} \varnothing \\
g_x^{00} + p_x &\xrightarrow{b_f^{xx}} g_x^{10} & \qquad g_y^{00} + p_y &\xrightarrow{b_f^{yy}} g_y^{01} \\
g_x^{00} + p_x &\xleftarrow{b_r^{xx}} g_x^{10} & \qquad g_y^{00} + p_y &\xleftarrow{b_r^{yy}} g_y^{01} \\
g_x^{00} + p_y &\xrightarrow{b_f^{xy}} g_x^{01} & \qquad g_y^{00} + p_x &\xrightarrow{b_f^{yx}} g_y^{10} \\
g_x^{00} + p_y &\xleftarrow{b_r^{xy}} g_x^{01} & \qquad g_y^{00} + p_x &\xleftarrow{b_r^{yx}} g_y^{10}
\end{aligned}
$$

Constraints:

$$g_x^{00} + g_x^{10} + g_x^{01} = G_x$$
$$g_y^{00} + g_y^{10} + g_y^{01} = G_y$$

mRNA ODEs:

$$\dot{m}_x = k_{00}^x g_x^{00} + k_{10}^x g_x^{10} + k_{01}^x g_x^{01} - d_m^x m_x$$
$$\dot{m}_y = k_{00}^y g_y^{00} + k_{10}^y g_y^{10} + k_{01}^y g_y^{01} - d_m^y m_y$$

Protein SDES:

$$\begin{aligned}\dot{p}_x =& k_p^x m_x - d_p^x p_x + b_r^{xx} g_x^{10} - b_f^{xx} g_x^{00} p_x + b_r^{yx} g_y^{10} - b_f^{yx} g_y^{00} p_x \\ &+ \sqrt{k_p^x m_x + d_p^x p_x + b_r^{xx} g_x^{10} + b_f^{xx} g_x^{00} p_x + b_r^{yx} g_y^{10} + b_f^{yx} g_y^{00} p_x}\ \eta_x(t) \\ \dot{p}_y =& k_p^y m_y - d_p^y p_y + b_r^{yy} g_y^{01} - b_f^{yy} g_y^{00} p_y + b_r^{xy} g_x^{01} - b_f^{xy} g_x^{00} p_y \\ &+ \sqrt{k_p^y m_y + d_p^y p_y + b_r^{yy} g_y^{01} + b_f^{yy} g_y^{00} p_y + b_r^{xy} g_x^{01} + b_f^{xy} g_x^{00} p_y}\ \eta_y(t)\end{aligned}$$

mRNA at QSS forces:

$$m_x = \frac{k_{00}^x g_x^{00} + k_{10}^x g_x^{10} + k_{01}^x g_x^{01}}{d_m^x}$$
$$m_y = \frac{k_{00}^y g_y^{00} + k_{10}^y g_y^{10} + k_{01}^y g_y^{01}}{d_m^y}$$

Binding at QSS forces:

$$b_r^{xx} g_x^{10} = b_f^{xx} g_x^{00} p_x$$
$$b_r^{yx} g_y^{10} = b_f^{yx} g_y^{00} p_x$$
$$b_r^{yy} g_y^{01} = b_f^{yy} g_y^{00} p_y$$
$$b_r^{xy} g_x^{01} = b_f^{xy} g_x^{00} p_y$$

In other words,

$$
\begin{aligned}
g_x^{10} &= \frac{b_f^{xx}}{b_r^{xx}} g_x^{00} p_x \\
g_y^{10} &= \frac{b_f^{yx}}{b_r^{yx}} g_y^{00} p_x \\
g_y^{01} &= \frac{b_f^{yy}}{b_r^{yy}} g_y^{00} p_y \\
g_x^{01} &= \frac{b_f^{xy}}{b_r^{xy}} g_x^{00} p_y
\end{aligned}
$$

Define

$$
B^{ij} := \frac{b_f^{ij}}{b_r^{ij}}
$$

for $i, j \in \{x, y\}$. Then we have

$$
\begin{aligned}
g_x^{10} &= B^{xx} g_x^{00} p_x \\
g_y^{10} &= B^{yx} g_y^{00} p_x \\
g_y^{01} &= B^{yy} g_y^{00} p_y \\
g_x^{01} &= B^{xy} g_x^{00} p_y
\end{aligned}
$$

Substituting these into our gene constraints yields

$$
\begin{aligned}
G_x &= g_x^{00} + g_x^{10} + g_x^{01} = g_x^{00} + B^{xx} g_x^{00} p_x + B^{xy} g_x^{00} p_y = g_x^{00} \left[1 + B^{xx} p_x + B^{xy} p_y\right] \\
G_y &= g_y^{00} \left[1 + B^{yy} p_y + B^{yx} p_x\right] \\
\implies \quad g_x^{00}(p_x, p_y) &= \frac{G_x}{1 + B^{xx} p_x + B^{xy} p_y} \\
\implies \quad g_y^{00}(p_x, p_y) &= \frac{G_y}{1 + B^{yy} p_y + B^{yx} p_x}
\end{aligned}
$$

Similarly, we also have

$$
\begin{aligned}
g_x^{10} &= \frac{G_x B^{xx} p_x}{1 + B^{xx} p_x + B^{xy} p_y} \\
g_y^{10} &= \frac{G_y B^{yx} p_x}{1 + B^{yy} p_y + B^{yx} p_x} \\
g_y^{01} &= \frac{G_y B^{yy} p_y}{1 + B^{yy} p_y + B^{yx} p_x} \\
g_x^{01} &= \frac{G_x B^{xy} p_y}{1 + B^{xx} p_x + B^{xy} p_y}
\end{aligned}
$$

Substituting m_x and m_y into the protein SDEs yields

$$
\begin{aligned}
\dot{p}_x =& k_p^x \frac{k_{00}^x g_x^{00} + k_{10}^x g_x^{10} + k_{01}^x g_x^{01}}{d_m^x} - d_p^x p_x \\
&+ \sqrt{k_p^x \frac{k_{00}^x g_x^{00} + k_{10}^x g_x^{10} + k_{01}^x g_x^{01}}{d_m^x} + d_p^x p_x + b_r^{xx} g_x^{10} + b_f^{xx} g_x^{00} p_x + b_r^{yx} g_y^{10} + b_f^{yx} g_y^{00} p_x}\ \eta_x(t) \\
\dot{p}_y =& k_p^y \frac{k_{00}^y g_y^{00} + k_{10}^y g_y^{10} + k_{01}^y g_y^{01}}{d_m^y} - d_p^y p_y \\
&+ \sqrt{k_p^y \frac{k_{00}^y g_y^{00} + k_{10}^y g_y^{10} + k_{01}^y g_y^{01}}{d_m^y} + d_p^y p_y + b_r^{yy} g_y^{01} + b_f^{yy} g_y^{00} p_y + b_r^{xy} g_x^{01} + b_f^{xy} g_x^{00} p_y}\ \eta_y(t)
\end{aligned}
$$

Substituting our QSS binding results into the protein SDEs yields

$$
\begin{aligned}
\dot{p}_x =& \frac{k_p^x G_x}{d_m^x} \frac{k_{00}^x + k_{10}^x B^{xx} p_x + k_{01}^x B^{xy} p_y}{1 + B^{xx} p_x + B^{xy} p_y} - d_p^x p_x \\
&+ \sqrt{\frac{k_p^x G_x}{d_m^x} \frac{k_{00}^x + k_{10}^x B^{xx} p_x + k_{01}^x B^{xy} p_y}{1 + B^{xx} p_x + B^{xy} p_y} + d_p^x p_x + 2 b_f^{xx} g_x^{00} p_x + 2 b_f^{yx} g_y^{00} p_x}\ \eta_x(t) \\
\dot{p}_y =& \frac{k_p^y G_y}{d_m^y} \frac{k_{00}^y + k_{10}^y B^{yx} p_x + k_{01}^y B^{yy} p_y}{1 + B^{yy} p_y + B^{yx} p_x} - d_p^y p_y \\
&+ \sqrt{\frac{k_p^y G_y}{d_m^y} \frac{k_{00}^y + k_{10}^y B^{yx} p_x + k_{01}^y B^{yy} p_y}{1 + B^{yy} p_y + B^{yx} p_x} + d_p^y p_y + 2 b_f^{yy} g_y^{00} p_y + 2 b_f^{xy} g_x^{00} p_y}\ \eta_y(t)
\end{aligned}
$$