

Appendix1: Two gene circuits.

The Liouville-master equations for two gene circuits are systems of four PDEs in four variables x_1, y_1, x_2, y_2 representing the protein and mRNA of the first gene G_1 and second gene G_2 , respectively. There are five different types of such circuits $G_1 \rightarrow G_2$, $G_1 \dashv G_2$, $G_1 \rightarrow G_2 \rightarrow G_1$, $G_1 \rightarrow G_2 \dashv G_1$, $G_1 \dashv G_2 \dashv G_1$ where $\rightarrow, \dashv$ stand for activation and repression, respectively.

The set of two promoters have four discrete states $1 = (0, 0)$, $2 = (1, 0)$, $3 = (0, 1)$, $4 = (1, 1)$. The respective probabilities densities are $p_1(x_1, y_1, x_2, y_2, t)$, $p_2(x_1, y_1, x_2, y_2, t)$, $p_3(x_1, y_1, x_2, y_2, t)$, $p_4(x_1, y_1, x_2, y_2, t)$.

The corresponding Liouville-master equations are the following:

For the circuit $G_1 \rightarrow G_2$.

$$\begin{aligned}\frac{\partial p_1}{\partial t} &= -\frac{\partial[(by_1 - ax_1)p_1]}{\partial x_1} - \frac{\partial[(k_0 - \rho y_1)p_1]}{\partial y_1} - \frac{\partial[(by_2 - ax_2)p_1]}{\partial x_2} - \frac{\partial[(k_0 - \rho y_2)p_1]}{\partial y_2} + h_2 p_3 + h_1 p_2 - (f_1 + f_2 x_1) p_1, \\ \frac{\partial p_2}{\partial t} &= -\frac{\partial[(by_1 - ax_1)p_2]}{\partial x_1} - \frac{\partial[(k_1 - \rho y_1)p_2]}{\partial y_1} - \frac{\partial[(by_2 - ax_2)p_2]}{\partial x_2} - \frac{\partial[(k_0 - \rho y_2)p_2]}{\partial y_2} + f_1 p_1 + h_2 p_4 - (h_1 + f_2 x_1) p_2, \\ \frac{\partial p_3}{\partial t} &= -\frac{\partial[(by_1 - ax_1)p_3]}{\partial x_1} - \frac{\partial[(k_0 - \rho y_1)p_3]}{\partial y_1} - \frac{\partial[(by_2 - ax_2)p_3]}{\partial x_2} - \frac{\partial[(k_1 - \rho y_2)p_3]}{\partial y_2} + h_1 p_4 + f_2 x_1 p_1 - (h_2 + f_1) p_3, \\ \frac{\partial p_4}{\partial t} &= -\frac{\partial[(by_1 - ax_1)p_4]}{\partial x_1} - \frac{\partial[(k_1 - \rho y_1)p_4]}{\partial y_1} - \frac{\partial[(by_2 - ax_2)p_4]}{\partial x_2} - \frac{\partial[(k_1 - \rho y_2)p_4]}{\partial y_2} + f_1 p_3 + f_2 x_1 p_2 - (h_1 + h_2) p_4.\end{aligned}$$

For the circuit $G_1 \dashv G_2$.

$$\begin{aligned}\frac{\partial p_1}{\partial t} &= -\frac{\partial[(by_1 - ax_1)p_1]}{\partial x_1} - \frac{\partial[(k_0 - \rho y_1)p_1]}{\partial y_1} - \frac{\partial[(by_2 - ax_2)p_1]}{\partial x_2} - \frac{\partial[(k_0 - \rho y_2)p_1]}{\partial y_2} + h_2 x_1 p_3 + h_1 p_2 - (f_1 + f_2) p_1, \\ \frac{\partial p_2}{\partial t} &= -\frac{\partial[(by_1 - ax_1)p_2]}{\partial x_1} - \frac{\partial[(k_1 - \rho y_1)p_2]}{\partial y_1} - \frac{\partial[(by_2 - ax_2)p_2]}{\partial x_2} - \frac{\partial[(k_0 - \rho y_2)p_2]}{\partial y_2} + f_1 p_1 + h_2 x_1 p_4 - (h_1 + f_2) p_2, \\ \frac{\partial p_3}{\partial t} &= -\frac{\partial[(by_1 - ax_1)p_3]}{\partial x_1} - \frac{\partial[(k_0 - \rho y_1)p_3]}{\partial y_1} - \frac{\partial[(by_2 - ax_2)p_3]}{\partial x_2} - \frac{\partial[(k_1 - \rho y_2)p_3]}{\partial y_2} + h_1 p_4 + f_2 p_1 - (h_2 x_1 + f_1) p_3, \\ \frac{\partial p_4}{\partial t} &= -\frac{\partial[(by_1 - ax_1)p_4]}{\partial x_1} - \frac{\partial[(k_1 - \rho y_1)p_4]}{\partial y_1} - \frac{\partial[(by_2 - ax_2)p_4]}{\partial x_2} - \frac{\partial[(k_1 - \rho y_2)p_4]}{\partial y_2} + f_1 p_3 + f_2 p_2 - (h_1 + h_2 x_1) p_4.\end{aligned}$$

For the circuit $G_1 \rightarrow G_2 \rightarrow G_1$.

$$\begin{aligned}
\frac{\partial p_1}{\partial t} &= -\frac{\partial[(by_1 - ax_1)p_1]}{\partial x_1} - \frac{\partial[(k_0 - \rho y_1)p_1]}{\partial y_1} - \frac{\partial[(by_2 - ax_2)p_1]}{\partial x_2} - \frac{\partial[(k_0 - \rho y_2)p_1]}{\partial y_2} + h_2 p_3 + h_1 p_2 - (f_1 x_2 + f_2 x_1)p_1, \\
\frac{\partial p_2}{\partial t} &= -\frac{\partial[(by_1 - ax_1)p_2]}{\partial x_1} - \frac{\partial[(k_1 - \rho y_1)p_2]}{\partial y_1} - \frac{\partial[(by_2 - ax_2)p_2]}{\partial x_2} - \frac{\partial[(k_0 - \rho y_2)p_2]}{\partial y_2} + f_1 x_2 p_1 + h_2 p_4 - (h_1 + f_2 x_1)p_2, \\
\frac{\partial p_3}{\partial t} &= -\frac{\partial[(by_1 - ax_1)p_3]}{\partial x_1} - \frac{\partial[(k_0 - \rho y_1)p_3]}{\partial y_1} - \frac{\partial[(by_2 - ax_2)p_3]}{\partial x_2} - \frac{\partial[(k_1 - \rho y_2)p_3]}{\partial y_2} + h_1 p_4 + f_2 x_1 p_1 - (h_2 + f_1 x_2)p_3, \\
\frac{\partial p_4}{\partial t} &= -\frac{\partial[(by_1 - ax_1)p_4]}{\partial x_1} - \frac{\partial[(k_1 - \rho y_1)p_4]}{\partial y_1} - \frac{\partial[(by_2 - ax_2)p_4]}{\partial x_2} - \frac{\partial[(k_1 - \rho y_2)p_4]}{\partial y_2} + f_1 x_2 p_3 + f_2 x_1 p_2 - (h_1 + h_2)p_4.
\end{aligned}$$

For the circuit $G_1 \rightarrow G_2 \dashv G_1$.

$$\begin{aligned}
\frac{\partial p_1}{\partial t} &= -\frac{\partial[(by_1 - ax_1)p_1]}{\partial x_1} - \frac{\partial[(k_0 - \rho y_1)p_1]}{\partial y_1} - \frac{\partial[(by_2 - ax_2)p_1]}{\partial x_2} - \frac{\partial[(k_0 - \rho y_2)p_1]}{\partial y_2} + h_2 p_3 + h_1 x_2 p_2 - (f_1 + f_2 x_1)p_1, \\
\frac{\partial p_2}{\partial t} &= -\frac{\partial[(by_1 - ax_1)p_2]}{\partial x_1} - \frac{\partial[(k_1 - \rho y_1)p_2]}{\partial y_1} - \frac{\partial[(by_2 - ax_2)p_2]}{\partial x_2} - \frac{\partial[(k_0 - \rho y_2)p_2]}{\partial y_2} + f_1 p_1 + h_2 p_4 - (h_1 x_2 + f_2 x_1)p_2, \\
\frac{\partial p_3}{\partial t} &= -\frac{\partial[(by_1 - ax_1)p_3]}{\partial x_1} - \frac{\partial[(k_0 - \rho y_1)p_3]}{\partial y_1} - \frac{\partial[(by_2 - ax_2)p_3]}{\partial x_2} - \frac{\partial[(k_1 - \rho y_2)p_3]}{\partial y_2} + h_1 x_2 p_4 + f_2 x_1 p_1 - (h_2 + f_1)p_3, \\
\frac{\partial p_4}{\partial t} &= -\frac{\partial[(by_1 - ax_1)p_4]}{\partial x_1} - \frac{\partial[(k_1 - \rho y_1)p_4]}{\partial y_1} - \frac{\partial[(by_2 - ax_2)p_4]}{\partial x_2} - \frac{\partial[(k_1 - \rho y_2)p_4]}{\partial y_2} + f_1 p_3 + f_2 x_1 p_2 - (h_1 x_2 + h_2)p_4.
\end{aligned}$$

For the circuit $G_1 \dashv G_2 \dashv G_1$.

$$\begin{aligned}
\frac{\partial p_1}{\partial t} &= -\frac{\partial[(by_1 - ax_1)p_1]}{\partial x_1} - \frac{\partial[(k_0 - \rho y_1)p_1]}{\partial y_1} - \frac{\partial[(by_2 - ax_2)p_1]}{\partial x_2} - \frac{\partial[(k_0 - \rho y_2)p_1]}{\partial y_2} + h_2 x_1 p_3 + h_1 x_2 p_2 - (f_1 + f_2)p_1, \\
\frac{\partial p_2}{\partial t} &= -\frac{\partial[(by_1 - ax_1)p_2]}{\partial x_1} - \frac{\partial[(k_1 - \rho y_1)p_2]}{\partial y_1} - \frac{\partial[(by_2 - ax_2)p_2]}{\partial x_2} - \frac{\partial[(k_0 - \rho y_2)p_2]}{\partial y_2} + f_1 p_1 + h_2 x_1 p_4 - (h_1 x_2 + f_2)p_2, \\
\frac{\partial p_3}{\partial t} &= -\frac{\partial[(by_1 - ax_1)p_3]}{\partial x_1} - \frac{\partial[(k_0 - \rho y_1)p_3]}{\partial y_1} - \frac{\partial[(by_2 - ax_2)p_3]}{\partial x_2} - \frac{\partial[(k_1 - \rho y_2)p_3]}{\partial y_2} + h_1 x_2 p_4 + f_2 p_1 - (h_2 x_1 + f_1)p_3, \\
\frac{\partial p_4}{\partial t} &= -\frac{\partial[(by_1 - ax_1)p_4]}{\partial x_1} - \frac{\partial[(k_1 - \rho y_1)p_4]}{\partial y_1} - \frac{\partial[(by_2 - ax_2)p_4]}{\partial x_2} - \frac{\partial[(k_1 - \rho y_2)p_4]}{\partial y_2} + f_1 p_3 + f_2 p_2 - (h_1 x_2 + h_2 x_1)p_4.
\end{aligned}$$