

Supplementary Informations

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MASTER EQUATIONS

16 Master equations for the canonical gene regulatory circuit of two mutually opposing proteins that positively self-regulate themselves, as in Fig. 1, are given as following:

$$\begin{aligned}
 \frac{dP_{1111}(n_A, n_B)}{dt} = & \\
 & -\frac{h_{AA}}{2}[n_A(n_A - 1)]P_{1111}(n_A, n_B) + f_{AA}P_{0111}(n_A - 2, n_B) \\
 & -\frac{h_{AB}}{2}[n_B(n_B - 1)]P_{1111}(n_A, n_B) + f_{AB}P_{1011}(n_A, n_B - 2) \\
 & -\frac{h_{BA}}{2}[n_A(n_A - 1)]P_{1111}(n_A, n_B) + f_{BA}P_{1101}(n_A - 2, n_B) \\
 & -\frac{h_{BB}}{2}[n_B(n_B - 1)]P_{1111}(n_A, n_B) + f_{BB}P_{1110}(n_A, n_B - 2) \\
 & +k_A[(n_A + 1)P_{1111}(n_A + 1, n_B) - n_AP_{1111}(n_A, n_B)] \\
 & +k_B[(n_B + 1)P_{1111}(n_A, n_B + 1) - n_BP_{1111}(n_A, n_B)] \\
 & +g_{11}^A[P_{1111}(n_A - 1, n_B) - P_{1111}(n_A, n_B)] \\
 & +g_{11}^B[P_{1111}(n_A, n_B - 1) - P_{1111}(n_A, n_B)]
 \end{aligned} \tag{1}$$

$$\begin{aligned}
 \frac{dP_{1011}(n_A, n_B)}{dt} = & \\
 & -\frac{h_{AA}}{2}[n_A(n_A - 1)]P_{1011}(n_A, n_B) + f_{AA}P_{0011}(n_A - 2, n_B) \\
 & +\frac{h_{AB}}{2}[(n_B + 2)(n_B + 1)]P_{1111}(n_A, n_B + 2) - f_{AB}P_{1011}(n_A, n_B) \\
 & -\frac{h_{BA}}{2}[n_A(n_A - 1)]P_{1011}(n_A, n_B) + f_{BA}P_{1001}(n_A - 2, n_B) \\
 & -\frac{h_{BB}}{2}[n_B(n_B - 1)]P_{1011}(n_A, n_B) + f_{BB}P_{1010}(n_A, n_B - 2) \\
 & +k_A[(n_A + 1)P_{1011}(n_A + 1, n_B) - n_AP_{1011}(n_A, n_B)] \\
 & +k_B[(n_B + 1)P_{1011}(n_A, n_B + 1) - n_BP_{1011}(n_A, n_B)] \\
 & +g_{10}^A[P_{1011}(n_A - 1, n_B) - P_{1011}(n_A, n_B)] \\
 & +g_{11}^B[P_{1011}(n_A, n_B - 1) - P_{1011}(n_A, n_B)]
 \end{aligned} \tag{2}$$

$$\begin{aligned}
& \frac{dP_{0111}(n_A, n_B)}{dt} = \\
& + \frac{h_{AA}}{2} [(n_A + 2)(n_A + 1)] P_{1111}(n_A + 2, n_B) - f_{AA} P_{0111}(n_A, n_B) \\
& - \frac{h_{AB}}{2} [n_B(n_B - 1)] P_{0111}(n_A, n_B) + f_{AB} P_{0011}(n_A, n_B - 2) \\
& - \frac{h_{BA}}{2} [n_A(n_A - 1)] P_{0111}(n_A, n_B) + f_{BA} P_{0101}(n_A - 2, n_B) \\
& - \frac{h_{BB}}{2} [n_B(n_B - 1)] P_{0111}(n_A, n_B) + f_{BB} P_{0110}(n_A, n_B - 2) \\
& + k_A [(n_A + 1) P_{0111}(n_A + 1, n_B) - n_A P_{0111}(n_A, n_B)] \\
& + k_B [(n_B + 1) P_{0111}(n_A, n_B + 1) - n_B P_{0111}(n_A, n_B)] \\
& + g_{01}^A [P_{0111}(n_A - 1, n_B) - P_{0111}(n_A, n_B)] \\
& + g_{11}^B [P_{0111}(n_A, n_B - 1) - P_{0111}(n_A, n_B)] \tag{3}
\end{aligned}$$

$$\begin{aligned}
& \frac{dP_{0011}(n_A, n_B)}{dt} = \\
& + \frac{h_{AA}}{2} [(n_A + 2)(n_A + 1)] P_{1011}(n_A + 2, n_B) - f_{AA} P_{0011}(n_A, n_B) \\
& + \frac{h_{AB}}{2} [(n_B + 2)(n_B + 1)] P_{0111}(n_A, n_B + 2) - f_{AB} P_{0011}(n_A, n_B) \\
& - \frac{h_{BA}}{2} [n_A(n_A - 1)] P_{0011}(n_A, n_B) + f_{BA} P_{0001}(n_A - 2, n_B) \\
& - \frac{h_{BB}}{2} [n_B(n_B - 1)] P_{0011}(n_A, n_B) + f_{BB} P_{0010}(n_A, n_B - 2) \\
& + k_A [(n_A + 1) P_{0011}(n_A + 1, n_B) - n_A P_{0011}(n_A, n_B)] \\
& + k_B [(n_B + 1) P_{0011}(n_A, n_B + 1) - n_B P_{0011}(n_A, n_B)] \\
& + g_{00}^A [P_{0011}(n_A - 1, n_B) - P_{0011}(n_A, n_B)] \\
& + g_{11}^B [P_{0011}(n_A, n_B - 1) - P_{0011}(n_A, n_B)] \tag{4}
\end{aligned}$$

$$\begin{aligned}
& \frac{dP_{1110}(n_A, n_B)}{dt} = \\
& -\frac{h_{AA}}{2}[n_A(n_A - 1)]P_{1110}(n_A, n_B) + f_{AA}P_{0110}(n_A - 2, n_B) \\
& -\frac{h_{AB}}{2}[n_B(n_B - 1)]P_{1110}(n_A, n_B) + f_{AB}P_{1010}(n_A, n_B - 2) \\
& -\frac{h_{BA}}{2}[n_A(n_A - 1)]P_{1110}(n_A, n_B) + f_{BA}P_{1100}(n_A - 2, n_B) \\
& +\frac{h_{BB}}{2}[(n_B + 2)(n_B + 1)]P_{1111}(n_A, n_B + 2) - f_{BB}P_{1110}(n_A, n_B) \\
& \quad +k_A[(n_A + 1)P_{1110}(n_A + 1, n_B) - n_AP_{1110}(n_A, n_B)] \\
& \quad +k_B[(n_B + 1)P_{1110}(n_A, n_B + 1) - n_BP_{1110}(n_A, n_B)] \\
& \quad +g_{11}^A[P_{1110}(n_A - 1, n_B) - P_{1110}(n_A, n_B)] \\
& \quad +g_{10}^B[P_{1110}(n_A, n_B - 1) - P_{1110}(n_A, n_B)]
\end{aligned} \tag{5}$$

$$\begin{aligned}
& \frac{dP_{1010}(n_A, n_B)}{dt} = \\
& -\frac{h_{AA}}{2}[n_A(n_A - 1)]P_{1010}(n_A, n_B) + f_{AA}P_{0010}(n_A - 2, n_B) \\
& +\frac{h_{AB}}{2}[(n_B + 2)(n_B + 1)]P_{1110}(n_A, n_B + 2) - f_{AB}P_{1010}(n_A, n_B) \\
& -\frac{h_{BA}}{2}[n_A(n_A - 1)]P_{1010}(n_A, n_B) + f_{BA}P_{1000}(n_A - 2, n_B) \\
& +\frac{h_{BB}}{2}[(n_B + 2)(n_B + 1)]P_{1011}(n_A, n_B + 2) - f_{BB}P_{1010}(n_A, n_B) \\
& \quad +k_A[(n_A + 1)P_{1010}(n_A + 1, n_B) - n_AP_{1010}(n_A, n_B)] \\
& \quad +k_B[(n_B + 1)P_{1010}(n_A, n_B + 1) - n_BP_{1010}(n_A, n_B)] \\
& \quad +g_{10}^A[P_{1010}(n_A - 1, n_B) - P_{1010}(n_A, n_B)] \\
& \quad +g_{10}^B[P_{1010}(n_A, n_B - 1) - P_{1010}(n_A, n_B)]
\end{aligned} \tag{6}$$

$$\begin{aligned}
& \frac{dP_{0110}(n_A, n_B)}{dt} = \\
& + \frac{h_{AA}}{2} [(n_A + 2)(n_A + 1)] P_{1110}(n_A + 2, n_B) - f_{AA} P_{0110}(n_A, n_B) \\
& \quad - \frac{h_{AB}}{2} [n_B(n_B - 1)] P_{0110}(n_A, n_B) + f_{AB} P_{0010}(n_A, n_B - 2) \\
& \quad - \frac{h_{BA}}{2} [n_A(n_A - 1)] P_{0110}(n_A, n_B) + f_{BA} P_{0100}(n_A - 2, n_B) \\
& + \frac{h_{BB}}{2} [(n_B + 2)(n_B + 1)] P_{0111}(n_A, n_B + 2) - f_{BB} P_{0110}(n_A, n_B) \\
& \quad + k_A [(n_A + 1) P_{0110}(n_A + 1, n_B) - n_A P_{0110}(n_A, n_B)] \\
& \quad + k_B [(n_B + 1) P_{0110}(n_A, n_B + 1) - n_B P_{0110}(n_A, n_B)] \\
& \quad + g_{01}^A [P_{0110}(n_A - 1, n_B) - P_{0110}(n_A, n_B)] \\
& \quad + g_{10}^B [P_{0110}(n_A, n_B - 1) - P_{0110}(n_A, n_B)] \tag{7}
\end{aligned}$$

$$\begin{aligned}
& \frac{dP_{0010}(n_A, n_B)}{dt} = \\
& + \frac{h_{AA}}{2} [(n_A + 2)(n_A + 1)] P_{1010}(n_A + 2, n_B) - f_{AA} P_{0010}(n_A, n_B) \\
& + \frac{h_{AB}}{2} [(n_B + 2)(n_B + 1)] P_{0110}(n_A, n_B + 2) - f_{AB} P_{0010}(n_A, n_B) \\
& \quad - \frac{h_{BA}}{2} [n_A(n_A - 1)] P_{0010}(n_A, n_B) + f_{BA} P_{0000}(n_A - 2, n_B) \\
& + \frac{h_{BB}}{2} [(n_B + 2)(n_B + 1)] P_{0011}(n_A, n_B + 2) - f_{BB} P_{0010}(n_A, n_B) \\
& \quad + k_A [(n_A + 1) P_{0010}(n_A + 1, n_B) - n_A P_{0010}(n_A, n_B)] \\
& \quad + k_B [(n_B + 1) P_{0010}(n_A, n_B + 1) - n_B P_{0010}(n_A, n_B)] \\
& \quad + g_{00}^A [P_{0010}(n_A - 1, n_B) - P_{0010}(n_A, n_B)] \\
& \quad + g_{10}^B [P_{0010}(n_A, n_B - 1) - P_{0010}(n_A, n_B)] \tag{8}
\end{aligned}$$

$$\begin{aligned}
& \frac{dP_{1101}(n_A, n_B)}{dt} = \\
& -\frac{h_{AA}}{2}[n_A(n_A - 1)]P_{1101}(n_A, n_B) + f_{AA}P_{0101}(n_A - 2, n_B) \\
& -\frac{h_{AB}}{2}[n_B(n_B - 1)]P_{1101}(n_A, n_B) + f_{AB}P_{1001}(n_A, n_B - 2) \\
& +\frac{h_{BA}}{2}[(n_A + 2)(n_A + 1)]P_{1111}(n_A + 2, n_B) - f_{BA}P_{1101}(n_A, n_B) \\
& -\frac{h_{BB}}{2}[n_B(n_B - 1)]P_{1101}(n_A, n_B) + f_{BB}P_{1100}(n_A, n_B - 2) \\
& \quad +k_A[(n_A + 1)P_{1101}(n_A + 1, n_B) - n_AP_{1101}(n_A, n_B)] \\
& \quad +k_B[(n_B + 1)P_{1101}(n_A, n_B + 1) - n_BP_{1101}(n_A, n_B)] \\
& \quad +g_{11}^A[P_{1101}(n_A - 1, n_B) - P_{1101}(n_A, n_B)] \\
& \quad +g_{01}^B[P_{1101}(n_A, n_B - 1) - P_{1101}(n_A, n_B)] \tag{9}
\end{aligned}$$

$$\begin{aligned}
& \frac{dP_{1001}(n_A, n_B)}{dt} = \\
& -\frac{h_{AA}}{2}[n_A(n_A - 1)]P_{1001}(n_A, n_B) + f_{AA}P_{0001}(n_A - 2, n_B) \\
& +\frac{h_{AB}}{2}[(n_B + 2)(n_B + 1)]P_{1101}(n_A, n_B + 2) - f_{AB}P_{1001}(n_A, n_B) \\
& +\frac{h_{BA}}{2}[(n_A + 2)(n_A + 1)]P_{1011}(n_A + 2, n_B) - f_{BA}P_{1001}(n_A, n_B) \\
& -\frac{h_{BB}}{2}[n_B(n_B - 1)]P_{1001}(n_A, n_B) + f_{BB}P_{1000}(n_A, n_B - 2) \\
& \quad +k_A[(n_A + 1)P_{1001}(n_A + 1, n_B) - n_AP_{1001}(n_A, n_B)] \\
& \quad +k_B[(n_B + 1)P_{1001}(n_A, n_B + 1) - n_BP_{1001}(n_A, n_B)] \\
& \quad +g_{10}^A[P_{1001}(n_A - 1, n_B) - P_{1001}(n_A, n_B)] \\
& \quad +g_{01}^B[P_{1001}(n_A, n_B - 1) - P_{1001}(n_A, n_B)] \tag{10}
\end{aligned}$$

$$\begin{aligned}
& \frac{dP_{0101}(n_A, n_B)}{dt} = \\
& + \frac{h_{AA}}{2} [(n_A + 2)(n_A + 1)] P_{1101}(n_A + 2, n_B) - f_{AA} P_{0101}(n_A, n_B) \\
& \quad - \frac{h_{AB}}{2} [n_B(n_B - 1)] P_{0101}(n_A, n_B) + f_{AB} P_{0001}(n_A, n_B - 2) \\
& + \frac{h_{BA}}{2} [(n_A + 2)(n_A + 1)] P_{0111}(n_A + 2, n_B) - f_{BA} P_{0101}(n_A, n_B) \\
& \quad - \frac{h_{BB}}{2} [n_B(n_B - 1)] P_{0101}(n_A, n_B) + f_{BB} P_{0100}(n_A, n_B - 2) \\
& \quad + k_A [(n_A + 1) P_{0101}(n_A + 1, n_B) - n_A P_{0101}(n_A, n_B)] \\
& \quad + k_B [(n_B + 1) P_{0101}(n_A, n_B + 1) - n_B P_{0101}(n_A, n_B)] \\
& \quad + g_{01}^A [P_{0101}(n_A - 1, n_B) - P_{0101}(n_A, n_B)] \\
& \quad + g_{01}^B [P_{0101}(n_A, n_B - 1) - P_{0101}(n_A, n_B)] \tag{11}
\end{aligned}$$

$$\begin{aligned}
& \frac{dP_{0001}(n_A, n_B)}{dt} = \\
& + \frac{h_{AA}}{2} [(n_A + 2)(n_A + 1)] P_{1001}(n_A + 2, n_B) - f_{AA} P_{0001}(n_A, n_B) \\
& + \frac{h_{AB}}{2} [(n_B + 2)(n_B + 1)] P_{0101}(n_A, n_B + 2) - f_{AB} P_{0001}(n_A, n_B) \\
& + \frac{h_{BA}}{2} [(n_A + 2)(n_A + 1)] P_{0011}(n_A + 2, n_B) - f_{BA} P_{0001}(n_A, n_B) \\
& \quad - \frac{h_{BB}}{2} [n_B(n_B - 1)] P_{0001}(n_A, n_B) + f_{BB} P_{0000}(n_A, n_B - 2) \\
& \quad + k_A [(n_A + 1) P_{0001}(n_A + 1, n_B) - n_A P_{0001}(n_A, n_B)] \\
& \quad + k_B [(n_B + 1) P_{0001}(n_A, n_B + 1) - n_B P_{0001}(n_A, n_B)] \\
& \quad + g_{00}^A [P_{0001}(n_A - 1, n_B) - P_{0001}(n_A, n_B)] \\
& \quad + g_{01}^B [P_{0001}(n_A, n_B - 1) - P_{0001}(n_A, n_B)] \tag{12}
\end{aligned}$$

$$\begin{aligned}
& \frac{dP_{1100}(n_A, n_B)}{dt} = \\
& -\frac{h_{AA}}{2}[n_A(n_A - 1)]P_{1100}(n_A, n_B) + f_{AA}P_{0100}(n_A - 2, n_B) \\
& -\frac{h_{AB}}{2}[n_B(n_B - 1)]P_{1100}(n_A, n_B) + f_{AB}P_{1000}(n_A, n_B - 2) \\
& +\frac{h_{BA}}{2}[(n_A + 2)(n_A + 1)]P_{1110}(n_A + 2, n_B) - f_{BA}P_{1100}(n_A, n_B) \\
& +\frac{h_{BB}}{2}[(n_B + 2)(n_B + 1)]P_{1101}(n_A, n_B + 2) - f_{BB}P_{1100}(n_A, n_B) \\
& \quad +k_A[(n_A + 1)P_{1100}(n_A + 1, n_B) - n_AP_{1100}(n_A, n_B)] \\
& \quad +k_B[(n_B + 1)P_{1100}(n_A, n_B + 1) - n_BP_{1100}(n_A, n_B)] \\
& \quad +g_{11}^A[P_{1100}(n_A - 1, n_B) - P_{1100}(n_A, n_B)] \\
& \quad +g_{00}^B[P_{1100}(n_A, n_B - 1) - P_{1100}(n_A, n_B)]
\end{aligned} \tag{13}$$

$$\begin{aligned}
& \frac{dP_{1000}(n_A, n_B)}{dt} = \\
& -\frac{h_{AA}}{2}[n_A(n_A - 1)]P_{1000}(n_A, n_B) + f_{AA}P_{0000}(n_A - 2, n_B) \\
& +\frac{h_{AB}}{2}[(n_B + 2)(n_B + 1)]P_{1100}(n_A, n_B + 2) - f_{AB}P_{1000}(n_A, n_B) \\
& +\frac{h_{BA}}{2}[(n_A + 2)(n_A + 1)]P_{1010}(n_A + 2, n_B) - f_{BA}P_{1000}(n_A, n_B) \\
& +\frac{h_{BB}}{2}[(n_B + 2)(n_B + 1)]P_{1001}(n_A, n_B + 2) - f_{BB}P_{1000}(n_A, n_B) \\
& \quad +k_A[(n_A + 1)P_{1000}(n_A + 1, n_B) - n_AP_{1000}(n_A, n_B)] \\
& \quad +k_B[(n_B + 1)P_{1000}(n_A, n_B + 1) - n_BP_{1000}(n_A, n_B)] \\
& \quad +g_{10}^A[P_{1000}(n_A - 1, n_B) - P_{1000}(n_A, n_B)] \\
& \quad +g_{00}^B[P_{1000}(n_A, n_B - 1) - P_{1000}(n_A, n_B)]
\end{aligned} \tag{14}$$

$$\begin{aligned}
& \frac{dP_{0100}(n_A, n_B)}{dt} = \\
& + \frac{h_{AA}}{2} [(n_A + 2)(n_A + 1)] P_{1100}(n_A + 2, n_B) - f_{AA} P_{0100}(n_A, n_B) \\
& \quad - \frac{h_{AB}}{2} [n_B(n_B - 1)] P_{0100}(n_A, n_B) + f_{AB} P_{0000}(n_A, n_B - 2) \\
& + \frac{h_{BA}}{2} [(n_A + 2)(n_A + 1)] P_{0110}(n_A + 2, n_B) - f_{BA} P_{0100}(n_A, n_B) \\
& + \frac{h_{BB}}{2} [(n_B + 2)(n_B + 1)] P_{0101}(n_A, n_B + 2) - f_{BB} P_{0100}(n_A, n_B) \\
& \quad + k_A [(n_A + 1) P_{0100}(n_A + 1, n_B) - n_A P_{0100}(n_A, n_B)] \\
& \quad + k_B [(n_B + 1) P_{0100}(n_A, n_B + 1) - n_B P_{0100}(n_A, n_B)] \\
& \quad + g_{01}^A [P_{0100}(n_A - 1, n_B) - P_{0100}(n_A, n_B)] \\
& \quad + g_{00}^B [P_{0100}(n_A, n_B - 1) - P_{0100}(n_A, n_B)] \tag{15}
\end{aligned}$$

$$\begin{aligned}
& \frac{dP_{0000}(n_A, n_B)}{dt} = \\
& + \frac{h_{AA}}{2} [(n_A + 2)(n_A + 1)] P_{1000}(n_A + 2, n_B) - f_{AA} P_{0000}(n_A, n_B) \\
& + \frac{h_{AB}}{2} [(n_B + 2)(n_B + 1)] P_{0100}(n_A, n_B + 2) - f_{AB} P_{0000}(n_A, n_B) \\
& + \frac{h_{BA}}{2} [(n_A + 2)(n_A + 1)] P_{0010}(n_A + 2, n_B) - f_{BA} P_{0000}(n_A, n_B) \\
& + \frac{h_{BB}}{2} [(n_B + 2)(n_B + 1)] P_{0001}(n_A, n_B + 2) - f_{BB} P_{0000}(n_A, n_B) \\
& \quad + k_A [(n_A + 1) P_{0000}(n_A + 1, n_B) - n_A P_{0000}(n_A, n_B)] \\
& \quad + k_B [(n_B + 1) P_{0000}(n_A, n_B + 1) - n_B P_{0000}(n_A, n_B)] \\
& \quad + g_{00}^A [P_{0000}(n_A - 1, n_B) - P_{0000}(n_A, n_B)] \\
& \quad + g_{00}^B [P_{0000}(n_A, n_B - 1) - P_{0000}(n_A, n_B)] \tag{16}
\end{aligned}$$

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