Electronic Supplementary Material

Silent transcription intervals and translational bursting lead to diverse phenotypic switching

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Content

Supplementary Notes

S1. Derivation of initiation-time distribution and renewal function

S1.1 Initiation-time distribution

For the queuing model, a key step for deriving the exact protein distribution is to derive the analytical expression of the initiation-time distribution $f_{\text{ini}}(t)$. From Fig. 1 in the main text, we can know that the promoter in the ON state can either produce protein bursting or switch back to OFF state. Specifically, the gene in the ON state can lead to protein bursting in a single step or make multistep trips to the OFF state before protein bursting occurs. A simple calculation yields the following explicit expression of the initiation-time distribution in the Laplace domain [1]

$$\tilde{f}_{\text{ini}}(s) = \frac{r_{\text{syn}}}{s + r_{\text{syn}} + r_{\text{on}}\left(1 - \tilde{f}_{\text{off}}(s)\right)}, \tag{S1}$$

where $\tilde{f}_{\text{ini}}(s)$ and $\tilde{f}_{\text{off}}(s)$ are the Laplace transforms of $f_{\text{ini}}(t)$ and $f_{\text{off}}(t)$, respectively. Then, the initiation-time distribution $f_{\text{ini}}(t)$ can be obtained by calculating the inverse Laplace transform of $\tilde{f}_{\text{ini}}(s)$:

$f_{\text{ini}}(t) = \mathcal{L}^{-1}\left\{r_{\text{syn}}\Big/\left[s + r_{\text{syn}} + r_{\text{on}}\left(1 - \tilde{f}_{\text{off}}(s)\right)\right]\right\}$. In addition, if the survival function of the OFF state is defined as

$F_{\text{off}}(t) = \int_t^\infty f_{\text{off}}(x)dx$ whose Laplace transform is denoted by $\tilde{F}_{\text{off}}(s)$, we can show $\tilde{F}_{\text{off}}(s) = \left(1 - \tilde{f}_{\text{off}}(s)\right)\Big/s$.

Substituting this expression into Eq. S1, we immediately obtain the following expression

$$\tilde{f}_{\text{ini}}(s) = r_{\text{syn}}\Big/\left(r_{\text{syn}} + s + sr_{\text{on}}\tilde{F}_{\text{off}}(s)\right) \tag{S2}$$

In the following, we consider that the waiting time for gene activation follows an Erlang distribution of the form $f_{\text{off}}(t) = \left(r_{\text{off}}\right)^{k_{\text{off}}} t^{k_{\text{off}}-1} e^{-r_{\text{off}}t}\Big/\Gamma(k_{\text{off}})$, where r_{off} is the scale parameter and k_{off} is the shape parameter characterizing the number of reaction steps [2]. Then, the mean silent time is $\langle \tau_{\text{off}} \rangle = k_{\text{off}}/r_{\text{off}}$.

To derive the analytical expression of initiation-time distribution, we first compute the Laplace transform of the survival function $F_{\text{off}}(t)$ and the result is $\tilde{F}_{\text{off}}(s) = \sum_{i=0}^{k_{\text{off}}-1} \left(r_{\text{off}}\right)^i \Big/\left(r_{\text{off}} + s\right)^{i+1}$. Substituting this expression into Eq. S2, we obtain the Laplace transform of initiation-time distribution $f_{\text{ini}}(t)$:

$$\tilde{f}_{\text{ini}}(s) = \frac{r_{\text{syn}}\left(s + r_{\text{off}}\right)^{k_{\text{off}}}}{s\left(s + r_{\text{off}}\right)^{k_{\text{off}}} + r_{\text{syn}}\left(s + r_{\text{off}}\right)^{k_{\text{off}}} + r_{\text{on}}s\sum_{j=1}^{k_{\text{off}}} r_{\text{off}}^{j-1}\left(s + r_{\text{off}}\right)^{k_{\text{off}}-j}}. \tag{S3}$$

Note that the Laplace transform function $f_{\text{ini}}(s)$ can be rewritten as the following rational function

$$\tilde{f}_{\text{ini}}(s) = \frac{r_{\text{syn}}P(s)}{Q(s)} = \frac{r_{\text{syn}}\left(p_{k_{\text{off}}}s^{k_{\text{off}}} + \cdots + p_1 s + p_0\right)}{q_{k_{\text{off}}+1}s^{k_{\text{off}}+1} + \cdots + q_1 s + q_0},$$ (S4)

where p_i $(i=1,2,\cdots,k_{\text{off}})$, and q_j $(j=1,2,\cdots,k_{\text{off}}+1)$ are constant coefficients determined by Eq. S3.

Assume that $Q(s)$ has l real roots and m pairs of complex roots (i.e., $l+2m = k_{\text{off}}+1$). In principle,

$\tilde{f}_{\text{ini}}(s)$ can be decomposed into the summation of real part and complex part

$$\tilde{f}_{\text{ini}}(s) = \sum_{j=1}^{l}\frac{c_j}{s+\lambda_j} + \sum_{j=1}^{m}\frac{d_j s + g_j}{\left(s+\omega_j\right)^2 + \phi_j^2},$$ (S5)

where constants $c_j, d_j, g_j, \lambda_j, \omega_j$ and ϕ_j can be determined according to the partial fraction expansion.

Using the inverse Laplace transform to Eq. S5, we obtain the following initiation-time distribution

$$f_{\text{ini}}(t) = \sum_{j=1}^{l} c_j e^{-\lambda_j t} + \sum_{j=1}^{m} d_j e^{-\omega_j t}\left(\cos\left(\phi_j t\right) + \rho_j \sin\left(\phi_j t\right)\right),$$ (S6)

where $\rho_j = \left(g_j - \omega_j d_j\right)/\left(\phi_j d_j\right)$. Eq. S6 implies that the analytical expression of initiation-time distribution

can be obtained if its Laplace transform can be written in the forms of partial fractions.

S1.2 Renewal function

As is well known, renewal function is important in the queuing theory since many results on statistical

quantities such as binominal moments can be analytically obtained based on the renewal function (see

subsection 2.2 for details). If a renewal function is defined as the mean number of renewal events, we

can derive its analytical expression. In fact, in our case, the renew function $R(t)$ takes the form [3]

$$R(t) = F_{\text{ini}}(t) + \int_0^t R(t-\tau)f_{\text{ini}}(\tau)d\tau,$$ (S7)

where $F_{\text{ini}}(t)$ is the cumulative function of the initiation-time distribution $f_{\text{ini}}(t)$, i.e., $F_{\text{ini}}(t) = \int_0^t f_{\text{ini}}(\tau)d\tau$.

Applying the Laplace transform to Eq. S7, we have

$$\tilde{R}(s) = \tilde{f}_{\text{ini}}(s)/\left(s - s\tilde{f}_{\text{ini}}(s)\right)$$ (S8)

where $\tilde{R}(s)$ is the Laplace transform of the renewal function. Then the renewal function can be obtained

by computing the inverse of Laplace transform $R(t) = \mathcal{L}^{-1}\left\{\tilde{f}_{\text{ini}}(s)/\left(s - s\tilde{f}_{\text{ini}}(s)\right)\right\}$.

In addition, substituting the expression of $\tilde{f}_{ini}(s)$ in Eq. (S2) into $\tilde{R}(s)$ yields

$$\tilde{R}(s) = \frac{r_{syn}\langle \tau_{on} \rangle}{s^2 \left(\langle \tau_{on} \rangle + \tilde{F}_{off}(s) \right)}, \tag{S9}$$

where $\langle \tau_{on} \rangle = 1/r_{on}$ is the mean ON time. Similarly, the renewal function can be obtained by computing

the inverse of Laplace transform $R(t) = \mathcal{L}^{-1} \left\{ r_{syn}\langle \tau_{on} \rangle / s^2 \left(\langle \tau_{on} \rangle + \tilde{F}_{off}(s) \right) \right\}$.

Next, we derive the analytical results for renewal function $R(t)$ when the waiting time for gene

activation follows an Erlang distribution. Substituting the expression $\tilde{F}_{off}(s) = \sum_{i=0}^{k_{off}-1} (r_{off})^i / (r_{off}+s)^{i+1}$ into Eq.

S9, we obtain the Laplace transform of the renewal function $R(t)$ as follows

$$\tilde{R}(s) = \frac{r_{syn}(s+r_{off})^{k_{off}}}{s^2 \left((s+r_{off})^{k_{off}} + r_{on} \sum_{j=1}^{k_{off}} r_{off}^{j-1}(s+r_{off})^{k_{off}-j} \right)}, \tag{S10}$$

Note that the Laplace transform $\tilde{R}(s)$ in Eq. S10 can be given by the following rational function

$$\tilde{R}(s) = \frac{r_{syn}P(s)}{s^2 V(s)} = \frac{r_{syn}\left(p_{k_{off}} s^{k_{off}} + \cdots + p_1 s + p_0 \right)}{s^2 \left(v_{k_{off}} s^{k_{off}} + \cdots + v_1 s + v_0 \right)}, \tag{S11}$$

where $v_i (i = 1, 2, \cdots, k_{off})$ is constant-coefficient determined by Eq. S10, and $p_i (i = 1, 2, \cdots, k_{off})$ has the

same expression as in Eq. S4. Assuming $V(s)$ has l_1 real roots and m_1 pairs of complex roots (i.e.,

$l_1 + 2m_1 = k_{off}$). By using the partial fraction expansion, $\tilde{R}(s)$ can be decomposed into the summation of

real part and complex part

$$\tilde{R}(s) = \sum_{j=1}^{2} \frac{a_j}{s^j} + \sum_{j=1}^{l_1} \frac{f_j}{s+\theta_j} + \sum_{j=1}^{m_1} \frac{h_j s + u_j}{(s+\sigma_j)^2 + \psi_j^2}, \tag{S12}$$

where coefficients $a_j, f_j, h_j, u_j, \theta_j, \sigma_j,$ and ψ_j are obtained from the partial fraction expansion. Using the

inverse Laplace transform to Eq. S12, we obtain the renewal function

$$R(t) = a_1 + a_2 t + \sum_{j=1}^{l_1} f_j e^{-\theta_j t} + \sum_{j=1}^{m_1} h_j e^{-\sigma_j t} \left(\cos(\psi_j t) + \xi_j \sin(\psi_j t) \right), \tag{S13}$$

where $\xi_j = \left[u_j - \sigma_j h_j \right] / (\psi_j h_j)$. Eq. S13 implies that the analytical renewal function can be obtained if its

Laplace transform can be written the partial fractions.

S2. Derivation of analytical moments

S2.1 Time-dependent binomial moments

Here, we consider that the waiting time for gene activation follows an Erlang distribution. Substituting Eq. S13 into Eq. 3 in the main text, we obtain the time-dependent first-order binomial moment, i.e., the time-dependent protein average $b_1^{\text{protein}}(t)$:

$$
\begin{aligned}
b_1^{\text{protein}}(t) ={}& \frac{\langle B \rangle a_2}{r_{\text{deg}}}\left(1-e^{-r_{\text{deg}}t}\right) + \sum_{j=1}^{l_1} \frac{\langle B \rangle f_j \theta_j}{\theta_j - r_{\text{deg}}}\left(e^{-\theta_j t}-e^{-r_{\text{deg}}t}\right) \\
&+ \sum_{j=1}^{m_1} \frac{\langle B \rangle h_j \left(\sigma_j - \xi_j \psi_j\right)}{\left(\sigma_j - r_{\text{deg}}\right)^2 + \psi_j^2}\left[\left(\sigma_j - r_{\text{deg}}\right)e^{-\sigma_j t}\cos\left(\psi_j t\right)-\psi_j e^{-\sigma_j t}\sin\left(\psi_j t\right)-\left(\sigma_j - r_{\text{deg}}\right)e^{-r_{\text{deg}}t}\right] \quad \text{(S14)} \\
&+ \sum_{j=1}^{m_1} \frac{\langle B \rangle h_j \left(\xi_j \sigma_j + \psi_j\right)}{\left(\sigma_j - r_{\text{deg}}\right)^2 + \psi_j^2}\left[\left(\sigma_j - r_{\text{deg}}\right)e^{-\sigma_j t}\sin\left(\psi_j t\right)+\psi_j e^{-\sigma_j t}\cos\left(\psi_j t\right)-\psi_j e^{-r_{\text{deg}}t}\right].
\end{aligned}
$$

In addition, we can also give the analytical expressions for the time-dependent second-order binomial moment $b_2^{\text{protein}}(t)$ and time-dependent noise $\eta_{\text{protein}}^2(t)$, is defined as the ratio of the variance over the squared mean: $\eta_{\text{protein}}^2(t) = \left(2b_2^{\text{protein}}(t)+b_1^{\text{protein}}(t)-\left(b_1^{\text{protein}}(t)\right)^2\right)\Big/\left(b_1^{\text{protein}}(t)\right)^2$, but we omit them due to the complexity of their expressions.

S2.2 Steady-state binomial moments

According to Eq. 4 in the main text, we give analytical expressions of steady-state binomial moments. For example, the second-order binomial moment is given by

$$
b_2^{\text{protein}} = \frac{r_{\text{syn}}^2 \langle \tau_{\text{on}} \rangle^2 \langle B \rangle^2}{2r_{\text{deg}}^2 \left(\langle \tau_{\text{on}} \rangle + \langle \tau_{\text{off}} \rangle\right)\left(\langle \tau_{\text{on}} \rangle + F_{\text{off}}\left(r_{\text{deg}}\right)\right)} + \frac{b_2^{\text{burst}} r_{\text{syn}} \langle \tau_{\text{on}} \rangle}{2r_{\text{deg}}\left(\langle \tau_{\text{on}} \rangle + \langle \tau_{\text{off}} \rangle\right)}, \quad \text{(S15)}
$$

the third-order binomial moment by

$$
b_3^{\text{protein}} = \frac{r_{\text{mean}}}{3r_{\text{deg}}}\left[\left(\frac{r_{\text{syn}} \langle \tau_{\text{on}} \rangle}{r_{\text{deg}}}\right)^2 \frac{\langle B \rangle^3}{\prod_{i=1}^{2} i\left(\langle \tau_{\text{on}} \rangle + \tilde{F}_{\text{off}}\left(i r_{\text{deg}}\right)\right)} + \frac{r_{\text{syn}} \langle \tau_{\text{on}} \rangle}{r_{\text{deg}}} \frac{\sum_{i=1}^{2} i\left(\langle \tau_{\text{on}} \rangle + \tilde{F}_{\text{off}}\left(i r_{\text{deg}}\right)\right)}{\prod_{i=1}^{2} i\left(\langle \tau_{\text{on}} \rangle + \tilde{F}_{\text{off}}\left(i r_{\text{deg}}\right)\right)} b_2^{\text{burst}} \langle B \rangle + b_3^{\text{burst}}\right], \quad \text{(S16)}
$$

and the fourth-order binomial moment by

$$b_4^{\text{protein}} = \frac{r_{\text{mean}}}{4r_{\text{deg}}} \left\{ \left(\frac{r_{\text{syn}} \langle \tau_{\text{on}} \rangle}{r_{\text{deg}}} \right)^3 \frac{\langle B \rangle^4}{\prod_{i=1}^{3} i \left(\langle \tau_{\text{on}} \rangle + \tilde{F}_{\text{off}} \left(i r_{\text{deg}} \right) \right)} + \left(\frac{r_{\text{syn}} \langle \tau_{\text{on}} \rangle}{r_{\text{deg}}} \right)^2 \frac{\sum_{i=1}^{3} i \left(\langle \tau_{\text{on}} \rangle + \tilde{F}_{\text{off}} \left(i r_{\text{deg}} \right) \right)}{\prod_{i=1}^{3} i \left(\langle \tau_{\text{on}} \rangle + \tilde{F}_{\text{off}} \left(i r_{\text{deg}} \right) \right)} b_2^{\text{burst}} \langle B \rangle^2 \right.$$

$$\left. + \frac{r_{\text{syn}} \langle \tau_{\text{on}} \rangle}{r_{\text{deg}}} \left[\frac{\sum_{i=1,3} i \left(\langle \tau_{\text{on}} \rangle + \tilde{F}_{\text{off}} \left(i r_{\text{deg}} \right) \right)}{\prod_{i=1,3} i \left(\langle \tau_{\text{on}} \rangle + \tilde{F}_{\text{off}} \left(i r_{\text{deg}} \right) \right)} b_3^{\text{burst}} \langle B \rangle + \frac{\left(b_2^{\text{burst}} \right)^2}{2 \left(\langle \tau_{\text{on}} \rangle + \tilde{F}_{\text{off}} \left(2 r_{\text{deg}} \right) \right)} \right] + b_4^{\text{burst}} \right\}. \tag{S17}$$

Interestingly, binomial moments and central moments have the following relationships

$$\mu_k^{\text{protein}} = \left(-b_1^{\text{protein}} \right)^k + \sum_{i=0}^{k-1} \sum_{j=0}^{k-i} M \left(k, i, j \right) \left(j! \right) \left(b_1^{\text{protein}} \right)^i b_j^{\text{protein}}, \tag{S18}$$

where $M \left(k, i, j \right) = (-1)^i \binom{k}{i} S \left(k - i, j \right)$ with $S \left(n, k \right) = \sum_{i=0}^{k} (-1)^{k-i} \binom{k}{i} i^n$ being the Stirling number of the second kind.

S3. Derivation of analytical distributions

Here, we consider two representative protein burst distributions: (1) Constant distribution, that is, $P \left(B = 1 \right) = 1, P(B = k) = 0, k = 0, 2, 3, \cdots$; (2) Geometric distribution, that is, $P(B = k) = \langle B \rangle^k / \left(1 + \langle B \rangle \right)^{k+1}$, $k = 0, 1, 2, \cdots$. For both distributions, we derive the analytical expressions of steady-state binomial moments and probability distributions.

S3.1 Constant burst-size distribution

This case means that binomial moments are $b_1^{\text{burst}} = \langle B \rangle = 1$, $b_i^{\text{burst}} = 0 (i = 2, 3, \cdots)$. Substituting them into Eq. 4 in the main text, we obtain the following expression

$$b_n^{\text{protein}} = \frac{r_{\text{syn}} \langle \tau_{\text{on}} \rangle}{\left(\langle \tau_{\text{on}} \rangle + \langle \tau_{\text{off}} \rangle \right) r_{\text{deg}}} \frac{1}{n} \prod_{i=1}^{n-1} \tilde{R} \left(i r_{\text{deg}} \right) i r_{\text{deg}}. \tag{S19}$$

Combining Eq. S19 with the expression of $R \left(s \right)$ in Eq. S11, we further obtain the analytical expression for the steady-state binomial moments

$$b_n^{\text{protein}} = \frac{\left(r_{\text{syn}} r_{\text{deg}}^{-1} \right)^n}{n!} \frac{\prod_{j=1}^{k_{\text{off}}} \left(\beta_j r_{\text{deg}}^{-1} \right)_n}{\prod_{j=1}^{k_{\text{off}}} \left(\alpha_j r_{\text{deg}}^{-1} \right)_n}, \tag{S20}$$

where $-\beta_j$ and $-\alpha_j \left(j = 1, 2, \cdots, k_{\text{off}} \right)$ are the roots of algebraic equations $p_{k_{\text{off}}} s^{k_{\text{off}}} + \cdots + p_1 s + p_0 = 0$ and $v_{k_{\text{off}}} s^{k_{\text{off}}} + \cdots + v_1 s + v_0 = 0$, respectively, and we have defined symbol $\left(v \right)_n = v \left(v - 1 \right) \cdots \left(v - n + 1 \right), n = 1, 2, \cdots$.

Substituting Eq. S20 into Eq. 7 in the main text, we obtain the steady-state protein distribution of the form

$$P(m) = \frac{\left(r_{\mathrm{syn}} r_{\mathrm{deg}}^{-1}\right)^m}{m!} \frac{\prod_{j=1}^{k_{\mathrm{off}}} \left(\beta_j r_{\mathrm{deg}}^{-1}\right)_m}{\prod_{j=1}^{k_{\mathrm{off}}} \left(\alpha_j r_{\mathrm{deg}}^{-1}\right)_m} \, {}_{k_{\mathrm{off}}} F_{k_{\mathrm{off}}} \left(m + \beta_1 r_{\mathrm{deg}}^{-1}, \cdots, m + \beta_{k_{\mathrm{off}}} r_{\mathrm{deg}}^{-1}; m + \alpha_1 r_{\mathrm{deg}}^{-1}, \cdots, m + \alpha_{k_{\mathrm{off}}} r_{\mathrm{deg}}^{-1}; -r_{\mathrm{syn}} r_{\mathrm{deg}}^{-1}\right) \tag{S21}$$

where ${}_{k_{\mathrm{off}}} F_{k_{\mathrm{off}}}$ denotes a generalized hypergeometric function. If we recall the gene-product distribution in the case of a multistep process of gene activation [4], Eq. S21 indicates that non-exponential waiting time is indeed equivalent to a multistep process. In particular, for the exponential waiting time, i.e., $f_{\mathrm{off}}(t) = r_{\mathrm{off}} e^{-r_{\mathrm{off}} t}$, Eq. S21 reduces to

$$P(m) = \frac{\left(r_{\mathrm{syn}} r_{\mathrm{deg}}^{-1}\right)^m}{m!} \frac{\left(r_{\mathrm{off}} r_{\mathrm{deg}}^{-1}\right)_m}{\left((r_{\mathrm{off}} + r_{\mathrm{on}}) r_{\mathrm{deg}}^{-1}\right)_m} \, {}_1 F_1 \left(r_{\mathrm{off}} r_{\mathrm{deg}}^{-1} + m; (r_{\mathrm{off}} + r_{\mathrm{on}}) r_{\mathrm{deg}}^{-1} + m; -r_{\mathrm{syn}} r_{\mathrm{deg}}^{-1}\right), \tag{S22}$$

which is a known result but is here derived in a different manner [5].

S3.2 Burst size follows a geometric distribution

In this case, the binomial moments are $b_i^{\mathrm{burst}} = \langle B \rangle^i$. Substituting them into Eq. 4 in the main text, we obtain the following nth-order protein binomial moment

$$b_n^{\mathrm{protein}} = \frac{r_{\mathrm{syn}} \langle \tau_{\mathrm{on}} \rangle}{(\langle \tau_{\mathrm{on}} \rangle + \langle \tau_{\mathrm{off}} \rangle) r_{\mathrm{deg}}} \frac{\langle B \rangle^n}{n} \prod_{i=1}^{n-1} \left[1 + \tilde{R}(i r_{\mathrm{deg}}) i r_{\mathrm{deg}}\right]. \tag{S23}$$

Combining Eq. S23 with the expression of $R(s)$ in Eq. S11, we further obtain the analytical expression for the steady-state binomial moments

$$b_n^{\mathrm{protein}} = \frac{\langle B \rangle^n}{n!} \frac{\prod_{j=1}^{k_{\mathrm{off}}+1} \left(\gamma_j r_{\mathrm{deg}}^{-1}\right)_n}{\prod_{j=1}^{k_{\mathrm{off}}} \left(\alpha_j r_{\mathrm{deg}}^{-1}\right)_n}, \tag{S24}$$

where $-\gamma_j \ (j = 1, 2, \cdots, k_{\mathrm{off}} + 1)$ are the roots of $Q(s) = q_{k_{\mathrm{off}}+1} s^{k_{\mathrm{off}}+1} + \cdots + q_1 s + q_0 = 0$, and $\alpha_j \ (j = 1, 2, \cdots, k_{\mathrm{off}})$ are the same as in Eq. S20. Substituting Eq. S24 into Eq. 7 in the main text, we further obtain the steady-state protein distribution

$$P(m) = \frac{\langle B \rangle^m}{m!} \frac{\prod_{j=1}^{k_{\mathrm{off}}+1} \left(\gamma_j r_{\mathrm{deg}}^{-1}\right)_m}{\prod_{j=1}^{k_{\mathrm{off}}} \left(\alpha_j r_{\mathrm{deg}}^{-1}\right)_m} \, {}_{k_{\mathrm{off}}+1} F_{k_{\mathrm{off}}} \left(m + \gamma_1 r_{\mathrm{deg}}^{-1}, \cdots, m + \gamma_{k_{\mathrm{off}+1}} r_{\mathrm{deg}}^{-1}; m + \alpha_1 r_{\mathrm{deg}}^{-1}, \cdots, m + \alpha_{k_{\mathrm{off}}} r_{\mathrm{deg}}^{-1}; -\langle B \rangle\right), \tag{S25}$$

where $_{k_{off+1}}F_{k_{off}}$ denotes a generalized hypergeometric function.

In particular, for the exponentially distributed OFF waiting time, i.e., $f_{off}(t) = r_{off}e^{-r_{off}t}$, the steady-state protein distribution are

$$P(m) = \frac{\langle B \rangle^m}{m!} \frac{\left(\gamma_1 r_{deg}^{-1}\right)_m \left(\gamma_2 r_{deg}^{-1}\right)_m}{\left(\alpha r_{deg}^{-1}\right)_m} {}_2F_1\left(\begin{array}{c} m+\gamma_1 r_{deg}^{-1}, m+\gamma_2 r_{deg}^{-1} \\ m+\alpha r_{deg}^{-1} \end{array}\middle| -\langle B \rangle\right),$$
(S26)

where $\gamma_{1,2} = \frac{1}{2}\left(r_{syn} + r_{on} + r_{off}\right) \pm \sqrt{\left(r_{syn} + r_{on} + r_{off}\right)^2 - 4r_{syn}r_{off}}$, $\alpha = r_{on} + r_{off}$. This results has been also derived in previous work yet in a different fashion [6].

S4. Estimating the bimodality of steady-state distribution

It is well-known that there is a strongly relation between the modality of a given distribution and the skewness (defined as $S = \mu_3 / (\mu_2)^{3/2}$, where μ_2 and μ_3 are the second and third central moments, respectively) and kurtosis (defined as $K = \mu_4 / (\mu_2)^2$, where μ_4 is the fourth central moment) of the distribution [7-9]. In fact, the bimodality of a given distribution can be measured by the relation $K - S^2 \geq 1$ and it will converge into one when the sample size tends to infinite [8]. Previous studies have demonstrated the use of $K - S^2$ as a measure for the modality of a distribution [7]. Here, we define the bimodality coefficient (BC):

$$BC = \frac{1}{K - S^2},$$
(S27)

which is bounded between 0 and 1. Specifically, $BC = 5/9$ is the case of uniform distribution, and $BC > 5/9$ means the bimodality is more clear with BC close to 1, whereas $BC < 5/9$ is the unimodal distribution.

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