Supporting Online Material for

Promoter-mediated transcriptional dynamics

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In this supplementary material, we first derive the analytical expression of $\mathbf{a}_0$ used in the main text, then give some detailed processes for the derivation of analytical distributions in particular cases, and finally list some parameter values used in figures shown in the main text.

A. Analytical expression of $\mathbf{a}_0$

Based on the iterative Eq. (16) with $n=0$ in the main article and using the conservative condition for probability, we have the following algebraic equation

$$\begin{aligned}\mathbf{u}_N\mathbf{a}_0 &= 1\\ \mathbf{A}\mathbf{a}_0 &= \mathbf{0}\end{aligned} \tag{A1}$$

To give the analytical expressions of components of the vector $\mathbf{a}_0$, we let $\mathbf{M}_k$ represent an $(N-1)\times(N-1)$ matrix, which is the minor one of the $N\times N$ matrix $\mathbf{A}$ by crossing out the kth row and kth column of its entry a_{kk}. Denote by $0,-\alpha_1,-\alpha_2,\cdots,-\alpha_{N-1}$ the eigenvalues of matrix $\mathbf{A}$ and by $-\beta_1^{(k)},-\beta_2^{(k)},\cdots,-\beta_{N-1}^{(k)}$ the eigenvalues of matrix $\mathbf{M}_k$. Note that $-\mathbf{A}$ is an M-matrix, so the real part of each α_i is positive. Therefore, with loss of generality, we assume $\alpha_i>0$. With the similar reason, we also assume $\beta_i^{(k)}>0$. In addition, we introduce two symbols

$$f_{\mathbf{A}}(n)=\det(n\mathbf{I}_N-\mathbf{A})=n\prod_{i=1}^{N-1}(n+\alpha_i),\quad f_{\mathbf{M}_k}(n)=\det(n\mathbf{I}_{N-1}-\mathbf{M}_k)=\prod_{i=1}^{N-1}\left(n+\beta_i^{(k)}\right) \tag{A2}$$

which are practically the characteristic polynomial of $\mathbf{A}$ and $\mathbf{M}_k$, respectively. Now, we show

$$a_0^{(k)} = \prod_{i=1}^{N-1} \frac{\beta_i^{(k)}}{\alpha_i}, \quad 1 \le k \le N \tag{A3}$$

In fact, $\mathbf{A}\mathbf{A}^* = \det(\mathbf{A})\mathbf{I} = \mathbf{0}$ due to $\det(\mathbf{A}) = 0$. In addition, as a consequence of Laplace's formula for the determinant of matrix $\mathbf{A}$, we have $\mathbf{A}\begin{pmatrix} \det(\mathbf{M}_1) \\ \vdots \\ \det(\mathbf{M}_N) \end{pmatrix} = \mathbf{0}$, where $\det(\mathbf{M}_k) = (-1)^{N-1} \prod_{i=1}^{N-1} \beta_i^{(k)}$. Note that the null space of $\mathbf{A}$ is of one dimension due to $rank(\mathbf{A}) = N-1$. Thus, combining $\mathbf{A}\mathbf{a}_0 = \mathbf{0}$, we know that $\mathbf{a}_0 = c\begin{pmatrix} \det(\mathbf{M}_1) \\ \vdots \\ \det(\mathbf{M}_N) \end{pmatrix}$, where c is a constant. The condition $\mathbf{u}_N \mathbf{a}_0 = 1$ gives $c = 1 \big/ \sum_{k=1}^{N} \det(\mathbf{M}_k)$. A direct computation yields $\left.\frac{df_{\mathbf{A}}(\mu)}{d\mu}\right|_{\mu=0} = \prod_{i=1}^{N-1} \alpha_i$. On the other hand, Jacobi's formula gives

$$\left.\frac{df_{\mathbf{A}}(\mu)}{d\mu}\right|_{\mu=0} = \left.\frac{d\det(\mu\mathbf{I}_N - \mathbf{A})}{d\mu}\right|_{\mu=0} = tr\left((\mu\mathbf{I}_N - \mathbf{A})^* \frac{d(\mu\mathbf{I}_N - \mathbf{A})}{d\mu} \right)\Bigg|_{\mu=0} = (-1)^{N-1} \sum_{k=1}^{N} \det(\mathbf{M}_k) = \sum_{k=1}^{N} \prod_{i=1}^{N-1} \beta_i^{(k)}$$

The combination of both yields the equality $\sum_{k=1}^{N} \prod_{i=1}^{N-1} \beta_i^{(k)} = \prod_{i=1}^{N-1} \alpha_i$. Using this fact combined with the expressions of c and $\det(\mathbf{M}_k)$, we immediately know that Eqn. (A3) holds.

Finally, we point out that if matrix $\mathbf{A}$ is symmetric, then the adjacency matrix $(n\mathbf{I}_N - \mathbf{A})^*$ is also symmetric for any n.

B. Derivation of analytical distributions in particular cases

Case 1 $\Lambda = \mu\mathbf{I}_N$

Such a case corresponds to a model of constitutive gene expression with the same transcription rate. Using the above symbols, we have $b_n = \mathbf{u}_N \mathbf{a_n}$ due to $b_n = \sum_{i=1}^{N} a_n^{(i)}$, and $b_n = \frac{1}{n}\mathbf{u}_N \mathbf{\Lambda} \mathbf{a}_{n-1} = \frac{\mu}{n}\mathbf{u}_N \mathbf{a}_{n-1}$. Thus, we obtain $b_n = \frac{\mu}{n} b_{n-1} = \frac{\mu^n}{n!}$. According to Eq. (1) in the main text, we compute and obtain

$$P(m) = \sum_{k=m}^{\infty} (-1)^{k-m} \binom{k}{m} b_k = \sum_{k=m}^{\infty} (-1)^{k-m} \binom{k}{m} \frac{\mu^k}{k!} = e^{-\mu} \frac{\mu^m}{m!}, \quad m = 0,1,2,\cdots \tag{B1}$$

which is a Poisson distribution with characteristic parameter μ. Eqn. (B1) indicates that the mRNA distribution is independent of the pattern of transitions between activity states of the promoter. In other words, whatever transitions among activity states are, does the static mRNA obey the same Poisson distribution determined completely by the transcription rate.

Case 2 $\mathbf{\Lambda} = \mu \begin{pmatrix} \mathbf{0}_{(N-1)} & \mathbf{0} \\ \mathbf{0} & 1 \end{pmatrix}$

Such a case corresponds to the gene model where the promoter has one ON and multiple OFFs. It follows from Eq. (16) in the main text that

$$\begin{pmatrix} * \\ a_n^{(N)} \end{pmatrix} = \mathbf{a}_n = \frac{1}{\det(n\mathbf{I}-\mathbf{A})} (n\mathbf{I}-\mathbf{A})^* \mathbf{\Lambda} \mathbf{a}_{n-1} = \frac{\mu}{\det(n\mathbf{I}-\mathbf{A})} \begin{pmatrix} * & * \\ * & \det(n\mathbf{I}_{N-1} - \mathbf{M}_N) \end{pmatrix} \begin{pmatrix} \mathbf{O} & \mathbf{O} \\ \mathbf{O} & 1 \end{pmatrix} \begin{pmatrix} * \\ a_{n-1}^{(N)} \end{pmatrix}$$
$$= \frac{\mu}{f_{\mathbf{A}}(n)} \begin{pmatrix} * \\ f_{M_N}(n) a_{n-1}^{(N)} \end{pmatrix} = \begin{pmatrix} * \\ \frac{\mu f_{M_N}(n)}{f_{\mathbf{A}}(n)} a_{n-1}^{(N)} \end{pmatrix}$$

Using the expressions of $f_{\mathbf{A}}(n)$ and $f_{M_N}(n)$, we can obtain

$$\mathrm{a}_n^{(N)} = \frac{\mu^n}{n!} \frac{\prod_{i=1}^{N-1} \left(\beta_i^{(N)}\right)_{n+1}}{\prod_{i=1}^{N-1} (\alpha_i)_{n+1}} \frac{\prod_{i=1}^{N-1} \alpha_i}{\prod_{i=1}^{N-1} \beta_i^{(N)}} \mathrm{a}_0^{(N)} \tag{B2}$$

Furthermore, according to $b_n = \frac{1}{n}\mathbf{u}_N \mathbf{\Lambda} \mathbf{a}_{n-1}$, we compute and obtain

$$b_n = \frac{\mu^n}{n!} \frac{\prod_{i=1}^{N-1} \left(\beta_i^{(N)}\right)_{n}}{\prod_{i=1}^{N-1} (\alpha_i)_{n}} \frac{\prod_{i=1}^{N-1} \alpha_i}{\prod_{i=1}^{N-1} \beta_i^{(N)}} \mathrm{a}_0^{(N)} \tag{B3}$$

Furthermore, combined with $a_0^{(N)}=\frac{\prod_{i=1}^{N-1}\beta_i^{(N)}}{\prod_{i=1}^{N-1}\alpha_i}$, Eq. (B3) implies that the total static generating function is

$$G(s)={}_{N-1}F_{N-1}\left(\begin{matrix}\beta_1^{(N)},\cdots,\beta_{N-1}^{(N)}\\ \alpha_1,\cdots,\alpha_{N-1}\end{matrix}\middle|;\mu s\right) \tag{B4}$$

Again according to Eq. (1) in the main text, we compute and obtain

$$\begin{aligned}P(m)&=a_0^{(N)}\frac{\prod_{i=1}^{N-1}\alpha_i}{\prod_{i=1}^{N-1}\beta_i^{(N)}}\sum_{k=m}^{\infty}(-1)^{k-m}\binom{k}{m}\frac{\mu^k}{k!}\frac{\prod_{i=1}^{N-1}\left(\beta_i^{(N)}\right)_k}{\prod_{i=1}^{N-1}(\alpha_i)_k}\\ &=a_0^{(N)}\frac{\prod_{i=1}^{N-1}\alpha_i}{\prod_{i=1}^{N-1}\beta_i^{(N)}}\sum_{k=0}^{\infty}(-1)^{k}\binom{k+m}{m}\frac{\mu^{k+m}}{(k+m)!}\frac{\prod_{i=1}^{N-1}\left(\beta_i^{(N)}\right)_{k+m}}{\prod_{i=1}^{N-1}(\alpha_i)_{k+m}}\\ &=a_0^{(N)}\frac{\mu^m}{m!}\frac{\prod_{i=1}^{N-1}\alpha_i}{\prod_{i=1}^{N-1}\beta_i^{(N)}}\frac{\prod_{i=1}^{N-1}(\beta_i)_m}{\prod_{i=1}^{N-1}(\alpha_i)_m}\sum_{k=0}^{\infty}\frac{\prod_{i=1}^{N-1}\left(m+\beta_i^{(N)}\right)_k}{\prod_{i=1}^{N-1}(m+\alpha_i)_k}\frac{(-\mu)^k}{k!}\end{aligned}$$

Using Eq. (A3), we obtain the analytical expression of mRNA distribution as

$$P(m)=\frac{\mu^m}{m!}\prod_{i=1}^{N-1}\frac{\left(\beta_1^{(N)}\right)_m}{(\alpha_i)_m}\,{}_{N-1}F_{N-1}\left(\begin{matrix}m+\beta_1^{(N)},\cdots,m+\beta_{N-1}^{(N)}\\ m+\alpha_1,\cdots,m+\alpha_{N-1}\end{matrix}\middle|;-\mu\right),\quad m=0,1,2,\cdots \tag{B5}$$

where ${}_nF_n\left(\begin{matrix}a_1,\cdots,a_n\\ b_1,\cdots,b_n\end{matrix}\middle|;\sigma\right)$ is a confluent hypergeometric function (1).

It is worth being pointed out that if $N=2$ that corresponds to the common ON-OFF model, then Eqn. (B5) can reproduce the result obtained previously (2,3). That is,

$$P(m)=\frac{\mu^m}{m!}\frac{\Gamma\left(m+\beta_1^{(2)}\right)}{\Gamma(m+\alpha_1)}\frac{\Gamma(\alpha_1)}{\Gamma(\beta_1)}\,{}_1F_1\left(\begin{matrix}m+\beta_1^{(2)}\\ m+\alpha_1\end{matrix}\middle|;-\mu\right),\quad m=0,1,2,\cdots \tag{B6}$$

where $\alpha_1=\lambda_{12}+\lambda_{21}$, $\beta_1^{(1)}=\lambda_{12}$, $\beta_1^{(2)}=\lambda_{21}$

Case 3 $\Lambda=\mu\begin{pmatrix}\mathbf{I}_{(N-1)} & \mathbf{0}\\ \mathbf{0} & 0\end{pmatrix}$

Such a case corresponds to the gene model where the promoter has $(N-1)$ active states with the same transcription rate. Correspondingly, Eq. (11) at steady state in the main article becomes

$$\begin{aligned}&\sum_{k=1,\neq i}^{N}\lambda_{ki}G_k-\sum_{k=1,\neq i}^{N}\lambda_{ik}G_i-s\frac{\partial G_i}{\partial s}+\mu sG_i=0,\quad i=1,2,\cdots,N-1\\&\sum_{k=1}^{N-1}\lambda_{kN}G_k-\sum_{k=1}^{N-1}\lambda_{Nk}G_N-s\frac{\partial G_N}{\partial s}=0\end{aligned}\tag{B7}$$

One will see that solving Eq. (B7) can become **Case 2**. In fact, the transformations $G_i=e^{\mu s}F_i$ $(1\le i\le N)$ will transform Eq. (B7) into

$$\begin{aligned}&\sum_{k=1,\neq i}^{N}\lambda_{ki}F_k-\sum_{k=1,\neq i}^{N}\lambda_{ik}F_i-\tau\frac{\partial F_i}{\partial \tau}=0,\quad i=1,2,\cdots,N-1\\&\sum_{k=1}^{N-1}\lambda_{kN}F_k-\sum_{k=1}^{N-1}\lambda_{Nk}F_N-\tau\frac{\partial F_N}{\partial \tau}+\mu\tau F_N=0\end{aligned}\tag{B8}$$

with $\tau=-s$, which is nothing but the gene model with one ON with the transcription rate μ and $(N-1)$ OFFs. According to discussion in **Case 2**, we have

$$F(\tau)={}_{N-1}F_{N-1}\left(\left.\begin{matrix}\beta_1^{(N)},\cdots,\beta_{N-1}^{(N)}\\\alpha_1,\cdots,\alpha_{N-1}\end{matrix}\right|;\mu\tau\right)\tag{B9}$$

Note that $G(z)=e^{\mu s}F(-s)=e^{\mu(z-1)}{}_{N-1}F_{N-1}\left(\left.\begin{matrix}\beta_1^{(N)},\cdots,\beta_{N-1}^{(N)}\\\alpha_1,\cdots,\alpha_{N-1}\end{matrix}\right|;\mu(1-z)\right)$. Therefore, using the relationship between probability distribution and generating function, we have

$$\begin{aligned}P(m)&=\frac{1}{m!}\frac{d^m}{dz^m}G(z)\bigg|_{z=0}\\&=\frac{e^{-\mu}}{m!}\sum_{k=0}^{m}\binom{m}{k}\mu^{m-k}(-1)^k\prod_{i=1}^{N-1}\frac{\left(\beta_1^{(N)}\right)_k}{(\alpha_i)_k}{}_{N-1}F_{N-1}\left(\left.\begin{matrix}k+\beta_1^{(N)},\cdots,k+\beta_{N-1}^{(N)}\\k+\alpha_1,\cdots,k+\alpha_{N-1}\end{matrix}\right|;\mu\right)\end{aligned}\tag{B10}$$

C. The parameter values used in computation in Fig. 1

(A) $\mathbf{A}=\left(\begin{array}{c|cc}-0.2&1&1\\\hline 0.1&-1.1&0.1\\0.1&0.1&-1.1\end{array}\right)$, $\mu=(0,10,30)$, $\delta=1$;

(B) $\mathbf{A}=\left(\begin{array}{c|cc}-2&0.1&0.1\\\hline 1&-1.1&0.1\\1&1&-0.2\end{array}\right)$, $\mu=(0,10,30)$, $\delta=1$;

(C) $\mathbf{A}=\left(\begin{array}{c|cc} -0.3 & 0.1 & 0.1 \\ \hline 0.2 & -1.1 & 0.1 \\ 0.1 & 1 & -0.2 \end{array}\right)$, $\mu=(0,10,30)$, $\delta=1$;

(D) $\mathbf{A}=\left(\begin{array}{c|cc} -2 & 0.02 & 0.02 \\ \hline 1 & -0.12 & 0.1 \\ 1 & 0.1 & -0.12 \end{array}\right)$, $\mu=(0,10,30)$, $\delta=1$;

(E) $\mathbf{A}=\left(\begin{array}{c|cc} -0.2 & 0.02 & 0.02 \\ \hline 0.1 & -0.12 & 0.1 \\ 0.1 & 0.1 & -0.12 \end{array}\right)$, $\mu=(0,10,30)$, $\delta=1$;

(F) $\mathbf{A}=\begin{pmatrix} -0.09 & 0.02 & 0.02 \\ 0.04 & -0.07 & 0.04 \\ 0.05 & 0.05 & -0.06 \end{pmatrix}$, $\mu=(5,20,45)$, $\delta=1$.

D. The parameter values used in computation in Fig. 2

(A)(C) $\mathbf{A}=\left(\begin{array}{c|cc} -4 & 0.2 & 0.2 \\ \hline 2 & -0.6 & 0.2 \\ 2 & 0.4 & -0.4 \end{array}\right)$, $\mu=(0,10,90)$, $\delta=1$;

(B)(D) $$\mathbf{A}=\left(\begin{array}{ccccccccc|c} -4 & 4 & & & & & & & & \\ & -4 & 4 & & & & & & & \\ & & -4 & 4 & & & & & & \\ & & & -4 & 4 & & & & & \\ & & & & -4 & 4 & & & & \\ & & & & & -4 & 4 & & & \\ & & & & & & -4 & 4 & & \\ & & & & & & & -4 & 4 & \\ & & & & & & & & -4 & 0.08 \\ \hline 4 & & & & & & & & & -0.08 \end{array}\right), \quad \mu=(0,0,0,0,0,0,0,0,0,90),$$

$\delta=1$.

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