Supporting information: Controlling gene expression timing through gene regulatory architecture

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S3 Text: Toy-model for power-law behavior

In order to determine the dependence of peak MFPT (response time for deterministic system) on regulatory strength (α) and TF-binding rate (k_{off}), we probe a simple toy model of auto-regulation. In this model, we ignore the mRNA dynamics and also consider the binding and unbinding events are fast enough to attain quasi-static equilibrium. If there are x TF present at any time the probability that the gene is free (P_{f}) or bound (P_{b}) can be expressed as

$$P_{\text{f}} = \frac{k_{\text{off}}}{k_{\text{on}}x + k_{\text{off}}} = \frac{1}{\sigma x + 1}, \quad P_{\text{b}} = \frac{k_{\text{on}}x}{k_{\text{on}}x + k_{\text{off}}} = \frac{\sigma x}{\sigma x + 1}. \tag{1}$$

Here, $\sigma = k_{\text{on}}/k_{\text{off}}$. Now the rate of change of x can be expressed as

$$\begin{aligned} \frac{dx}{dt} &= r_0 P_{\text{f}} + r P_{\text{b}} - \gamma x, \\ &= r_0 \frac{1+\alpha\sigma x}{1+\sigma x} - \gamma x. \end{aligned} \tag{2}$$

r_0 and r being the basal production rate and production rate when TF is bound. The regulatory strength $\alpha = r/r_0$ is same as previously defined. The above differential equation can be solved exactly to obtain,

$$\begin{aligned} \ln(C) - \gamma\sigma t &= A\ln(x-a-b) + B\ln(x-a+b), \\ a &= \frac{r_0\alpha\sigma - \gamma}{2\gamma\sigma}, \quad b = \sqrt{a^2 + \frac{r_0}{\gamma\sigma}}, \\ A &= \frac{1+\sigma(a+b)}{2b}, \quad B = \frac{-1+\sigma(b-a)}{2b}. \end{aligned} \tag{3}$$

Here, $\ln(C) = A\ln(-a-b) + B\ln(-a+b)$ is a constant of integration obtained using initial condition, $x(t=0)=0$. Furthermore the steady state expression x_{ss} is given by $x_{\text{ss}} = a+b$ for $t=\infty$. The response time (τ), time to reach a certain fraction (f) of x_{ss}, after doing a little bit algebra is expressed as

$$\tau = -\frac{\ln(1-f)}{\gamma} + \frac{B}{\gamma\sigma}\left[\ln(1-f) - \ln\left(1 + f\frac{a+b}{b-a}\right)\right]. \tag{4}$$

Eqn. 4, is a non-monotonic function with a complex dependence on the threshold fraction (f) and off-rate ($k_{\text{off}} = k_{\text{on}}/\sigma$). The first term in the expression is basically the response time for a constitutive gene, $\tau_{\text{cons}} = -\ln(1-f)/\gamma = \ln(2)/\gamma$ for $f = 0.5$. In principle, to obtain peak response time, one can maximize eqn. 4. However, in this case, cannot be solved explicitly. In Fig. 1, we show the results obtained using Eqn. 4 which closely match with the full deterministic model.

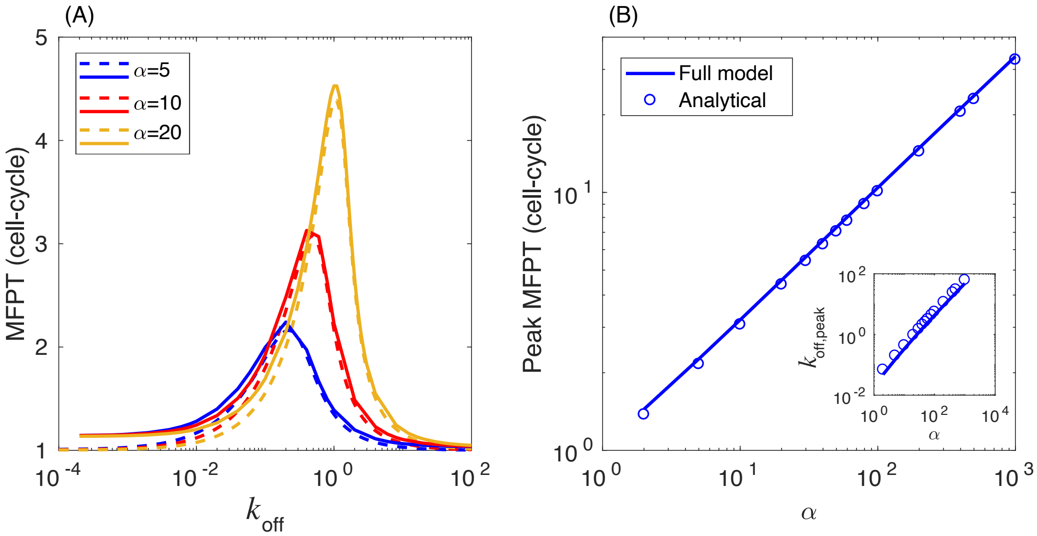

Fig 1. Comparison of the full deterministic model and the simplified toy-model without mRNA dynamics. (A) MFPT (response time) as a function of k_{off} from deterministic model (solid lines) and from Eqn. 4 for simplified toy-model for varying regulatory strengths (α). (B) Peak MFPT versus α as well as k_{off} at peak versus α (inset) from the toy-model matches well with the full deterministic model.