

# A model for the spatio-temporal design of gene regulatory circuits

## Supplementary Information

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### 1 Quasi steady state mRNA

The system of Ordinary Differential Equations was simplified using the quasi-steady-state assumption for mRNA:

$$m_i^*(P_i) = \frac{\beta_{\text{transc}}(P_i + \alpha_{\text{leak},i})}{k_{\text{Dm}} + \mu} \quad (\text{S1})$$

replacing equations 3 and 6 with:

$$\frac{dR_{\text{local}}}{dt} = \beta_{\text{transl}} m_R^*(P_R) - (k_{\text{Dp}} + \mu)R_{\text{local}} - k_{\text{unb}}R_{\text{local}} - \frac{P_{\text{gfp}}R_{\text{local}}}{\tau_{\text{s,local}}} \quad (\text{S2})$$

$$\frac{d\text{FP}}{dt} = \beta_{\text{transl}} m_{\text{gfp}}^*(P_{\text{gfp}}) - (k_{\text{Dp}} + \mu)\text{FP} \quad (\text{S3})$$

### 2 Derivation of $\tau_{\text{local}}$

To get the local search time at a specific inter-genic distance we solve Equation 7:

$$\rho(x, t) = \frac{e^{-\frac{x^2}{4Dt} - k_{\text{un}}t}}{2\sqrt{\pi}\sqrt{Dt}} \quad (\text{S4})$$

Now we calculate the average time it takes for the TFs to bind within this limit:

$$\frac{\int_0^\infty tk_{\text{bind}}\rho(x, t)dt}{\int_0^\infty k_{\text{bind}}\rho(x, t)dt} = \frac{\int_0^\infty t\rho(x, t)dt}{\int_0^\infty \rho(x, t)dt} = \frac{\sqrt{k_{\text{un}}}|x| + \sqrt{D}}{2\sqrt{D}k_{\text{un}}} \quad (\text{S5})$$

If this is compared against the solution  $\frac{|x|}{2\sqrt{D}k_{\text{un}}}$  in Wunderlich and Mirny (1), we see that there is an extra term of  $\frac{\sqrt{D/k_{\text{un}}}}{2\sqrt{D}k_{\text{un}}}$ , referred to as  $\alpha$ . This parameter defines the effect of non-immediately binding. Let  $0 < \alpha < 1$ ,  $\lim_{k_{\text{bind}} \rightarrow \infty} \alpha = 0$  and  $\lim_{k_{\text{bind}} \rightarrow 0} \alpha = 1$ .

By substituting we obtain:

$$\tau_{\text{local}} = \frac{d + \alpha\sqrt{D/k_{\text{un}}}}{2\sqrt{D}k_{\text{un}}} \quad (\text{S6})$$

where we fill in the distance between the source and target,  $d$ , for  $|x|$ .

Solving the binding rate from the global search time returns a value for a TF and a location to be ca.  $5000s^{-1}$  (using the parameters  $M$  and  $\tau_{\text{global}}$ ), hence  $\alpha \approx 0$ .

## References

1. Wunderlich, Z., and Mirny, L. A. (2008) Spatial effects on the speed and reliability of protein-DNA search. *Nucleic Acids Research* 36, 3570–3578.