## **Supporting Information**

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## SI Text

**Analytical results: Mean and Covariance.** Here, we explain how to derive and solve the equations for the moments of the particle fields. The generating functions for the gene expression system in the main text satisfy

$$\begin{pmatrix} \frac{\partial}{\partial \tau} - \mathbf{D} \Delta_{\xi_0} \end{pmatrix} \mathbf{u} = \begin{bmatrix} au_1(u_2 - 1) \\ \gamma (bu_2(u_3 - 1) - (u_2 - 1)) \\ -(u_3 - 1) \end{bmatrix} \\
= \underbrace{\begin{bmatrix} 0 & a & 0 \\ 0 & -\gamma & b\gamma \\ 0 & 0 & -1 \end{bmatrix}}_{\mathbf{A}} (\mathbf{u} - \mathbf{1}) \\
+ \begin{bmatrix} a(u_1 - 1)(u_2 - 1) \\ b\gamma(u_2 - 1)(u_3 - 1) \\ 0 \end{bmatrix}, \quad [S1]$$

where  $\mathbf{D} = d_3^{-1} \operatorname{diag}(0, D_2, D_3)$  and  $\mathbf{1} = (1, 1, 1)^T$ .

We can obtain equations for the first and second moments by taking functional derivatives of Eq. S1 with respect to  $s_i(\xi)$ , i = 1, 2, 3 and evaluating at  $s_i(\xi) = 1, i = 1, 2, 3, \xi \in \mathbb{R}^d$ . Using the notation described in the main text, we introduce the matrix of means,  $[\mathbf{M}]_{ij} = M_{j|i}$ , and the matrix of second moments

$$\begin{aligned} [\Theta_{i}]_{jk} &= \Theta_{jk|i} = \left( \frac{\delta^{2} u_{i}}{\delta s_{j}(\xi) \delta s_{k}(\xi')} + \delta_{jk} \delta(\xi - \xi') \frac{\delta u_{i}}{\delta s_{j}(\xi)} \right) \Big|_{s=1}, \\ \Theta &= \begin{pmatrix} \Theta_{1} \\ \Theta_{2} \\ \Theta_{3} \end{pmatrix}. \end{aligned} [S2]$$

After differentiating and evaluating Eq. S1 as mentioned above, we obtain

$$\left(\frac{\partial}{\partial \tau} - \mathbf{D}\Delta_{\xi_0}\right) \mathbf{M} = \mathbf{A}\mathbf{M},$$
 [S3]

$$\left( \frac{\partial}{\partial \tau} - (\textbf{D} \otimes \textbf{I}) \Delta_{\xi_0} \right) \Theta = (\textbf{A} \otimes \textbf{I}) \Theta + \begin{pmatrix} \textbf{F}_1 \\ \textbf{F}_2 \\ 0 \end{pmatrix}, \quad \quad \textbf{[S4]}$$

where **A** is defined in Eq. S1,  $\otimes$  is the matrix tensor product,  $\mathbf{F}_2 = \mathbf{F}(\tau, \xi, \xi' | \xi_0)$  is given in the main text, and

$$\begin{split} \mathbf{F}_{1} = & \mathbf{F}_{1}(\tau, \xi, \xi' | \xi_{0}) \\ = & \begin{bmatrix} 0 & M_{1|1} M'_{2|2} & M_{1|1} M'_{3|2} \\ M_{2|2} M'_{1|1} & M_{2|2} M'_{2|1} + M_{2|1} M'_{2|2} & M_{2|2} M'_{3|1} + M_{2|1} M'_{3|2} \\ M_{3|2} M'_{1|1} & M_{3|2} M'_{2|1} + M_{3|1} M'_{2|2} & M_{3|2} M'_{3|1} + M_{3|1} M'_{3|2} \end{bmatrix}. \end{split}$$

The moments satisfy the initial conditions  $M_{j|i}(0,\xi|\xi_0)=\delta_{ij}\delta(\xi-\xi_0)$  and  $\Theta_{jk|i}(0,\xi,\xi'|\xi_0)=\delta_{ij}\delta_{jk}\delta(\xi-\xi_0)\delta(\xi'-\xi_0)$ . Analytical solution of these equations is accomplished by split-

Analytical solution of these equations is accomplished by splitting  $\mathbf{A} = \mathbf{A}_d + \mathbf{A}_u$  into diagonal and strictly upper diagonal parts, introducing an integrating factor to absorb the term involving  $\mathbf{A}_d$  and solving the remaining equations iteratively using standard

Green's function or transform methods for the inhomogeneous heat equation. The solutions for the **M** are given in the main text. The second moments are

$$\begin{split} \Theta_{1}(t,\xi,\xi'|\xi_{0}) &= \delta(\xi - \xi') \begin{bmatrix} M_{1|1} & 0 & 0 \\ 0 & M_{2|1} & 0 \\ 0 & 0 & M_{3|1} \end{bmatrix} (\tau,\xi|\xi_{0}) \\ &+ a \int_{0}^{\tau} \mathbf{F}_{1}(\tau_{1},\xi,\xi'|\xi_{0}) \mathrm{d}\tau_{1} + ab\gamma \int_{0}^{\tau} \int_{0}^{\tau_{1}} e^{-\gamma(\tau_{1} - \tau_{2})} \\ &\times \int_{\mathbb{R}^{d}} f(\kappa_{2}^{2}\gamma(\tau_{1} - \tau_{2}),\zeta|\xi_{0}) \mathbf{F}_{2}(\tau_{2},\xi,\xi'|\zeta) \mathrm{d}\zeta \mathrm{d}\tau_{2} \mathrm{d}\tau_{1} \end{split} \tag{S6}$$

$$\begin{split} \Theta_{2}(t,\xi,\xi'|\xi_{0}) &= \delta(\xi - \xi') \begin{bmatrix} 0 & 0 & 0 \\ 0 & M_{2|2} & 0 \\ 0 & 0 & M_{3|2} \end{bmatrix} (\tau,\xi|\xi_{0}) \\ &+ b\gamma \int_{0}^{\tau} e^{-\gamma(\tau - \tau_{1})} \int_{\mathbb{R}^{d}} f(\kappa_{2}^{2}\gamma(\tau - \tau_{1}), \zeta|\xi_{0}) \\ &\times \mathbf{F}_{2}(\tau_{1},\xi,\xi'|\zeta) d\zeta d\tau_{1} \end{split} \tag{S7}$$

$$\Theta_{3}(\tau, \xi, \xi'|\xi_{0}) = \delta(\xi - \xi') \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & M_{3|3} \end{bmatrix} (\tau, \xi|\xi_{0}).$$
 [S8]

We are primarily interested in obtaining expressions for the covariance

$$\mathbf{C}_{1}(t,\xi,\xi'|\xi_{0}) = \mathbf{\Theta}_{1} - \mathbf{M}_{1}^{T}(t,\xi|\xi_{0})\mathbf{M}_{1}(t,\xi'|\xi_{0}).$$
 [S9]

It turns out that the second term in the solution for  $\Theta_1$  is exactly

$$\begin{split} a \int_0^\tau \mathbf{F}_1(\tau_1, \xi, \xi'|\xi_0) \mathrm{d}\tau_1 &= \mathbf{M}_{1:}^T(t, \xi|\xi_0) \mathbf{M}_{1:}(t, \xi'|\xi_0) \\ &- \delta(\xi - \xi') \begin{bmatrix} M_{1|1}(\tau, \xi|\xi_0) & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}, \end{split}$$
 [S10]

so it cancels with the matrix of the products of means and part of the first term. The first and third terms remain and yield the expressions listed in the main text. From these solutions of the moment equations, we can derive expressions for other statistical quantities such as variance densities and radial distribution functions.

The Steady-State Limit: Means. We compute the  $\tau \to \infty$  limit of the means and radial correlation functions in a number of ways in order to verify our results. Recall that the Laplace transform of a function  $g = g(\tau)$  is given by

$$(\mathscr{L}g)(s) = \int_{0^{-}}^{\infty} e^{-s\tau} g(\tau) d\tau.$$
 [S11]

The Laplace transform is particularly useful for calculating large time limits (1) via the identity Using this identity, the long-term mRNA density can be calculated:

$$\begin{split} \lim_{\tau \to \infty} & M_{2|1}(\tau, \xi | \xi_0) = a \underset{s\downarrow 0}{\lim} \mathcal{L}[e^{-\gamma \tau} f(\kappa_2^2 \gamma \tau, \xi | \xi_0)](s) \\ &= a \underset{s\downarrow 0}{\lim} \mathcal{L}[f(\kappa_2^2 \gamma \tau, \xi | \xi_0)](s + \gamma) \\ &= \frac{a}{\kappa_2^2 \gamma} \underset{s\downarrow 0}{\lim} \mathcal{L}[f(\tau, \xi | \xi_0)] \left(\frac{s + \gamma}{\kappa_2^2 \gamma}\right) \\ &= \frac{a}{\kappa_2^2 \gamma} L_d \left(\frac{1}{\kappa_2^2}, |\xi - \xi_0|\right), \end{split} \tag{S13}$$

where  $L_d$  is given by Eq. **S78**. Using the identity from Eq. **S80**, we can verify that  $\int_{\mathbb{R}^d} M_{2|1}(\infty, \xi|\xi_0) = a/\gamma = v_0/d_0 = m_2$ . Employing the same technique and a judicious change of variables, we can compute the  $\tau \to \infty$  limit of  $M_{3|1}$  when  $\kappa_2 \neq \kappa_3$ :

$$\begin{split} \lim_{\tau \to \infty} & M_{3|1}(\tau, \xi | \xi_0) = \frac{ab}{\kappa_3^2 - \kappa_2^2} \left( L_d \left( \frac{1}{\kappa_3^2}, |\xi - \xi_0| \right) \right. \\ & \left. - L_d \left( \frac{1}{\kappa_2^2}, |\xi - \xi_0| \right) \right). \end{split} \tag{S14}$$

The case  $\kappa_2 = \kappa_3$  is given by the limit

$$\lim_{\kappa_2 \to \kappa_3} \lim_{\tau \to \infty} M_{3|1}(\tau, \xi | \xi_0) = \frac{ab}{4\pi \kappa_3^4} L_{d-2} \left( \frac{1}{\kappa_3^2}, |\xi - \xi_0| \right). \tag{S15}$$

Typically  $\kappa_3 \gg \kappa_2$ , so for regions a moderate distance  $|\xi| \gg \kappa_2$  from the DNA source, we have

$$M_{3|1}(\infty, \xi|\xi_0) \approx \frac{ab}{\kappa_3^2} L_d\left(\frac{1}{\kappa_3^2}, |\xi - \xi_0|\right).$$
 [S16]

With the aid of the identity in Eq. **S80**, we can integrate  $M_{3|1}(\infty, \xi|\xi_0)$  over  $\mathbb{R}^d$  to see that the mean total number of particles agrees with the nonspatial result:

$$\int_{\mathbb{R}^d} M_{3|1}(\infty, \xi|\xi_0) d\xi = ab = v_0 v_1 / (d_0 d_1) = m_3.$$
 [S17]

The Steady-State Limit: Radial Correlation Functions. Due to the symmetry of the covariance densities and the Gaussian structure of the diffusion mechanism, it is possible to compute tractable analytical expressions for  $\Gamma_{ij}$ . In the main text, we define the radial correlation functions using Dirac delta functions. A more rigorous definition is given by

$$\begin{split} \int_{0}^{\tilde{r}} z^{d-1} \Gamma_{ij}(\tau, z) \mathrm{d}z &= \frac{1}{A_{d}} \int_{\mathbb{R}^{d}} \int_{\mathbb{R}^{d}} H(\tilde{r} - |\zeta - \zeta'|) \\ &\times C_{ij|1}(\tau, \zeta, \zeta') \mathrm{d}\zeta \mathrm{d}\zeta', \end{split} \tag{S18}$$

where H is the Heaviside function  $H(r)=0, r\leq 0, H(r)=1, r>0$  and  $A_d$  is the surface area of the d-dimensional sphere. Formally, we can think of Eq. **S18** as

$$\tilde{r}^{d-1}\Gamma_{ij}(\tau,\tilde{r}) = \frac{1}{A_d} \int_{\mathbb{R}^d} \int_{\mathbb{R}^d} \delta_{\tilde{r}}(|\zeta - \zeta'|) C_{ij|1}(\tau,\zeta,\zeta') d\zeta d\zeta'$$

$$\equiv \int_{(\zeta,\zeta')} \in \mathbb{R}^{2d} C_{ij|1}(\tau,\zeta,\zeta') d\zeta d\zeta', \quad [S19]$$

$$|\zeta - \zeta'| = \tilde{r}$$

where  $\delta_{\tilde{r}}(x) = \delta(x - \tilde{r})$ . Note that we are using an "unnormalized" version of the delta function in the sense that,  $\iint \delta(|\zeta - \zeta'| - \tilde{r}) \mathrm{d}\zeta \mathrm{d}\zeta' = A_d \tilde{r}^{d-1}$ . Also note that if the integrand  $C_{ij|1}$  possesses integrable singularities [in  $(\zeta, \zeta')$ ], the definition in the main text should be used rather than the formal delta function definition.

In both the mRNA-Pr (i = 2, j = 3) and the Pr-Pr (i = 3, j = 3) cases, the expressions involve terms of the form

$$\iint \delta(|\zeta - \zeta'| - \tilde{r}) \int f(T_3, \eta) f(T_1, \zeta - \eta) f(T_2, \zeta' - \eta) d\eta d\zeta d\zeta'.$$
[S20]

We can change the order of integration in Eq. **S20** and make a change of variables  $\zeta \mapsto \zeta - \zeta' + \eta$ ,  $\zeta' \mapsto \zeta' + \eta$  to simplify:

$$\begin{aligned} \text{Eq.} \mathbf{S20} &= \int f(T_3, \eta) \mathrm{d}\eta \int \delta(|\zeta| - \tilde{r}) \int f(T_2, \zeta') f(T_1, \zeta - \zeta') \mathrm{d}\zeta' \mathrm{d}\zeta \\ &= \int \delta(|\zeta| - \tilde{r}) f(T_1 + T_2, \zeta) \mathrm{d}\zeta \\ &= A_d \int_0^\infty r^{d-1} \delta(r - \tilde{r}) f(T_1 + T_2, r) \mathrm{d}r \\ &= A_d \tilde{r}^{d-1} f(T_1 + T_2, \tilde{r}), \end{aligned} \tag{S21}$$

recalling that  $f(\tau,\zeta)$  depends only on  $\tau$  and  $|\zeta|$ .  $\delta(|\zeta-\zeta'|-\tilde{r})$  is the Dirac delta distribution on the sphere  $|\zeta|=\tilde{r}$  in  $\mathbb{R}^d$ . With this identity we can obtain tractable analytic expressions for the radial correlation function  $\Gamma$ .

To facilitate comparison of these analytical expression to Monte Carlo estimates, we introduce the radial distribution functions (rdfs)  $\rho_{ii}(r)$  and  $\tilde{\rho}_{ij}(r)$ . The rdfs are defined by

$$\int_{0}^{\tilde{r}} z^{d-1} \rho_{ij}(\tau, z) dz = \frac{1}{A_d} \int_{\mathbb{R}^d} \int_{\mathbb{R}^d} H(\tilde{r} - |\zeta - \zeta'|) \times \mathbb{E}(X_{\tau}^i(\zeta) X_{\tau}^j(\zeta')) d\zeta d\zeta'$$
 [S22]

and

$$\int_{0}^{\tilde{r}} z^{d-1} \tilde{\rho}_{ij}(\tau, z) dz = \frac{1}{A_d} \int_{\mathbb{R}^d} \int_{\mathbb{R}^d} H(\tilde{r} - |\zeta - \zeta'|) \times M_{i|1}(\tau, \zeta) M_{i|1}(\tau, \zeta') d\zeta' d\zeta.$$
 [S23]

If the spatial dimension d=3, the background term  $\tilde{\rho}_{ij} \equiv \rho_{ij} - \Gamma_{ij}$  can also be computed analytically. The computation of this integral serves two purposes. Firstly, it allows us to analytically compute the effective radial distribution function  $\rho_{ij} = \Gamma_{ij} + \tilde{\rho}_{ij}$ . Secondly, since it is costly to estimate  $\tilde{\rho}_{ij}$  by straightforward Monte Carlo methods, having an analytic expression for  $\tilde{\rho}_{ij}$  is essential for comparing the theory to simulation. Fig. S1 shows  $\rho$  computed from analytics and simulation. The subfigures with error bars give the relative differences plus/minus one standard deviation of the sample estimates.

The following three subsections detail the calculation of the rcf  $\Gamma$  and the background term  $\tilde{\rho}$  for the mRNA-Protein and Protein-Protein fields.

 $C_{23|1}(\tau, \zeta, \zeta') = \mathbf{II}_{23},$  [S24]

where  $II_{23} =$ 

$$ab\gamma \int_0^{\tau} \int_0^{\tau_1} \int e^{-\gamma \tau_1 - \tau_2} f(\kappa_2^2 \gamma(\tau_1 - \tau_2), \eta)$$

$$\times f(\kappa_2^2 \gamma \tau_2, \zeta - \eta) f(\kappa_3^2 \tau_2, \zeta' - \eta) d\eta d\tau_2 d\tau_1.$$
 [S25]

Applying the above manipulations,

$$\begin{split} A_d\tilde{r}^{d-1}\Gamma_{23} &= \iint \delta(|\zeta-\zeta'|-\tilde{r})\mathbf{H}_{23}(\tau,\zeta,\zeta')\mathrm{d}\zeta\mathrm{d}\zeta' \\ &= ab\gamma \iint \delta(|\zeta-\zeta'|-\tilde{r}) \int_0^\tau \int_0^{\tau_1} e^{-\gamma\tau_1-\tau_2} \\ &\times \int f(\kappa_2^2\gamma(\tau_1-\tau_2),\eta)f(\kappa_2^2\gamma\tau_2,\eta-\zeta') \\ &\times f(\kappa_3^2\tau_2,\eta-\zeta)\mathrm{d}\eta\mathrm{d}\tau_2\mathrm{d}\tau_1\mathrm{d}\zeta\mathrm{d}\zeta' \\ &= ab\gamma A_d\tilde{r}^{d-1} \int_0^\tau \int_0^{\tau_1} e^{-\gamma\tau_1-\tau_2} f((\kappa_2^2\gamma+\kappa_3^2)\tau_2,\tilde{r})\mathrm{d}\tau_2\mathrm{d}\tau_1. \end{split}$$

In the limit as  $\tau \to \infty$ , we can exchange the order of integration to obtain

$$\Gamma_{23}(\tilde{r}) = ab\gamma \int_{0}^{\infty} \int_{0}^{\tau_{1}} e^{-\gamma\tau_{1}-\tau_{2}} f((\kappa_{2}^{2}\gamma + \kappa_{3}^{2})\tau_{2}, \tilde{r}) d\tau_{2} d\tau_{1}$$

$$= ab\gamma \int_{0}^{\infty} \int_{\tau_{2}}^{\infty} e^{-\gamma\tau_{1}-\tau_{2}} f((\kappa_{2}^{2}\gamma + \kappa_{3}^{2})\tau_{2}, \tilde{r}) d\tau_{1} d\tau_{2}$$

$$= ab\gamma \frac{1}{\gamma} \int_{0}^{\infty} e^{-(1+\gamma)\tau_{2}} f((\kappa_{2}^{2}\gamma + \kappa_{3}^{2})\tau_{2}, \tilde{r}) d\tau_{2}$$

$$= ab \int_{0}^{\infty} e^{-(1+\gamma)\tau_{2}} (4\pi\hat{\kappa}^{2}\tau_{2})^{-d/2} e^{-\tilde{r}^{2}/(4\hat{\kappa}^{2}\tau_{2})} d\tau_{2}, \quad [S27]$$

where  $\hat{\kappa}^2 = \kappa_2^2 \gamma + \kappa_3^2$ . In the  $\tau \to \infty$  limit, we can obtain an explicit expression for  $\Gamma_{23}$ :

$$\Gamma_{23}(\infty, \tilde{r}) = \frac{ab}{\hat{\kappa}^2} L_d \left( \frac{1+\gamma}{\hat{\kappa}^2}, \tilde{r} \right).$$
 [S28]

**Protein-protein** ( $\Gamma_{33}$ ). The unconvolved form of the protein-protein covariance is

$$C_{33|1}(\tau, \zeta, \zeta'|\zeta_0) = \delta(\zeta - \zeta')M_{3|1}(\tau, \zeta|\zeta_0) + \mathbf{II}_{33},$$
 [S29]

where

$$\begin{split} \mathbf{II}_{33} &= ab\gamma \int_{0}^{\tau} \int_{0}^{\tau_{1}} e^{-\gamma(\tau_{1} - \tau_{2})} \int f(\kappa_{2}^{2} \gamma(\tau_{1} - \tau_{2}), \eta) \\ &\times \mathbf{F}_{33}(\tau_{2}, \zeta, \zeta' | \eta) \mathrm{d} \eta \mathrm{d} \tau_{2} \mathrm{d} \tau_{1} \\ &= a(b\gamma)^{2} \int_{0}^{\tau} \int_{0}^{\tau_{1}} \int_{0}^{\tau_{2}} e^{-\gamma(\tau_{1} - \tau_{2})} e^{-\gamma(\tau_{2} - \tau_{3}) - \tau_{2} - \tau_{3}} \\ &\times \int f(\kappa_{2}^{2} \gamma(\tau_{1} - \tau_{2}), \eta) \\ &\times [f(\kappa_{2}^{2} \gamma(\tau_{2} - \tau_{3}) + \kappa_{3}^{2} \tau_{3}, \zeta - \eta) f(\kappa_{3}^{2} \tau_{2}, \zeta' - \eta) \\ &+ f(\kappa_{2}^{2} \gamma(\tau_{2} - \tau_{3}) + \kappa_{3}^{2} \tau_{3}, \zeta' - \eta) f(\kappa_{3}^{2} \tau_{2}, \zeta - \eta)] \mathrm{d} \eta \mathrm{d} \tau_{3} \mathrm{d} \tau_{2} \mathrm{d} \tau_{1}. \end{split}$$

Plugging  $C_{33|1}$  into the definition of  $\Gamma$  we see that the first term is

$$\begin{split} &\int_{\mathbb{R}^d} \int_{\mathbb{R}^d} H(\tilde{r} - |\zeta - \zeta'|) \delta(\zeta - \zeta') M_{3|1}(\tau, \zeta) \mathrm{d}\zeta \mathrm{d}\zeta' \\ &= \int_{\mathbb{R}^d} M_{3|1}(\tau, \zeta) \mathrm{d}\zeta = ab \end{split} \tag{S31}$$

for all  $\tilde{r}>0$ . This means that  $\Gamma_{33}$  is a distribution that can formally be written as

$$A_d \tilde{r}^{d-1} \Gamma_{33}(\tau, \tilde{r}) = \delta(\tilde{r}) ab +$$
" $\mathbf{II}_{33}$ term". [S32]

The second term, after some manipulation as discussed above, gives

"
$$\mathbf{II}_{33}$$
term" = 
$$\iint \delta(\tilde{r} - |\zeta - \zeta'|) \mathbf{II}_{33} d\zeta d\zeta'$$
$$= 2a(b\gamma)^2 A_d \tilde{r}^{d-1} \int_0^{\tau} \int_0^{\tau_1} \int_0^{\tau_2} \Phi d\tau_3 d\tau_2 d\tau_1, \quad [\mathbf{S33}]$$

where

$$\Phi = e^{-\gamma(\tau_1 - \tau_2) - \gamma(\tau_2 - \tau_3) - \tau_2 - \tau_3} f(\kappa_2^2 \gamma(\tau_2 - \tau_3) + \kappa_3^2 (\tau_2 + \tau_3), \tilde{r}).$$
[S34]

We take the limit as  $\tau \to \infty$  and rearrange the order of integration. Letting  $\kappa^2 = (\gamma \kappa_2^2 + \kappa_3^2)/(\gamma + 1)$  and changing variables gives

$$\Phi = e^{-\gamma S_3} e^{-(1-\kappa^2/\kappa_3^2)S_2} e^{-S_1/\kappa_3^2} f(S_1, \tilde{r}),$$
 [S35]

where  $S_1 = (\kappa_2^2 \gamma + \kappa_3^2)(\tau_2 - \tau_3) + 2\kappa_3^2 \tau_3$ ,  $S_2 = (1 + \gamma)(\tau_2 - \tau_3)$ ,  $S_3 = (\tau_1 - \tau_2)$ . In the limit  $\tau \to \infty$ , the integral in Eq. S33 becomes

"II<sub>33</sub> term" = 
$$\frac{a(b\gamma)^2}{(1+\gamma)\kappa_3^2} A_d \tilde{r}^{d-1} \int_0^\infty \int_0^{S_1/\kappa^2} \int_0^\infty \Phi dS_3 dS_2 dS_1.$$
 [S36]

Performing the integrals for  $S_3$  and  $S_2$  and simplifying gives

"II<sub>33</sub> term" = 
$$\frac{ab^2}{\kappa_3^2 - \kappa_2^2} A_d \tilde{r}^{d-1} \int_0^\infty [1 - e^{-(1/\kappa_3^2 - 1/\kappa^2)S_1}] e^{-S_1/\kappa_3^2} f(S_1, \tilde{r}) dS_1.$$
 [S37]

An explicit form can be obtained using Eq. S77:

$$\begin{split} A_d\tilde{r}^{d-1}\Gamma_{33}(\infty,\tilde{r}) &= \delta(\tilde{r})ab \\ &+ A_d\tilde{r}^{d-1}\frac{ab^2}{\kappa_3^2 - \kappa_2^2} \left(L_d(\frac{1}{\kappa_3^2},\tilde{r})\right. \\ &- L_d\left(\frac{1+\gamma}{\gamma\kappa_2^2 + \kappa_3^2},\tilde{r}\right)\right). \end{split} \tag{S38}$$

**The term**  $\tilde{\rho}$ . As mentioned above, the background term  $\tilde{\rho}$  (Eq. S23) relating the rdf  $\rho$  and the rcf  $\Gamma$  is a useful quantity that is slightly more difficult to estimate directly using Monte Carlo techniques than  $\rho$  in that it requires the generation of independent samples of the fields. We can calculate this quantity either analytically or by using quadrature.

We restrict ourselves to the case d=3 and change to radial coordinates and use the fact that the mean densities are radially symmetric. We note also that the integral over the angular coor-

dinates depends only on the radial lengths r, r' and  $\tilde{r}$ . Furthermore, this quantity either vanishes or is equal to the solid angle of the spherical cap of a cone with angle  $\tilde{\theta}(r, r', \tilde{r})$ . The key result is that

$$\begin{split} B_3(r,r',\tilde{r}) &\equiv \int_0^{2\pi} \int_0^\pi \int_0^{2\pi} \int_0^\pi H(\tilde{r}-|\zeta-\zeta'|) \mathrm{d}\phi' \mathrm{d}\phi' \mathrm{d}\phi \mathrm{d}\theta \\ &= \begin{cases} 8\pi^2 (1-\cos\tilde{\theta}(r,r',\tilde{r})), & |\tilde{r}-r| \leq r' \leq r+\tilde{r} \\ 16\pi^2, & r \leq \tilde{r},r' \leq \tilde{r}-r \\ 0, & \text{otherwise} \end{cases} \end{split}$$

where  $\tilde{\theta}$  is given by

$$\cos \tilde{\theta}(r, r', \tilde{r}) = \frac{1}{2} \frac{r^2 + (r')^2 - \tilde{r}^2}{rr'}.$$
 [S40]

We can then write the integral from Eq. S23 as

$$\begin{split} [\mathbf{S23}] &= 4\pi^2 \int_0^\infty \int_{|r-\tilde{r}|}^{r+\tilde{r}} r r' (\tilde{r}^2 - (r-r')^2) \\ &\times M_{i|1}(\tau,r) M_{j|1}(\tau,r') \mathrm{d}r' \mathrm{d}r \\ &+ 16\pi^4 \int_0^R \int_0^{\tilde{r}-r} r^2 (r')^2 M_{i|1}(\tau,r) M_{j|1}(\tau,r') \mathrm{d}r' \mathrm{d}r. \end{split}$$
 [S41]

These integrals can be computed in closed form. For example, in the limit as  $\tau \to \infty$ , the mean densities happen to be linear combinations of functions  $L_3$  (Eq. S78), and Eq. S23 can be written in terms of integrals of the form

$$I(s, s', \tilde{r}) \equiv \int_0^\infty \int_0^\infty B_3(r, r', \tilde{r}) L_3(s, r) L_3(s', r') dr dr'.$$
 [S42]

The quantity in Eq. **S42** can be calculated explicitly using symbolic math software such as Maple. The resulting expression is extremely long, so we omit its presentation here.

We can now write the rdfs (for dimension d=3) in terms of the function in Eq. **S42**. We can then analytically compute  $\rho_{ii}(\infty, \tilde{r}) = \Gamma_{ii}(\infty, \tilde{r}) + \tilde{\rho}_{ij}(\infty, \tilde{r})$ , though we omit the details here.

**Comparison to simulation.** We verified Eqs. 23, 29, and 30 in the main text by comparing integrals of these densities over regions with exact Monte Carlo simulations. For our simulations, we used an event-driven algorithm that is a slight modification of the Gillespie algorithm (2): Over a given time interval of length  $\Delta t$ , each molecule of type i moves by a random amount in a random direction so that its displacement is a Gaussian random variable with a mean of zero and covariance of  $D_i \Delta t$ . Since diffusion is occurring in free space, there are no boundary conditions to implement.

As an example, to check the validity of our expression for  $M_{2|1}(\infty, \xi|0)$  in Eq. 23, we use simulations to estimate the mean number of steady-state mRNAs between two spheres of radius  $r_i$  and  $r_i + \Delta r_i$ . This number should equal the integral of  $M_{2|1}$  over the volume:

$$\int_{r_i}^{r_i + \Delta r_i} 4\pi r^2 \frac{a}{\gamma} \frac{e^{-r/\kappa_2}}{4\pi r \kappa_2^2} dr = -\frac{a}{\gamma} e^{-r/\kappa_2} (1 + r/\kappa_2) \Big|_{r=r_i}^{r=r_i + \Delta r_i}, \quad [S43]$$

as we show in Fig. S2.

**Limiting Cases.** The limit of fast degradation of mRNA compared to protein. For the following calculation, we assume that we are in  $\mathbb{R}^3$  with no bounding walls and that the DNA molecule is at  $\xi_0=0$ . Accordingly, we suppress the dependence on  $\xi_0$  in our notation. The limit  $\gamma\to\infty$  with a and b fixed can be achieved by fixing  $v_2$ ,  $d_3$  and letting both  $d_2$ ,  $v_3\to\infty$ . Since we also fix  $D_2$  and  $D_3$ , we have that  $\kappa_2\to 0$ . From Eqs. S13 and S14, we get, for  $\gamma\to\infty$ ,

$$\lim_{\gamma \to \infty} M_{2|1}(\infty, \xi) = 0, \qquad \lim_{\gamma \to \infty} M_{3|1}(\infty, \xi) = ab \frac{e^{-|\xi|/\kappa_3}}{4\pi |\xi| \kappa_3^2}. \quad \textbf{[S44]}$$

In the following, we will use the identity

$$\lim_{\gamma \to \infty} \gamma \int_0^{\tau} e^{-\gamma t} g(t) dt = g(0)$$
 [S45]

for  $\tau > 0$ , which can be checked using integration by parts.

To get  $C_{33|1}$  in the limit  $\gamma \to \infty$ , we start with Eqs. 21 and 22 in the main text. We need to find the expressions for  $M_{3|3}$  and  $M_{3|2}$  in the  $\gamma \to \infty$  limit. For the calculation of  $M_{3|2}$ , we use the change of variables  $t = \tau - \tau_1$  to get

$$\lim_{\gamma \to \infty} M_{3|2}(\tau, \xi) = \lim_{\gamma \to \infty} b\gamma \int_0^{\tau} e^{-\gamma(\tau - \tau_1) - \tau_1} f(\kappa_2^2 \gamma(\tau - \tau_1) + \kappa_3^2 \tau_1, \xi) d\tau_1$$

$$= \lim_{\gamma \to \infty} b\gamma \int_0^{\tau} e^{-\gamma t} e^{-(\tau - t)} f(\kappa_2^2 \gamma t + \kappa_3^2 (\tau - t), \xi) dt$$

$$= be^{-\tau} f(\kappa_2^2 \tau, \xi) \qquad [S46]$$

and from Eq. 23

$$M_{3|3}(\tau,\xi|\xi_0) = e^{-\tau} f(\kappa_3^2 \tau,\xi), \tag{S47} \label{eq:S47}$$

which does not depend on γ. Using the change of variables

$$au_1 = x + y, au_2 = y, au_3 = dy, au_4 = dx, au_5 = dx, au_7 = dx, au_8 = dx, a$$

we obtain

$$\begin{split} \lim_{\gamma \to \infty} C_{33|1}(\xi, \xi') &= \delta(\xi - \xi') M_{3|1} + \lim_{\gamma \to \infty} ab\gamma \int_0^\infty \int_0^{\tau_1} e^{-\gamma(\tau_1 - \tau_2)} \\ &\times \int_{\mathbf{R}^d} f(\kappa_2^2 \gamma(\tau_1 - \tau_2), \zeta) F_{33}(\tau_2, \xi, \xi' | \zeta) d\zeta d\tau_1 d\tau_2 \\ &= \delta(\xi - \xi') M_{3|1} + ab \int_0^\infty \lim_{\gamma \to \infty} \gamma \int_0^\infty e^{-\gamma x} \\ &\times \int_{\mathbf{R}^d} f(\kappa_2^2 \gamma x, \zeta) F_{33}(y, \xi, \xi' | \zeta) d\zeta dx dy \\ &= \delta(\xi - \xi') M_{3|1} \\ &+ ab \int_0^\infty \int_{\mathbf{R}^d} f(0, \zeta) F_{33}(y, \xi, \xi' | \zeta) d\zeta dy \\ &= \delta(\xi - \xi') M_{3|1} + ab \int_0^\infty F_{33}(y, \xi, \xi' | \zeta) d\zeta dy. \quad \textbf{[S49]} \end{split}$$

Recall that

$$F_{33}(y,\xi,\xi') = M_{3|3}M'_{3|2} + M_{3|2}M'_{3|3} = 2be^{-2y}f(\kappa_3^2y,\xi)f(\kappa_3^2y,\xi').$$
 [S50]

The integral of  $F_{33}$  can be evaluated:

where  $K_2$  is the order 2 modified Bessel function of the second kind (3). Defining

$$\theta = (|\xi|^2 + |\xi'|^2)/\kappa_3^2,$$
 [S52]

we obtain

$$\lim_{\gamma \to \infty} C_{33|1}(\infty, \xi, \xi') = \delta(\xi - \xi') M_{3|1}(\infty, \xi) 
+ 2ab^2 \frac{K_2(\sqrt{2}\sqrt{|\xi|^2 + |\xi'|^2}/\kappa_3)}{4\pi^3 \kappa_3^4 (|\xi|^2 + |\xi'|^2)} 
= \delta(\xi - \xi') M_{3|1}(\infty, \xi) + \frac{ab^2}{2\pi^3 \kappa_3^6} \frac{K_2(\sqrt{2\theta})}{\theta}.$$
[S53]

Now, we consider the deviation of protein distribution from Poisson. Consider a cubic volume of length  $\Delta \xi$  on each side. We imagine measuring the number of protein molecules contained in the volume at a given point in time. To determine how far the distribution of this variable differs from being Poissonian, we compute the variance divided by the mean which is the Fano factor. Assuming that  $\Delta \xi$  is small, so that  $M_{3|1}(\infty, \xi)$  and  $C_{33|1}(\infty, \xi, \xi')$  are effectively constant over the volume, the mean number of particles is approximately

$$\Delta \xi^3 M_{3|1}(\infty, \xi)$$
 [S54]

and the variance is approximately

$$\Delta \xi^3 M_{3|1}(\infty,\xi) + \Delta \xi^6 \frac{ab^2}{2\pi^3 \kappa_4^3} \frac{K_2(2|\xi|/\kappa_3)}{|\xi|^2}.$$
 [S55]

So we have

Fano factor 
$$= 1 + \frac{\Delta \xi^6 \frac{ab^2}{2\pi^3 \kappa_3^4} \frac{K_2(2|\xi|/\kappa_3)}{|\xi|^2}}{\Delta \xi^3 M_{3|1}(\infty, \xi)} = 1 + \frac{\Delta \xi^3 \frac{ab^2}{2\pi^3 \kappa_3^4} \frac{K_2(2|\xi|/\kappa_3)}{|\xi|^2}}{ab \frac{e^{-|\xi|/\kappa_3}}{4\pi |\xi| \kappa_3^2}}$$

$$= 1 + \Delta \xi^3 \frac{b}{2\pi^2 \kappa_3^2 |\xi|} K_2(2|\xi|/\kappa_2) \exp(|\xi|/\kappa_3)$$

$$= b \left(\frac{\Delta \xi}{\kappa_3}\right)^3 \frac{K_2(2|\xi|/\kappa_2) \exp(|\xi|/\kappa_3)}{2\pi^2 |\xi|/\kappa_3}$$

$$= 1 + b \left(\frac{\Delta \xi}{\kappa_3}\right)^3 \mathcal{S}(|\xi|/\kappa_3),$$
 [S56]

where

$$\mathscr{G}(z) = \frac{K_2(2z)\exp(z)}{2\pi^2z}.$$
 [S57]

Limit of fast protein diffusion. Here, we obtain expressions for  $M_{3|1}$  in a closed region with reflecting walls, in the limit of  $\gamma \to \infty$  and of  $L/\kappa_3 \to 0$ . For the purposes of this calculation, we may assume that protein molecules originate at a single fixed DNA molecule at  $\xi_0$  at a constant rate. (These assumptions would not give the correct result for  $C_{33|1}$ .) Recall that we have rescaled time so that the rate of protein decay is 1.

Let our domain be  $L\Gamma$ , where  $\Gamma$  is a reference region with length 1 and L has units of length. We obtain for the mean density

of protein at  $\xi$ 

$$M_{3|1}(\xi|\xi_0) = ab \int_0^\infty e^{-\tau} f_L(\kappa_3^2 \tau, \xi|\xi_0) dy.$$
 [S58]

Here,  $f_L$  is the diffusion kernel of a particle diffusing at rate 1 within  $L\Gamma$  with reflecting boundary conditions. A scaling argument yields that

$$f_L(y,\zeta|\zeta_0) = L^{-d}f(y/L^2,\zeta/L|\zeta_0/L),$$
 [S59]

where f is the corresponding diffusion kernel for L = 1.

We use the eigenfunction expansion of  $f(t, \zeta|\zeta_0)$ , dropping the dependence on  $\zeta_0$ . Using separation of variables in the diffusion equation gives

$$f(t,\zeta) = \sum_{j=0}^{\infty} e^{-\lambda_j t} c_j \phi_j(\zeta),$$
 [S60]

where  $c_j$  are constants,  $\lambda_j$  are the eigenvalues of the Laplacian on the domain, and  $\phi_j$  are the corresponding orthogonal eigenfunctions. We use the normalization  $\int_{\Gamma} \phi_j(\zeta)^2 d\zeta = 1$ . Now,

$$\delta(\zeta - \zeta_0) = f(0, \zeta) = \sum_{j=0}^{\infty} c_j \phi_j(\zeta).$$
 [S61]

Integrating both sides against  $\phi_i(\zeta)$  gives

$$\phi_j(\zeta_0) = \int_{\Gamma} \delta(\zeta - \zeta_0) \phi_j(\zeta) d\zeta = c_j.$$
 [S62]

So,

$$f(t,\zeta|\zeta_0) = \sum_{i=0}^{\infty} e^{-\lambda_j t} \phi_j(\zeta_0) \phi_j(\zeta)$$
 [S63]

and

$$\begin{split} f_L(y,\zeta|\zeta_0) &= L^{-d}f(y/L^2,\zeta/L|\zeta_0/L) \\ &= L^{-d}\sum_{i=0}^\infty e^{-\lambda_i y/L^2}\phi_j(\zeta_0/L)\phi_j(\zeta/L). \end{split} \tag{S64}$$

The reflecting boundary conditions tell us that  $\phi_0$  is constant and  $\lambda_0 = 0$ . All the other  $\lambda_i$  are positive. Since

$$\int_{\Gamma} \{\phi_0(\zeta|\zeta_0)\}^2 d\zeta = 1,$$
 [S65]

we have  $\phi_0(\zeta|\zeta_0) = \operatorname{vol}(\Gamma)^{-1/2}$  for all  $\zeta$ .

Looking at mean protein concentration gives

$$\begin{split} M_{3|1}(\xi|\xi_{0}) &= ab \int_{0}^{\infty} e^{-y} f_{L}(\kappa_{3}^{2}y, \xi|\xi_{0}) dy \\ &= \frac{ab}{L^{d}} \int_{0}^{\infty} e^{-y} \sum_{j=0}^{\infty} e^{-y\lambda_{j}\kappa_{3}^{2}/L^{2}} c_{j} \phi_{j}(\xi/L) dy \\ &= \frac{ab}{L^{d}} \sum_{j=0}^{\infty} \left[ \int_{0}^{\infty} e^{-y-y\lambda_{j}\kappa_{3}^{2}/L^{2}} dy \right] c_{j} \phi_{j}(\xi/L) \\ &= \frac{ab}{L^{d}} \sum_{j=0}^{\infty} \frac{1}{1 + \lambda_{j}\kappa_{3}^{2}/L^{2}} c_{j} \phi_{j}(\xi/L) \\ &= \frac{ab}{L^{d}} c_{0} \phi_{0}(\xi/L) \\ &+ \frac{ab}{L^{d}} \sum_{j=1}^{\infty} \frac{L^{2}}{\lambda_{j}\kappa_{3}^{2}} \frac{1}{L^{2}/(\kappa_{3}^{2}\lambda_{j}) + 1} c_{j} \phi_{j}(\xi/L) \\ &= \frac{ab}{L^{d} \text{vol}(\Gamma)} \\ &+ \frac{ab}{L^{d}} \sum_{j=1}^{\infty} \frac{L^{2}}{\kappa_{3}^{2}} \frac{1}{\lambda_{j}} c_{j} \phi_{j}(\xi/L) \sum_{i=0}^{\infty} \left(\frac{L^{2}}{\kappa_{3}^{2}}\right)^{i} (-\lambda_{j})^{-i} \\ &= \frac{ab}{L^{d} \text{vol}(\Gamma)} \\ &+ \frac{ab}{L^{d} \text{vol}(\Gamma)} \sum_{i=0}^{\infty} \left(\frac{L^{2}}{\kappa_{3}^{2}}\right)^{i+1} \text{vol}(\Gamma) \sum_{j=1}^{\infty} c_{j} \phi_{j}(\xi/L) (-\lambda_{j})^{-i} \\ &= \frac{ab}{L^{d} \text{vol}(\Gamma)} + \frac{ab}{L^{d} \text{vol}(\Gamma)} \sum_{i=1}^{\infty} \left(\frac{L^{2}}{\kappa_{3}^{2}}\right)^{i} \eta_{i}(\xi/L). \end{split}$$

Here,  $\eta_i(\xi/L)$  is a dimensionless quantity depending on  $\xi$ ,  $\xi_0$  and the geometry of  $\Gamma$ .

**Kuramoto Lengths for Proteins in Budding Yeast.** There have been few direct measurements of the diffusion coefficient of proteins in budding yeast, and we therefore estimated diffusion coefficients using the molecular mass of the protein (obtained from www.uniprot.org) and the measured value of the diffusion coefficient of the kinase Fus3p (4). For a spherical protein, Stokes' law relates the diffusion coefficient, D, to the radius, R, of the protein (5):

$$D = \frac{kT}{6\pi\eta R},$$
 [S67]

where k is Boltzmann's constant and T is temperature. The coefficient of viscosity is denoted  $\eta$ . Assuming each protein is also uniformly dense, then the mass, M, of a protein is proportional to the volume of a sphere or  $R^3$ . Consequently, the ratio of two diffusion coefficients obeys

$$\frac{D}{D'} = \frac{R'}{R} = \left(\frac{M'}{M}\right)^{\frac{1}{3}}$$
 [S68]

for uniformly dense, spherical proteins. We used Eq.  $\mathbf{S68}$  to estimate diffusion coefficients with D' being the diffusion coefficent and M' being the molecular mass of Fus3p. To find the Kuramoto lengths, we took the square root of the diffusion coefficient multipled by the lifetime of the protein using the data of Belle et al. (6). We emphasize that our results are only approximate: They rely on the accuracy of the measurement of the diffusion

sion coefficient of Fus3p and assume that cytoplasmic proteins are uniformly dense spheres.

Using gene ontologies (www.geneontology.org), we asked if particular classes of proteins had on average relatively small or large Kuramoto lengths. Given the large absolute Kuramoto lengths of all the proteins we investigated, there may, however, be little selection on exact values, but rather only to maintain values larger than the cell diameter. Proceeding nevertheless, we found that proteins involved in responses to chemical stimuli and stress, in sporulation, transporters, signal transduction, and in the generation of energy all had relatively low Kuramoto lengths despite having relatively high diffusion coefficients. These proteins may then be rapidly degraded to maintain higher local concentrations, perhaps for both specificity (7) and efficiency.

**Regulated Expression of Genes.** The model presented in the main text considers constituitively expressed genes, wherein the DNA is always active. We can extend our framework to genes that have regulated expression.

To do this, we consider four species of molecule: Active DNA, Inactive DNA, mRNA, and protein. Active DNA produces mRNA exactly as DNA does in the model in the main text. Inactive DNA does not produce mRNA. With rate  $k_0$  inactive DNA switches into active DNA, and with rate  $k_1$  active DNA switches into inactive DNA. This system also satisfies the criterion for a branching process: Once a particle is produced, its subsequent evolution and that of its offspring are independent of all other particles in the system. As in the main text, we rescale time by the rate of protein decay  $d_3$  and use parameters  $\kappa_0 = k_0/d_3$ ,  $\kappa_1 = k_1/d_3$ .

We first deal with the spatially homogeneous case. Let  $N_i$  be the number of molecules of species i, where i=0 for inactive DNA, i=1 for active DNA, and i=2, 3 are for mRNA and protein, respectively. We define the generating functions as

$$g(t, s_0, s_1, s_2, s_3) = \mathbb{E}\left[\prod_{i=0}^3 s_i^{N_i(t)}\right]$$
 [S69]

and

$$u_j(t, s_0, s_1, s_2, s_3) = g(t, s_0, s_1, s_2, s_3 | 1 \text{ molecule of species } j).$$
[S70]

Hence,

$$g = \prod_{j=0}^{3} \prod_{k=1}^{N_j(0)} u_j = \prod_{j=0}^{3} u_j^{N_j(0)}.$$
 [S71]

Following a similar derivation as in the main text, we obtain the following equations for the  $u_i$ :

$$\frac{\partial}{\partial \tau} \begin{bmatrix} u_0 \\ u_1 \\ u_2 \\ u_3 \end{bmatrix} = \begin{bmatrix} \kappa_0(u_1 - u_0) \\ \kappa_1(u_0 - u_1) + au_1(u_2 - 1) \\ \gamma[bu_2(u_3 - 1) - (u_2 - 1)] \\ -(u_3 - 1) \end{bmatrix}.$$

To include the effects of diffusion we allow mRNA and protein to diffuse through a region  $\Gamma$  as in the main text, but fix the position of the DNA, regardless of whether it is active or not. The generating functions depend on functions  $s_i = s_i(\xi)$  for  $\xi$  in  $\Gamma$  and i = 0, ..., 3. We let

$$g(t, s_0, s_1, s_2, s_3) = \mathbb{E}\left[\prod_{i=0}^{3} \prod_{k=1}^{N_i(t)} s_i(x_i^{(k)}(t))\right]$$
 [S72]

 $u_j(t, s_0, s_1, s_2, s_3 | \xi_0) = g(t, s_0, s_1, s_2, s_3 | 1 \text{ molecule of species } j \text{ at } \xi_0),$ [S73]

which gives

$$g(t, s_0, s_1, s_2, s_3) = \prod_{i=0}^{3} \prod_{k=1}^{N_j(0)} u_j(t, s_0, s_1, s_2, s_3 | x_j^{(k)}(0)).$$
 [S74]

Similarly, the equations for the  $u_i$  are

$$\left(\frac{\partial}{\partial \tau} - \mathbf{D}\Delta_{\xi_0}\right)\mathbf{u} = \begin{bmatrix} \kappa_0(u_1 - u_0) \\ \kappa_1(u_0 - u_1) + au_1(u_2 - 1) \\ \gamma(bu_2(u_3 - 1) - (u_2 - 1)) \\ -(u_3 - 1) \end{bmatrix}, \quad [S75]$$

where  $\mathbf{D} = d_3^{-1} \operatorname{diag}(0, 0, D_2, D_3)$ .

**Appendix.** Recall that  $f(\tau, \xi | \xi_0)$  is the Gaussian density given by

$$f(\tau, \xi | \xi_0) = f(\tau, |\xi - \xi_0|) \equiv (4\pi\tau)^{-\frac{d}{2}} e^{-\frac{|\xi - \xi_0|^2}{4\tau}}.$$
 [S76]

The Laplace transform of f (in  $\tau$ ) is given by

- 1. Arfken GB, Weber HJ (2005) Mathematical Methods for Physicists (Academic, London).
- Gillespie DT (1977) Exact stochastic simulation of coupled chemical reactions. J Phys Chem 81:2340–2361.
- Wolfram Alpha LLC. (2011) Wolfram Alpha: Computational Knowledge Engine (www. wolframalpha.com).
- Maeder CI, et al. (2007) Spatial regulation of Fus3 MAP kinase activity through a reaction-diffusion mechanism in yeast pheromone signalling. Nat Cell Biol 9:1319–1326.

for  $\zeta > 0$ , where

$$L_{d}(s,\zeta) \equiv \frac{1}{(2\pi)^{\frac{d}{2}}} \left(\frac{\zeta}{\sqrt{s}}\right)^{1-\frac{d}{2}} K_{\frac{d}{2}-1}(\sqrt{s}\zeta) = \begin{cases} \frac{1}{2\sqrt{s}} e^{-\sqrt{s}\zeta}, & d = 1\\ \frac{1}{2\pi} K_{0}(\sqrt{s}\zeta), & d = 2\\ \frac{1}{4\pi\zeta} e^{-\sqrt{s}\zeta}, & d = 3 \end{cases}$$
[S78]

and  $K_n$  is a modified Bessel function of the second kind with degree n (8).  $L_d$  satisfies the scaling relations

$$L_d(s, \sqrt{a}\zeta) = a^{1-\frac{d}{2}}L_d(as, \zeta)$$
 [S79]

for d = 1, 2, 3. There are two useful identities involving integrals of  $L_d$  over  $\mathbb{R}^d$ . They can be computed using symbolic software such as Maple:

$$\begin{split} & \int_{\mathbb{R}^d} L_d(s,\zeta) \mathrm{d}\zeta = A_d \int_0^\infty r^{d-1} L_d(s,r) \mathrm{d}r = \frac{1}{s}, \\ & \int_{\mathbb{R}^d} L_{d-2}(s,\zeta) \mathrm{d}\zeta = A_d \int_0^\infty r^{d-1} L_{d-2}(s,r) \mathrm{d}r = \frac{2\pi}{s^2}. \end{split} \tag{S80}$$

- 5. Berg HC (1993) Random Walks in Biology (Princeton Univ Press, Princeton).
- Belle A, Tanay A, Bitincka L, Shamir R, O'Shea EK (2006) Quantification of protein halflives in the budding yeast proteome. Proc Natl Acad Sci USA 103:13004–13009.
- 7. Kholodenko BN, Hancock JF, Kolch W (2010) Signalling ballet in space and time. *Nat Rev Mol Cell Riol* 11:414–426
- Andrews GE, Askey R, Roy R (2001) Special Functions (Cambridge Univ Press, Cambridge, UK).

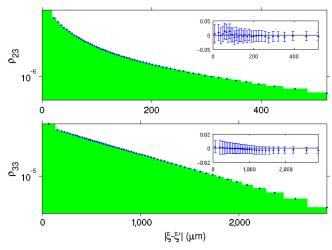


Fig. S1. Comparison of Monte Carlo estimates (blue points) and analytic expression (green solid areas) for rdfs  $\rho$ . The subplots show the relative difference of the MC estimates and theory with error bars corresponding to the standard deviation of the estimates. The parameters used are the same as in the main text, but with  $D_3 = 50 \ \mu\text{m}^2 \,\text{s}^{-1}$ .

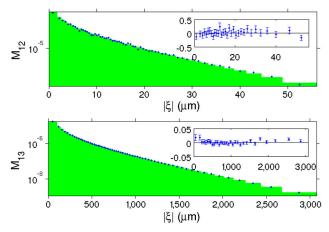


Fig. 52. Comparison of Monte Carlo estimates (blue points) and analytic expression (green solid areas) for means  $M_{2|1}=M_{12}$  and  $M_{3|1}=M_{13}$ . The subplots show the relative difference of the MC estimates and theory with error bars corresponding to the standard deviation of the estimates. The parameters used are the same as in the main text, but with  $D_3=50~\mu m^2\,s^{-1}$ .

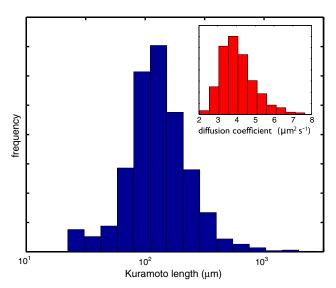


Fig. S3. The Kuramoto length for cytoplasmic proteins in budding yeast is expected to be larger than then the cell diameter (approximately 4  $\mu$ m). Using a diffusion coefficient of 4.2  $\mu$ m<sup>2</sup> s<sup>-1</sup> for Fus3p (4), measurements of protein half-lives (6) and molecular masses (www.uniprot.org), we estimated the diffusion coefficient (*Inset*) and the Kuramoto length for approximately 1,400 cytoplasmic proteins in budding yeast.