Optimization of information transmission through a noisy biochemical pathway explains the choice of reaction rates SUPPLEMENTARY

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Estimated Parameters

1. k_1 = 1078.4 nM^{-1} min^{-1}
2. S_{basal} = 86.68 min^{-1}
3. P_{basal} = 2036.6 min^{-1}
4. j_x = 0.7653 nM min^{-1}
5. N_{G_x} = 0.3344
6. d_x = 0.0304 min^{-1}
7. K_{GFP} = 3.7001 nM
8. j_{GFP} = 0.0594 nM min^{-1}
9. d_{GFP} = 0.0363 min^{-1}
10. $N_{G_{GFP}}$ = 0.2281
11. k_2 = 2652.9 nM^{-1} min^{-1}
12. j_P = 0.0174 nM min^{-1}
13. N_{G_P} = 2.6023
14. K_2 = 0.2081 nM
15. d_P = 0.0174 min^{-1}

The mean and variance of the one stage phosphorylation cascade

In the schematic diagram of a one-stage phosphoryltion cycle shown below, S corresponds to the signaling molecule. $X_1(X_2)$ represents the dephosphorylated (phosphorylated) form of the signaling protein X.

$$X_1 \underset{\beta}{\overset{\alpha_0+\alpha_1 S}{\rightleftharpoons}} X_2$$

The dynamics of the active protein concentration is given by

$$\frac{dx_2}{dt} = (\alpha_0 + \alpha_1 s)X_T - \{(\alpha_0 + \alpha_1 s) + \beta\} x_2 \tag{1}$$

The steady state value of active $X(x_2)$ is given by

$$x_{2s} = \frac{(\alpha_0 + \alpha_1 s)X_T}{(\alpha_0 + \alpha_1 s) + \beta} \tag{2}$$

The linearized equation around a steady state with adding a Gaussian white noise term

$$\frac{d\Delta x_2}{dt} = -\{(\alpha_0+\alpha_1 s)+\beta\}\,\Delta x_2+\xi_1(t) \tag{3}$$

$$\langle \xi_1(t_1)\rangle = 0 \tag{4}$$

$$\langle \xi_1(t_1)\,\xi_1(t_2)\rangle = 2\beta x_{2s}\delta(t_1-t_2) \tag{5}$$

The variance in the active protein concentration

$$\sigma_x^2 = \left\langle \Delta x_2^2 \right\rangle = \frac{(\alpha_0+\alpha_1 s)\beta X_T}{(\alpha_0+\alpha_1 s+\beta)^2} \tag{6}$$

Functional Relationship of Fisher Information with amplification and noise

The probability distributions are assumed to be normal at each value of the input

$$p(\mathrm{x}\mid\theta) = \frac{1}{\sqrt{2\pi\sigma(\theta)^2}} e^{-\frac{1}{2}\left(\frac{x-\mu(\theta)}{\sigma(\theta)}\right)^2} \tag{7}$$

$$\frac{-\partial}{\partial\theta}\log[p(\mathrm{x}\mid\theta)] = \frac{(x-\mu)}{\sigma^2}\frac{\partial\mu}{\partial\theta}+\frac{1}{\sigma}\left(\frac{(x-\mu)^2}{\sigma^2}-1\right)\frac{\partial\sigma}{\partial\theta} \tag{8}$$

$$\left(\frac{\partial}{\partial\theta}\log[p(\mathrm{x}\mid\theta)]\right)^2 = \frac{(x-\mu)^2}{\sigma^4}\left(\frac{\partial\mu}{\partial\theta}\right)^2+\frac{1}{\sigma^2}\left(\frac{(x-\mu)^4}{\sigma^4}+1-2\frac{(x-\mu)^2}{\sigma^2}\right)\left(\frac{\partial\sigma}{\partial\theta}\right)^2+\frac{1}{\sigma^3}\left(\frac{(x-\mu)^3}{\sigma^2}-(x-\mu)\right) \times\left(\frac{\partial\mu}{\partial\theta}\right)\left(\frac{\partial\sigma}{\partial\theta}\right) \tag{9}$$

Taking average over x while the cross term vanishes due to zero moments of the odd exponents for normal distribution and $\left\langle (x-\mu)^4\right\rangle = 3\sigma^4; \left\langle (x-\mu)^2\right\rangle = \sigma^2$, we obtain

$$\left\langle \left(\frac{\partial}{\partial\theta}\log[p(\mathrm{x}\mid\theta)]\right)^2 \right| = \frac{1}{\sigma^2}\left[\left(\frac{\partial\mu}{\partial\theta}\right)^2+2\left(\frac{\partial\sigma}{\partial\theta}\right)^2\right] \tag{10}$$

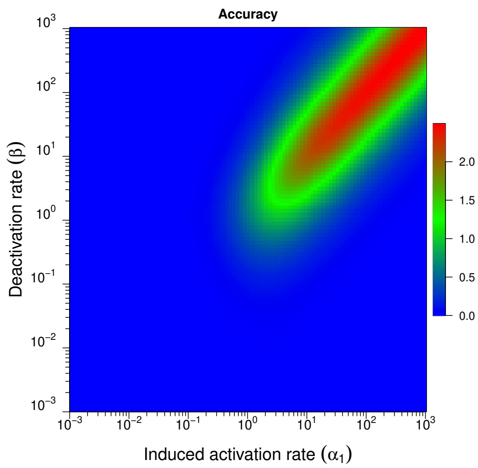
now,

$$\frac{1}{\sigma^2}\left(\frac{\partial\sigma}{\partial\theta}\right)^2 = \left(\frac{1}{\sigma}\frac{\partial\sigma}{\partial\theta}\right)^2 \tag{11}$$

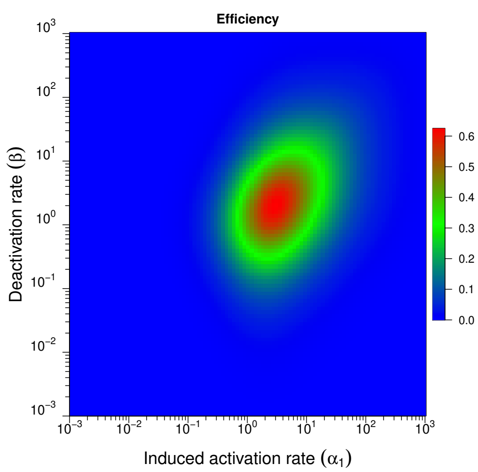
Thus, the first term in Equation S10 would contain the total number of molecule (X_T) while the second term is independent of X_T. Hence, the Fisher information when X_T is large can be approximated as,

$$F(\theta) = \left\langle \left(\frac{\partial}{\partial\theta}\log[p(\mathrm{x}\mid\theta)]\right)^2 \right| \approx \frac{1}{\sigma^2}\left(\frac{\partial\mu}{\partial\theta}\right)^2 \tag{12}$$

Figures



(a)



(b)

Figure S1. The optimization of information transmission from the analytical calculation in 2-dimension.(a) The heatmap displays the accuracy as function of the induced activation rate (α_1) and the deactivation rate (β) **(b)** The heatmap displays the efficiency as function of the induced activation rate ($alpha_1$) and deactivation rate ($beta$)

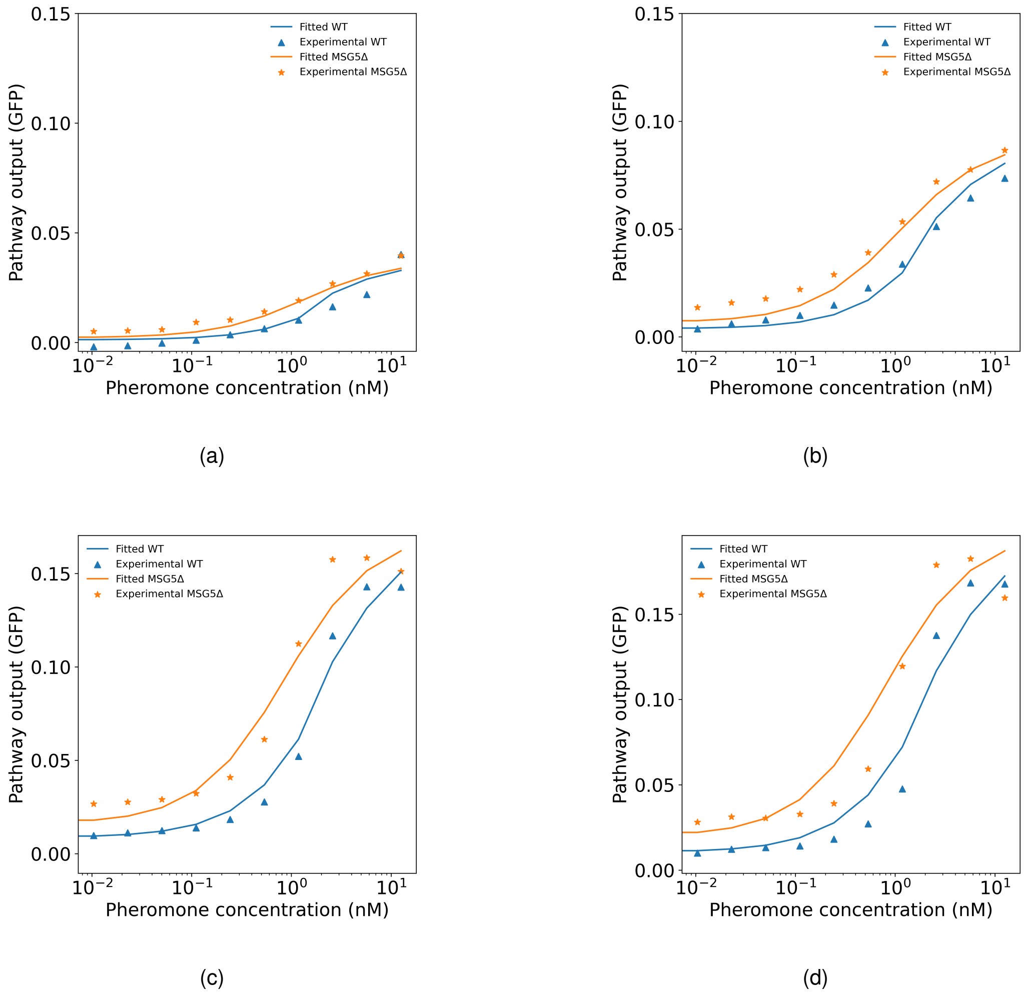
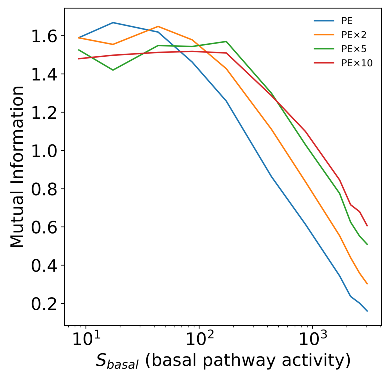
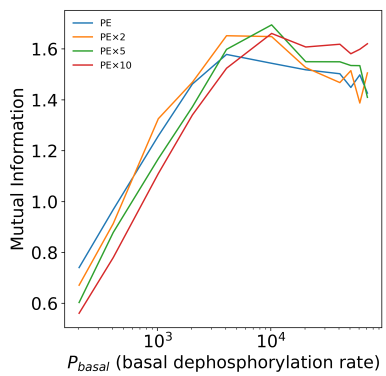


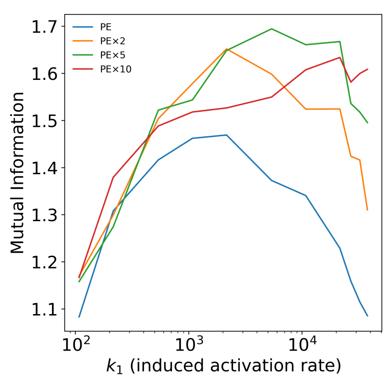
Figure S2. The fitted curves along with the experimentally measured GFP output values at the various time lapse indices shown for the WT and the MSG5Δ strain as indicated **(a)** First time-lapse index **(b)** Second time-lapse index **(c)** Fourth time-lapse index **(d)** Fifth time-lapse index



(a)



(b)



(c)

Figure S3. **(a)**Mutual information vs S_{basal} at four different values of the induced activation rate (k_1) as indicated in the legend while keeping other parameter values fixed at estimated values. PE corresponds to the estimated parameter value of k_1.**(b)**Mutual information vs P_{basal} at four different values of the induced activation rate (k_1) as indicated in the legend while keeping other parameter values fixed at estimated values. PE corresponds to the estimated parameter value of k_1. **(c)**Mutual information vs k_1 at four different values of the induced activation rate (P_{basal}) as indicated in the legend while keeping other parameter values fixed at estimated values. PE corresponds to the estimated parameter value of P_{basal}.

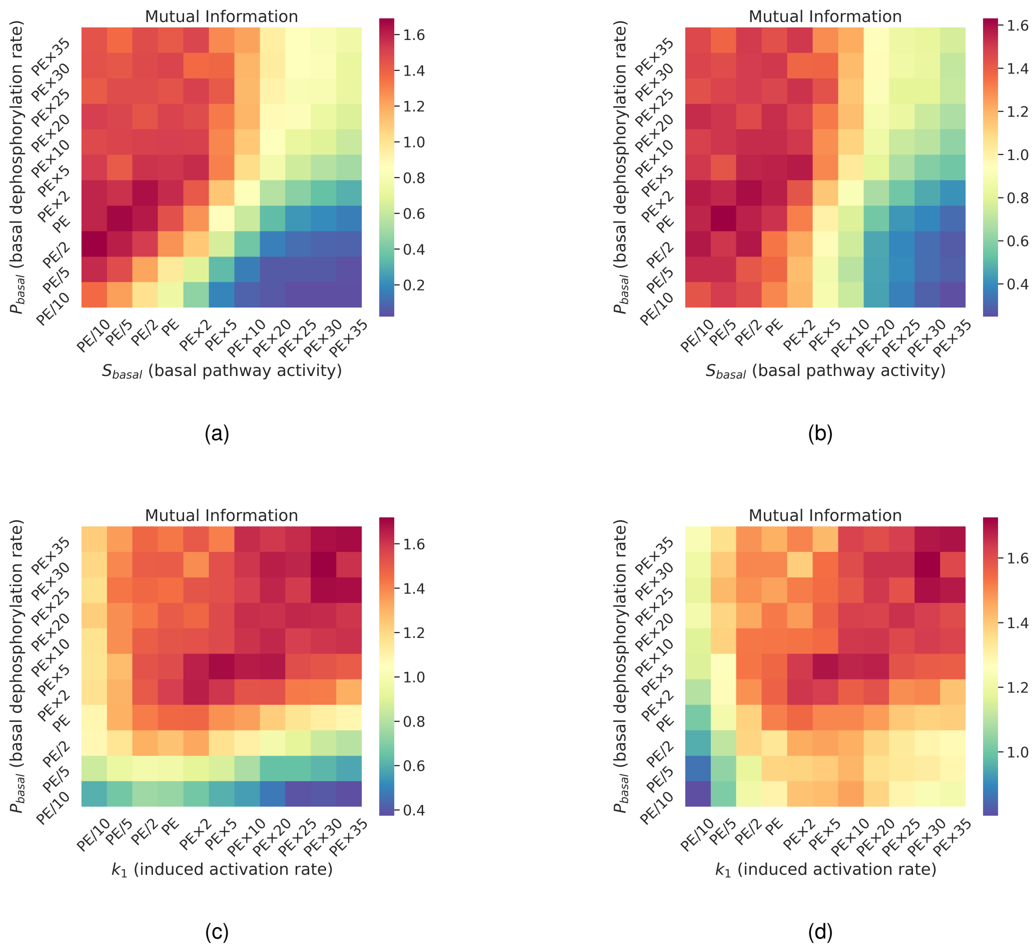


Figure S4. **(a)** Heatmap shows the mutual information as function of S_{basal} and P_{basal}. The PE on x-axis corresponds to estimated value of the induced activation rate (S_{basal}) while The PE on y-axis corresponds to estimated value of the basal deactivation rate (P_{basal}). **(b)** Heatmap shows the accuracy as function of S_{basal} and P_{basal} for WT in presence of the induced feedback loop. The PE on x-axis corresponds to estimated value of the basal pathway activity (S_{basal}) while The PE on y-axis corresponds to estimated value of the basal deactivation rate (P_{basal}). **(c)** Heatmap shows the mutual information as function of k_1 and P_{basal}. The PE on x-axis corresponds to estimated value of the induced activation rate (k_1) while The PE on y-axis corresponds to estimated value of the basal deactivation rate (P_{basal}). **(d)** Heatmap shows the accuracy as function of k_1 and P_{basal} for WT in presence of the induced feedback loop. The PE on x-axis corresponds to estimated value of the basal pathway activity (k_1) while The PE on y-axis corresponds to estimated value of the basal deactivation rate (P_{basal}).