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Supplementary Materials for the paper entitled "Mathematical modeling deciphers the benefits of alternatively-designed conserved activatory and inhibitory gene circuits"

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Deterministic Simulation of the Models when Protein Number is Small

In this section, the deterministic models were solved numerically when the protein number was 100 molec/cell to compare with the results of the stochastic simulation given in Section 5. We used the same parameter settings that had been used before for the deterministic simulations except the value for the parameter α_p . This parameter was set to $\alpha_p = 0.5$ molec/minute to reflect small protein number. We then run the deterministic simulations as γ changes between 1 and 20, and k varies from 5 to 100. The results are given in Figures S.1-S.2, and Tables S.1-S.2.

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| | $mP(\mathrm{molec/cell})$ | $mT(\min)$ | $D(\min)$ |
|------------|---------------------------|------------|-----------|
| A_{md^-} | 407 | 63 | 85 |
| A_{ms^+} | 945 | 36 | 108 |
| A_{pd^-} | 191 | 49 | 88 |
| A_{ps^+} | 960 | 29 | 107 |

Table S.1: The values for the metrics mP, mT and D for the activation mechanisms when the steady state protein level is 100 molec/cell, and the signal parameters are k = 100 and $\gamma = 20$.

Table S.2: The values for the metrics mP, mT and D for the inhibition mechanisms when steady state protein level is 100 molec/cell, and the signal profile parameters are k = 100 and $\gamma = 20$.

| | $mP(\mathrm{molec/cell})$ | $mT(\min)$ | $D(\min)$ |
|------------|---------------------------|------------|-----------|
| I_{md^+} | 59 | 29 | 116 |
| I_{ms^-} | 60 | 36 | 110 |
| I_{pd^+} | 52 | 2 | 133 |
| I_{ps^-} | 59 | 29 | 108 |



Figure S.1: A_{md^-} , A_{ms^+} , A_{pd^-} and A_{ps^+} mechanisms' dynamics when changing the signal profile, with the amplitude γ ranging from a 1-fold change to a 21-fold change and the signal persistency k ranging from 5 to 100 minutes when the steady state protein level is 100 molecule per cell.



Figure S.2: I_{md^+} , I_{ms^-} , I_{pd^+} and I_{ps^-} mechanisms' dynamics and characteristics when changing the signal profile with the signal amplitude γ ranging from a 1-fold change to a 21-fold change and the signal persistency k ranging from 5 to 100 minutes when the steady state protein level is 100 molecule per cell