Supplementary Materials for the paper entitled "Dynamics matter: Differences and similarities between alternatively designed mechanisms"

I. The Analytical Solutions of the Models

Consider the following initial value problem (IVP)

$$\frac{dP}{dt} = a - bP, \quad P(t_0) = P_0$$

The solution of this IVP is

$$P(t) = \frac{a}{b} + \left(P_0 - \frac{a}{b}\right) e^{-b(t-t_0)} \tag{S.1}$$

For signal profiles $S(t)$ in Eq.(4), our original models M_1-M_4 can be approximated by the following two different initial value problems,

$$\frac{dP}{dt} = \begin{cases} a - bP, & P(0) = P_0 \quad \text{if } 0 \le t < k \\ \alpha - \beta P, & P(k) = A \quad \text{if } t \ge k \end{cases} \tag{S.2}$$

From Eqs. (S.1) and (S.2), the solutions of these IVPs respectively become

$$P(t) = \begin{cases} \frac{a}{b} + \left(P_0 - \frac{a}{b}\right) e^{-bt} & , \quad \text{if } 0 \le t < k \\ \frac{\alpha}{\beta} + \left(A - \frac{\alpha}{\beta}\right) e^{-\beta(t-k)} & , \quad \text{if } t \ge k \end{cases} \tag{S.3}$$

where the value of A is chosen so that $P(t)$ is continuous throughout the time course. Similarly, in the following equations for the mechanisms M_1, M_2, M_3, M_4, the constants A_1, A_2, A_3, A_4 are taken to be such that P_1, P_2, P_3, P_4 are the continuous functions of time t.

II. Increased degradation rate mechanism(M_1)

For the same $S(t)$ profile, using Eq. (S.2), the model for mechanism M_1 can be written as

$$\frac{dP_1}{dt} = \begin{cases} \alpha - \beta(1+\gamma)P_1, & P_1(0) = \frac{\alpha}{\beta} \quad \text{if } 0 \le t < k \\ \alpha - \beta P_1, & P_1(k) = A_1 \quad \text{if } t \ge k \end{cases} \tag{S.4}$$

From Eq. (S.3), the solution of Eq. (S.4) becomes

$$P_1(t) = \begin{cases} \frac{\alpha}{(1+\gamma)\beta} + \frac{\alpha}{\beta}\frac{\gamma}{(1+\gamma)}e^{-\beta(1+\gamma)t} & , \text{ if } 0 \le t < k \\ \frac{\alpha}{\beta} + \left(A_1 - \frac{\alpha}{\beta}\right)e^{-\beta(t-k)} & , \text{ if } t \ge k \end{cases} \tag{S.5}$$

For $0 < t < k$, the time derivative of Eq. (S.5)

$$P_1'(t) = -\alpha\gamma e^{-\beta(1+\gamma)t} < 0$$

Since this derivative is always negative, the solution $P_1(t)$ is a decreasing function of t and it takes its minimum value on $[0,k]$ at the high endpoint k as

$$P_1(k) = \frac{\alpha}{(1+\gamma)\,\beta} + \left(\frac{\alpha}{\beta} - \frac{\alpha}{(1+\gamma)\,\beta}\right)e^{-\beta(1+\gamma)k} \tag{S.6}$$

III. Decreased production rate mechanism(M_2)

By using Eq. (S.2), the model M_2 can be written as

$$\frac{dP_2}{dt} = \begin{cases} \frac{\alpha}{1+\gamma} - \beta P_2, & P_2(0) = \frac{\alpha}{\beta} \quad \text{if } 0 \le t < k \\ \alpha - \beta P_2, & P_2(k) = A_2 \quad \text{if } t \ge k \end{cases} \tag{S.7}$$

for the same $S(t)$ function in Eq.(4). By Eq.(S.3), the solution of (S.7) has the following form

$$P_2(t) = \begin{cases} \frac{\alpha}{(1+\gamma)\beta} + \frac{\alpha}{\beta}\frac{\gamma}{(1+\gamma)}e^{-\beta t} & , \text{ if } 0 \le t < k \\ \frac{\alpha}{\beta} + \left(A_2 - \frac{\alpha}{\beta}\right)e^{-\beta(t-k)} & , \text{ if } t \ge k \end{cases} \tag{S.8}$$

For $0 < t < k$, the time derivative of Eq.(S.8) is

$$P_2'(t) = -\frac{\alpha\gamma}{1+\gamma}e^{-\beta t} < 0$$

which is always negative. Therefore, the solution $P_2(t)$ is a decreasing function of t over the interval $[0,k]$ and it takes its minimum value on $[0,k]$ at the high endpoint k as

$$P_2(k) = \frac{\alpha}{(1+\gamma)\,\beta} + \left(\frac{\alpha}{\beta} - \frac{\alpha}{(1+\gamma)\,\beta}\right)e^{-\beta k} \tag{S.9}$$

IV. Decreased degradation rate mechanism(M_3)

Again, using Eq.(S.2), the model for mechanism M_3 becomes

$$\frac{dP_3}{dt} = \begin{cases} \alpha - \frac{\beta P_3}{(1+\gamma)}, & P_3(0) = \frac{\alpha}{\beta} \quad \text{if } \ 0 \le t < k \\ \alpha - \beta P_3, & P_3(k) = A_3 \quad \text{if } \ t \ge k \end{cases} \tag{S.10}$$

for the same signal function as above. From Eq.(S.3), the solution of Eq. (S.10) is

$$P_3(t) = \begin{cases} \frac{\alpha(1+\gamma)}{\beta} - \frac{\alpha\gamma}{\beta} e^{-\frac{\beta t}{(1+\gamma)}} & , \ \text{if } \ 0 \le t < k \\ \frac{\alpha}{\beta} + \left(A_3 - \frac{\alpha}{\beta}\right) e^{-\beta(t-k)} & , \ \text{if } \ t \ge k \end{cases} \tag{S.11}$$

For $0 < t < k$, the time derivative of Eq. (S.11) becomes

$$P_3'(t) = \frac{\alpha\gamma}{1+\gamma} e^{-\frac{\beta t}{(1+\gamma)}} > 0$$

Since this derivative is always positive, the solution $P_3(t)$ is an increasing function of t and takes its highest value on $[0, k]$ at the higher endpoint k as

$$P_3(k) = \frac{\alpha\,(1+\gamma)}{\beta} - \frac{\alpha\gamma}{\beta} e^{-\frac{\beta k}{(1+\gamma)}} \tag{S.12}$$

V. Increased production rate mechanism(M_4)

By using Eq. (S.2), the model M_4 will have the following form

$$\frac{dP_4}{dt} = \begin{cases} \alpha(1+\gamma) - \beta P_4, & P_4(0) = \frac{\alpha}{\beta} \quad \text{if } \ 0 \le t < k \\ \alpha - \beta P_4, & P_4(k) = A_4 \quad \text{if } t \ge k \end{cases} \tag{S.13}$$

for the same signal profile as above. By Eq.(S.3), the solution of Eq.(S.13) has the following solution

$$P_4(t) = \begin{cases} \frac{\alpha(1+\gamma)}{\beta} - \frac{\alpha\gamma}{\beta} e^{-\beta t} & , \ \text{if } \ 0 \le t < k \\ \frac{\alpha}{\beta} + \left(A_4 - \frac{\alpha}{\beta}\right) e^{-\beta(t-k)} & , \ \text{if } \ t \ge k \end{cases} \tag{S.14}$$

For $0 < t < k$, the time derivative of Eq. (S.14) becomes

$$P_4'(t) = \alpha\gamma e^{-\beta t} > 0$$

This is always positive, which makes the solution $P_4(t)$ an increasing function of t over the interval

$[0, k]$. This solution attains its highest value on $[0, k]$ at the higher endpoint k, which is equal to

$$P_4(k) = \frac{\alpha(1+\gamma)}{\beta} - \frac{\alpha\gamma}{\beta} e^{-\beta k} \tag{S.15}$$

VI. Comparison of the signal induced activation mechanisms

Maximum protein abundance (mP): From Eqs.(S.12) and (S.15), we have $P_3(k) < P_4(k)$ since $e^{-\beta k} < e^{-\frac{\beta k}{(1+\gamma)}}$ for any positive k, β and γ. In fact, for any $t \in [0, k]$, $P_3(t) < P_4(t)$ must hold. This observation suggests that mP levels are lower in mechanism M_3 compared to mechanism M_4, and this result does not depend on α and β values.

Minimal response time (mT): Theoretically, the time required to reach minimal $P_3(t)$ and $P_4(t)$ values are equal to k for both models. However, since $e^{-\beta t} < e^{-\frac{\beta}{1+\gamma}t}$ for any positive t, β and γ, $P_4(t)$ increases faster than $P_3(t)$. Since mT is defined as time required to reach 90% of its maximum value, which makes it longer for $P_3(t)$. This observation suggests that mT is shorter for mechanism M_4 in comparison to mechanism M_3, and this result is independent from the values of the parameters α and β.

Duration (D): Since the signal becomes zero when at $t = k$ minutes, the same differential equation with different initial conditions describes the dynamics of both $P_3(t)$ and $P_4(t)$ dynamics for $t \geq k$. Since $A_3 = P_3(k)$ and $A_4 = P_4(k)$, $A_3 < A_4$ must hold. This leads to $P_3(t) < P_4(t)$ for all $t > k$. We also know that for any $t \in [0, k]$, $P_3(t) < P_4(t)$ is true, which makes D shorter for mechanism M_3. Our numerical simulations agree with this result, and show a slight variation between the two mechanisms.

Integrated Response (IR): Since mP is larger and D is longer for mechanism M_4, the integrated response IR becomes larger for this mechanism. Our numerical simulations support this result.