

Electronic Supplementary Information for: Properties of composite pulse-generating motifs

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1 Parameter Values

Parameter	Value	Reference & Remarks
α_{r_o}	$1.5 \times 10^{-3} \text{ nM} \cdot \text{min}^{-1}$	Approx transcription rate of 1.2kb/min for a 1.2kb long RNA in a diploid cell ^[1]
α_{r_c}	$1.5 \times 10^{-3} \text{ nM} \cdot \text{min}^{-1}$	Same as α_{r_o}
α_{p_o}	1.65 min^{-1}	Translation rate of 400 amino acid (aa) protein at 11 aa/sec ^[2]
α_{p_c}	1.65 min^{-1}	Same as α_{p_o}
β_{r_o}	$1.2 \times 10^{-3} \text{ min}^{-1}$	Average human mRNA degradation rate ^[3]
β_{r_c}	$1.2 \times 10^{-3} \text{ min}^{-1}$	Same as β_{r_o}
β_{p_o}	$1.3 \times 10^{-4} \text{ min}^{-1}$	Average human protein degradation rate ^[3]
β_{p_c}	$1.3 \times 10^{-4} \text{ min}^{-1}$	Same as β_{p_o}
$K_{r_o}^I$	100 nM	Arbitrary
$K_{r_o}^{p_c}$	30 nM	Average Hill constant ^[4]
$K_{r_c}^I$	100 nM	Same as $K_{r_o}^I$
$K_{r_c}^{p_o}$	30 nM	Average Hill constant ^[4]
$K_{r_o}^{p_c}$	50 nM	Similar to $K_{r_o}^{p_c}$
$K_{r_o}^{p_c}$	$1/K_{r_o}^{p_c}$	Assumed
$K_{p_o}^{p_c}$	$1/K_{r_o}^{p_c}$	Assumed

Tab. S1: Basal parameter values

2 Analytical expressions for steady state

2.1 rfORn

$$\frac{d}{dt}[r_o] = \alpha_{r_o} \frac{[I]}{K_{\frac{I}{r_o}} + [I]} \times \frac{K_{\frac{p_o}{r_o}}}{K_{\frac{p_o}{r_o}} + [p_c]} - \beta_{r_o}[r_o] \quad (2.1.1)$$

$$\frac{d}{dt}[r_c] = \alpha_{r_o} \frac{\frac{[I]}{K_{\frac{I}{r_o}}} + \frac{[p_o]}{K_{\frac{p_o}{r_c}}}}{1 + \frac{[I]}{K_{\frac{I}{r_o}}} + \frac{[p_o]}{K_{\frac{p_o}{r_c}}}} - \beta_{r_c}[r_c] \quad (2.1.2)$$

$$\frac{d}{dt}[p_o] = \alpha_{p_o}[r_o] - \beta_{p_o}[p_o] \quad (2.1.3)$$

$$\frac{d}{dt}[p_c] = \alpha_{p_c}[r_c] - \beta_{p_c}[p_c] \quad (2.1.4)$$

2.1.1 Steady state

$$[p_o] = \frac{\alpha_{p_o}}{\beta_{p_o}}[r_o] \quad (2.1.5)$$

$$[p_c] = \frac{\alpha_{p_c}}{\beta_{p_c}}[r_c] \quad (2.1.6)$$

$$\begin{aligned} [r_c] &= \frac{\alpha_{r_c}}{\beta_{r_c}} \frac{\frac{[I]}{K_{\frac{I}{r_c}}} + \frac{\alpha_{p_o}}{\beta_{p_o}}[r_o]}{1 + \frac{[I]}{K_{\frac{I}{r_c}}} + \frac{\alpha_{p_o}}{\beta_{p_o}}[r_o]} \\ &= \mathcal{S}_{r_c} \frac{K_{\frac{p_o}{r_c}}[I] + K_{\frac{I}{r_c}}\mathcal{S}_{p_o}[r_o]}{K_{\frac{p_o}{r_c}}K_{\frac{I}{r_c}} + K_{\frac{p_o}{r_c}}[I] + K_{\frac{I}{r_c}}\mathcal{S}_{p_o}[r_o]} \end{aligned} \quad (2.1.7)$$

$$[r_o] = \frac{\alpha_{r_o}}{\beta_{r_o}} \frac{[I]}{K_{\frac{I}{r_o}} + [I]} \times \frac{K_{\frac{p_o}{r_o}}}{K_{\frac{p_o}{r_o}} + \frac{\alpha_{p_c}}{\beta_{p_c}}[r_c]}$$

$$a = -\mathcal{S}_{p_o}K_{\frac{I}{r_c}}([I] + K_{\frac{I}{r_o}})(K_{\frac{p_o}{r_o}} + \mathcal{S}_c)$$

$$b = [I] \left(K'_{\frac{I}{r_o}} (\mathcal{S}_o - K_{\frac{p_o}{r_c}}) - K'_{\frac{I}{r_c}} (K_{\frac{p_o}{r_o}} + \mathcal{S}_c) \right) - [I]^2 (K_{\frac{p_o}{r_o}}K_{\frac{p_o}{r_c}} + K_{\frac{p_o}{r_c}}\mathcal{S}_c) - K'_{\frac{I}{r_o}}K'_{\frac{I}{r_c}}$$

$$c = [I]K_{\frac{p_o}{r_o}}K_{\frac{p_o}{r_c}}\mathcal{S}_{r_o}([I] + K_{\frac{I}{r_c}})$$

$$\text{where } \mathcal{S}_x = \mathcal{S}_{p_x}\mathcal{S}_{r_x}, \quad K'_{\frac{I}{r_c}} = K_{\frac{I}{r_o}}K_{\frac{p_o}{r_c}}, \quad K'_{\frac{I}{r_o}} = K_{\frac{I}{r_c}}K_{\frac{p_o}{r_o}}$$

$$[r_o] = \frac{-b + \sqrt{b^2 - 4ac}}{2a} \quad (2.1.8)$$

2.1.2 Jacobian

$$\begin{bmatrix} -\beta_{r_o} & 0 & 0 & \frac{\alpha_{r_o}[I]K_{\frac{p_o}{r_o}}}{(K_{\frac{I}{r_o}}+[I])(K_{\frac{p_o}{r_o}}+[p_c])^2} \\ 0 & -\beta_{r_c} & \frac{\alpha_{r_c}K_{\frac{I}{r_c}}^2K_{\frac{p_o}{r_c}}}{(K_{\frac{I}{r_c}}K_{\frac{p_o}{r_c}}+K_{\frac{p_o}{r_c}}[I]+K_{\frac{I}{r_c}}[p_o])^2} & 0 \\ \alpha_{p_o} & 0 & -\beta_{p_o} & 0 \\ 0 & \alpha_{p_c} & 0 & -\beta_{p_c} \end{bmatrix}$$

2.2 rfANDn

$$\frac{d}{dt}[r_o] = \alpha_{r_o} \frac{[I]}{K_{r_o} + [I]} \times \frac{K_{r_o}^{p_o}}{K_{r_o}^{p_o} + [p_c]} - \beta_{r_o}[r_o] \quad (2.2.1)$$

$$\frac{d}{dt}[r_c] = \alpha_{r_c} \frac{[I]}{K_{r_c} + [I]} \times \frac{[p_o]}{K_{r_c}^{p_o} + [p_o]} - \beta_{r_c}[r_c] \quad (2.2.2)$$

$$\frac{d}{dt}[p_o] = \alpha_{p_o}[r_o] - \beta_{p_o}[p_o] \quad (2.2.3)$$

$$\frac{d}{dt}[p_c] = \alpha_{p_c}[r_c] - \beta_{p_c}[p_c] \quad (2.2.4)$$

2.2.1 Steady state

$$[p_o] = \frac{\alpha_{p_o}}{\beta_{p_o}}[r_o] \quad (2.2.5)$$

$$[p_c] = \frac{\alpha_{p_c}}{\beta_{p_c}}[r_c] \quad (2.2.6)$$

$$[r_c] = \mathcal{S}_{r_c} \frac{\mathcal{S}_{p_o}[I][r_o]}{K_{r_c} K_{r_c}^{p_o} + K_{r_c} \mathcal{S}_{p_o}[r_o] + \mathcal{S}_{p_o}[I][r_o] + K_{r_c}^{p_o}[I]}$$

$$[r_o] = \mathcal{S}_{r_o} \frac{[I]}{K_{r_o} + [I]} \times \frac{K_{r_o}^{p_c}}{K_{r_o}^{p_c} + \mathcal{S}_{p_c}[r_c]}$$

$$a = -\mathcal{S}_{p_o} ([I] + K_{r_o}) \left(K'_{r_o} + [I](K_{r_o}^{p_c} + \mathcal{S}_c) \right)$$

$$b = [I](K'_{r_o} \mathcal{S}_o - K_{r_o}^{p_o} K'_{r_o} - K_{r_o}^{p_c} K'_{r_c}) + [I]^2(K_{r_o}^{p_c} \mathcal{S}_o - K_{r_o}^{p_o} K_{r_o}^{p_c}) - K'_{r_o} K'_{r_c}$$

$$c = [I]K_{r_o}^{p_c} K_{r_c}^{p_o} \mathcal{S}_{r_o}([I] + K_{r_o})$$

$$\text{where } \mathcal{S}_x = \mathcal{S}_{p_x} \mathcal{S}_{r_x}, \quad K'_{r_c} = K_{r_o} K_{r_c}^{p_o}, \quad K'_{r_o} = K_{r_c} K_{r_o}^{p_c}$$

$$[r_o] = \frac{-b + \sqrt{b^2 - 4ac}}{2a} \quad (2.2.7)$$

2.2.2 Jacobian

$$\begin{bmatrix} -\beta_{r_o} & 0 & 0 & -\frac{\alpha_{r_o}[I]K_{r_o}^{p_c}}{(K_{r_o} + [I])(K_{r_o}^{p_c} + [p_c])^2} \\ 0 & -\beta_{r_c} & \frac{\alpha_{r_c}[I]K_{r_c}^{p_o}}{(K_{r_c} + [I])(K_{r_c}^{p_o} + [p_o])^2} & 0 \\ \alpha_{p_o} & 0 & -\beta_{p_o} & 0 \\ 0 & \alpha_{p_c} & 0 & -\beta_{p_c} \end{bmatrix}$$

2.3 rdORn

$$\frac{d}{dt}[r_o] = \alpha_{r_o} \frac{[I]}{K_{r_o}^I + [I]} - \beta_{r_o}[r_o](1 + \lambda_{r_o}^{p_c}[p_c]) \quad (2.3.1)$$

$$\frac{d}{dt}[r_c] = \alpha_{r_o} \frac{\frac{[I]}{K_{r_o}^I} + \frac{[p_o]}{K_{r_c}^{p_o}}}{1 + \frac{[I]}{K_{r_o}^I} + \frac{[p_o]}{K_{r_c}^{p_o}}} - \beta_{r_c}[r_c] \quad (2.3.2)$$

$$\frac{d}{dt}[p_o] = \alpha_{p_o}[r_o] - \beta_{p_o}[p_o] \quad (2.3.3)$$

$$\frac{d}{dt}[p_c] = \alpha_{p_c}[r_c] - \beta_{p_c}[p_c] \quad (2.3.4)$$

2.3.1 Steady state

$$[p_o] = \frac{\alpha_{p_o}}{\beta_{p_o}}[r_o] \quad (2.3.5)$$

$$[p_c] = \frac{\alpha_{p_c}}{\beta_{p_c}}[r_c] \quad (2.3.6)$$

$$\begin{aligned} [r_c] &= \frac{\alpha_{r_c}}{\beta_{r_c}} \frac{\frac{[I]}{K_{r_c}^I} + \frac{\alpha_{p_o}[r_o]}{K_{r_c}^{p_o}}}{1 + \frac{[I]}{K_{r_c}^I} + \frac{\alpha_{p_o}[r_o]}{K_{r_c}^{p_o}}} \\ &= \mathcal{S}_{r_c} \frac{K_{r_c}^{p_o}[I] + K_{r_c}^I \mathcal{S}_{p_o}[r_o]}{K_{r_c}^{p_o} K_{r_c}^I + K_{r_c}^{p_o}[I] + K_{r_c}^I \mathcal{S}_{p_o}[r_o]} \end{aligned} \quad (2.3.7)$$

$$[r_o] = \mathcal{S}_{r_o} \frac{[I]}{(K_{r_o}^I + [I])(1 + \lambda_{r_o}^{p_c} \mathcal{S}_{p_c}[r_c])}$$

$$a = -K_{r_c}^I \mathcal{S}_{p_o}([I] + K_{r_o}^I)(1 + \lambda_{r_o}^{p_c} \mathcal{S}_c)$$

$$b = [I] \left(K_{r_c}^I \mathcal{S}_o - K_{r_c}^I K_{r_c}^{p_o} - K_{r_c}^I (1 + \lambda_{r_o}^{p_c} \mathcal{S}_c) \right) - [I]^2 K_{r_c}^{p_o} (1 + \lambda_{r_o}^{p_c} \mathcal{S}_c) - K_{r_c}^I K_{r_c}^I$$

$$c = [I] K_{r_c}^{p_o} \mathcal{S}_{r_o} ([I] + K_{r_c}^I)$$

$$\text{where } \mathcal{S}_x = \mathcal{S}_{p_x} \mathcal{S}_{r_x}, \quad K'_{r_c} = K_{r_o}^I K_{r_c}^{p_o}$$

$$[r_o] = \frac{-b + \sqrt{b^2 - 4ac}}{2a} \quad (2.3.8)$$

2.3.2 Jacobian

$$\begin{bmatrix} -\beta_{r_o}(1 + \lambda_{r_o}^{p_c}[p_c]) & 0 & 0 & -\beta_{r_o} \lambda_{r_o}^{p_c}[r_o] \\ 0 & -\beta_{r_c} & \frac{\alpha_{r_c} K_{r_c}^I K_{r_c}^{p_o}}{(K_{r_c}^I K_{r_c}^{p_o} + K_{r_c}^{p_o}[I] + K_{r_c}^I [p_o])^2} & 0 \\ \alpha_{p_o} & 0 & -\beta_{p_o} & 0 \\ 0 & \alpha_{p_c} & 0 & -\beta_{p_c} \end{bmatrix}$$

2.4 rdANDn

$$\frac{d}{dt}[r_o] = \alpha_{r_o} \frac{[I]}{K_{r_o}^I + [I]} - \beta_{r_o}[r_o](1 + \lambda_{r_o}^{p_c}[p_c]) \quad (2.4.1)$$

$$\frac{d}{dt}[r_c] = \alpha_{r_c} \frac{[I]}{K_{r_c}^I + [I]} \times \frac{[p_o]}{K_{r_c}^{p_o} + [p_o]} - \beta_{r_c}[r_c] \quad (2.4.2)$$

$$\frac{d}{dt}[p_o] = \alpha_{p_o}[r_o] - \beta_{p_o}[p_o] \quad (2.4.3)$$

$$\frac{d}{dt}[p_c] = \alpha_{p_c}[r_c] - \beta_{p_c}[p_c] \quad (2.4.4)$$

2.4.1 Steady state

$$[p_o] = \frac{\alpha_{p_o}}{\beta_{p_o}}[r_o] \quad (2.4.5)$$

$$[p_c] = \frac{\alpha_{p_c}}{\beta_{p_c}}[r_c] \quad (2.4.6)$$

$$[r_c] = \mathcal{S}_{r_c} \frac{\mathcal{S}_{p_o}[I][r_o]}{K_{r_c}^I K_{r_c}^{p_o} + K_{r_c}^I \mathcal{S}_{p_o}[r_o] + \mathcal{S}_{p_o}[I][r_o] + K_{r_c}^{p_o}[I]} \quad (2.4.7)$$

$$[r_o] = \mathcal{S}_{r_o} \frac{[I]}{(K_{r_o}^I + [I])(1 + \lambda_{r_o}^{p_c} \mathcal{S}_{p_c}[r_c])}$$

$$a = -\mathcal{S}_{p_o}([I] + K_{r_o}^I)(K_{r_c}^I + [I](1 + \lambda_{r_o}^{p_c} \mathcal{S}_c))$$

$$b = ((\mathcal{S}_o - K_{r_o}^{p_o})[I] - K_{r_o}^I K_{r_c}^{p_o}) ([I] + K_{r_c}^I)$$

$$c = [I] K_{r_c}^{p_o} \mathcal{S}_{r_o} ([I] + K_{r_c}^I)$$

where $\mathcal{S}_x = \mathcal{S}_{p_x} \mathcal{S}_{r_x}$

$$[r_o] = \frac{-b + \sqrt{b^2 - 4ac}}{2a} \quad (2.4.8)$$

2.4.2 Jacobian

$$\begin{bmatrix} -\beta_{r_o}(1 + \lambda_{r_o}^{p_c}[p_c]) & 0 & 0 & -\beta_{r_o}\lambda_{r_o}^{p_c}[r_o] \\ 0 & -\beta_{r_c} & \frac{\alpha_{r_c}[I]K_{r_c}^{p_o}}{(K_{r_c}^I + [I])(K_{r_c}^{p_o} + [p_o])^2} & 0 \\ \alpha_{p_o} & 0 & -\beta_{p_o} & 0 \\ 0 & \alpha_{p_c} & 0 & -\beta_{p_c} \end{bmatrix}$$

2.5 pfORn

$$\frac{d}{dt}[r_o] = \alpha_{r_o} \frac{[I]}{K_{\frac{I}{r_o}} + [I]} - \beta_{r_o}[r_o] \quad (2.5.1)$$

$$\frac{d}{dt}[r_c] = \alpha_{r_o} \frac{\frac{[I]}{K_{\frac{I}{r_o}}} + \frac{[p_o]}{K_{\frac{p_o}{r_c}}}}{1 + \frac{[I]}{K_{\frac{I}{r_o}}} + \frac{[p_o]}{K_{\frac{p_o}{r_c}}}} - \beta_{r_c}[r_c] \quad (2.5.2)$$

$$\frac{d}{dt}[p_o] = \alpha_{p_o}[r_o] \frac{K_{\frac{p_o}{r_c}}}{K_{\frac{p_o}{r_c}} + [p_c]} - \beta_{p_o}[p_o] \quad (2.5.3)$$

$$\frac{d}{dt}[p_c] = \alpha_{p_c}[r_c] - \beta_{p_c}[p_c] \quad (2.5.4)$$

2.5.1 Steady state

$$[p_c] = \frac{\alpha_{p_c}}{\beta_{p_c}}[r_c] \quad (2.5.5)$$

$$\begin{aligned} [r_c] &= \frac{\alpha_{r_c}}{\beta_{r_c}} \frac{\frac{[I]}{K_{\frac{I}{r_c}}} + \frac{[p_o]}{K_{\frac{p_o}{r_c}}}}{1 + \frac{[I]}{K_{\frac{I}{r_c}}} + \frac{[p_o]}{K_{\frac{p_o}{r_c}}}} \\ &= \mathcal{S}_{r_c} \frac{K_{\frac{p_o}{r_c}}[I] + K_{\frac{I}{r_c}}[p_o]}{K_{\frac{p_o}{r_c}}K_{\frac{I}{r_c}} + K_{\frac{p_o}{r_c}}[I] + K_{\frac{I}{r_c}}[p_o]} \end{aligned} \quad (2.5.6)$$

$$[r_o] = \mathcal{S}_{r_o} \frac{[I]}{K_{\frac{I}{r_o}} + [I]} \quad (2.5.7)$$

$$\begin{aligned} [p_o] &= \frac{\alpha_{p_o}}{\beta_{p_o}}[r_o] \frac{K_{\frac{p_o}{r_c}}}{K_{\frac{p_o}{r_c}} + [p_c]} \\ &= \mathcal{S}_o \frac{[I]}{K_{\frac{I}{r_o}} + [I]} \times \frac{K_{\frac{p_o}{r_c}}}{K_{\frac{p_o}{r_c}} + \mathcal{S}_{p_c}[r_c]} \end{aligned}$$

$$a = -K_{\frac{I}{r_c}}([I] + K_{\frac{I}{r_o}})(K_{\frac{p_o}{r_c}} + \mathcal{S}_c)$$

$$b = [I](K'_{\frac{I}{p_o}}\mathcal{S}_o - K'_{\frac{I}{p_o}}K_{\frac{p_o}{r_c}} - K'_{\frac{I}{r_c}}K_{\frac{p_o}{p_o}} - K'_{\frac{I}{r_c}}\mathcal{S}_c) - [I]^2(K_{\frac{p_o}{r_c}}K_{\frac{p_o}{r_c}} + K_{\frac{p_o}{r_c}}\mathcal{S}_c) - K'_{\frac{I}{p_o}}K'_{\frac{I}{r_c}}$$

$$c = [I]K_{\frac{p_o}{r_c}}K_{\frac{p_o}{r_c}}\mathcal{S}_o([I] + K_{\frac{I}{r_c}})$$

$$\text{where } \mathcal{S}_x = \mathcal{S}_{p_x}\mathcal{S}_{r_x}, \quad K'_{\frac{I}{r_c}} = K_{\frac{I}{r_o}}K_{\frac{p_o}{r_c}}, \quad K'_{\frac{I}{p_o}} = K_{\frac{I}{r_c}}K_{\frac{p_o}{p_o}}$$

$$[p_o] = \frac{-b + \sqrt{b^2 - 4ac}}{2a} \quad (2.5.8)$$

2.5.2 Jacobian

$$\begin{bmatrix} -\beta_{r_o} & 0 & 0 & 0 \\ 0 & -\beta_{r_c} & \frac{\alpha_{r_c} K_{\frac{I}{r_c}}^2 K_{\frac{p_o}{r_c}}}{(K_{\frac{I}{r_c}} K_{\frac{p_o}{r_c}} + K_{\frac{p_o}{r_c}} [I] + K_{\frac{I}{r_c}} [p_o])^2} & 0 \\ \alpha_{p_o} \frac{K_{\frac{p_c}{p_o}}}{K_{\frac{p_c}{p_o}} + [p_c]} & 0 & -\beta_{p_o} & -\alpha_{p_o} [r_o] \frac{K_{\frac{p_c}{p_o}}}{(K_{\frac{p_c}{p_o}} + [p_c])^2} \\ 0 & \alpha_{p_c} & 0 & -\beta_{p_c} \end{bmatrix}$$

2.6 pfANDn

$$\frac{d}{dt}[r_o] = \alpha_{r_o} \frac{[I]}{K_{r_o} + [I]} - \beta_{r_o}[r_o] \quad (2.6.1)$$

$$\frac{d}{dt}[r_c] = \alpha_{r_c} \frac{[I]}{K_{r_c} + [I]} \times \frac{[p_o]}{K_{r_c}^{p_o} + [p_o]} - \beta_{r_c}[r_c] \quad (2.6.2)$$

$$\frac{d}{dt}[p_o] = \alpha_{p_o}[r_o] \frac{K_{p_o}}{K_{p_o}^{p_o} + [p_c]} - \beta_{p_o}[p_o] \quad (2.6.3)$$

$$\frac{d}{dt}[p_c] = \alpha_{p_c}[r_c] - \beta_{p_c}[p_c] \quad (2.6.4)$$

2.6.1 Steady state

$$[p_c] = \frac{\alpha_{p_c}}{\beta_{p_c}}[r_c] \quad (2.6.5)$$

$$[r_c] = \mathcal{S}_{r_c} \frac{[I][p_o]}{K_{r_c} K_{r_c}^{p_o} + K_{r_c} [p_o] + [I][p_o] + K_{r_c}^{p_o} [I]} \quad (2.6.6)$$

$$[p_o] = \frac{\alpha_{p_o}}{\beta_{p_o}}[r_o] \frac{K_{p_o}}{K_{p_o}^{p_o} + [p_c]}$$

$$[r_o] = \mathcal{S}_{r_o} \frac{[I]}{K_{r_o} + [I]} \quad (2.6.7)$$

$$= \mathcal{S}_o \frac{[I]}{K_{r_o} + [I]} \times \frac{K_{p_o}}{K_{p_o}^{p_o} + \mathcal{S}_{p_c}[r_c]}$$

$$a = -([I] + K_{r_o}) \left(K'_{p_o} + [I](K_{p_o}^{p_o} + \mathcal{S}_c) \right)$$

$$b = [I](K'_{p_o} \mathcal{S}_o - K_{r_o} K'_{p_o} - K_{p_o} K'_{r_o}) + [I]^2(K_{p_o}^{p_o} \mathcal{S}_o - K_{r_o} K_{p_o}^{p_o}) - K'_{p_o} K'_{r_o}$$

$$c = [I] K_{p_o}^{p_o} K_{r_o} \mathcal{S}_o ([I] + K_{r_o})$$

where $\mathcal{S}_x = \mathcal{S}_{p_x} \mathcal{S}_{r_x}$, $K'_{r_c} = K_{r_o} K_{r_c}^{p_o}$, $K'_{p_o} = K_{r_c} K_{p_o}^{p_o}$

$$[p_o] = \frac{-b + \sqrt{b^2 - 4ac}}{2a} \quad (2.6.8)$$

2.6.2 Jacobian

$$\begin{bmatrix} -\beta_{r_o} & 0 & 0 & 0 \\ 0 & -\beta_{r_c} & \frac{\alpha_{r_c} [I] K_{r_c}^{p_o}}{(K_{r_c} + [I])(K_{r_c}^{p_o} + [p_o])^2} & 0 \\ \alpha_{p_o} \frac{K_{p_o}}{K_{p_o}^{p_o} + [p_c]} & 0 & -\beta_{p_o} & -\alpha_{p_o} [r_o] \frac{K_{p_o}}{(K_{p_o}^{p_o} + [p_c])^2} \\ 0 & \alpha_{p_c} & 0 & -\beta_{p_c} \end{bmatrix}$$

2.7 pdORn

$$\frac{d}{dt}[r_o] = \alpha_{r_o} \frac{[I]}{K_{r_o} + [I]} - \beta_{r_o}[r_o] \quad (2.7.1)$$

$$\frac{d}{dt}[r_c] = \alpha_{r_o} \frac{\frac{[I]}{K_{r_o}} + \frac{[p_o]}{K_{r_c}^{p_o}}}{1 + \frac{[I]}{K_{r_o}} + \frac{[p_o]}{K_{r_c}^{p_o}}} - \beta_{r_c}[r_c] \quad (2.7.2)$$

$$\frac{d}{dt}[p_o] = \alpha_{p_o}[r_o] - \beta_{p_o}[p_o](1 + \lambda_{p_o}^{p_c}[p_c]) \quad (2.7.3)$$

$$\frac{d}{dt}[p_c] = \alpha_{p_c}[r_c] - \beta_{p_c}[p_c] \quad (2.7.4)$$

2.7.1 Steady state

$$[p_c] = \frac{\alpha_{p_c}}{\beta_{p_c}}[r_c] \quad (2.7.5)$$

$$[r_o] = \mathcal{S}_{r_o} \frac{[I]}{K_{r_o} + [I]} \quad (2.7.6)$$

$$\begin{aligned} [r_c] &= \mathcal{S}_{r_c} \frac{\frac{[I]}{K_{r_c}} + \frac{[p_o]}{K_{r_c}^{p_o}}}{1 + \frac{[I]}{K_{r_c}} + \frac{[p_o]}{K_{r_c}^{p_o}}} \\ &= \mathcal{S}_{r_c} \frac{K_{r_c}^{p_o}[I] + K_{r_c}[p_o]}{K_{r_c}^{p_o}K_{r_c} + K_{r_c}^{p_o}[I] + K_{r_c}[p_o]} \end{aligned} \quad (2.7.7)$$

$$[r_o] = \mathcal{S}_{r_o} \frac{[I]}{K_{r_o} + [I]} \quad (2.7.8)$$

$$[p_o] = \frac{\mathcal{S}_{r_o}\mathcal{S}_{p_o}}{(1 + \lambda_{p_o}^{p_c}\mathcal{S}_{p_c}[r_c])} \times \frac{[I]}{K_{r_o} + [I]}$$

$$a = -K_{r_c}([I] + K_{r_o})(1 + \lambda_{r_o}^{p_c}\mathcal{S}_c)$$

$$b = [I] \left(K_{r_c} \mathcal{S}_o - K_{r_c} K_{r_c}^{p_o} - K_{r_c}' (1 + \lambda_{p_o}^{p_c} \mathcal{S}_c) \right) - [I]^2 K_{r_c}^{p_o} (1 + \lambda_{p_o}^{p_c} \mathcal{S}_c) - K_{r_c} K_{r_c}'$$

$$c = [I] K_{r_c}^{p_o} \mathcal{S}_o ([I] + K_{r_c})$$

where $\mathcal{S}_x = \mathcal{S}_{p_x} \mathcal{S}_{r_x}$, $K_{r_c}' = K_{r_o} K_{r_c}^{p_o}$

$$[p_o] = \frac{-b + \sqrt{b^2 - 4ac}}{2a} \quad (2.7.9)$$

2.7.2 Jacobian

$$\begin{bmatrix} -\beta_{r_o} & 0 & 0 & 0 \\ 0 & -\beta_{r_c} & \frac{\alpha_{r_c} K_{r_c}^2 K_{r_c}^{p_o}}{(K_{r_c} K_{r_c}^{p_o} + K_{r_c}^{p_o}[I] + K_{r_c}[p_o])^2} & 0 \\ \alpha_{p_o} & 0 & -\beta_{p_o}(1 + \lambda_{p_o}^{p_c}[p_c]) & -\beta_{p_o} \lambda_{p_o}^{p_c}[p_o] \\ 0 & \alpha_{p_c} & 0 & -\beta_{p_c} \end{bmatrix}$$

2.8 pdANDn

$$\frac{d}{dt}[r_o] = \alpha_{r_o} \frac{[I]}{K_{r_o} + [I]} - \beta_{r_o}[r_o] \quad (2.8.1)$$

$$\frac{d}{dt}[r_c] = \alpha_{r_c} \frac{[I]}{K_{r_c} + [I]} \times \frac{[p_o]}{K_{r_c}^{p_o} + [p_o]} - \beta_{r_c}[r_c] \quad (2.8.2)$$

$$\frac{d}{dt}[p_o] = \alpha_{p_o}[r_o] - \beta_{p_o}[p_o](1 + \lambda_{p_o}^{p_c}[p_c]) \quad (2.8.3)$$

$$\frac{d}{dt}[p_c] = \alpha_{p_c}[r_c] - \beta_{p_c}[p_c] \quad (2.8.4)$$

2.8.1 Steady state

$$[r_o] = \mathcal{S}_{r_o} \frac{[I]}{K_{r_o} + [I]} \quad (2.8.5)$$

$$[p_c] = \frac{\alpha_{p_c}}{\beta_{p_c}} [r_c] \quad (2.8.6)$$

$$[r_c] = \mathcal{S}_{r_c} \frac{[I][p_o]}{K_{r_c} K_{r_c}^{p_o} + K_{r_c} [p_o] + [I][p_o] + K_{r_c}^{p_o} [I]} \quad (2.8.7)$$

$$[p_o] = \frac{\mathcal{S}_{r_o} \mathcal{S}_{p_o}}{(1 + \lambda_{p_o}^{p_c} \mathcal{S}_{r_c} [r_c])} \times \frac{[I]}{K_{r_o} + [I]}$$

$$a = -[I](K_{r_c} + K_{r_o}(1 + \lambda_{r_o}^{p_c} \mathcal{S}_c)) - [I]^2(1 + \lambda_{r_o}^{p_c} \mathcal{S}_c) - K_{r_c} K_{r_o}$$

$$b = \left((\mathcal{S}_o - K_{r_c}^{p_o})[I] - K_{r_o} K_{r_c}^{p_o} \right) \left([I] + K_{r_c} \right)$$

$$c = [I] K_{r_c}^{p_o} \mathcal{S}_o ([I] + K_{r_c})$$

where $\mathcal{S}_x = \mathcal{S}_{p_x} \mathcal{S}_{r_x}$

$$[p_o] = \frac{-b + \sqrt{b^2 - 4ac}}{2a} \quad (2.8.8)$$

2.8.2 Jacobian

$$\begin{bmatrix} -\beta_{r_o} & 0 & 0 & 0 \\ 0 & -\beta_{r_c} & \frac{\alpha_{r_c} [I] K_{r_c}^{p_o}}{(K_{r_c} + [I])(K_{r_c}^{p_o} + [p_o])^2} & 0 \\ \alpha_{p_o} & 0 & -\beta_{p_o}(1 + \lambda_{p_o}^{p_c}[p_c]) & -\beta_{p_o} \lambda_{p_o}^{p_c}[p_o] \\ 0 & \alpha_{p_c} & 0 & -\beta_{p_c} \end{bmatrix}$$

2.9 rfANDp

$$\frac{d}{dt}[r_o] = \alpha_{r_o} \frac{[I]}{K_{r_o} + [I]} \times \frac{K_{r_o}}{K_{r_o}^{p_o} + [p_c]} - \beta_{r_o}[r_o] \quad (2.9.1)$$

$$\frac{d}{dt}[r_c] = \alpha_{r_c} \frac{[I]}{K_{r_c} + [I]} \times \frac{K_{r_c}}{K_{r_c}^{p_o} + [p_o]} - \beta_{r_c}[r_c] \quad (2.9.2)$$

$$\frac{d}{dt}[p_o] = \alpha_{p_o}[r_o] - \beta_{p_o}[p_o] \quad (2.9.3)$$

$$\frac{d}{dt}[p_c] = \alpha_{p_c}[r_c] - \beta_{p_c}[p_c] \quad (2.9.4)$$

2.9.1 Steady state

$$[p_o] = \frac{\alpha_{p_o}}{\beta_{p_o}}[r_o] \quad (2.9.5)$$

$$[p_c] = \frac{\alpha_{p_c}}{\beta_{p_c}}[r_c] \quad (2.9.6)$$

$$[r_c] = \mathcal{S}_{r_c} \frac{[I] K_{r_c}^{p_o}}{K_{r_c}^I K_{r_c}^{p_o} + K_{r_c}^I \mathcal{S}_{p_o}[r_o] + \mathcal{S}_{p_o}[I][r_o] + K_{r_c}^{p_o}[I]}$$

$$[r_o] = \mathcal{S}_{r_o} \frac{[I]}{K_{r_o}^I + [I]} \times \frac{K_{r_o}^{p_c}}{K_{r_o}^{p_c} + \mathcal{S}_{p_c}[r_c]}$$

$$a = -\mathcal{S}_{p_o} K_{r_o}^{p_c} ([I] + K_{r_c}^I) ([I] + K_{r_o}^I)$$

$$b = -[I]^2 (K_{r_o}^{p_c} K_{r_c}^{p_o} - \mathcal{S}_o K_{r_o}^{p_c} + \mathcal{S}_c K_{r_c}^{p_o}) - [I] \left(K_{r_c}^I (K_{r_o}^{p_c} + \mathcal{S}_c) + K_{r_o}^I (K_{r_c}^{p_o} - \mathcal{S}_o) \right) - K_{r_o}^I K_{r_c}^I$$

$$c = [I] K_{r_o}^{p_c} K_{r_c}^{p_o} \mathcal{S}_{r_o} ([I] + K_{r_c}^I)$$

where $\mathcal{S}_x = \mathcal{S}_{p_x} \mathcal{S}_{r_x}$, $K'_{r_c} = K_{r_o} K_{r_c}^{p_o}$, $K'_{r_o} = K_{r_c} K_{r_o}^{p_c}$

$$[r_o] = \frac{-b + \sqrt{b^2 - 4ac}}{2a} \quad (2.9.7)$$

2.9.2 Jacobian

$$\begin{bmatrix} -\beta_{r_o} & 0 & 0 & -\frac{\alpha_{r_o}[I] K_{r_o}^{p_c}}{(K_{r_o}^I + [I])(K_{r_o}^{p_c} + [p_c])^2} \\ 0 & -\beta_{r_c} & \frac{-\alpha_{r_c}[I] K_{r_c}^{p_o}}{(K_{r_c}^I + [I])(K_{r_c}^{p_o} + [p_o])^2} & 0 \\ \alpha_{p_o} & 0 & -\beta_{p_o} & 0 \\ 0 & \alpha_{p_c} & 0 & -\beta_{p_c} \end{bmatrix}$$

2.10 rdANDp

$$\frac{d}{dt}[r_o] = \alpha_{r_o} \frac{[I]}{K_{r_o} + [I]} - \beta_{r_o}[r_o](1 + \lambda_{r_o}^{p_c}[p_c]) \quad (2.10.1)$$

$$\frac{d}{dt}[r_c] = \alpha_{r_c} \frac{[I]}{K_{r_c} + [I]} \times \frac{K_{r_c}^{p_o}}{K_{r_c}^{p_o} + [p_o]} - \beta_{r_c}[r_c] \quad (2.10.2)$$

$$\frac{d}{dt}[p_o] = \alpha_{p_o}[r_o] - \beta_{p_o}[p_o] \quad (2.10.3)$$

$$\frac{d}{dt}[p_c] = \alpha_{p_c}[r_c] - \beta_{p_c}[p_c] \quad (2.10.4)$$

2.10.1 Steady state

$$[p_o] = \frac{\alpha_{p_o}}{\beta_{p_o}}[r_o] \quad (2.10.5)$$

$$[p_c] = \frac{\alpha_{p_c}}{\beta_{p_c}}[r_c] \quad (2.10.6)$$

$$[r_c] = \mathcal{S}_{r_c} \frac{[I] K_{r_c}^{p_o}}{K_{r_c} I K_{r_c}^{p_o} + K_{r_c} \mathcal{S}_{p_o}[r_o] + \mathcal{S}_{p_o}[I][r_o] + K_{r_c}^{p_o} [I]} \quad (2.10.7)$$

$$[r_o] = \mathcal{S}_{r_o} \frac{[I]}{(K_{r_o} + [I])(1 + \lambda_{r_o}^{p_c} \mathcal{S}_{p_c}[r_c])}$$

$$a = -\mathcal{S}_{p_o}([I] + K_{r_c})([I] + K_{r_o})$$

$$b = -[I]^2 \left(K_{r_c}^{p_o} (1 + \lambda_{r_o}^{p_c} \mathcal{S}_c) - \mathcal{S}_o \right) - [I] \left(K_{r_c} (K_{r_c}^{p_o} - \mathcal{S}_o) + K_{r_c}' (1 + \lambda_{r_o}^{p_c} \mathcal{S}_c) \right) - K_{r_c}' K_{r_o}$$

$$c = [I] K_{r_c}^{p_o} \mathcal{S}_{r_o} ([I] + K_{r_o})$$

where $\mathcal{S}_x = \mathcal{S}_{p_x} \mathcal{S}_{r_x}$

$$[r_o] = \frac{-b + \sqrt{b^2 - 4ac}}{2a} \quad (2.10.8)$$

2.10.2 Jacobian

$$\begin{bmatrix} -\beta_{r_o}(1 + \lambda_{r_o}^{p_c}[p_c]) & 0 & 0 & -\beta_{r_o} \lambda_{r_o}^{p_c}[r_o] \\ 0 & -\beta_{r_c} & \frac{-\alpha_{r_c} [I] K_{r_c}^{p_o}}{(K_{r_c} + [I])(K_{r_c}^{p_o} + [p_o])^2} & 0 \\ \alpha_{p_o} & 0 & -\beta_{p_o} & 0 \\ 0 & \alpha_{p_c} & 0 & -\beta_{p_c} \end{bmatrix}$$

2.11 pfANDp

$$\frac{d}{dt}[r_o] = \alpha_{r_o} \frac{[I]}{K_{r_o} + [I]} - \beta_{r_o}[r_o] \quad (2.11.1)$$

$$\frac{d}{dt}[r_c] = \alpha_{r_c} \frac{[I]}{K_{r_c} + [I]} \times \frac{[p_o]}{K_{r_c}^{p_o} + [p_o]} - \beta_{r_c}[r_c] \quad (2.11.2)$$

$$\frac{d}{dt}[p_o] = \alpha_{p_o}[r_o] \frac{K_{p_o}}{K_{p_o}^{p_o} + [p_c]} - \beta_{p_o}[p_o] \quad (2.11.3)$$

$$\frac{d}{dt}[p_c] = \alpha_{p_c}[r_c] - \beta_{p_c}[p_c] \quad (2.11.4)$$

2.11.1 Steady state

$$[p_c] = \frac{\alpha_{p_c}}{\beta_{p_c}}[r_c] \quad (2.11.5)$$

$$[r_c] = \mathcal{S}_{r_c} \frac{[I][p_o]}{K_{r_c} K_{r_c}^{p_o} + K_{r_c} [p_o] + [I][p_o] + K_{r_c}^{p_o} [I]} \quad (2.11.6)$$

$$[p_o] = \frac{\alpha_{p_o}}{\beta_{p_o}}[r_o] \frac{K_{p_o}}{K_{p_o}^{p_o} + [p_c]} \quad (2.11.7)$$

$$[r_o] = \mathcal{S}_{r_o} \frac{[I]}{K_{r_o} + [I]} \times \frac{K_{p_o}}{K_{p_o}^{p_o} + \mathcal{S}_{p_c}[r_c]}$$

$$a = -K_{p_o}^{p_c}([I] + K_{r_c})([I] + K_{r_o})$$

$$b = -[I]^2 \left(K_{p_o}^{p_c} (K_{r_o} - \mathcal{S}_o) + K_{r_o}^{p_o} \mathcal{S}_c \right) - [I] \left(K_{p_o}^{p_c} (K_{r_o} - \mathcal{S}_o) + K_{r_o}^{p_o} (K_{p_o}^{p_c} + \mathcal{S}_c) \right) - K_{p_o}^{p_c} K_{r_o}^{p_o}$$

$$c = [I] K_{p_o}^{p_c} K_{r_o}^{p_o} \mathcal{S}_o ([I] + K_{r_o})$$

where $\mathcal{S}_x = \mathcal{S}_{p_x} \mathcal{S}_{r_x}$, $K'_{r_c} = K_{r_o} K_{r_c}^{p_o}$, $K'_{p_o} = K_{r_o} K_{p_o}^{p_c}$

$$[p_o] = \frac{-b + \sqrt{b^2 - 4ac}}{2a} \quad (2.11.8)$$

2.11.2 Jacobian

$$\begin{bmatrix} -\beta_{r_o} & 0 & 0 & 0 \\ 0 & -\beta_{r_c} & \frac{-\alpha_{r_c}[I]K_{r_c}^{p_o}}{(K_{r_c} + [I])(K_{r_c}^{p_o} + [p_o])^2} & 0 \\ \alpha_{p_o} \frac{K_{p_o}^{p_c}}{K_{p_o}^{p_c} + [p_c]} & 0 & -\beta_{p_o} & -\alpha_{p_o}[r_o] \frac{K_{p_o}^{p_c}}{(K_{p_o}^{p_c} + [p_c])^2} \\ 0 & \alpha_{p_c} & 0 & -\beta_{p_c} \end{bmatrix}$$

2.12 pdANDp

$$\frac{d}{dt}[r_o] = \alpha_{r_o} \frac{[I]}{K_{r_o}^I + [I]} - \beta_{r_o}[r_o] \quad (2.12.1)$$

$$\frac{d}{dt}[r_c] = \alpha_{r_c} \frac{[I]}{K_{r_c}^I + [I]} \times \frac{[p_o]}{K_{r_c}^{p_o} + [p_o]} - \beta_{r_c}[r_c] \quad (2.12.2)$$

$$\frac{d}{dt}[p_o] = \alpha_{p_o}[r_o] - \beta_{p_o}[p_o](1 + \lambda_{p_o}^{p_c}[p_c]) \quad (2.12.3)$$

$$\frac{d}{dt}[p_c] = \alpha_{p_c}[r_c] - \beta_{p_c}[p_c] \quad (2.12.4)$$

2.12.1 Steady state

$$[r_o] = \mathcal{S}_{r_o} \frac{[I]}{K_{r_o}^I + [I]} \quad (2.12.5)$$

$$[p_c] = \frac{\alpha_{p_c}}{\beta_{p_c}}[r_c] \quad (2.12.6)$$

$$[r_c] = \mathcal{S}_{r_c} \frac{[I][p_o]}{K_{r_c}^I K_{r_c}^{p_o} + K_{r_c}^I [p_o] + [I][p_o] + K_{r_c}^{p_o}[I]} \quad (2.12.7)$$

$$[p_o] = \frac{\mathcal{S}_{r_o} \mathcal{S}_{p_o}}{(1 + \lambda_{p_o}^{p_c} \mathcal{S}_{r_c}[r_c])} \times \frac{[I]}{K_{r_o}^I + [I]}$$

$$a = -([I] + K_{r_c}^I)([I] + K_{r_o}^I)$$

$$b = -[I]^2 \left(K_{r_c}^{p_o} (1 + \lambda_{p_o}^{p_c} \mathcal{S}_c) - \mathcal{S}_o \right) - [I] \left(K_{r_c}^I (1 + \lambda_{p_o}^{p_c} \mathcal{S}_c) + K_{r_c}^I (K_{r_c}^{p_o} - \mathcal{S}_o) \right) - K_{r_c}^I K_{r_c}^I$$

$$c = [I] K_{r_c}^{p_o} \mathcal{S}_o ([I] + K_{r_c}^I)$$

where $\mathcal{S}_x = \mathcal{S}_{p_x} \mathcal{S}_{r_x}$

$$[p_o] = \frac{-b + \sqrt{b^2 - 4ac}}{2a} \quad (2.12.8)$$

2.12.2 Jacobian

$$\begin{bmatrix} -\beta_{r_o} & 0 & 0 & 0 \\ 0 & -\beta_{r_c} & \frac{-\alpha_{r_c}[I]K_{r_c}^{p_o}}{(K_{r_c}^I + [I])(K_{r_c}^{p_o} + [p_o])^2} & 0 \\ \alpha_{p_o} & 0 & -\beta_{p_o}(1 + \lambda_{p_o}^{p_c}[p_c]) & -\beta_{p_o}\lambda_{p_o}^{p_c}[p_o] \\ 0 & \alpha_{p_c} & 0 & -\beta_{p_c} \end{bmatrix}$$

3 Figures

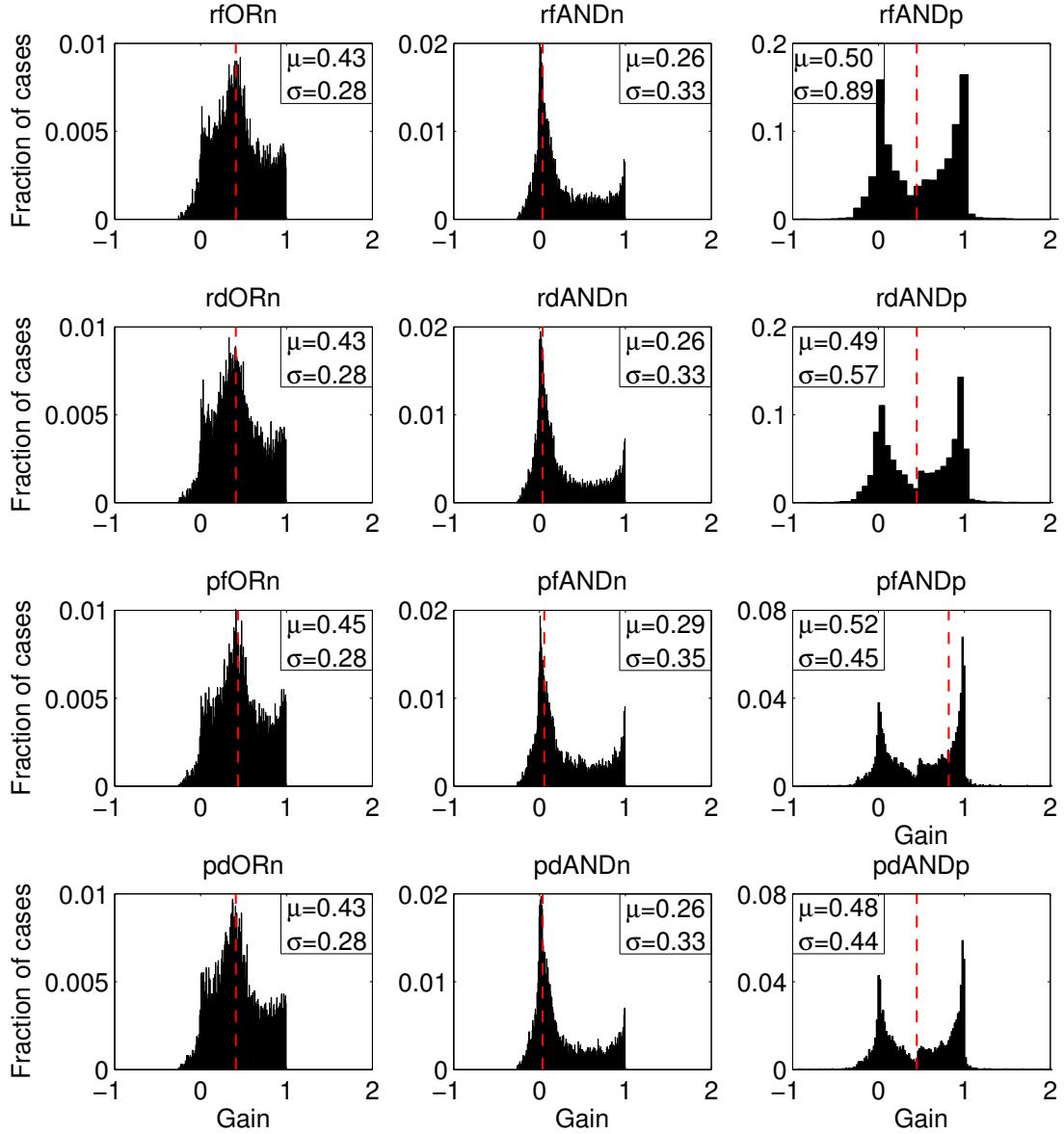


Fig. S1: Steady state gain distributions for the different composite motifs with a broad range of parameter variation (1/20 to 20 times the basal value). μ and σ indicate the mean and standard deviation of the corresponding distributions. The dashed vertical red line denotes the value of gain for the basal parameter set.

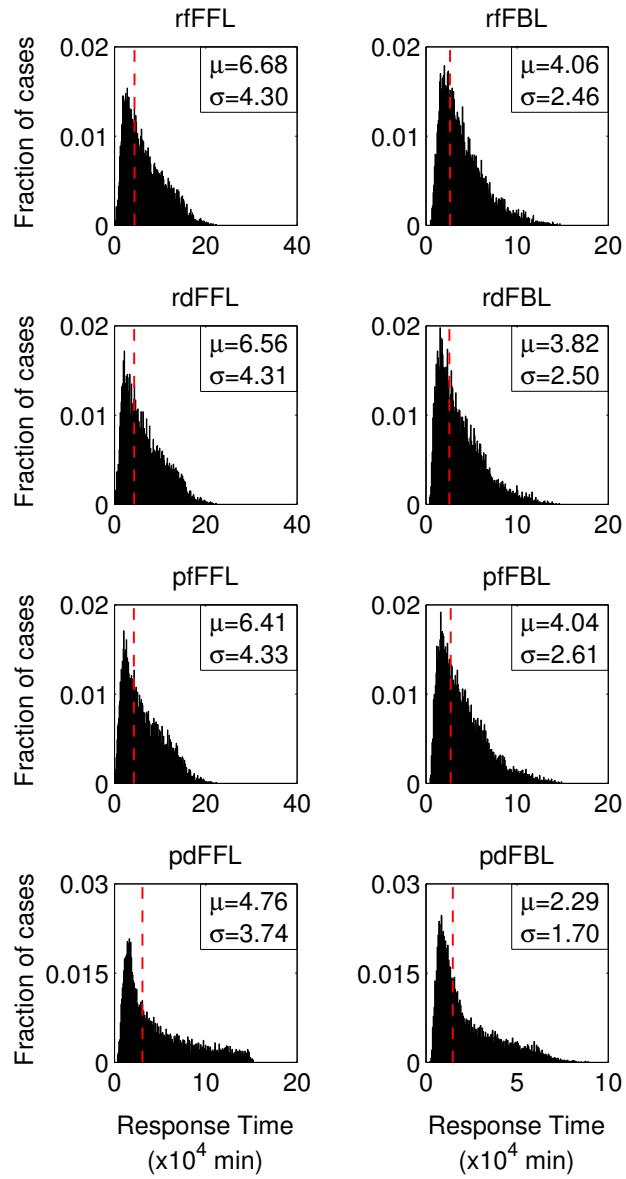


Fig. S2: Response time distributions for uncoupled feedforward and feedback motifs. μ and σ indicate the mean and standard deviation of the corresponding distributions. The dashed vertical red line denotes the value of gain for the basal parameter set.

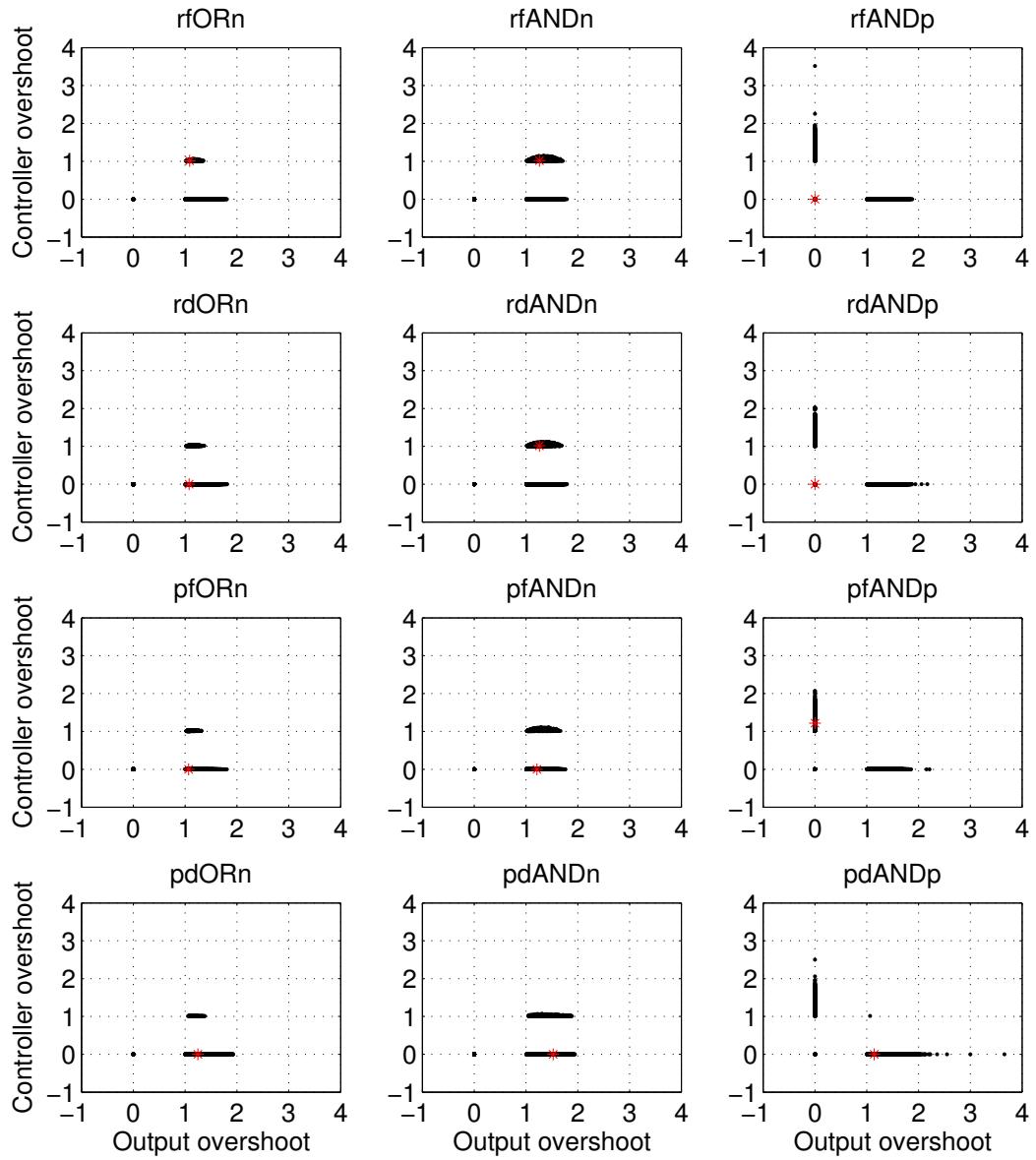


Fig. S3: Correlation between the overshoot of the output-protein and the controller-protein, for different composite motifs. The red asterisk denotes the value corresponding to the basal parameter set.

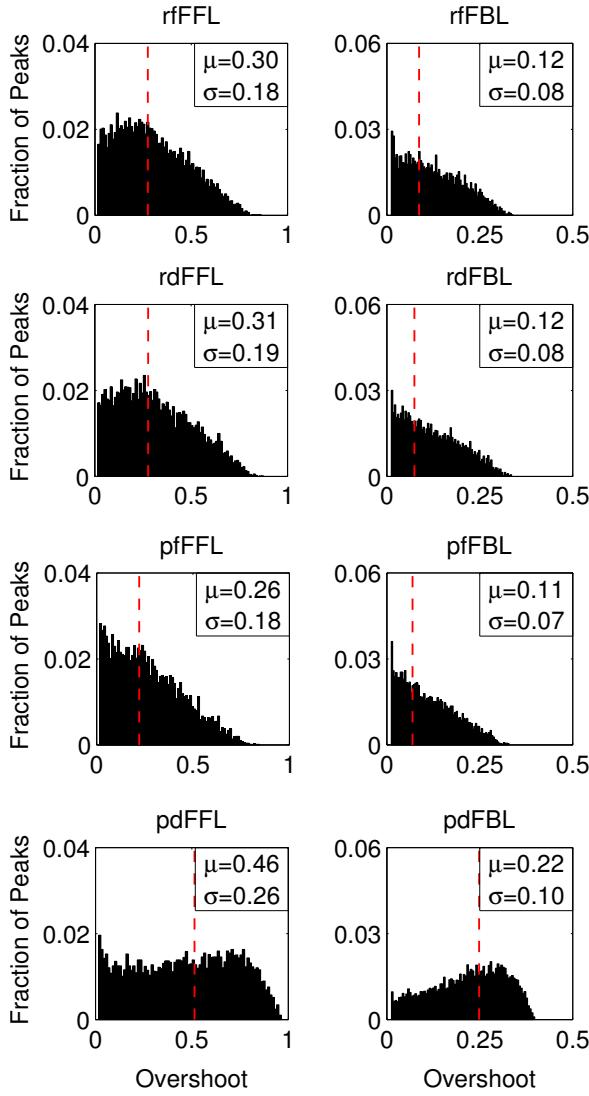


Fig. S4: Overshoot distributions for uncoupled feedforward and feedback motifs. μ and σ indicate the mean and standard deviation of the corresponding distributions. The dashed vertical red line denotes the value of overshoot for the basal parameter set.

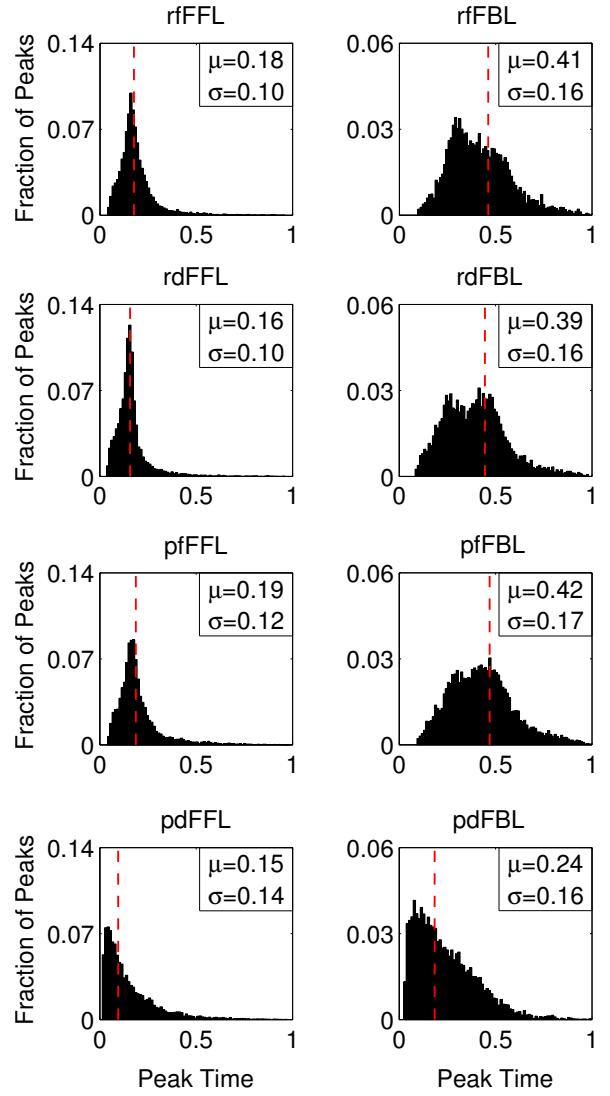


Fig. S5: Peak time distributions for uncoupled feedforward and feedback motifs. μ and σ indicate the mean and standard deviation of the corresponding distributions. The dashed vertical red line denotes the value of peak time for the basal parameter set.

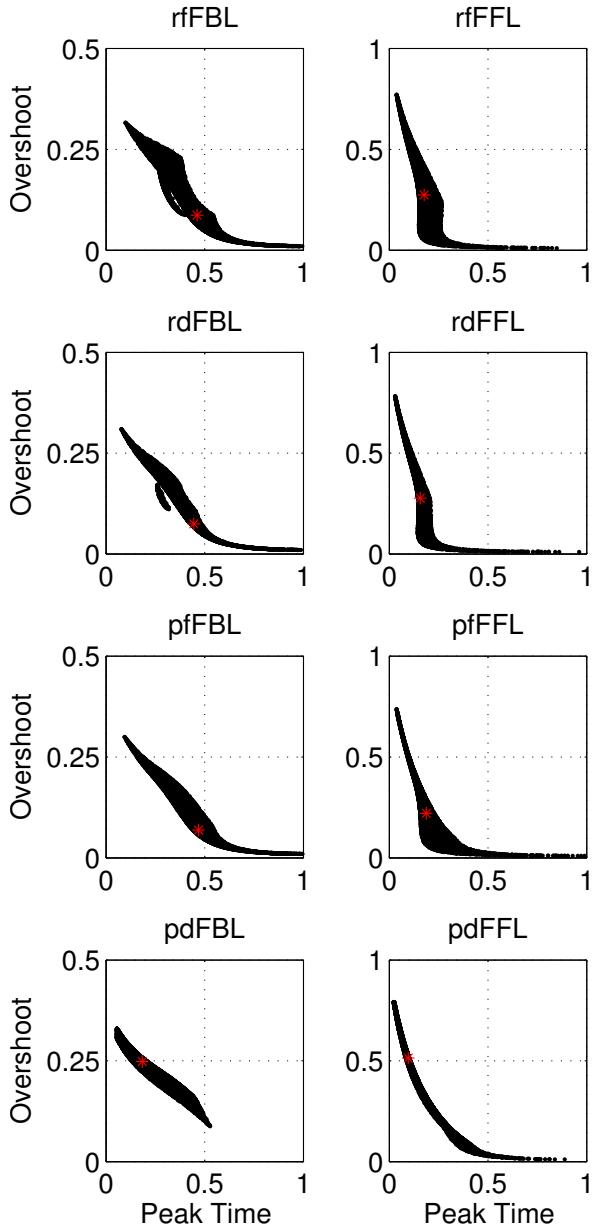


Fig. S6: Scatter plots between peak time and overshoot for the uncoupled feedforward and feedback motifs, when just the protein degradation rate constants are varied. Asterisks denote the values corresponding to the basal parameter set, when it shows peak.

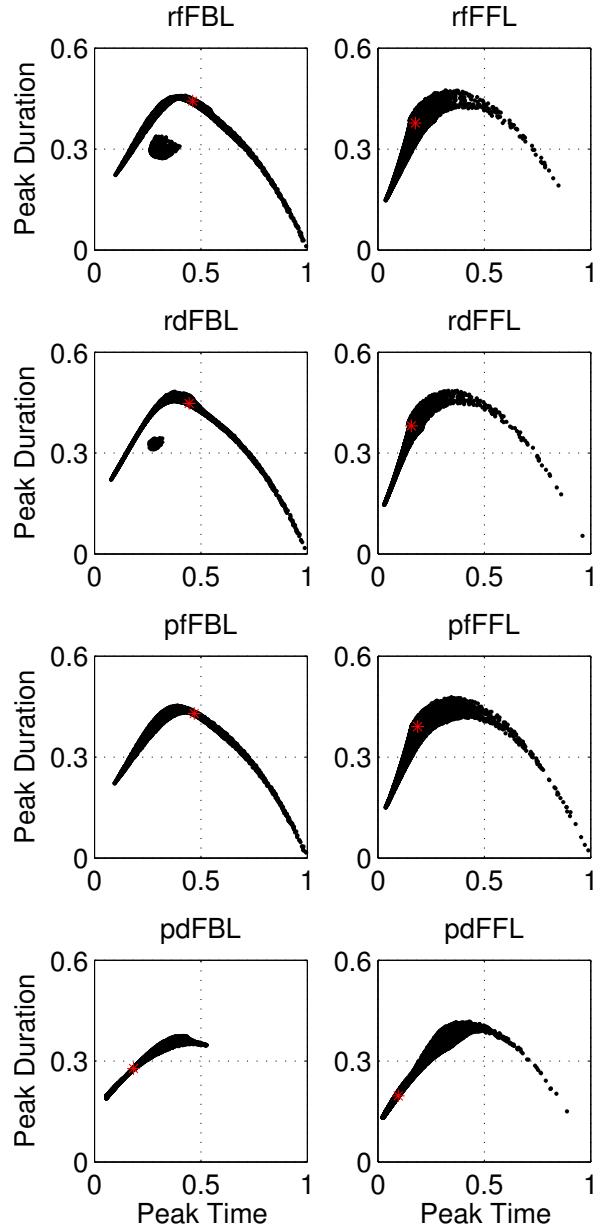


Fig. S7: Scatter plots between peak time and peak duration for the uncoupled feedforward and feedback motifs, when just the protein degradation rate constants are varied. Asterisks denote the values corresponding to the basal parameter set, when it shows peak.

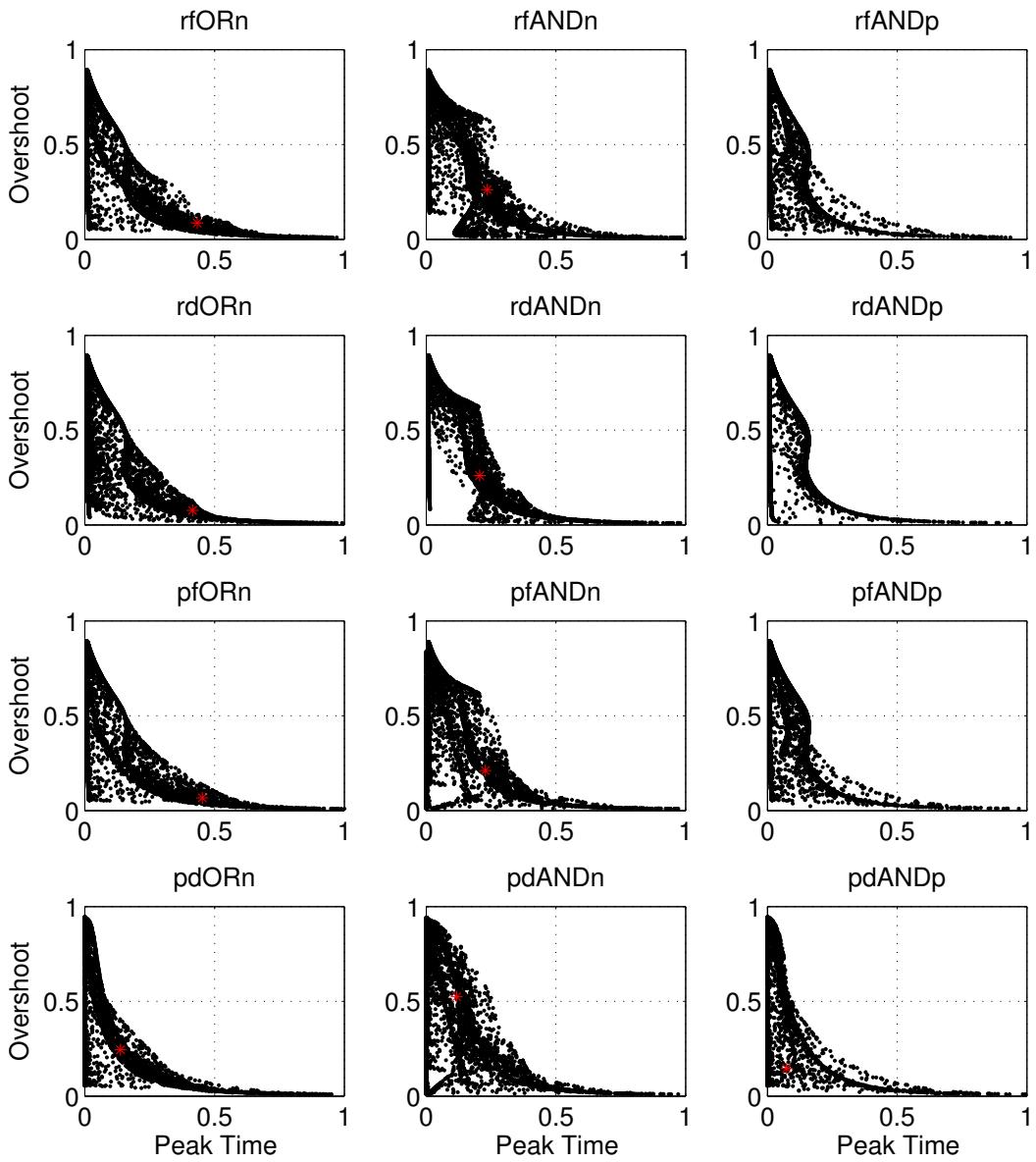


Fig. S8: Scatter plots between peak time and overshoot for the composite motifs, when just the RNA degradation rate constants are varied. Asterisks denote the values corresponding to the basal parameter set, when it shows peak.

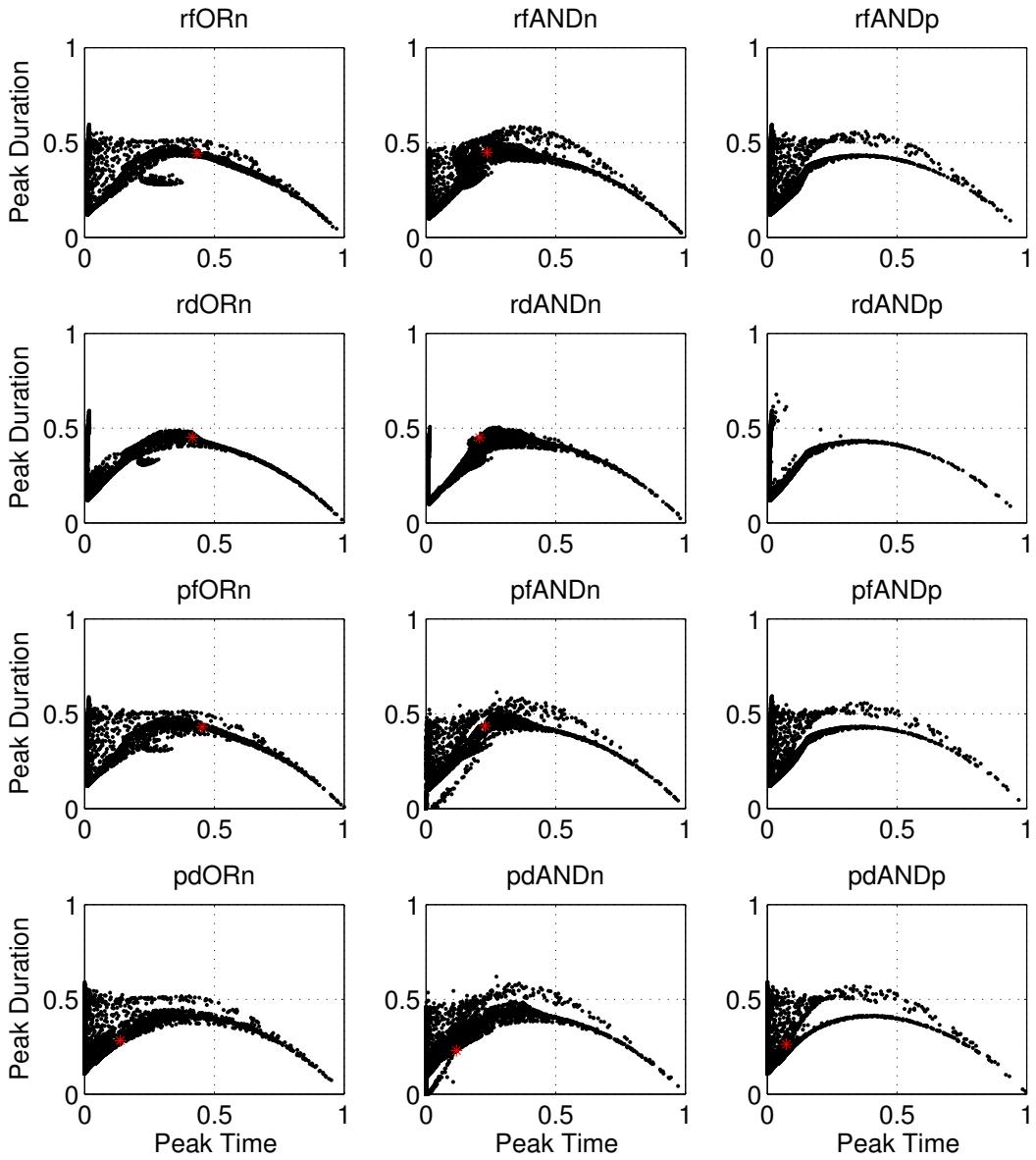


Fig. S9: Scatter plots between peak time and peak duration for the composite motifs, when just the RNA degradation rate constants are varied. Asterisks denote the values corresponding to the basal parameter set, when it shows peak.

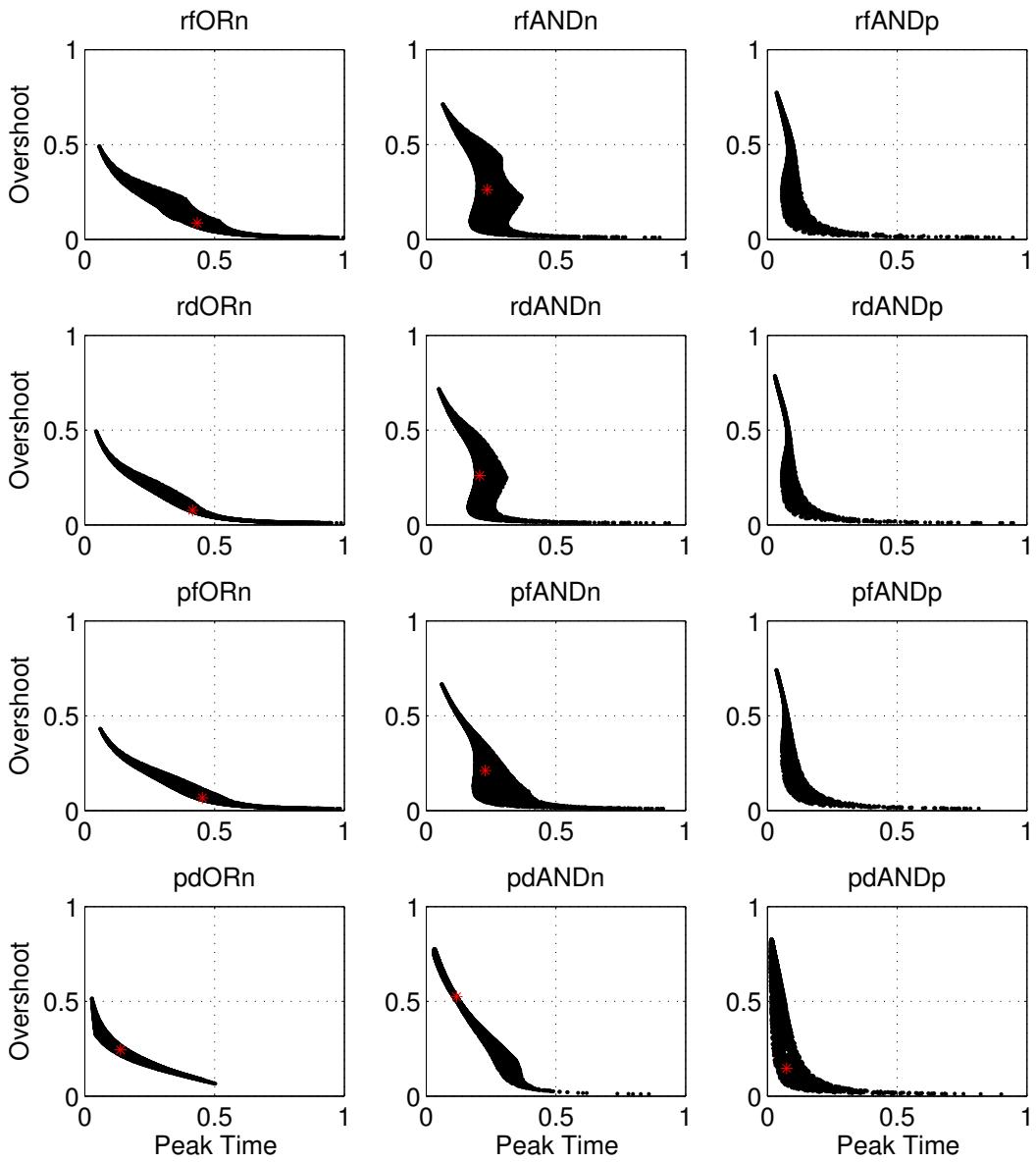


Fig. S10: Scatter plots between peak time and overshoot for composite motifs, when just the protein degradation rate constants are varied. Asterisks denote the values corresponding to the basal parameter set, when it shows peak.

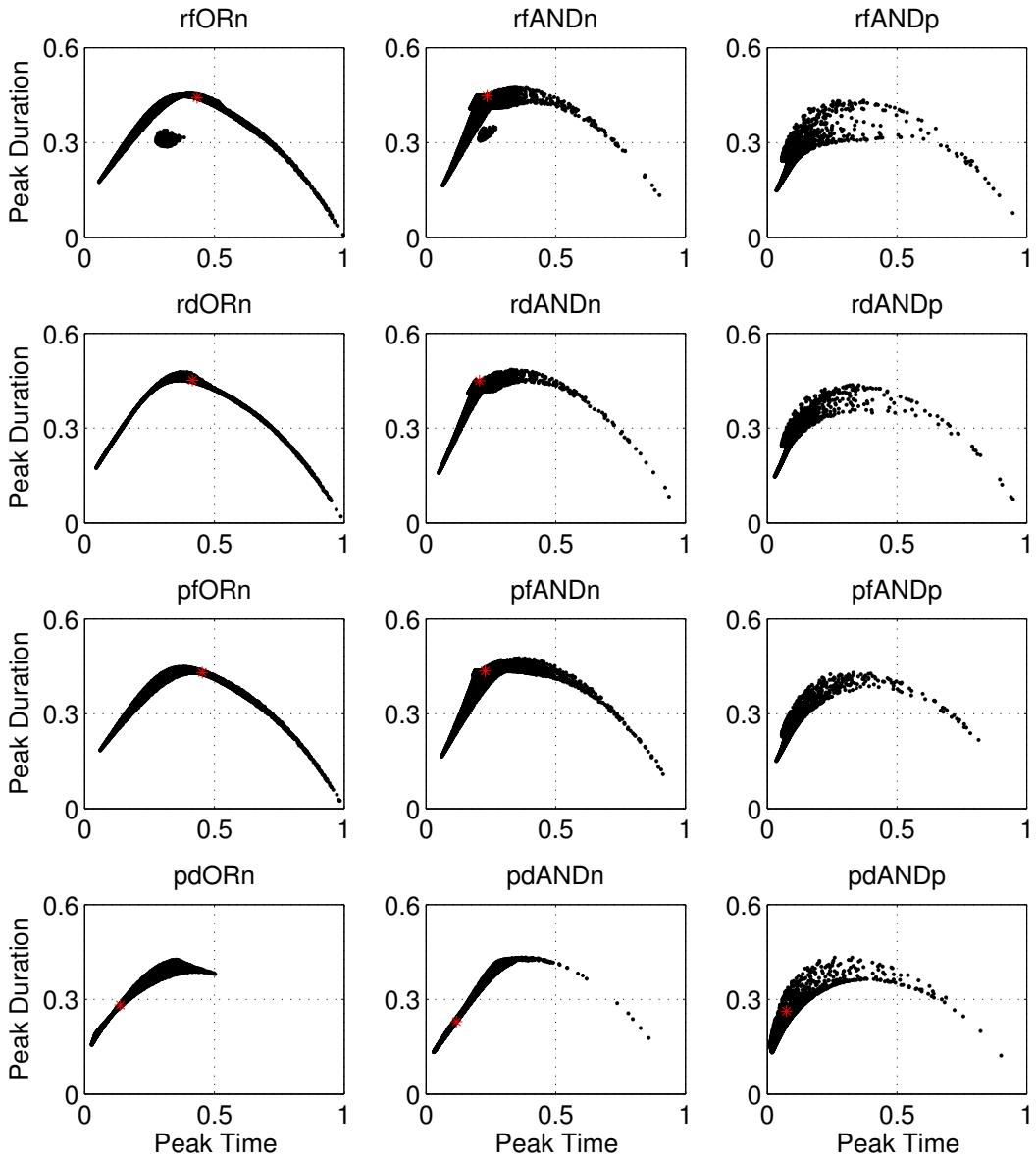


Fig. S11: Scatter plots between peak time and peak duration for composite motifs, when just the protein degradation rate constants are varied. Asterisks denote the values corresponding to the basal parameter set, when it shows peak.

4 Analytical solutions for a simplistic model of FFL

4.1 Equal degradation rates

$$\frac{dx}{dt} = \frac{\alpha_x I}{y} - x \quad (4.1.1)$$

$$\frac{dy}{dt} = \alpha_y I - y \quad (4.1.2)$$

Solving Equation 4.1.2:

$$\begin{aligned} \int \frac{dy}{\alpha_y I - y} &= \int dt \\ -\log(\alpha_y I - y) &= t + C \\ y &= \alpha_y I - C e^{-t} \\ \text{at } t_0 \quad C &= \alpha_y I - y_0 \\ y(t) &= \alpha_y I - (\alpha_y I - y_0) e^{-t} \end{aligned} \quad (4.1.3)$$

Substituting this expression of y in Equation 4.1.1:

$$\begin{aligned} \frac{dx}{dt} &= \frac{\alpha_x I}{\alpha_y I - (\alpha_y I - y_0) e^{-t}} - x \\ \frac{d}{dt}(x e^t) &= \frac{\alpha_x I e^t}{\alpha_y I - (\alpha_y I - y_0) e^{-t}} \\ x e^t &= \int \frac{\alpha_x I e^t e^t dt}{\alpha_y I e^t - (\alpha_y I - y_0)} \\ \text{Taking } z &= e^t \quad dz = e^t dt \\ x e^t &= \int \frac{\alpha_x I z \cdot dz}{\alpha_y I z - (\alpha_y I - y_0)} \\ &= \int \lambda dz + \int \frac{\alpha_x I - \lambda y_0}{\alpha_y I z - (\alpha_y I - y_0)} \quad (\lambda = \alpha_x / \alpha_y) \\ &= \lambda e^t + \frac{\alpha_x I - \lambda y_0}{\alpha_y I} \log(\alpha_y I e^t - (\alpha_y I - y_0)) + C \end{aligned}$$

$$\begin{aligned} x &= \lambda + e^{-t} \left(\frac{\alpha_x I - \lambda y_0}{\alpha_y I} \log(\alpha_y I e^t - (\alpha_y I - y_0)) + C \right) \\ C &= x_0 - \lambda - \frac{\alpha_x I - \lambda y_0}{\alpha_y I} \log(y_0) \\ x(t) &= \lambda + e^{-t} \left(x_0 - \lambda + \frac{\alpha_x I - \lambda y_0}{\alpha_y I} \log \left(\frac{\alpha_y I e^t - \alpha_y I + y_0}{y_0} \right) \right) \end{aligned} \quad (4.1.4)$$

For a step-up response $y_0 = \alpha_y I_0$ and $x_0 = \lambda$. Substituting this in Equation 4.1.4:

$$x(t) = \lambda + e^{-t} \left(\lambda \frac{I_f - I_0}{I_f} \log((G+1)e^t - G) \right) \quad (4.1.5)$$

Peak time

Differentiating Equation 4.1.5 and setting it to zero:

$$t_p = \min_t \left\{ t \mid \frac{e^t}{e^t - H} = \log((G+1)e^t - G) \right\} \quad (4.1.6)$$

$$H = \frac{I_f - I_0}{I_f} = \frac{G}{G+1}$$

Overshoot

$$\text{Overshoot} = \frac{x(t_p)}{\lambda} - 1 \quad (4.1.7)$$

Peak duration

$$\begin{aligned} \Delta t_{p/2} &= \max_{t \in (t_{\text{peak}}, \infty)} \left\{ t \mid \lambda + e^{-t} \left(\lambda \frac{I_f - I_0}{I_f} \log((G+1)e^t - G) \right) = \frac{x(t_p) + \lambda}{2} \right\} \\ &\quad - \min_{t \in (0, t_{\text{peak}})} \left\{ t \mid \lambda + e^{-t} \left(\lambda \frac{I_f - I_0}{I_f} \log((G+1)e^t - G) \right) = \frac{x(t_p) + \lambda}{2} \right\} \end{aligned} \quad (4.1.8)$$

4.2 Unequal degradation rates

$$\frac{dx}{dt} = \frac{\alpha_x I}{y} - \beta_x x \quad (4.2.1)$$

$$\frac{dy}{dt} = \alpha_y I - \beta_y y \quad (4.2.2)$$

Solving Equation 4.2.2 for y :

$$\begin{aligned} \int \frac{dy}{\alpha_y I - \beta_y y} &= \int dt \\ -\log(\alpha_y I - \beta_y y) &= \beta_y t + C \\ y &= \frac{\alpha_y}{\beta_y} I - C e^{-\beta_y t} \\ \text{at } t_0 \quad C &= \frac{\alpha_y}{\beta_y} I - y_0 \\ y(t) &= \mathcal{S}_y I + (y_0 - \mathcal{S}_y I) e^{-\beta_y t}; \quad \text{where } \mathcal{S}_y = \frac{\alpha_y}{\beta_y} \end{aligned} \quad (4.2.3)$$

Substituting this expression of y in Equation 4.2.1

$$\frac{dx}{dt} = \frac{\alpha_x I}{\mathcal{S}_y I + (y_0 - \mathcal{S}_y I) e^{-\beta_y t}} - \beta_x x$$

$$\frac{d}{dt}(x e^{\beta_x t}) = \frac{\alpha_x I e^{\beta_x t}}{\mathcal{S}_y I + (y_0 - \mathcal{S}_y I) e^{-\beta_y t}}$$

$$x e^{\beta_x t} = \int \frac{\alpha_x I e^{(\beta_x + \beta_y)t} dt}{\mathcal{S}_y I e^{\beta_y t} + y_0 - \mathcal{S}_y I}$$

Setting $\alpha_x / \mathcal{S}_y = p$ and $\frac{y_0 - \mathcal{S}_y I}{\mathcal{S}_y I} = q$

$$\begin{aligned} x e^{\beta_x t} &= p \int \frac{e^{(\beta_x + \beta_y)t} dt}{e^{\beta_y t} + q} \\ &= \frac{p e^{(\beta_x + \beta_y)t}}{q(\beta_x + \beta_y)} {}_2F_1\left(1, \frac{\beta_x + \beta_y}{\beta_y}, 2 + \frac{\beta_x}{\beta_y}; \frac{-e^{\beta_y t}}{q}\right) \end{aligned}$$

$${}_2F_1(a, b, c; z) = \sum_{n=0}^{\infty} \frac{(a)_n (b)_n}{(c)_n} \frac{z^n}{n!}$$

$$(r)_n = \begin{cases} 1 & n = 0 \\ r(r+1)\dots(r+n-1) & n > 0 \end{cases}$$

```

In[3]:= f = Exp[bx*t] * Exp[by*t] / (Exp[by*t] + q)
Integrate[f, t]
Out[3]= 
$$\frac{e^{bx t+by t}}{e^{by t}+q}$$

Out[4]= 
$$\frac{e^{(bx+by) t} \text{Hypergeometric2F1}\left[1, \frac{bx+by}{by}, 2+\frac{bx}{by}, -\frac{e^{by t}}{q}\right]}{(bx+by) q}$$


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Fig. S12: Analytical solution obtained using Wolfram Mathematica

$$x = \frac{p e^{\beta_y t}}{q(\beta_x + \beta_y)} \cdot {}_2F_1\left(1, \frac{\beta_x + \beta_y}{\beta_y}, 2 + \frac{\beta_x}{\beta_y}; \frac{-e^{\beta_y t}}{q}\right) + C$$

$$\text{at } t = 0, \quad C = x_0 - \frac{p}{q(\beta_x + \beta_y)} {}_2F_1\left(1, \frac{\beta_x + \beta_y}{\beta_y}, 2 + \frac{\beta_x}{\beta_y}; \frac{-1}{q}\right)$$

$$\begin{aligned} x &= \frac{\alpha_x I e^{\beta_y t}}{(y_0 - \mathcal{S}_y I)(\beta_x + \beta_y)} \cdot {}_2F_1\left(1, \frac{\beta_x + \beta_y}{\beta_y}, 2 + \frac{\beta_x}{\beta_y}; \frac{-\mathcal{S}_y I e^{\beta_y t}}{y_0 - \mathcal{S}_y I}\right) \\ &\quad + x_0 - \frac{\alpha_x I}{(y_0 - \mathcal{S}_y I)(\beta_x + \beta_y)} {}_2F_1\left(1, \frac{\beta_x + \beta_y}{\beta_y}, 2 + \frac{\beta_x}{\beta_y}; \frac{-\mathcal{S}_y I}{y_0 - \mathcal{S}_y I}\right) \end{aligned} \quad (4.2.4)$$

For step change $y_0 = \mathcal{S}_y I_0$, $x_0 = \lambda$ and $H = \frac{I_f - I_0}{I_0}$ where $\lambda = \mathcal{S}_x / \mathcal{S}_y$

$$x = \frac{\alpha_x e^{\beta_y t}}{\mathcal{S}_y H(\beta_x + \beta_y)} \cdot {}_2F_1 \left(1, \frac{\beta_x + \beta_y}{\beta_y}, 2 + \frac{\beta_x}{\beta_y}; \frac{-e^{\beta_y t}}{H} \right) \\ + \lambda - \frac{\alpha_x}{\mathcal{S}_y H(\beta_x + \beta_y)} {}_2F_1 \left(1, \frac{\beta_x + \beta_y}{\beta_y}, 2 + \frac{\beta_x}{\beta_y}; \frac{-1}{H} \right) \quad (4.2.5)$$

Peak time

$$t_p = \min_t \left\{ t \mid \frac{p\beta_y e^{\beta_y t}}{q(\beta_x + \beta_y)} {}_2F_1 \left(1, \frac{\beta_x + \beta_y}{\beta_y}, 2 + \frac{\beta_x}{\beta_y}; \frac{-e^{\beta_y t}}{q} \right) + \frac{p\beta_y}{q^2(2\beta_y + \beta_x)} {}_2F_1 \left(2, 1 + \frac{\beta_x + \beta_y}{\beta_y}, 3 + \frac{\beta_x}{\beta_y}; \frac{-e^{\beta_y t}}{q} \right) = 0 \right\} \quad (4.2.6)$$

$$\frac{\partial^k}{\partial z^k} [{}_2F_1(a, b, c; z)] = \frac{(a)_k (b)_k}{(c)_k} {}_2F_1(a+k, b+k, c+k; z)$$

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