

Table S1

GEF-only model

ODEs:

$$\begin{aligned}d(\text{RasGTP})/dt &= \text{ReactionFlux1} - \text{ReactionFlux2} \\d(\text{RasGDP})/dt &= -\text{ReactionFlux1} + \text{ReactionFlux2} \\d(\text{GEF})/dt &= -\text{ReactionFlux3} \\d([\text{R-GEF}])/dt &= \text{ReactionFlux3} - \text{ReactionFlux8} \\d(\text{R})/dt &= -\text{ReactionFlux3} + \text{ReactionFlux8} \\d(\text{delay1})/dt &= \text{ReactionFlux4} - \text{ReactionFlux5} \\d(\text{delay2})/dt &= \text{ReactionFlux5} - \text{ReactionFlux6} \\d(\text{delay3})/dt &= \text{ReactionFlux6} - \text{ReactionFlux7} \\d([\text{GEF-inactive}])/dt &= \text{ReactionFlux8}\end{aligned}$$

Fluxes:

$$\begin{aligned}\text{ReactionFlux1} &= k1 * [\text{R-GEF}] * \text{RasGDP} / (k2 + \text{RasGDP}) \\ \text{ReactionFlux2} &= \\ &k3 * \text{GAP_basal} * \text{RasGTP} / (k4 + \text{RasGTP}) \\ \text{ReactionFlux3} &= k5 * \text{R} * \text{GEF} \\ \text{ReactionFlux4} &= k_{\text{delay}} * \text{RasGTP} \\ \text{ReactionFlux5} &= k_{\text{delay}} * \text{delay1} \\ \text{ReactionFlux6} &= k_{\text{delay}} * \text{delay2} \\ \text{ReactionFlux7} &= k6 * \text{delay3} \\ \text{ReactionFlux8} &= k7 * \text{delay3} * [\text{R-GEF}]\end{aligned}$$

Parameter Values:

$$\begin{aligned}k1 &= 0.005 \\ k2 &= 50 \\ k3 &= 0.05 \\ k4 &= 50 \\ k5 &= 0.001 \\ k6 &= 0.1 \\ k7 &= 1 \\ k_{\text{delay}} &= 0.001 \\ \text{GAP_basal} &= \text{variable}\{\text{Null}=0, \text{Low}=1, \text{High}=8\}\end{aligned}$$

Initial Conditions:

$$\begin{aligned}\text{RasGTP} &= 0 \\ \text{RasGDP} &= 100 \\ \text{GEF} &= 100 \\ [\text{R-GEF}] &= 0 \\ \text{R} &= 100 \\ \text{delay1} &= 0 \\ \text{delay2} &= 0 \\ \text{delay3} &= 0 \\ [\text{GEF-inactive}] &= 0\end{aligned}$$

GAP-only model

ODEs:

$$\begin{aligned}d(\text{RasGTP})/dt &= \text{ReactionFlux1} - \text{ReactionFlux2} \\d(\text{RasGDP})/dt &= -\text{ReactionFlux1} + \text{ReactionFlux2} \\d(\text{GEF})/dt &= -\text{ReactionFlux3} \\d([\text{R-GEF}])/dt &= \text{ReactionFlux3} \\d(\text{R})/dt &= -\text{ReactionFlux3} \\d(\text{delay1})/dt &= \text{ReactionFlux4} - \text{ReactionFlux5} \\d(\text{delay2})/dt &= \text{ReactionFlux5} - \text{ReactionFlux6} \\d(\text{delay3})/dt &= \text{ReactionFlux6} - \text{ReactionFlux7} \\d([\text{GAP-active}])/dt &= \text{ReactionFlux8} \\d([\text{GAP-inactive}])/dt &= -\text{ReactionFlux8}\end{aligned}$$

Fluxes:

$$\begin{aligned}\text{ReactionFlux1} &= k_1 * [\text{R-GEF}] * \text{RasGDP} / (k_2 + \text{RasGDP}) \\ \text{ReactionFlux2} &= k_3 * [\text{GAP-active}] * \text{RasGTP} / (k_4 + \text{RasGTP}) \\ \text{ReactionFlux3} &= k_5 * \text{R} * \text{GEF} \\ \text{ReactionFlux4} &= k_{\text{delay}} * \text{RasGTP} \\ \text{ReactionFlux5} &= k_{\text{delay}} * \text{delay1} \\ \text{ReactionFlux6} &= k_{\text{delay}} * \text{delay2} \\ \text{ReactionFlux7} &= k_6 * \text{delay3} \\ \text{ReactionFlux8} &= k_7 * \text{delay3} * [\text{GAP-inactive}]\end{aligned}$$

Parameter Values:

$$\begin{aligned}k_1 &= 0.38 \\ k_2 &= 10 \\ k_3 &= 0.34 \\ k_4 &= 0.01 \\ k_5 &= 0.017 \\ k_6 &= 0.01 \\ k_7 &= 5.1 \\ k_{\text{delay}} &= 0.22\end{aligned}$$

Initial Conditions:

$$\begin{aligned}\text{RasGTP} &= 0 \\ \text{RasGDP} &= 100 \\ \text{GEF} &= 100 \\ [\text{R-GEF}] &= 0 \\ \text{R} &= 100 \\ \text{delay1} &= 0 \\ \text{delay2} &= 0 \\ \text{delay3} &= 0 \\ \text{GAP_active} &= 0 \\ \text{GAP_inactive} &= 100\end{aligned}$$