

Table 1. Variables of the quantitative model

Variable	Description
x_1	[free AtRGS1]
x_2	[AtRGS1:G α^{GDP} $\beta\gamma$ complex]
x_3	[AtRGS1:G α^{GTP} $\beta\gamma$ complex]
x_4	[AtRGS1:G α^{GDP} complex]
x_5	[AtRGS1:G α^{GTP} complex]
x_6	[G α^{GDP} $\beta\gamma$]
x_7	[G α^{GTP} $\beta\gamma$]
x_8	[G α^{GDP}]
x_9	[G α^{GTP}]
x_{10}	[G $\beta\gamma$]
x_{11}	[Phosphorylated AtRGS1]
x_{12}	[Internalized AtRGS1]
x_{13}	[Hypothetical D-glucose (co)receptor]
x_{14}	[Kinase 2] (not present in the one-kinase model)
x_{15}	[Kinase 1]
L	[D-glucose]

Table 2. Ordinary Differential Equations of the quantitative model

$$\begin{aligned} \frac{dx_1}{dt} &= -k_{17} \cdot x_1 \cdot x_7 - k_{18} \cdot x_1 \cdot x_9 - k_{12} \cdot x_1 + k_{24} \cdot x_5 + k_{25} \cdot x_3 + k_{27} \cdot x_{12} \\ \frac{dx_2}{dt} &= k_4 \cdot x_3 + k_8 \cdot x_4 \cdot x_{10} - k_6 \cdot x_2 - k_{16} \cdot x_2 \\ \frac{dx_3}{dt} &= k_6 \cdot x_2 - k_4 \cdot x_3 - k_{11} \cdot x_3 \cdot \frac{x_{13}^{k_{14}}}{k_{26}^{k_{14}} + x_{13}^{k_{14}}} - k_{25} \cdot x_3 + k_{17} \cdot x_1 \cdot x_7 + k_{13} \cdot x_5 \cdot x_{10} \\ \frac{dx_4}{dt} &= k_4 \cdot x_5 - k_6 \cdot x_4 - k_8 \cdot x_4 \cdot x_{10} + k_{16} \cdot x_2 \\ \frac{dx_5}{dt} &= k_6 \cdot x_4 + k_{11} \cdot x_3 \cdot \frac{x_{13}^{k_{14}}}{k_{26}^{k_{14}} + x_{13}^{k_{14}}} - k_4 \cdot x_5 - k_3 \cdot x_5 \cdot (x_{14} + x_{15}) + k_{30} \cdot x_{11} + k_{18} \cdot x_1 \cdot x_9 - k_2 \cdot x_5 - k_{24} \cdot x_5 - k_{13} \cdot x_5 \cdot x_{10} \\ \frac{dx_6}{dt} &= k_5 \cdot x_7 + k_7 \cdot x_8 \cdot x_{10} - k_6 \cdot x_6 - k_{28} \cdot x_6 \\ \frac{dx_7}{dt} &= k_6 \cdot x_6 - k_5 \cdot x_7 - k_{10} \cdot x_7 - k_{17} \cdot x_1 \cdot x_7 + k_9 \cdot x_9 \cdot x_{10} + k_{25} \cdot x_3 \\ \frac{dx_8}{dt} &= k_5 \cdot x_9 + k_{28} \cdot x_6 - k_6 \cdot x_8 - k_7 \cdot x_8 \cdot x_{10} \\ \frac{dx_9}{dt} &= k_{20} \cdot x_{11} + k_6 \cdot x_8 + k_{10} \cdot x_7 - k_5 \cdot x_9 - k_{18} \cdot x_1 \cdot x_9 - k_9 \cdot x_9 \cdot x_{10} + k_2 \cdot x_5 + k_{24} \cdot x_5 \\ \frac{dx_{10}}{dt} &= k_{10} \cdot x_7 + k_{11} \cdot x_3 \cdot \frac{x_{13}^{k_{14}}}{k_{26}^{k_{14}} + x_{13}^{k_{14}}} - k_8 \cdot x_4 \cdot x_{10} - k_7 \cdot x_8 \cdot x_{10} - k_9 \cdot x_9 \cdot x_{10} + k_{28} \cdot x_6 - k_{13} \cdot x_5 \cdot x_{10} + k_{16} \cdot x_2 \\ \frac{dx_{11}}{dt} &= k_3 \cdot x_5 \cdot (x_{14} + x_{15}) - k_{20} \cdot x_{11} - k_{30} \cdot x_{11} \\ \frac{dx_{12}}{dt} &= k_2 \cdot x_5 + k_{12} \cdot x_1 + k_{20} \cdot x_{11} - k_{27} \cdot x_{12} \\ \frac{dx_{13}}{dt} &= k_{15} \cdot (L - x_{13}) \\ \frac{dx_{14}}{dt} &= \begin{cases} k_1 \cdot \left(\frac{k_{21} \cdot x_{10}^2}{k_{22}^2 + x_{10}^2} - x_{14} \right), & \text{two-kinase model} \\ 0, & \text{one-kinase model} \end{cases} \\ \frac{dx_{15}}{dt} &= k_{19} \cdot \left(\frac{k_{23} \cdot x_{10}^2}{k_{29}^2 + x_{10}^2} - x_{15} \right) \end{aligned}$$

Table 3. Parameter set values used for the one-kinase model ($Md_{1kinase}^{top50}$) and the two-kinase model ($Md_{2kinase}^{top50}$)

Parameter	Description	Values in one-kinase model ($Md_{1kinase}^{top50}$)	Values in two-kinase model ($Md_{2kinase}^{top50}$)	Source
k₁	Deactivation rate of kinase 2	--	$6.21 \times 10^{-4} \text{ min}^{-1}$	estimated
k₂	Phosphorylation rate of AtRGS1	2.50 min^{-1}	2.15 min^{-1}	estimated
k₃	Kinase-dependent AtRGS1 internalization rate	$1.04 \times 10^{-2} \text{ molc}^{-1} \text{ min}^{-1}$	$7.29 \times 10^{-3} \text{ molc}^{-1} \text{ min}^{-1}$	estimated
k₄	AtRGS1-dependent GTP hydrolysis rate	1.89 min^{-1}	1.89 min^{-1}	[1]
k₅	Intrinsic GTP hydrolysis rate	$4.95 \times 10^{-2} \text{ min}^{-1}$	$4.95 \times 10^{-2} \text{ min}^{-1}$	[2]
k₆	Intrinsic nucleotide exchange rate	8.4 min^{-1}	8.4 min^{-1}	[3]
k₇	Association rate of $G\alpha^{GDP}$ and $G\beta\gamma$	$3.50 \times 10^{-2} \text{ molc}^{-1} \text{ min}^{-1}$	$3.50 \times 10^{-2} \text{ molc}^{-1} \text{ min}^{-1}$	[4]
k₈	Dissociation rate of $\text{AtRGS1}:G\alpha^{GDP}\beta\gamma$	$1.09 \times 10^{-2} \text{ molc}^{-1} \text{ min}^{-1}$	$4.91 \times 10^{-3} \text{ molc}^{-1} \text{ min}^{-1}$	estimated
k₉	Association rate of $G\alpha^{GTP}$ and $G\beta\gamma$	$1.01 \times 10^{-6} \text{ molc}^{-1} \text{ min}^{-1}$	$4.26 \times 10^{-6} \text{ molc}^{-1} \text{ min}^{-1}$	estimated
k₁₀	Dissociation rate of $G\alpha^{GTP}\beta\gamma$	$4.53 \times 10^{-6} \text{ min}^{-1}$	$4.65 \times 10^{-5} \text{ min}^{-1}$	estimated
k₁₁	D-glucose-dependent dissociation rate of $\text{AtRGS1}:G\alpha^{GTP}\beta\gamma$	20.06 min^{-1}	29.38 min^{-1}	estimated
k₁₂	Constitutive AtRGS1 internalization rate	6.04 min^{-1}	5.00 min^{-1}	estimated
k₁₃	Association rate of $\text{AtRGS1}:G\alpha^{GTP}$ and $G\beta\gamma$	$2.87 \times 10^{-4} \text{ molc}^{-1} \text{ min}^{-1}$	$6.61 \times 10^{-4} \text{ molc}^{-1} \text{ min}^{-1}$	estimated
k₁₄	Hill coefficient on hypothetical glucose (co)receptor X	2	2	estimated
k₁₅	Deactivation rate of the hypothetical glucose (co)receptor	$1.16 \times 10^{-1} \text{ min}^{-1}$	$2.31 \times 10^{-1} \text{ min}^{-1}$	estimated
k₁₆	Association rate of $\text{AtRGS1}:G\alpha^{GDP}$ and $G\beta\gamma$	$1.60 \times 10^{-3} \text{ min}^{-1}$	$5.44 \times 10^{-3} \text{ min}^{-1}$	estimated

k₁₇	Association rate of $G\alpha^{GTP}\beta\gamma$ and free AtRGS1	2.52×10^{-4} $\text{molc}^{-1}\text{min}^{-1}$	5.09×10^{-4} $\text{molc}^{-1}\text{min}^{-1}$	estimated
k₁₈	Association rate of $G\alpha^{GTP}$ and free AtRGS1	3.90×10^{-2} $\text{molc}^{-1}\text{min}^{-1}$	3.21×10^{-2} $\text{molc}^{-1}\text{min}^{-1}$	estimated
k₁₉	Deactivation rate of Kinase 1	$4.70 \times 10^{-3} \text{min}^{-1}$	$1.52 \times 10^{-2} \text{min}^{-1}$	estimated
k₂₀	Internalization rate of phosphorylated AtRGS1	$6.83 \times 10^1 \text{min}^{-1}$	$7.20 \times 10^1 \text{min}^{-1}$	estimated
k₂₁	$G\beta\gamma$ -dependent maximum activation of Kinase 2	--	$5.53 \times 10^3 \text{molc}$	estimated
k₂₂	K_m of kinase 2 activation	--	$4.25 \times 10^3 \text{molc}$	estimated
k₂₃	$G\beta\gamma$ -dependent maximum activation of Kinase 1	$9.84 \times 10^4 \text{molc}$	$5.57 \times 10^4 \text{molc}$	estimated
k₂₄	Dissociation rate of AtRGS1: $G\alpha^{GTP}$	$2.50 \times 10^{-3} \text{min}^{-1}$	$3.80 \times 10^{-3} \text{min}^{-1}$	estimated
k₂₅	Dissociation rate of AtRGS1: $G\alpha^{GTP}\beta\gamma$	$4.20 \times 10^{-3} \text{min}^{-1}$	$3.04 \times 10^{-3} \text{min}^{-1}$	estimated
k₂₆	K_m of the hypothetical glucose (co)receptor X	1.19 (a.u.)	1.92 (a.u.)	estimated
k₂₇	Tonic recycling rate of AtRGS1	$3.06 \times 10^{-1} \text{min}^{-1}$	$1.84 \times 10^{-1} \text{min}^{-1}$	estimated
k₂₈	Dissociation rate of $G\alpha^{GDP}\beta\gamma$	2.36min^{-1}	3.48min^{-1}	estimated
k₂₉	K_m of kinase 1 activation	$6.52 \times 10^4 \text{molc}$	$4.66 \times 10^4 \text{molc}$	estimated
k₃₀	Dephosphorylation rate of AtRGS1	3.84min^{-1}	2.41min^{-1}	estimated

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