

Supplementary information S8 (table) | Kinetic description of a bistable three-kinase cascade

Bistability (supplementary information S7 (figure)) emerges from inhibition of the rate of cytoplasmic phosphatase-2 by the active form M_3P . The spatio-temporal dynamics of the cascade is described by the reaction-diffusion system (equation 1 in BOX 4 of the main text). Both phosphorylated and unphosphorylated forms of kinases M_1 , M_2 and M_3 diffuse in the cytoplasm. The cell radius $L = 25 \mu\text{m}$, the diffusion coefficient D is assumed to be equal for all kinase forms, $D = 5 \mu\text{m}^2/\text{sec}$. Total concentrations of the unphosphorylated (M_i) form and phosphorylated form (M_iP) are assumed constant on the time scale considered, $M_i + M_iP = M_{tot}$. Eq. 1 can be solved for dimensionless variables M_iP/M_{tot} , therefore, in the table the Michaelis constants (K_{mi} and K_{mpi} , $i=1,2,3$) and the maximal activities (V_{phos}^i) are normalized by M_{tot} .

Reaction	Rate expression	Kinetic constants
Membrane kinase $M_1 \rightarrow M_1P$	$v_{kin}^{mem} = \frac{V_{kin}^{mem} M_1}{(K_{m1} + M_1)}$	$V_{kin}^{mem} / M_{tot} = (1.5 L/3) \mu\text{m s}^{-1}$ $K_{m1}/M_{tot} = 0.5$
Cytoplasmic phosphatase-1 $M_1P \rightarrow M_1$	$v_{phos}^1 = \frac{V_{phos}^1 M_1P}{(K_{mp1} + M_1P)}$	$V_{phos}^1 / M_{tot} = 3 \text{ s}^{-1}$ $K_{mp1}/M_{tot} = 0.7$
Kinase M_1P $M_2 \rightarrow M_2P$	$v_{kin}^1 = \frac{k_2^{cat} M_1P \cdot M_2}{(K_{m2} + M_2)}$	$k_2^{cat} = 9 \text{ s}^{-1}$ $K_{m2}/M_{tot} = 0.7$
Cytoplasmic phosphatase-2 $M_2P \rightarrow M_2$	$v_{phos}^2 = V_{phos}^2 \frac{M_2P}{(K_{mp2} + M_2P)(1 + (M_3P/K_1)^2)}$	$V_{phos}^2 / M_{tot} = 9 \text{ s}^{-1}$ $K_{mp2}/M_{tot} = 0.7, K_1/M_{tot} = 0.15$
Kinase M_2P $M_3 \rightarrow M_3P$	$v_{kin}^2 = \frac{k_3^{cat} M_2P \cdot M_3}{(K_{m3} + M_3)}$	$k_3^{cat} = 9 \text{ s}^{-1}$ $K_{m3}/M_{tot} = 0.5$
Cytoplasmic phosphatase-3 $M_3P \rightarrow M_3$	$v_{phos}^3 = V_{phos}^3 \frac{M_3P}{(K_{mp3} + M_3P)}$	$V_{phos}^3 / M_{tot} = 3 \text{ s}^{-1}$ $K_{mp3}/M_{tot} = 0.7$

The traveling wave shown in BOX 4 of the main text (see figure, panel B) was calculated for the input impulse of $V_{kin}^{mem} / M_{tot} = (7.5 L/3) \mu\text{m s}^{-1}$ in the time range from 0 to 30 sec, and $V_{kin}^{mem} / M_{tot} = 0$ at $t > 30$ s, using the reaction diffusion equations (equation 1 in BOX 4) with the rate expressions and parameters given in supplementary information S8 (table). Note that in the absence of bistability, the phosphorylation signal cannot reach the distance of $20 \mu\text{m}$, since it will be terminated by cytoplasmic phosphatases.