Supporting information for Kholodenko *et al.* (2002) *Proc. Natl. Acad. Sci. USA*, 10.1073/pnas.192442699

Table 1. Rate equations and parameter values of the MAPK cascade model

Rate equation	Parameter values
$v_1 = \dfrac{k_1^{cat} \cdot [RasGTP] \cdot [MKKK]}{(K_{11} + [MKKK] + [MKKKP] \cdot K_{11}/K_{12}) \cdot (1 + [MAPKPP]/K_i)}$	$k_1^{cat} = 1$; [RasGTP] =20; $K_{11} = 300$; $K_{12} = 20$; $K_i = 100$
$v_2 = \dfrac{k_2^{cat} \cdot [RasGTP] \cdot [MKKKP]}{(K_{11} + [MKKK] + [MKKKP] \cdot K_{11}/K_{12}) \cdot (1 + [MAPKPP]/K_i)}$	$k_2^{cat} = 15$; $[MKKK]_{total} = 200$
$v_3 = \dfrac{V_3^{max} \cdot [MKKKPP]}{(K_{31} + [MKKKPP] + [MKKKP] \cdot K_{31}/K_{32} + [MKKK] \cdot K_{31}/K_{33})}$	$V_3^{max} = 18.8$; $K_{31} = 22$; $K_{32} = 18$; $K_{33} = 80$
$v_4 = \dfrac{V_4^{max} \cdot [MKKKP]}{(K_{31} + [MKKKPP] + [MKKKP] \cdot K_{31}/K_{32} + [MKKK] \cdot K_{31}/K_{33})}$	$V_4^{max} = 16.4$
$v_5 = \dfrac{k_5^{cat} \cdot [MKK] \cdot [MKKKPP]}{(K_{51} + [MKK] + [MKKP] \cdot K_{51}/K_{52})}$	$k_5^{cat} = 1$; $K_{51} = 300$; $K_{52} = 20$
$v_6 = \dfrac{k_6^{cat} \cdot [MKKP] \cdot [MKKKPP]}{(K_{51} + [MKK] + [MKKP] \cdot K_{51}/K_{52})}$	$k_6^{cat} = 15$; $[MKK]_{total} = 180$
$v_7 = \dfrac{V_7^{max} \cdot [MKKPP] \cdot (1 + A \cdot [MAPKPP]/K_{mp})}{(K_{71} + [MKKPP] + [MKKP] \cdot K_{71}/K_{72} + [MKK] \cdot K_{71}/K_{73}) \cdot (1 + [MAPKPP]/K_{mp})}$	$V_7^{max} = 18.8$; $K_{71} = 22$; $K_{72} = 18$; $K_{73} = 80$; $A = 5$; $K_{mp} = 100$
$v_8 = \dfrac{V_8^{max} \cdot [MKKP] \cdot (1 + A \cdot [MAPKPP]/K_{mp})}{(K_{71} + [MKKPP] + [MKKP] \cdot K_{71}/K_{72} + [MKK] \cdot K_{71}/K_{73}) \cdot (1 + [MAPKPP]/K_{mp})}$	$V_8^{max} = 16.4$
$v_9 = \dfrac{k_9^{cat} \cdot [MKKPP] \cdot [MAPK]}{(K_{91} + [MAPK] + [MAPKP] \cdot K_{91}/K_{92})}$	$k_9^{cat} = 1$; $K_{91} = 300$; $K_{92} = 20$
$v_{10} = \dfrac{k_{10}^{cat} \cdot [MKKPP] \cdot [MAPKP]}{(K_{91} + [MAPK] + [MAPKP] \cdot K_{91}/K_{92})}$	$k_{10}^{cat} = 15$; $[MAPK]_{total} = 360$
$v_{11} = \dfrac{V_{11}^{max} \cdot [MAPKPP]}{(K_{111} + [MAPKPP] + [MAPKP] \cdot K_{111}/K_{112} + [MAPK] \cdot K_{111}/K_{113})}$	$V_{11}^{max} = 8.4$; $K_{111} = 22$; $K_{112} = 18$; $K_{113} = 80$
$v_{12} = \dfrac{V_{12}^{max} \cdot [MAPKP]}{(K_{111} + [MAPKPP] + [MAPKP] \cdot K_{111}/K_{112} + [MAPK] \cdot K_{111}/K_{113})}$	$V_{12}^{max} = 7.3$

Concentrations and the Michaelis constants (K_{ij}, $i = 1, 3, 5, 7, 9, 11$; $j = 1, 2, 3$; K_{mp}; K_i) are given in nM. The catalytic rate constants (k_i^{cat} , i = 1, 2, 5, 6, 9, 10) and maximal enzyme rates (V_i^{max}, i = 3, 4, 7, 8, 11, 12) are expressed in s^{-1} and $nM \cdot s^{-1}$, respectively. The kinetic equations and moiety conservations derived from the stoichiometry are the following: d[MKKK-P]/$dt = v_1 - v_2 + v_3 - v_4$; d[MKKK-PP]/$dt = v_2 - v_3$; d[MKK-P]/dt = $v_5 - v_6 + v_7 - v_8$; d[MKK-PP]/$dt = v_6 - v_7$; d[MAPK-P]/$dt = v_9 - v_{10} + v_{11} - v_{12}$; d[MAPK-PP]/$dt = v_{10} - v_{11}$; $[MKKK]_{total}$ = [MKKK] + [MKKK-P] + [MKKK-PP]; $[MKK]_{total}$ = [MKK] + [MKK-P] + [MKK-PP]; $[MAPK]_{total}$ = [MAPK] + [MAPK-P] + [MAPK-PP]. MAPK, mitogen-activated protein kinase; MKK, MAPK kinase; MKKK, MKK kinase; P, monophosphorylated form; PP, bisphosphorylated form.