

Additional file 1 —Mathematical model

Mathematical model of the MAP kinase signalling pathway

Based on the chemical reactions of the MAP kinase signalling pathway listed in the manuscript, the dynamics of this pathway is modelled by the following system with 15 differential equations and 21 unknown parameters.

$$\begin{aligned}
 \frac{d[pRaf - MEK]}{dt} &= a_1[pRaf][MEK] - (d_1 + k_1)[pRaf - MEK], \\
 \frac{d[MEK]}{dt} &= -a_1[pRaf][MEK] + d_1[pRaf - MEK] + k_3[pMEK - MEKP], \\
 \frac{d[pMEK]}{dt} &= k_2[ppMEK - MEKP] + d_3[pMEK - MEKP] - a_3[pMEK][MEKP], \\
 \frac{d[ppMEK]}{dt} &= k_1[pRaf - MEK] + d_2[ppMEK - MEKP] - a_2[ppMEK][MEKP] \\
 &\quad + (d_4 + k_4)[ppMEK - ERK] - a_4[ppMEK][ERK] - a_5[ppMEK][pERK] \\
 &\quad + (d_5 + k_5)[ppMEK - pERK], \\
 \frac{d[pMEK - MEKP]}{dt} &= a_3[pMEK][MEKP] - (d_3 + k_3)[pMEK - MEKP], \\
 \frac{d[ppMEK - MEKP]}{dt} &= a_2[ppMEK][MEKP] - (d_2 + k_2)[ppMEK - MEKP], \\
 \frac{d[MEKP]}{dt} &= (d_2 + k_2)[ppMEK - MEKP] - a_2[ppMEK][MEKP] \\
 &\quad + (d_3 + k_3)[pMEK - MEKP] - a_3[pMEK][MEKP], \\
 \frac{d[ERK]}{dt} &= -a_4[ppMEK][ERK] + d_4[ppMEK - ERK] + k_7[pERK - ERKP], \\
 \frac{d[pERK]}{dt} &= k_4[ppMEK - ERK] + d_7[pERK - ERKP] - a_7[pERK][ERKP] \\
 &\quad + d_5[ppMEK - pERK] - a_5[ppMEK][pERK] + k_6[ppERK - ERKP], \\
 \frac{d[ppERK]}{dt} &= k_5[ppMEK - pERK] + d_6[ppERK - ERKP] - a_6[ppERK][ERKP], \\
 \frac{d[pERK - ERKP]}{dt} &= a_7[pERK][ERKP] - (d_7 + k_7)[pERK - ERKP], \\
 \frac{d[ppERK - ERKP]}{dt} &= a_6[ppERK][ERKP] - (d_6 + k_6)[ppERK - ERKP], \\
 \frac{d[ERKP]}{dt} &= -a_6[ppERK][ERKP] + (d_6 + k_6)[ppERK - ERKP] \\
 &\quad - a_7[pERK][ERKP] + (d_7 + k_7)[pERK - ERKP], \\
 \frac{d[ppMEK - ERK]}{dt} &= a_4[ppMEK][ERK] - (d_4 + k_4)[ppMEK - ERK], \\
 \frac{d[ppMEK - pERK]}{dt} &= a_5[ppMEK][pERK] - (d_5 + k_5)[ppMEK - pERK].
 \end{aligned} \tag{0.1}$$