We used the two member MAPK scaffold model (cite PNAS paper) as a basis for our model with the following alterations. First, RAF (MAPKKK) dynamics were removed and a basal level of RAF activation was assumed. Second, we spacially partition the cell into "front" and "back" compartments, each with subcellular regions of cytoplasm, membrane and vesicles. Scaffold is capable of recycling through those three subcellular regions and is initially only cytoplasmic. MAPK components are cytoplasmic however they can be recruited to vesicle scaffolds, which can further catalyze the creation of dually phosphorylated MAPK.

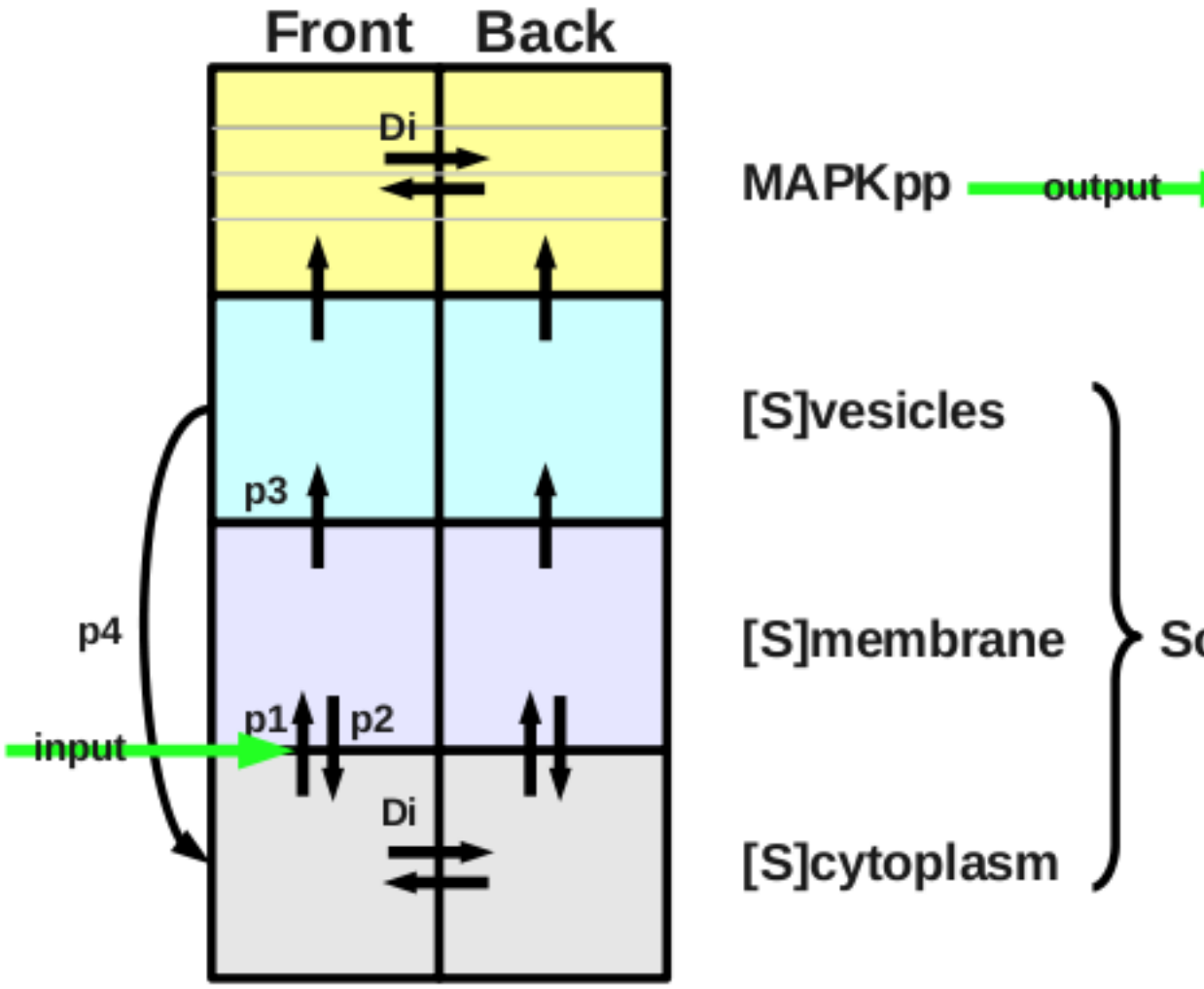
Translocation of cytoplasmic scaffold to the membrane occurs at a rate proportional to input dose. Translocation of membrane scaffold to vesicles occurs at a biphasic rate dependent on membrane scaffold. The readout for the model is the amount of dually phosphorylated MAPK.

Simulation was carried out through temporal integration of the system to steady state until an equilibrium tolerance was reached.

X-p phosphorylation, X-Ph phosphatase, X-k, kinase

$$\mathrm{p3}(0) = (\mathrm{p3bSmem}(0)(t) + \mathrm{p3a}) \left(\frac{1 - \mathrm{p3d}}{e^{\mathrm{p3f}(\mathrm{Smem}(0)(t) - \mathrm{p3e})} + 1} + \mathrm{p3d} \right) \tag{1}$$

$$\mathrm{MI} = \frac{\mathrm{MAPKpp}_{\mathrm{front}} - \mathrm{MAPKpp}_{\mathrm{back}}}{dx * \mathrm{maxdose}} \tag{2}$$


Front
Back
Di
MAPKpp
output
[S]vesicles
p3
p4
[S]membrane
p1
p2
input
Di
[S]cytoplasm

a_1	1
a˙10	5
a_2	0.5
a_3	3.3
a_4	10
a_5	3.3
a_6	10
a_7	20
a_8	5
a_9	20
Stot	0
d_1	0.4
d˙10	0.4
d_2	0.5
d_3	0.42
d_4	0.8
d_5	0.4
d_6	0.8
d_7	0.6
d_8	0.4
d_9	0.6
k_1	0.1
k˙10	0.1
k_2	0.1
k_3	0.1
k_4	0.1
k_5	0.1
k_6	0.1
k_7	0.1
k_8	0.1
k_9	0.1
MAPKPhtot	0.3
MAPKtot	0.4
MEKPhtot	0.2
MEKtot	0.2
of_1	0.05
of_2	0.05
of_3	0.05
of_4	0.5
on_1	10
on_2	10
RAFp	0.14
RAFPhtot	0.3
RAFtot	0.3
p_2	0.1
Di	0.0001
$p_1(0)$	0.1
$p_3(0)$	0.1
$p_4(0)$	0.1
$p_1(1)$	0.1
$p_3(1)$	0.1
$p_4(1)$	0.1

$$
\begin{aligned}
S'_{\mathrm{cyto}}(0,t) &= p_4(0)C_1(0,t) + \mathrm{Di}(S_{\mathrm{cyto}}(1,t) - S_{\mathrm{cyto}}(0,t)) - p_1(0)S_{\mathrm{cyto}}(0,t) + p_2 S_{\mathrm{mem}}(0,t)\\
\mathrm{MEK}'(0,t) &= -a_3\mathrm{RAFpMEK}(0,t) - \mathrm{on}_1\mathrm{MEK}(0,t)(C_1(0,t) + C_4(0,t) + C_5(0,t))\\
&\quad + \mathrm{of}_1(C_2(0,t) + C_6(0,t) + C_9(0,t)) + d_3\mathrm{MEKRAFp}(0,t)\\
&\quad + \mathrm{Di}(\mathrm{MEK}(1,t) - \mathrm{MEK}(0,t)) + k_4\mathrm{MEKpMEKPh}(0,t)\\
\mathrm{MEKRAFp}'(0,t) &= a_3\mathrm{RAFpMEK}(0,t) + (-d_3 - k_3)\mathrm{MEKRAFp}(0,t)\\
&\quad + \mathrm{Di}(\mathrm{MEKRAFp}(1,t) - \mathrm{MEKRAFp}(0,t))\\
\mathrm{MEKp}'(0,t) &= -a_4\mathrm{MEKp}(0,t)(-\mathrm{MEKpMEKPh}(0,t) - \mathrm{MEKppMEKPh}(0,t)\\
&\quad + \mathrm{MEKPhtot}) - a_5\mathrm{RAFpMEKp}(0,t) + d_4\mathrm{MEKpMEKPh}(0,t)\\
&\quad + d_5\mathrm{MEKpRAFp}(0,t) + \mathrm{Di}(\mathrm{MEKp}(1,t) - \mathrm{MEKp}(0,t))\\
&\quad + k_3\mathrm{MEKRAFp}(0,t) + k_6\mathrm{MEKppMEKPh}(0,t)\\
\mathrm{MEKpMEKPh}'(0,t) &= a_4\mathrm{MEKp}(0,t)(-\mathrm{MEKpMEKPh}(0,t) - \mathrm{MEKppMEKPh}(0,t)\\
&\quad + \mathrm{MEKPhtot}) + (-d_4 - k_4)\mathrm{MEKpMEKPh}(0,t)\\
&\quad + \mathrm{Di}(\mathrm{MEKpMEKPh}(1,t) - \mathrm{MEKpMEKPh}(0,t))\\
\mathrm{MEKpRAFp}'(0,t) &= a_5\mathrm{RAFpMEKp}(0,t) + (-d_5 - k_5)\mathrm{MEKpRAFp}(0,t)\\
&\quad + \mathrm{Di}(\mathrm{MEKpRAFp}(1,t) - \mathrm{MEKpRAFp}(0,t))\\
\mathrm{MEKpp}'(0,t) &= -a_6\mathrm{MEKpp}(0,t)(-\mathrm{MEKpMEKPh}(0,t) - \mathrm{MEKppMEKPh}(0,t)\\
&\quad + \mathrm{MEKPhtot})\\
&\quad - a_7\mathrm{MAPK}(0,t)\mathrm{MEKpp}(0,t) - a_9\mathrm{MAPKp}(0,t)\mathrm{MEKpp}(0,t)\\
&\quad + \mathrm{of}_3(C_3(0,t) + C_7(0,t) + C_8(0,t)) + d_6\mathrm{MEKppMEKPh}(0,t)\\
&\quad + (d_7 + k_7)\mathrm{MAPKMEKpp}(0,t) + (d_9 + k_9)\mathrm{MAPKpMEKpp}(0,t)\\
&\quad + \mathrm{Di}(\mathrm{MEKpp}(1,t) - \mathrm{MEKpp}(0,t)) + k_5\mathrm{MEKpRAFp}(0,t)\\
\mathrm{MEKppMEKPh}'(0,t) &= a_6\mathrm{MEKpp}(0,t)(-\mathrm{MEKpMEKPh}(0,t) - \mathrm{MEKppMEKPh}(0,t)\\
&\quad + \mathrm{MEKPhtot}) - (d_6 + k_6)\mathrm{MEKppMEKPh}(0,t)\\
&\quad + \mathrm{Di}(\mathrm{MEKppMEKPh}(1,t) - \mathrm{MEKppMEKPh}(0,t))\\
\mathrm{MAPK}'(0,t) &= -a_7\mathrm{MAPK}(0,t)\mathrm{MEKpp}(0,t)\\
&\quad - \mathrm{on}_2\mathrm{MAPK}(0,t)(C_1(0,t) + C_2(0,t) + C_3(0,t))\\
&\quad + \mathrm{of}_2(C_4(0,t) + C_6(0,t) + C_7(0,t)) + d_7\mathrm{MAPKMEKpp}(0,t)\\
&\quad + \mathrm{Di}(\mathrm{MAPK}(1,t) - \mathrm{MAPK}(0,t)) + k_8\mathrm{MAPKpMAPKPh}(0,t)\\
\mathrm{MAPKMEKpp}'(0,t) &= a_7\mathrm{MAPK}(0,t)\mathrm{MEKpp}(0,t) + (-d_7 - k_7)\mathrm{MAPKMEKpp}(0,t)\\
&\quad + \mathrm{Di}(\mathrm{MAPKMEKpp}(1,t) - \mathrm{MAPKMEKpp}(0,t))\\
\mathrm{MAPKp}'(0,t) &= -a_8\mathrm{MAPKp}(0,t)(-\mathrm{MAPKpMAPKPh}(0,t)\\
&\quad - \mathrm{MAPKppMAPKPh}(0,t) + \mathrm{MAPKPhtot})\\
&\quad - a_9\mathrm{MAPKp}(0,t)\mathrm{MEKpp}(0,t) + d_8\mathrm{MAPKpMAPKPh}(0,t)\\
&\quad + d_9\mathrm{MAPKpMEKpp}(0,t) + \mathrm{Di}(\mathrm{MAPKp}(1,t) - \mathrm{MAPKp}(0,t))\\
&\quad + \mathrm{k\dot{}10}\mathrm{MAPKppMAPKPh}(0,t) + k_7\mathrm{MAPKMEKpp}(0,t)\\
\mathrm{MAPKpMEKpp}'(0,t) &= a_9\mathrm{MAPKp}(0,t)\mathrm{MEKpp}(0,t)\\
&\quad + (-d_9 - k_9)\mathrm{MAPKpMEKpp}(0,t)\\
&\quad + \mathrm{Di}(\mathrm{MAPKpMEKpp}(1,t) - \mathrm{MAPKpMEKpp}(0,t))
\end{aligned}
$$

$$
\begin{aligned}
\mathrm{MAPKpp}'(0,t) &= -\mathrm{a\dot{}10MAPKpp}(0,t)(-\mathrm{MAPKpMAPKPh}(0,t) \\
&\qquad - \mathrm{MAPKppMAPKPh}(0,t) + \mathrm{MAPKPhtot}) \\
&\quad + \mathrm{of}_4(C_5(0,t) + C_8(0,t) + C_9(0,t)) + \mathrm{d\dot{}10MAPKppMAPKPh}(0,t) \\
&\quad + \mathrm{Di}(\mathrm{MAPKpp}(1,t) - \mathrm{MAPKpp}(0,t)) + k_9\mathrm{MAPKpMEKpp}(0,t) \\
\mathrm{MAPKpMAPKPh}'(0,t) &= a_8\mathrm{MAPKp}(0,t)(-\mathrm{MAPKpMAPKPh}(0,t) \\
&\qquad - \mathrm{MAPKppMAPKPh}(0,t) + \mathrm{MAPKPhtot}) \\
&\quad + (-d_8 - k_8)\mathrm{MAPKpMAPKPh}(0,t) \\
&\quad + \mathrm{Di}(\mathrm{MAPKpMAPKPh}(1,t) - \mathrm{MAPKpMAPKPh}(0,t)) \\
\mathrm{MAPKppMAPKPh}'(0,t) &= \mathrm{a\dot{}10MAPKpp}(0,t)(-\mathrm{MAPKpMAPKPh}(0,t) \\
&\qquad - \mathrm{MAPKppMAPKPh}(0,t) + \mathrm{MAPKPhtot}) \\
&\quad - (\mathrm{d\dot{}10} + \mathrm{k\dot{}10})\mathrm{MAPKppMAPKPh}(0,t) \\
&\quad + \mathrm{Di}(\mathrm{MAPKppMAPKPh}(1,t) - \mathrm{MAPKppMAPKPh}(0,t)) \\
C_1'(0,t) &= -C_1(0,t)(\mathrm{on}_2\mathrm{MAPK}(0,t) + \mathrm{on}_1\mathrm{MEK}(0,t)) - p_4(0)C_1(0,t) \\
&\quad + \mathrm{of}_1C_2(0,t) + \mathrm{of}_3C_3(0,t) + \mathrm{of}_2C_4(0,t) + \mathrm{of}_4C_5(0,t) + p_3(0)S_{\mathrm{mem}}(0,t) \\
C_2'(0,t) &= \mathrm{on}_1C_1(0,t)\mathrm{MEK}(0,t) - k_5\mathrm{RAFp}C_2(0,t) \\
&\quad - C_2(0,t)(\mathrm{on}_2\mathrm{MAPK}(0,t) + \mathrm{of}_1) + \mathrm{of}_2C_6(0,t) + \mathrm{of}_4C_9(0,t) \\
C_3'(0,t) &= k_5\mathrm{RAFp}C_2(0,t) - \mathrm{on}_2C_3(0,t)\mathrm{MAPK}(0,t) \\
&\quad - \mathrm{of}_3C_3(0,t) + \mathrm{of}_2C_7(0,t) + \mathrm{of}_4C_8(0,t) \\
C_4'(0,t) &= \mathrm{on}_2C_1(0,t)\mathrm{MAPK}(0,t) - C_4(0,t)(\mathrm{on}_1\mathrm{MEK}(0,t) + \mathrm{of}_2) \\
&\quad + \mathrm{of}_1C_6(0,t) + \mathrm{of}_3C_7(0,t) \\
C_5'(0,t) &= -C_5(0,t)(\mathrm{on}_1\mathrm{MEK}(0,t) + \mathrm{of}_4) + \mathrm{of}_3C_8(0,t) + \mathrm{of}_1C_9(0,t) \\
C_6'(0,t) &= \mathrm{on}_2C_2(0,t)\mathrm{MAPK}(0,t) + \mathrm{on}_1C_4(0,t)\mathrm{MEK}(0,t) \\
&\quad - k_5\mathrm{RAFp}C_6(0,t) + (-\mathrm{of}_1 - \mathrm{of}_2)C_6(0,t) \\
C_7'(0,t) &= \mathrm{on}_2C_3(0,t)\mathrm{MAPK}(0,t) + k_5\mathrm{RAFp}C_6(0,t) \\
&\quad - k_9C_7(0,t) - \mathrm{of}_2C_7(0,t) - \mathrm{of}_3C_7(0,t) \\
C_8'(0,t) &= k_9C_7(0,t) - (\mathrm{of}_3 + \mathrm{of}_4)C_8(0,t) + k_5\mathrm{RAFp}C_9(0,t) \\
C_9'(0,t) &= \mathrm{on}_1C_5(0,t)\mathrm{MEK}(0,t) - k_5\mathrm{RAFp}C_9(0,t) + (-\mathrm{of}_1 - \mathrm{of}_4)C_9(0,t) \\
S_{\mathrm{mem}}'(0,t) &= p_1(0)S_{\mathrm{cyto}}(0,t) - p_2S_{\mathrm{mem}}(0,t) - p_3(0)S_{\mathrm{mem}}(0,t) \\
S_{\mathrm{cyto}}'(1,t) &= p_4(1)C_1(1,t) + \mathrm{Di}(S_{\mathrm{cyto}}(0,t) - S_{\mathrm{cyto}}(1,t)) - p_1(1)S_{\mathrm{cyto}}(1,t) + p_2S_{\mathrm{mem}}(1,t) \\
\mathrm{MEK}'(1,t) &= -a_3\mathrm{RAFpMEK}(1,t) - \mathrm{on}_1\mathrm{MEK}(1,t)(C_1(1,t) + C_4(1,t) + C_5(1,t)) \\
&\quad + \mathrm{of}_1(C_2(1,t) + C_6(1,t) + C_9(1,t)) + d_3\mathrm{MEKRAFp}(1,t) \\
&\quad + \mathrm{Di}(\mathrm{MEK}(0,t) - \mathrm{MEK}(1,t)) + k_4\mathrm{MEKpMEKPh}(1,t) \\
\mathrm{MEKRAFp}'(1,t) &= a_3\mathrm{RAFpMEK}(1,t) + (-d_3 - k_3)\mathrm{MEKRAFp}(1,t) \\
&\quad + \mathrm{Di}(\mathrm{MEKRAFp}(0,t) - \mathrm{MEKRAFp}(1,t)) \\
\mathrm{MEKp}'(1,t) &= -a_4\mathrm{MEKp}(1,t)(-\mathrm{MEKpMEKPh}(1,t) - \mathrm{MEKppMEKPh}(1,t) \\
&\quad + \mathrm{MEKPhtot}) - a_5\mathrm{RAFpMEKp}(1,t) + d_4\mathrm{MEKpMEKPh}(1,t) \\
&\quad + d_5\mathrm{MEKpRAFp}(1,t) + \mathrm{Di}(\mathrm{MEKp}(0,t) - \mathrm{MEKp}(1,t)) \\
&\quad + k_3\mathrm{MEKRAFp}(1,t) + k_6\mathrm{MEKppMEKPh}(1,t)
\end{aligned}
$$

$$\begin{aligned}
\mathrm{MEKpMEKPh}'(1,t) &= a_4\mathrm{MEKp}(1,t)(-\mathrm{MEKpMEKPh}(1,t) - \mathrm{MEKppMEKPh}(1,t)\\
&\quad + \mathrm{MEKPhtot}) + (-d_4 - k_4)\mathrm{MEKpMEKPh}(1,t)\\
&\quad + \mathrm{Di}(\mathrm{MEKpMEKPh}(0,t) - \mathrm{MEKpMEKPh}(1,t))\\
\mathrm{MEKpRAFp}'(1,t) &= a_5\mathrm{RAFpMEKp}(1,t) + (-d_5 - k_5)\mathrm{MEKpRAFp}(1,t)\\
&\quad + \mathrm{Di}(\mathrm{MEKpRAFp}(0,t) - \mathrm{MEKpRAFp}(1,t))\\
\mathrm{MEKpp}'(1,t) &= -a_6\mathrm{MEKpp}(1,t)(-\mathrm{MEKpMEKPh}(1,t) - \mathrm{MEKppMEKPh}(1,t)\\
&\quad + \mathrm{MEKPhtot})\\
&\quad - a_7\mathrm{MAPK}(1,t)\mathrm{MEKpp}(1,t) - a_9\mathrm{MAPKp}(1,t)\mathrm{MEKpp}(1,t)\\
&\quad + \mathrm{of}_3(C_3(1,t) + C_7(1,t) + C_8(1,t)) + d_6\mathrm{MEKppMEKPh}(1,t)\\
&\quad + (d_7 + k_7)\mathrm{MAPKMEKpp}(1,t) + (d_9 + k_9)\mathrm{MAPKpMEKpp}(1,t)\\
&\quad + \mathrm{Di}(\mathrm{MEKpp}(0,t) - \mathrm{MEKpp}(1,t)) + k_5\mathrm{MEKpRAFp}(1,t)\\
\mathrm{MEKppMEKPh}'(1,t) &= a_6\mathrm{MEKpp}(1,t)(-\mathrm{MEKpMEKPh}(1,t) - \mathrm{MEKppMEKPh}(1,t)\\
&\quad + \mathrm{MEKPhtot}) - (d_6 + k_6)\mathrm{MEKppMEKPh}(1,t)\\
&\quad + \mathrm{Di}(\mathrm{MEKppMEKPh}(0,t) - \mathrm{MEKppMEKPh}(1,t))\\
\mathrm{MAPK}'(1,t) &= -a_7\mathrm{MAPK}(1,t)\mathrm{MEKpp}(1,t)\\
&\quad - \mathrm{on}_2\mathrm{MAPK}(1,t)(C_1(1,t) + C_2(1,t) + C_3(1,t))\\
&\quad + \mathrm{of}_2(C_4(1,t) + C_6(1,t) + C_7(1,t)) + d_7\mathrm{MAPKMEKpp}(1,t)\\
&\quad + \mathrm{Di}(\mathrm{MAPK}(0,t) - \mathrm{MAPK}(1,t)) + k_8\mathrm{MAPKpMAPKPh}(1,t)\\
\mathrm{MAPKMEKpp}'(1,t) &= a_7\mathrm{MAPK}(1,t)\mathrm{MEKpp}(1,t) + (-d_7 - k_7)\mathrm{MAPKMEKpp}(1,t)\\
&\quad + \mathrm{Di}(\mathrm{MAPKMEKpp}(0,t) - \mathrm{MAPKMEKpp}(1,t))\\
\mathrm{MAPKp}'(1,t) &= -a_8\mathrm{MAPKp}(1,t)(-\mathrm{MAPKpMAPKPh}(1,t)\\
&\quad - \mathrm{MAPKppMAPKPh}(1,t) + \mathrm{MAPKPhtot})\\
&\quad - a_9\mathrm{MAPKp}(1,t)\mathrm{MEKpp}(1,t) + d_8\mathrm{MAPKpMAPKPh}(1,t)\\
&\quad + d_9\mathrm{MAPKpMEKpp}(1,t) + \mathrm{Di}(\mathrm{MAPKp}(0,t) - \mathrm{MAPKp}(1,t))\\
&\quad + \mathrm{k\dot{}10MAPKppMAPKPh}(1,t) + k_7\mathrm{MAPKMEKpp}(1,t)\\
\mathrm{MAPKpMEKpp}'(1,t) &= a_9\mathrm{MAPKp}(1,t)\mathrm{MEKpp}(1,t)\\
&\quad + (-d_9 - k_9)\mathrm{MAPKpMEKpp}(1,t)\\
&\quad + \mathrm{Di}(\mathrm{MAPKpMEKpp}(0,t) - \mathrm{MAPKpMEKpp}(1,t))\\
\mathrm{MAPKpp}'(1,t) &= -\mathrm{a\dot{}10MAPKpp}(1,t)(-\mathrm{MAPKpMAPKPh}(1,t)\\
&\quad - \mathrm{MAPKppMAPKPh}(1,t) + \mathrm{MAPKPhtot})\\
&\quad + \mathrm{of}_4(C_5(1,t) + C_8(1,t) + C_9(1,t)) + \mathrm{d\dot{}10MAPKppMAPKPh}(1,t)\\
&\quad + \mathrm{Di}(\mathrm{MAPKpp}(0,t) - \mathrm{MAPKpp}(1,t)) + k_9\mathrm{MAPKpMEKpp}(1,t)\\
\mathrm{MAPKpMAPKPh}'(1,t) &= a_8\mathrm{MAPKp}(1,t)(-\mathrm{MAPKpMAPKPh}(1,t)\\
&\quad - \mathrm{MAPKppMAPKPh}(1,t) + \mathrm{MAPKPhtot})\\
&\quad + (-d_8 - k_8)\mathrm{MAPKpMAPKPh}(1,t)\\
&\quad + \mathrm{Di}(\mathrm{MAPKpMAPKPh}(0,t) - \mathrm{MAPKpMAPKPh}(1,t))\\
\mathrm{MAPKppMAPKPh}'(1,t) &= \mathrm{a\dot{}10MAPKpp}(1,t)(-\mathrm{MAPKpMAPKPh}(1,t)\\
&\quad - \mathrm{MAPKppMAPKPh}(1,t) + \mathrm{MAPKPhtot})\\
&\quad - (\mathrm{d\dot{}10} + \mathrm{k\dot{}10})\mathrm{MAPKppMAPKPh}(1,t)\\
&\quad + \mathrm{Di}(\mathrm{MAPKppMAPKPh}(0,t) - \mathrm{MAPKppMAPKPh}(1,t))
\end{aligned}$$

$$
\begin{aligned}
C_1'(1,t) &= -C_1(1,t)(\mathrm{on}_2\mathrm{MAPK}(1,t) + \mathrm{on}_1\mathrm{MEK}(1,t)) - p_4(1)C_1(1,t) \\
&\quad + \mathrm{of}_1 C_2(1,t) + \mathrm{of}_3 C_3(1,t) + \mathrm{of}_2 C_4(1,t) + \mathrm{of}_4 C_5(1,t) + p_3(1)S_{\mathrm{mem}}(1,t) \\
C_2'(1,t) &= \mathrm{on}_1 C_1(1,t)\mathrm{MEK}(1,t) - k_5\mathrm{RAFp}C_2(1,t) \\
&\quad - C_2(1,t)(\mathrm{on}_2\mathrm{MAPK}(1,t) + \mathrm{of}_1) + \mathrm{of}_2 C_6(1,t) + \mathrm{of}_4 C_9(1,t) \\
C_3'(1,t) &= k_5\mathrm{RAFp}C_2(1,t) - \mathrm{on}_2 C_3(1,t)\mathrm{MAPK}(1,t) \\
&\quad - \mathrm{of}_3 C_3(1,t) + \mathrm{of}_2 C_7(1,t) + \mathrm{of}_4 C_8(1,t) \\
C_4'(1,t) &= \mathrm{on}_2 C_1(1,t)\mathrm{MAPK}(1,t) - C_4(1,t)(\mathrm{on}_1\mathrm{MEK}(1,t) + \mathrm{of}_2) \\
&\quad + \mathrm{of}_1 C_6(1,t) + \mathrm{of}_3 C_7(1,t) \\
C_5'(1,t) &= -C_5(1,t)(\mathrm{on}_1\mathrm{MEK}(1,t) + \mathrm{of}_4) + \mathrm{of}_3 C_8(1,t) + \mathrm{of}_1 C_9(1,t) \\
C_6'(1,t) &= \mathrm{on}_2 C_2(1,t)\mathrm{MAPK}(1,t) + \mathrm{on}_1 C_4(1,t)\mathrm{MEK}(1,t) \\
&\quad - k_5\mathrm{RAFp}C_6(1,t) + (-\mathrm{of}_1 - \mathrm{of}_2)C_6(1,t) \\
C_7'(1,t) &= \mathrm{on}_2 C_3(1,t)\mathrm{MAPK}(1,t) + k_5\mathrm{RAFp}C_6(1,t) \\
&\quad - k_9 C_7(1,t) - \mathrm{of}_2 C_7(1,t) - \mathrm{of}_3 C_7(1,t) \\
C_8'(1,t) &= k_9 C_7(1,t) - (\mathrm{of}_3 + \mathrm{of}_4)C_8(1,t) + k_5\mathrm{RAFp}C_9(1,t) \\
C_9'(1,t) &= \mathrm{on}_1 C_5(1,t)\mathrm{MEK}(1,t) - k_5\mathrm{RAFp}C_9(1,t) + (-\mathrm{of}_1 - \mathrm{of}_4)C_9(1,t) \\
S_{\mathrm{mem}}'(1,t) &= p_1(1)S_{\mathrm{cyto}}(1,t) - p_2 S_{\mathrm{mem}}(1,t) - p_3(1)S_{\mathrm{mem}}(1,t)
\end{aligned}
$$