# SUPPLEMENTAL MATERIAL

TABLE I: parameters in G-protein cycle

| parameter | value | References and Notes |
|---|---|---|
| k1 | $0.12nM^{-1}min^{-1}$ | $2 \times 10^6 M^{-1}s^{-1}$ (12) |
| k2 | $0.6min^{-1}$ | 0.01 $s^{-1}$ (12) |
| k3 | $0.24min^{-1}$ | $4 \times 10^{-3}s^{-1}$ (12) |
| k4 | $320nM \cdot min^{-1}$ | fit to the time-course of G protein activation |
| k5 | 7 nM | (12).(See Fig.2A ) |
| k6 | $30nM \cdot min^{-1}$ | $4(molecules/cell)s^{-1}$ (12) |
| k7 | $0.024min^{-1}$ | $4 \times 10^{-4}s^{-1}$ (12) |
| k8 | $0.0048min^{-1}$ | $10^{-5}(molecules/cell)^{-1}s^{-1}$ (12) |
| k9 | $115nM \cdot min^{-1}$ | fit to the time-course of G protein activation |
| k10 | 60 nM | (12)(See Fig.2A), |
| k11 | $20nM \cdot min^{-1}$ | and experimental data that G protein increased from |
| k12 | $0.08min^{-1}$ | 8000 molecules/cell to 12000 molecules/cell (8) |
| k13 | $0.24min^{-1}$ | $4 \times 10^{-3}s^{-1}$ (12) |
| k14 | $0.025nM^{-1}min^{-1}$ | $0.11s^{-1}$ (12) |
| k15 | $480nM^{-1}min^{-1}$ | $1(molecule/cell)^{-1}s^{-1}$(12) |

TABLE II: parameters in recruitment of scaffolds

| parameter | value | References and Notes |
|---|---|---|
| k16 | $0.05nM^{-1}min^{-1}$ | $t_{1/2} = 8.22s$ for Ste5s' recovery |
| k17 | $5min^{-1}$ | at shmoo tips (49) |
| k18 | $0.00007nM^{-1}min^{-1}$ | fit to (24) |
| k19 | $0.001min^{-1}$ | (See Fig.2C. ) |
| k22 | $0.3min^{-1}$ | Ste5 undergoes continuous shuttle without pheromone induction, and yet most are sequestered in the nucleus. Thus, the exportation speed is assumed to be slow. |
| k23 | $30min^{-1}$ | $t_{1/2} = 2s$ for the recovery of ste5 in the nucleus. (49) |

TABLE III: dephosphorylation

| protein | a1 ($nM^{-1}min^{-1}$) | d1 ($min^{-1}$) | p1 ($min^{-1}$) | a2 ($nM^{-1}min^{-1}$) | d2 ($min^{-1}$) | p2 ($min^{-1}$) |
|---|---|---|---|---|---|---|
| Ste11(MAPKKK) | 0.5 | 24 | 10 | 1 | 24 | 10 |
| Ste7(MAPKK) | 0.5 | 24 | 10 | 0.5 | 24 | 10 |
| Fus3(MAPK) | 0.2 | 10 | 30 | 0.4 | 20 | 30 |

TABLE IV: phosphorylation in cytosol

| protein | a3 ($nM^{-1}min^{-1}$) | d3 ($min^{-1}$) | p3 ($min^{-1}$) | a4 ($nM^{-1}min^{-1}$) | d4 ($min^{-1}$) | p4 ($min^{-1}$) |
|---|---|---|---|---|---|---|
| Ste7(MAPKK) | 1 | 36 | 10 | 1 | 36 | 10 |
| Fus3(MAPK) | 0.1 | 36 | 10 | 0.1 | 36 | 10 |

Notes: Equations of reaction in this part are all in the following form: $S + E \underset{d_n}{\overset{a_n}{\rightleftharpoons}} SE \xrightarrow{p_n} S^* + E$.

As for the underset n:
1: dephosphorylation of the once phosphorylated kinase; 2: dephosphorylation of the twice phosphorylated kinase; 3: once phosphorylation; 4: twice phosphorylation. Parameters are estimated in analogy to Ref.11.

TABLE V: Other reactions in the cytosol

| parameter | value | References |
|---|---|---|
| k24 | 1.2 $nM^{-1}min^{-1}$ | Ref.23 |
| k25 | $24min^{-1}$ | Ref.23 |
| k26 | 0.0015 $nM^{-1}min^{-1}$ | Ref.40 |
| k27 | 0.1 $min^{-1}$ | Ref.41 |

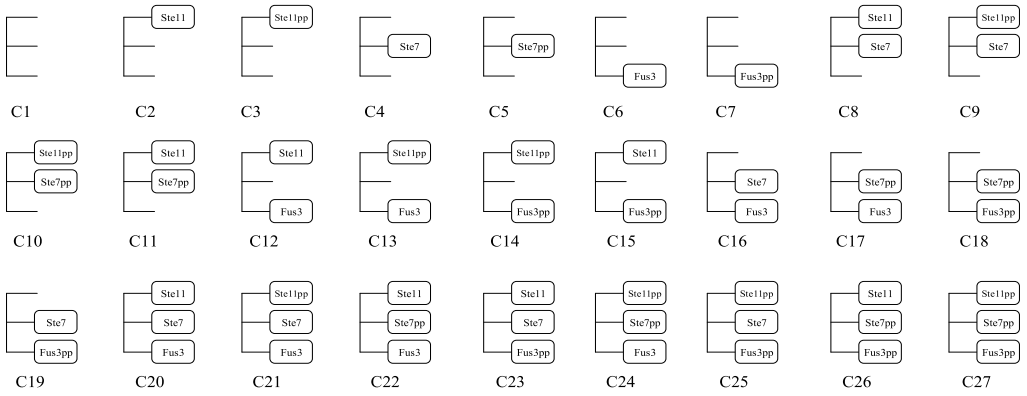


FIG. 1: 27 kinds of scaffold-kinase complexes

| | | |
|---|---|---|
| $C1 + MEKK \rightleftharpoons C2$ | $C1 + MEKK** \rightleftharpoons C3$ | $C1 + MEK \rightleftharpoons C4$ |
| $C1 + MEK** \leftarrow C5$ | $C1 + MAPK \rightleftharpoons C6$ | $C1 + MAPK** \leftarrow C7$ |
| $C2 \rightarrow C3$ | $C2 + MEK \rightleftharpoons C8$ | $C2 + MEK** \leftarrow C11$ |
| $C2 + MAPK \rightleftharpoons C12$ | $C2 + MAPK** \leftarrow C15$ | $C3 + MEK \rightleftharpoons C9$ |
| $C3 + MEK** \leftarrow C10$ | $C3 + MAPK \rightleftharpoons C13$ | $C3 + MAPK** \leftarrow C14$ |
| $C4 + MEKK \rightleftharpoons C8$ | $C4 + MEKK** \rightleftharpoons C9$ | $C4 + MAPK \rightleftharpoons C16$ |
| $C4 + MAPK** \leftarrow C19$ | $C5 + MEKK** \rightleftharpoons C10$ | $C5 + MEKK \rightleftharpoons C11$ |
| $C5 + MAPK \rightleftharpoons C17$ | $C5 + MAPK** \leftarrow C18$ | $C6 + MEKK \rightleftharpoons C12$ |
| $C6 + MEKK** \rightleftharpoons C13$ | $C6 + MEK \rightleftharpoons C16$ | $C6 + MEK** \leftarrow C17$ |
| $C7 + MEKK** \rightleftharpoons C14$ | $C7 + MEKK \rightleftharpoons C15$ | $C7 + MEK** \leftarrow C18$ |
| $C7 + MEK \rightleftharpoons C19$ | $C8 \rightarrow C9$ | $C8 + MAPK \rightleftharpoons C20$ |
| $C8 + MAPK** \leftarrow C23$ | $C9 \rightarrow C10$ | $C9 + MAPK \rightleftharpoons C21$ |
| $C9 + MAPK** \leftarrow C25$ | $C10 \leftarrow C11$ | $C10 + MAPK \rightleftharpoons C24$ |
| $C10 + MAPK** \leftarrow C27$ | $C11 + MAPK \rightleftharpoons C22$ | $C11 + MAPK** \leftarrow C26$ |
| $C12 \leftarrow C13$ | $C12 + MEK \rightleftharpoons C20$ | $C12 + MEK** \leftarrow C22$ |
| $C13 + MEK \rightleftharpoons C21$ | $C13 + MEK** \leftarrow C24$ | $C14 \leftarrow C15$ |
| $C14 + MEK \rightleftharpoons C25$ | $C14 + MEK** \leftarrow C27$ | $C15 + MEK \rightleftharpoons C23$ |
| $C15 + MEK** \leftarrow C26$ | $C16 + MEKK** \rightleftharpoons C21$ | $C16 + MEKK \rightleftharpoons C20$ |
| $C17 \rightarrow C18$ | $C17 + MEKK** \rightleftharpoons C24$ | $C17 + MEKK \rightleftharpoons C22$ |
| $C18 + MEKK** \rightleftharpoons C27$ | $C18 + MEKK \rightleftharpoons C26$ | $C19 + MEKK** \rightleftharpoons C25$ |
| $C19 + MEKK \rightleftharpoons C23$ | $C20 \rightarrow C21$ | $C21 \rightarrow C24$ |
| $C22 \rightarrow C24$ | $C22 \rightarrow C26$ | $C23 \rightarrow C25$ |
| $C24 \rightarrow C27$ | $C25 \rightarrow C27$ | $C26 \rightarrow C27$ |

TABLE VI: parameters in MAPK cascade on scaffold

| Protein | on ($nM^{-1}$ $\min^{-1}$) | off ($min^{-1}$) | **on ($nM^{-1}$ $\min^{-1}$) | **off ($min^{-1}$) | phosphorylation ($min^{-1}$) | References and notes |
|---|---|---|---|---|---|---|
| Ste11 (MAP KKK) | 1.2 | 10 | 1 | 10 | 20 | Ste11pp can rebind to the scafold (27) |
| Ste7 (MAP KK) | 1.2 | 0.1 | - | 0.5; 20 | 46 | Ste7pp in the scaffold undergoes hyperphosphorylation by Fus3pp, which accelerates Ste7's dissociation from the scaffold |
| Fus3 (MAPK) | 1.2 | 10 | - | 200 | 250 | $t_{1/2} = 0.3s$ for the recovery of Fuspp in shmoo tips(10,57) |

TABLE VII: parameters in downstream reactions

| protein | value | References and Notes |
|---|---|---|
| k28 | $6nMmin^{-1}$ | |
| k29 | $40nM$ | |
| k30 | $0.01min^{-1}$ | |
| k31 | $0.5nMmin^{-1}$ | |
| k32 | $10nM$ | |
| k33 | $2nMmin^{-1}$ | |
| k34 | $7nM$ | |
| k35 | $0.002min^{-1}$ | |
| k36 | $8nM^{-1}min^{-1}$ | |
| k37 | $1min^{-1}$ | |
| k38 | $10min^{-1}$ | |
| k39 | $10min^{-1}$ | |
| k40 | $0.1nM^{-1}min^{-1}$ | |
| k41 | $0.01min^{-1}$ | |
| k42 | $0.01nM^{-1}min^{-1}$ | |
| k43 | $0.1min^{-1}$ | |
| k44 | $32nMmin^{-1}$ | fit the time course of Sst2 determined in experiment (8) |
| k45 | $1nM$ | the same as k44 |
| k46 | $0.052min^{-1}$ | the sam as k44 |
| k47 | $10min^{-1}$ | $t_{1/2} = 4s$ for the recovery of Fus3in nucleus (57) |
| k48 | $14min^{-1}$ | $[Fus3_{in}]/[Fus3_{out}] = 1.4$ at $t = 0$ (45) |
| k49 | $8min^{-1}$ | $[Fus3_{in}]/[Fus3_{out}] = 2$ after 60 min treatment of |
| k50 | $15min^{-1}$ | $\alpha$-factor (45) |

TABLE VIII: initial amount of proteins

| Protein | value(nM) | notes and references |
|---|---|---|
| Ste2 | 1000 | 8000 mole/cell (8) |
| Sst2 | 250 | 2000 mole/cell (8) |
| G protein | 1000 | 8000 mole/cell (8) |
| Ste20 | 1000 | |
| Ste11 | 200 | less than 2000 mole/cell(1) |
| Fus3Ste7 | 200 | Total amount of Ste7 should be less than 2000 mole/cell, and about 95% of |
| Ste7 | 10 | Ste7 is in the form of Fus3Ste7 before pheromone induction (1) |
| $Fus3_{in}$ | 700 | about 5000 mole/cell (1), and before pheromone |
| $Fus3_{out}$ | 300 | induction, $[Fus3_{in}]/[Fus3_{out}] = 1.4$ (45) |
| MEKK-P | 100 | |
| MEK-P | 100 | |
| MAPK-Pin | 100 | |
| MAPK-Pout | 100 | |
| Ste5in | 125 | (1) |
| Ste5out | 0.1 | |
| Cdc28 | 100 | |

TABLE IX: mutants

| No. | Mutant | Behavior | Implementation | Reference |
|---|---|---|---|---|
| 1 | $Ste2^{300\triangle}$ (endocytosis of receptor Ste2 is impaired) | G protein activation levels up | k3=0.08 | Ref.12 |
| 2 | treated with cycloheximide(synthesis inhibitor) | G protein cycle is closed down | k31=k32=k44= k4=k9=0 | Ref.12 |
| 3 | SST2$\triangle$ | super-sensitivity upon pheromone induction | k44=0 | Ref.8 |
| 4 | $2 \times SST2$ | response upon pheromone reduces | k44=64, $[Sst2]_{t=0}$=500 nM | Ref.8 |
| 5 | $2 \times G\beta\gamma$ | super-sensitivity to pheromone induction | $[G\beta\gamma]_{t=0} = 1000nM$ | Ref.8 |
| 6 | negative feedbacks are cut down | activation of Fus3pp doesn't attenuate with time | k26=k27=k31= k44=0 | |
| 7 | dissociating speed for hyperphosphorylated Ste7pp is slowed down | activation of Fus3pp doesn't attenuate with time | $**off'_{KK} = 0.5$ | |
| 8 | dissociating speed for normal Ste7pp is enhanced | activation of Fus3pp decreases | $**off_{KK} = 20$ | |
| 9 | shuttle of the scaffold Ste5 is cut down | super-sensitivity to pheromone induction | k22=k23=0 | |
| 10 | Ste11 is continuously activated | Ste7pp is activated while Fus3pp is repressed down | $[Ste11pp]_{t=0} = 100nM$, d[Ste11pp]/dt=0, [$\alpha$-factor]=0 | |
| 11 | Ste7 is continuously activated | Fus3pp isn't activated | $[Ste7pp]_{t=0} = 100nM$, d[Ste7pp]/dt=0, [$\alpha$-factor]=0 | Ref.46 |

***ODE functions***:

$$\frac{d[Ste2]}{dt} = -k1[\alpha - factor][Ste2] + k2[Ste2_{active}] - k7[Ste2] + \frac{k4[Ste12_{active}]^2}{k5^2 + [Ste12_{active}]^2} + k6$$

$$\frac{d[Ste2_{active}]}{dt} = k1[\alpha - factor][Ste2] - k2[Ste2_{active}] - k3[Ste2_{active}]$$

$$\frac{d[Sst2_{active}]}{dt} = \frac{k44[Ste12_{active}]^2}{k45^2 + [Ste12_{active}]^2} - k46[Sst2_{active}]$$

$$\frac{d[G]}{dt} = -k8[Ste2_{active}][G] + k15[G_\alpha d][G_\beta\gamma] + \frac{k9[Ste12_{active}]^2}{k10^2 + [Ste12_{active}]^2} - k12[G] + k11$$

$$\frac{d[G_\alpha t]}{dt} = k8[Ste2_{active}][G] - k13[G_\alpha t] - k14[G_\alpha t][Sst2_{active}]$$

$$\frac{d[G_\alpha d]}{dt} = k13[G_\alpha t] + k14[G_\alpha t][Sst2_{active}] - k15[G_\alpha d][G_\beta\gamma]$$

$$\frac{d[G_\beta\gamma]}{dt} =$$
$$k8[Ste2_{active}][G] - k15[G_\alpha d][G_\beta\gamma] - k40[G_\beta\gamma][Far1pp_{out}] + k41[Far1ppG_\beta\gamma] - k16[Ste5_{out}][G_\beta\gamma] + k17G_\beta\gamma Ste5 - k18[G_\beta\gamma][Ste20] + k19G_\beta\gamma Ste20$$

$$\frac{d[Ste20]}{dt} = -k18[G_\beta\gamma][Ste20] + k19G_\beta\gamma Ste20 - k18[Ste20]G_\beta\gamma Ste5 + k19C1$$

$$\frac{d[MAPK - P_{out}]}{dt} = -a1_K[Fus3p][MAPK - P_{out}] + (d1_K + p1_K)[Fus3pMAPK - P] - a2_K[Fus3pp_{out}][MAPK - P_{out}] + (p2_K +$$
$$d2_K)[Fus3ppMAPK - P] + \frac{k31[Ste12_{active}]^2}{k5^2 + [Ste12_{active}]^2}$$

$$\frac{d[Fus3_{in}]}{dt} = -k47[Fus3_{in}] + k48[Fus3_{out}] + p1_K[Fus3p_{in}MAPK - P]$$

$$\frac{d[Fus3pp_{in}MAPK - P]}{dt} = a2_K[Fus3pp_{in}][MAPK - P_{in}] - d2_K[Fus3pp_{in}MAPK - P] - p2_K[Fus3pp_{in}MAPK - P]$$

$$\frac{d[Ste11]}{dt} = p1_{KKK}[Ste11pMEKK - P] + off_{KKK}(C2 + C8 + C11 + C12 + C15 + C20 + C22 + C23 + C26) - on_{KKK}[Ste11](C4 + C6 + C7 +$$
$$C1 + C16 + C17 + C18 + C19 + C5) - k26[Ste11][Fus3pp]$$

$$\frac{d[Fus3p_{in}MAPK - P]}{dt} = a1_K[Fus3p_{in}][MAPK - P_{in}] - d1_K[Fus3p_{in}MAPK - P] - p1_K[Fus3p_{in}MAPK - P]$$

$$\frac{d[Ste11p]}{dt} = -a1_{KKK}[Ste11p](W1 - [Ste11pMEKK - P] - [Ste11ppMEKK - P]) + d1_{KKK}[Ste11pMEKK - P] + p2_{KKK}[Ste11ppMEKK - P]$$

$$\frac{d[Ste11pMEKK - P]}{dt} = a1_{KKK}[Ste11p](W1 - [Ste11pMEKK - P] - [Ste11ppMEKK - P]) - (d1_{KKK} + p1_{KKK})[Ste11pMEKK - P]$$

$$\frac{d[Fus3p_{in}]}{dt} = p2_K[Fus3pp_{in}MAPK - P] - a1_K[Fus3p_{in}][MAPK - P_{in}] + d1_K[Fus3p_{in}MAPK - P]$$

$$\frac{d[Ste11pp]}{dt} = -a2_{KKK}[Ste11pp](W1 - [Ste11pMEKK - P] - [Ste11ppMEKK - P]) + d2_{KKK}[Ste11ppMEKK - P] - a3_{KK}[Ste11pp][Ste7] +$$
$$(d3_{KK} + p3_{KK})[Ste11ppSte7] - a4_{KK}[Ste11pp][Ste7p] + (d4_{KK} + p4_{KK})[Ste11ppSte7p] + **off_{KKK}(C3 + C10 + C9 + C13 + C14 + C21 +$$
$$C24 + C25 + C27) - **on_{KKK}[Ste11pp](C1 + C4 + C5 + C6 + C7 + C16 + C17 + C18 + C19)$$

$$\frac{d[Ste11ppMEKK - P]}{dt} = a2_{KKK}[Ste11pp](W1 - [Ste11pMEKK - P] - [Ste11ppMEKK - P]) - (d2_{KKK} + p2_{KKK})[Ste11ppMEKK - P]$$

$$\frac{d[Ste7]}{dt} = -a3_{KK}[Ste7][Ste11pp] + d3_{KK}[Ste11ppSte7] + p1_{KK}[Ste7pMEK - P] + off_{KK}(C4 + C8 + C9 + C16 + C19 + C20 + C21 + C23 +$$
$$C25) - on_{KK}[Ste7](C1 + C2 + C3 + C6 + C7 + C12 + C13 + C14 + C15) - k24[Ste7][Fus3_{out}] + k25[Fus3Ste7]$$

$$\frac{d[Ste11ppSte7]}{dt} = a3_{KK}[Ste11pp][Ste7] - (d3_{KK} + p3_{KK})[Ste11ppSte7]$$

$$\frac{d[Ste7p]}{dt} = -a1_{KK}(W2 - [Ste7pMEK - P] - [Ste7ppMEK - P])[Ste7p] + d1_{KK}[Ste7pMEK - P] + p3_{KK}[Ste11ppSte7] -$$
$$a4_{KK}[Ste7p][Ste11pp] + d4_{KK}[Ste11ppSte7p] + p2_{KK}[Ste7ppMEK - P]$$

$$\frac{d[Ste7pMEK - P]}{dt} = a1_{KK}[Ste7p](W2 - [Ste7pMEK - P] - [Ste7ppMEK - P]) - (d1_{KK} + p1_{KK})[Ste7pMEK - P]$$

$$\frac{d[Ste11ppSte7p]}{dt} = a4_{KK}[Ste11pp][Ste7p] - (d4_{KK} + p4_{KK})[Ste11ppSte7p]$$

$$\frac{d[Ste5_{out}]}{dt} = -k16[Ste5_{out}]([G_\beta\gamma] + G_\beta\gamma Ste20) + kl7(C1 + G_\beta\gamma Ste5) + k22[Ste5_{in}] - k23[Ste5_{out}]$$

$$\frac{d[Ste12_{active}]}{dt} = \frac{k28[Fus3pp_{in}]}{k29 + [Fus3pp_{in}]} - k30[Ste12_{active}]$$

$$\frac{d[Far1_{in}]}{dt} = \frac{k33[Ste12_{active}]^2}{k34^2 + [Ste12_{active}]^2} - k36[Far1_{in}][Fus3pp_{in}] - k35[Far1_{in}] + k37[Far1pp_{in}]$$

$$\frac{d[Far1pp_{in}]}{dt} = k36[Far1_{in}][Fus3pp_{in}] - k37[Far1pp_{in}] - k38[Far1pp_{in}] + k39[Far1pp_{out}] - k43[Far1pp_{in}][Cdc28] + k42[Far1ppCdc28]$$

$$\frac{d[Far1ppG_\beta\gamma]}{dt} = k40[G_\beta\gamma][Far1pp_{out}] - k41[Far1ppG_\beta\gamma]$$

$$\frac{d[Cdc28]}{dt} = k42[Far1ppCdc28] - k43[Far1pp_{in}][Cdc28]$$

$$\frac{d[Far1ppCdc28]}{dt} = -k42[Far1ppCdc28] + k43[Far1pp_{in}][Cdc28]$$

$$\frac{d[Ste7pp]}{dt} = -a2_{KK}[Ste7pp](W2 - [Ste7pMEK - P] - [Ste7ppMEK - P]) + d2_{KK}[Ste7ppMEK - P] + p4_{KK}[Ste11ppSte7p] -$$
$$a3_K[Ste7pp][Fus3_{out}] + (d3_K + p3_K)[Ste7ppFus3] - a4_K[Ste7pp][Fus3p] + (d4_K + p4_K)[Ste7ppFus3p] + **off_{KK}(C5 + C10 + C11 + C17 +$$
$$C22 + C24) + **off'_{KK}(C18 + C26 + C27) - k27[Ste7pp]$$

$$\frac{d[Ste7ppMEK - P]}{dt} = a2_{KK}[Ste7pp](W2 - [Ste7pMEK - P] - [Ste7ppMEK - P]) - (d2_{KK} + p2_{KK})[Ste7ppMEK - P]$$

$$\frac{d[Fus3_{out}]}{dt} = -a3_K[Ste7pp][Fus3_{out}] + d3_K[Ste7ppFus3] + p1_K[Fus3pMAPK - P] + off_K(C6 + C12 + C13 + C16 + C17 + C20 + C21 +$$
$$C22 + C24) - on_K[Fus3_{out}](C1 + C2 + C3 + C4 + C5 + C8 + C9 + C10 + C11) - k24[Ste7][Fus3_{out}] + k25[Fus3Ste7] + k47[Fus3_{in}] -$$
$$k48[Fus3_{out}] + \frac{k32[Ste12_{active}]^2}{k5^2 + [Ste12_{active}]^2}$$

$$\frac{d[Ste7ppFus3]}{dt} = a3_K[Ste7pp][Fus3_{out}] - (d3_K + p3_K)[Ste7ppFus3]$$

$$\frac{d[Fus3p]}{dt} =$$
$$-a1_K[Fus3p][MAPK - P_{out}] + d1_K[Fus3pMAPK - P] + p3_K[Ste7ppFus3] - a4_K[Ste7pp][Fus3p] + d4_K[Ste7ppFus3p] + p2_K[Fus3ppMAPK - P]$$

$$\frac{d[Fus3pMAPK - P]}{dt} = a1_K[Fus3p][MAPK - P_{out}] - (d1_K + p1_K)[Fus3pMAPK - P]$$

$$\frac{d[Ste7ppFus3p]}{dt} = a4_K[Ste7pp][Fus3p] - (d4_K + p4_K)[Ste7ppFus3p]$$

$$\frac{d[Fus3pp_{out}]}{dt} = -a2_K[Fus3pp_{out}][MAPK - P_{out}] + d2_K[Fus3ppMAPK - P] + p4_K[Ste7ppFus3p] + **off_K(C7 + C14 + C15 + C18 + C19 + C23 + C25 + C26 + C27) + k49[Fus3pp_{in}] - k50[Fus3pp_{out}]$$

$$\frac{d[Fus3ppMAPK - P]}{dt} = a2_K[Fus3pp_{out}][MAPK - P_{out}] - (d2_K + p2_K)[Fus3ppMAPK - P]$$

$$\frac{dC1}{dt} = -C1(on_{KKK}[Ste11] + **on_{KKK}[Ste11pp] + on_{KK}[Ste7] + on_K[Fus3_{out}]) + off_{KKK}C2 + **off_{KKK}C3 + off_{KK}C4 + **off_{KK}C5 + off_KC6 + **off_KC7 + k18[Ste20][G_\beta\gamma Ste5] - k19C1 + k16[G_\beta\gamma Ste20][Ste5_{out}] - k17C1$$

$$\frac{dC2}{dt} = on_{KKK}C1[Ste11] - off_{KKK}C2 - p_{KKK}C2 - on_{KK}[Ste7]C2 - on_K[Fus3_{out}]C2 + off_{KK}C8 + **off_{KK}C11 + off_KC12 + **off_KC15$$

$$\frac{dC3}{dt} = **on_{KKK}[Ste11pp]C1 + p_{KKK}C2 - on_{KK}[Ste7]C3 - on_K[Fus3_{out}]C3 + off_{KK}C9 + **off_{KK}C10 + off_KC13 + **off_KC14 - **off_{KKK}C3$$

$$\frac{dC4}{dt} = on_{KK}C1[Ste7] - off_{KK}C4 - on_{KKK}[Ste11]C4 - **on_{KKK}C4[Ste11pp] - on_K[Fus3_{out}]C4 + off_{KKK}C8 + **off_{KKK}C9 + off_KC16 + **off_KC19$$

$$\frac{dC5}{dt} = -**on_{KKK}[Ste11pp]C5 - on_{KKK}[Ste11]C5 - on_K[Fus3_{out}]C5 + **off_{KKK}C10 + off_{KKK}C11 + off_KC17 + **off_KC18 - **off_{KK}C5$$

$$\frac{dC6}{dt} = -***on_{KKK}[Ste11pp]C6 + on_KC1[Fus3_{out}] - off_KC6 - on_{KKK}[Ste11]C6 - on_{KK}[Ste7]C6 + off_{KKK}C12 + **off_{KKK}C13 + off_{KK}C16 + **off_{KK}C17$$

$$\frac{dC7}{dt} = -**on_{KKK}[Ste11pp]C7 - on_{KKK}[Ste11]C7 - on_{KK}[Ste7]C7 + **off_{KKK}C14 + off_{KKK}C15 + **off'_{KK}C18 + off_{KK}C19 - **off_KC7$$

$$\frac{dC8}{dt} = -p_{KKK}C8 - on_K[Fus3_{out}]C8 - (off_{KKK} + off_{KK})C8 + on_{KKK}[Ste11]C4 + on_{KK}[Ste7]C2 + off_KC20 + **off_KC23$$

$$\frac{dC9}{dt} = **on_{KKK}C4[Ste11pp] - p_{KK}C9 - (**off_{KKK} + off_{KK})C9 - on_K[Fus3_{out}]C9 + on_{KK}[Ste7]C3 + off_KC21 + **off_KC25 + p_{KKK}C8$$

$$\frac{dC10}{dt} = **on_{KKK}[Ste11pp]C5 - (**off_{KKK} + **off_{KK})C10 - on_K[Fus3_{out}]C10 + off_KC24 + **off_KC27 + p_{KKK}C11 + p_{KK}C9$$

$$\frac{dC11}{dt} = -p_{KKK}C11 - (off_{KKK} + **off_{KK})C11 - on_K[Fus3_{out}]C11 + on_{KKK}[Ste11]C5 + off_KC22 + **off_KC26$$

$$\frac{dC12}{dt} = -p_{KKK}C12 - on_{KK}[Ste7]C12 - (off_{KKK} + off_K)C12 + on_{KKK}[Ste11]C6 + on_K[Fus3_{out}]C2 + off_{KK}C20 + **off_{KK}C22$$

$$\frac{dC13}{dt} = **on_{KKK}[Ste11pp]C6 - (**off_{KKK} + off_K)C13 - on_{KK}[Ste7]C13 + on_K[Fus3_{out}]C3 + off_{KK}C21 + **off_{KK}C24 + p_{KKK}C12$$

$$\frac{dC14}{dt} = **on_{KKK}[Ste11pp]C7 - (**off_{KKK} + **off_K)C14 - on_{KK}[Ste7]C14 + off_{KK}C25 + **off'_{KK}C27 + p_{KKK}C15$$

$$\frac{dC15}{dt} = -p_{KKK}C15 - (off_{KKK} + **off_K)C15 - on_{KK}[Ste7]C15 + on_{KKK}[Ste11]C7 + off_{KK}C23 + **off'_{KK}C26$$

$$\frac{dC16}{dt} = -**on_{KKK}[Ste11pp]C16 - on_{KKK}[Ste11]C16 - (off_{KK} + off_K)C16 + on_{KK}[Ste7]C6 + on_K[Fus3_{out}]C4 + off_{KKK}C20 + **off_{KKK}C21$$

$$\frac{dC17}{dt} = -**on_{KKK}[Ste11pp]C17 - p_KC17 - (**off_{KK} + off_K)C17 - on_{KKK}[Ste11]C17 + on_K[Fus3_{out}]C5 + off_{KKK}C22 + **off_{KKK}C24$$

$$\frac{dC18}{dt} = -***on_{KKK}[Ste11pp]C18 - (**off'_{KK} + **off_K)C18 - on_{KKK}[Ste11]C18 + off_{KKK}C26 + **off_{KKK}C27 + p_KC17$$

$$\frac{dC19}{dt} = -***on_{KKK}[Ste11pp]C19 - (off_{KK} + **off_K)C19 - on_{KKK}[Ste11]C19 + on_{KK}[Ste7]C7 + off_{KKK}C23 + **off_{KKK}C25$$

$$\frac{dC20}{dt} = -(off_{KKK} + off_{KK} + off_K)C20 - (p_{KKK})C20 + on_{KKK}[Ste11]C16 + on_{KK}[Ste7]C12 + on_K[Fus3_{out}]C8$$

$$\frac{dC21}{dt} = **on_{KKK}[Ste11pp]C16 - (**off_{KKK} + off_{KK} + off_K)C21 - (p_{KK})C21 + on_{KK}[Ste7]C13 + on_K[Fus3_{out}]C9 + p_{KKK}C20$$

$$\frac{dC22}{dt} = -(off_{KKK} + **off_{KK} + off_K)C22 - (p_{KKK} + p_K)C22 + on_{KKK}[Ste11]C17 + on_K[Fus3_{out}]C11$$

$$\frac{dC23}{dt} = -(off_{KKK} + off_{KK} + **off_K)C23 - (p_{KKK})C23 + on_{KKK}[Ste11]C19 + on_{KK}[Ste7]C15$$

$$\frac{dC24}{dt} = **on_{KKK}[Ste11pp]C17 - (**off_{KKK} + **off_{KK} + off_K)C24 - p_KC24 + on_K[Fus3_{out}]C10 + p_{KKK}C22 + p_{KK}C21$$

$$\frac{dC25}{dt} = **on_{KKK}[Ste11pp]C19 - (**off_{KKK} + off_{KK} + **off_K)C25 - p_{KK}C25 + on_{KK}[Ste7]C14 + p_{KKK}C23$$

$$\frac{dC26}{dt} = -(off_{KKK} + **off'_{KK} + **off_K)C26 - p_{KKK}C26 + on_{KKK}[Ste11]C18 + p_KC22$$

$$\frac{dC27}{dt} = **on_{KKK}[Ste11pp]C18 - (**off_{KKK} + **off'_{KK} + **off_K)C27 + p_{KKK}C26 + p_{KK}C25 + p_KC24$$

$$\frac{d[Fus3Ste7]}{dt} = k24[Ste7][Fus3_{out}] - k25[Fus3Ste7]$$

$$\frac{d[Ste5_{in}]}{dt} = -k22[Ste5_{in}] + k23[Ste5_{out}]$$

$$\frac{d[Fus3pp_{in}]}{dt} = -k49[Fus3pp_{in}] + k50[Fus3pp_{out}] - a2_K[Fus3pp_{in}][MAPK - P_{in}] + d2_K[Fus3pp_{in}MAPK - P]$$

$$\frac{d[MAPK - P_{in}]}{dt} = -a1_K[Fus3p_{in}][MAPK - P_{in}] + (d1_K + p1_K)[Fus3p_{in}MAPK - P] - a2_K[Fus3pp_{in}][MAPK - P_{in}] + (p2_K + d2_K)[Fus3pp_{in}MAPK - P] + \frac{k31[Ste12_{active}]^2}{k5^2 + [Ste12_{active}]^2}$$

$$\frac{d[Far1pp_{out}]}{dt} = -k40[Far1pp_{out}][G_\beta\gamma] + k41[Far1ppG_\beta\gamma] + k38[Far1pp_{in}] - k39[Far1pp_{out}]$$

$$\frac{d[G_\beta\gamma Ste5]}{dt} = k16[G_\beta\gamma][Ste5_{out}] - k17[G_\beta\gamma Ste5] - k18[G_\beta\gamma Ste5][Ste20] + k19[C1]$$

$$\frac{d[G_\beta\gamma Ste20]}{dt} = -k16[G_\beta\gamma Ste20][Ste5_{out}] + k17[C1] + k18[G_\beta\gamma][Ste20] - k19[G_\beta\gamma Ste20]$$