**Figure S1 – The Flow Chart of the Crosstalk Model of IFN-gamma and IL-6 Signalling**

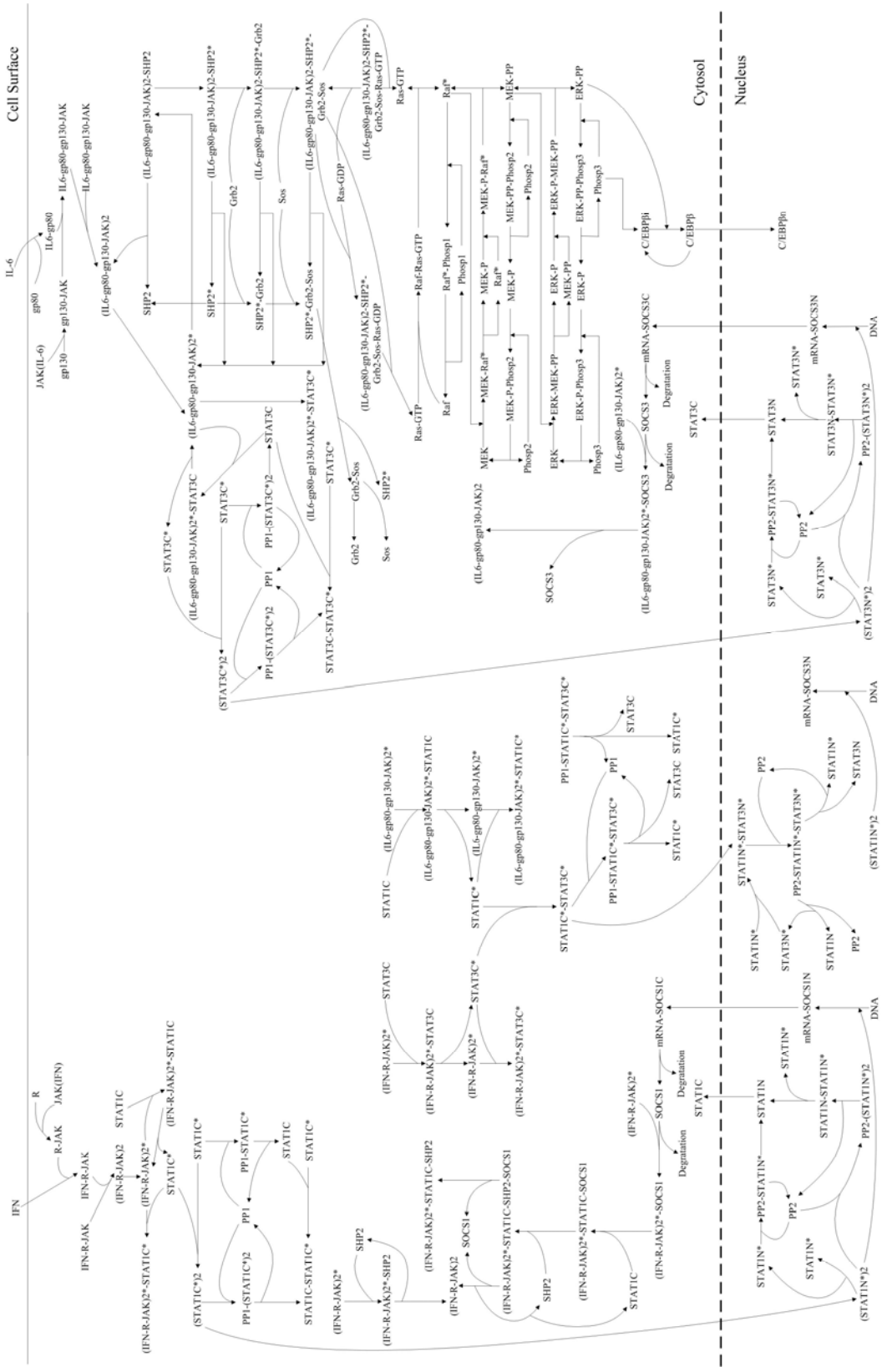

**Table S1. Parameters of new adding reactions**

| Parameter | Value | Description | Reference |
|---|---|---|---|
| n_kf1 | 0.001 | STAT3 binding at IFNR sites | Estimated |
| n_kr1 | 7.999422 | STAT3 dissociation from IFNR sites | Estimated |
| n_k2 | 3.999995 | STAT3 activation rate at IFNR sites | Estimated |
| n_kf3 | 0.00051 | STAT3C* binding at IFNR sites | Estimated |
| n_kr3 | 4.982769 | STAT3C* dissociation from IFNR sites | Estimated |
| n_kf4 | 0.002 | STAT1 binding at gp130 sites | Estimated |
| n_kr4 | 7.994572 | STAT1 dissociation from gp130 sites | Estimated |
| n_k5 | 3.999987 | STAT1 activation rate at gp130 sites | Estimated |
| n_kf6 | 0.000501 | STAT1C* binding at gp130 sites | Estimated |
| n_kr6 | 4.992048 | STAT1C* dissociation from gp130 sites | Estimated |
| n_kf7 | 0.001 | Max rate of (STAT1N*)2 inducing mRNA-SOCS3 | Estimated |
| n_kr7 | 400 | Km of (STAT1N*)2 inducing mRNA -SOCS3 | [1] |
| n_kf8 | 0.02 | STAT1/3 dimers formation in cytosol | [1-2] |
| n_kr8 | 0.1 | STAT1/3 dimers dissociation in cytosol | [1-2] |
| n_kf9 | 0.02 | STAT1/3 dimers formation in nucleus | [2] |
| n_kr9 | 0.1 | STAT1/3 dimers dissociation in nucleus | [2] |
| n_k10 | 0.005 | STAT1/3 dimers nuclear import | [1-2] |
| n_kf11 | 0.001 | PP1 combination with STAT1/3 dimers | [1-2] |
| n_kr11 | 0.2 | PP1 dissociation from STAT1/3 dimers | [1-2] |
| n_kf12 | 0.001 | PP2 combination with STAT1/3 dimers | [1-2] |
| n_kr12 | 0.2 | PP2 dissociation from STAT1/3 dimers | [1-2] |
| n_k13 | 0.0015 | STAT1 inactivation by PP1 within STAT1/3 dimers | Estimated |
| n_k14 | 0.0015 | STAT3 inactivation by PP1 within STAT1/3 dimers | Estimated |
| n_k15 | 0.0025 | STAT1 inactivation by PP2 within STAT1/3 dimers | Estimated |
| n_k16 | 0.0025 | STAT3 inactivation by PP2 within STAT1/3 dimers | Estimated |

First order rate constants are in units of $s^{-1}$ and second order rate constants are expressed in $nM^{-1}s^{-1}$. Michaelis constants are in nM.

**TableS2. Parameters of the IFNγ signalling part of the crosstalk model**

| Parameter | Value | Description | Reference |
|---|---|---|---|
| kf1 | 0.1 | IFNR combination with JAK | [1] |

| | | | |
|---|---|---|---|
| kb1 | 0.05 | IFNR dissociation from JAK | [1] |
| kf2 | 0.02 | IFN combination with R-JAK | [1] |
| kb2 | 0.02 | IFN dissociation from R-JAK | [1] |
| kf3 | 0.04 | (IFN-R-JAK)2 complex dimerization | [1] |
| kb3 | 0.2 | (IFN-R-JAK)2 complex dissociation | [1] |
| kf4 | 0.005 | (IFN-R-JAK)2 complex activation | [1] |
| kf5 | 0.008 | STAT1 binding at IFNR sites | [1] |
| kb5 | 0.8 | STAT1 dissociation from IFNR sites | [1] |
| kf6 | 0.4 | STAT1 activation rate at IFNR sites | [1] |
| kf7 | 0.005 | STAT1C* binding at IFNR sites | [1] |
| kb7 | 0.5 | STAT1C* dissociation from IFNR sites | [1] |
| kf8 | 0.02 | STAT1 homodimers formation in cytosol | [1] |
| kb8 | 0.1 | STAT1 homodimers dissociation in cytosol | [1] |
| kf9 | 0.001 | SHP2 binding at (IFN-R-JAK)2* complex | [1] |
| kb9 | 0.2 | SHP2 dissociation from (IFN-R-JAK)2* complex | [1] |
| kf10 | 0.003 | (IFN-R-JAK)2* complex inactivation of by SHP2 | [1] |
| kf11 | 0.001 | PP1 combination with STAT1C* | [1] |
| kb11 | 0.2 | PP1 dissociation from STAT1C* | [1] |
| kf12 | 0.003 | STAT1 inactivation by PP1 | [1] |
| kf13 | 2.00E-07 | STAT1C combination with STAT1C* | [1] |
| kb13 | 0.2 | STAT1C dissociation from STAT1C* | [1] |
| kf14 | 0.005 | STAT1 homodimers nuclear import | [1] |
| kf15 | 0.001 | PP2 combination with STAT1N* | [1] |
| kb15 | 0.2 | PP2 dissociation from STAT1N* | [1] |
| kf16 | 0.005 | STAT1 inactivation by PP2 | [1] |
| kf17 | 0.05 | STAT1 nuclear export | [1] |
| k18a | 0.01 | Max rate of (STAT1N*)2 inducing mRNA-SOCS1 | [1] |
| k18b | 400 | Km of (STAT1N*)2 inducing mRNA -SOCS1 | [1] |
| kf19 | 0.001 | mRNA of SOCS1 nuclear export | [1] |
| kf20 | 0.01 | Translation of SOCS1 | [1] |
| kf21 | 0.02 | SOCS1 binding at (IFN-R-JAK)2* complex | [1] |
| kb21 | 0.1 | SOCS1 dissociation from (IFN-R-JAK)2* complex | [1] |
| kf22 | 0.0005 | mRNA of SOCS1 degrading rate | [1] |
| kf23 | 0.0005 | SOCS1 degrading rate | [1] |
| kf24 | 0.001 | PP1 combination with (STAT1C*)2 | [1] |
| kb24 | 0.2 | PP1 dissociation from (STAT1C*)2 | [1] |
| kf25 | 0.003 | STAT1 inactivation by PP1 within (STAT1C*)2 | [1] |
| kf26 | 0.005 | STAT1 homodimers formation in nuclear | [1] |

| | | | |
|---|---|---|---|
| kb26 | 0.5 | STAT1 homodimers dissociation in nuclear | [1] |
| kf27 | 0.001 | PP2 combination with (STAT1N*)2 | [1] |
| kb27 | 0.2 | PP2 dissociation from (STAT1N*)2 | [1] |
| kf28 | 0.005 | STAT1 deactivation by PP2 within (STAT1N*)2 | [1] |
| kf29 | 2.00E-07 | STAT1N combination with STAT1N* | [1] |
| kb29 | 0.2 | STAT1N dissociation from STAT1N* | [1] |
| kf30 | 0.008 | STAT1C binding at (IFN-R-JAK)2*-SOCS1 complex | [1] |
| kb30 | 0.8 | STAT1C dissociation from (IFN-R-JAK)2*-SOCS1 complex | [1] |
| kf31 | 0.001 | SHP2 binding at (IFN-R-JAK)2*-STAT1C-SOCS1 complex | [1] |
| kb31 | 0.2 | SHP2 dissociation from (IFN-R-JAK)2*-STAT1C-SOCS1 complex | [1] |
| kf32 | 0.003 | (IFN-R-JAK)2*-STAT1C-SHP2-SOCS1 complex dissociation | [1] |
| kf33 | 0.0005 | SOCS1 dissociation from (IFN-R-JAK)2*-STAT1C-SHP2-SOCS1 complex | [1] |

First order rate constants are in units of $s^{-1}$ and second order rate constants are expressed in $nM^{-1}s^{-1}$. Michaelis constants are in nM.

**Table S3. Parameters of the IL-6 signalling part of the crosstalk model**

| Parameter | Value | Description | Reference |
|---|---|---|---|
| k1f | 0.1 | IL6 combination with gp80 | [2] |
| k1r | 0.05 | IL6 dissociation from gp80 | [2] |
| k2f | 0.1 | gp130 combination with JAK | [2] |
| k2r | 0.05 | gp130 dissociation from JAK | [2] |
| k3f | 0.02 | IL6-gp80-gp130-JAK formation | [2] |
| k3r | 0.02 | IL6-gp80-gp130-JAK dissociation | [2] |
| k6f | 0.04 | (IL6-gp80-gp130-JAK)2 complex dimerization | [2] |
| k6r | 0.2 | (IL6-gp80-gp130-JAK)2 complex dissociation | [2] |
| k7 | 0.005 | (IL6-gp80-gp130-JAK)2 complex activation | [2] |
| k8f | 0.008 | STAT3 binding at gp130 sites | [2] |
| k8r | 0.8 | STAT3 dissociation from gp130 sites | [2] |
| k9 | 0.4 | STAT3 activation rate at gp130 sites | [2] |
| k10f | 0.005 | STAT3C* binding at gp130 sites | [2] |
| k10r | 0.5 | STAT3C* dissociation from gp130 sites | [2] |
| k16f | 0.02 | STAT3 homodimers formation in cytosol | [2] |
| k16r | 0.1 | STAT3 homodimers dissociation in cytosol | [2] |

| | | | |
|---|---|---|---|
| k17f | 0.001 | SHP2 binding at (IL6-gp80-gp130-JAK)2* complex | [2] |
| k17r | 0.2 | SHP2 dissociation from (IL6-gp80-gp130-JAK)2* complex | [2] |
| k18 | 0.003 | (IL6-gp80-gp130-JAK)2* complex inactivation of by SHP2 | [2] |
| k19f | 0.001 | PP1 combination with STAT3C* | [2] |
| k19r | 0.2 | PP1 dissociation from STAT3C* | [2] |
| k20 | 0.003 | STAT3 inactivation by PP1 | [2] |
| k21f | 0.001 | PP1 combination with (STAT3C*)2 | [2] |
| k21r | 0.2 | PP1 dissociation from (STAT3C*)2 | [2] |
| k22 | 0.003 | STAT3 inactivation by PP1 within (STAT3C*)2 | [2] |
| k23f | 2.00E-07 | STAT3C combination with STAT3C* | [2] |
| k23r | 0.2 | STAT3C dissociation from STAT3C* | [2] |
| k24 | 0.005 | STAT3 homodimers nuclear import | [2] |
| k25f | 0.1 | STAT1 homodimers dissociation in nuclear | [2] |
| k25r | 0.02 | STAT1 homodimers formation in nuclear | [2] |
| k26f | 0.001 | PP1 combination with STAT3C* | [2] |
| k26r | 0.2 | PP1 dissociation from STAT3C* | [2] |
| k27 | 0.005 | STAT1 inactivation by PP1 | [2] |
| k28f | 0.001 | PP1 combination with (STAT3C*)2 | [2] |
| k28r | 0.2 | PP1 dissociation from (STAT3C*)2 | [2] |
| k29 | 0.005 | STAT3 inactivation by PP1 within (STAT3C*)2 | [2] |
| k30f | 0.2 | STAT3N dissociation from STAT3N* | [2] |
| k30r | 2.00E-07 | STAT3N combination with STAT3N* | [2] |
| k31 | 0.05 | STAT3 nuclear export | [2] |
| k32f | 0.01 | Max rate of (STAT3N*)2 inducing mRNA of SOCS3 | [2] |
| k32r | 400 | Km of (STAT3N*)2 inducing mRNA of SOCS3 | [2] |
| k33 | 0.001 | mRNA of SOCS3 nuclear export | [2] |
| k34 | 0.01 | Translation of SOCS3 | [2] |
| k35f | 5 | SOCS3 binding at (IL6-gp80-gp130-JAK)2* complex | [2] |
| k35r | 0.1 | SOCS3 dissociation from (IL6-gp80-gp130-JAK)2* complex | [2] |
| k36 | 0.0005 | mRNA of SOCS3 degrading rate | [2] |
| k37 | 0.0006 | SOCS3 degrading rate | [2] |
| k38 | 0.003 | (IL6-gp80-gp130-JAK)2* complex inactivation of by SHP2 | [2] |
| k39f | 6 | SHP2 activation within | [2] |

| | | | |
|---|---|---|---|
| | | (IL6-gp80-gp130-JAK)2*-SHP2 complex | |
| k39r | 0.06 | SHP2 deactivation within (IL6-gp80-gp130-JAK)2*-SHP2 complex | [2] |
| k40f | 0.01 | Grb2 binding at (IL6-gp80-gp130-JAK)2*-SHP2* complex | [2] |
| k40r | 0.55 | Grb2 dissociation from (IL6-gp80-gp130-JAK)2*-SHP2 complex | [2] |
| k41f | 0.01 | SOS binding at (IL6-gp80-gp130-JAK)2*-SHP2*-Grb2 complex | [2] |
| k41r | 0.0214 | SOS dissociation from (IL6-gp80-gp130-JAK)2*-SHP2-Grb2 complex | [2] |
| k42f | 0.015 | Ras-GDP binding at (IL6-gp80-gp130-JAK)2*-SHP2*-Grb2-SOS complex | [2] |
| k42r | 1.3 | Ras-GDP dissociation from (IL6-gp80-gp130-JAK)2*-SHP2-Grb2-SOS complex | [2] |
| k43f | 0.5 | Ras-GDP activation by (IL6-gp80-gp130-JAK)2*-SHP2*-Grb2-SOS complex | [2] |
| k43r | 0.0001 | Ras-GTP deactivation by (IL6-gp80-gp130-JAK)2*-SHP2*-Grb2-SOS complex | [2] |
| k44f | 0.001 | Raf combination with Ras-GTP | [2] |
| k44r | 0.0053 | Raf dissociation from Ras-GTP | [2] |
| k45f | 1 | Raf activation by Ras-GTP | [2] |
| k45r | 0.0007 | Raf* deactivation by Ras-GTP | [2] |
| k46f | 0.0079 | Ras-GTP* binding at (IL6-gp80-gp130-JAK)2*-SHP2*-Grb2-SOS complex | [2] |
| k46r | 0.4 | Ras-GTP* dissociation from (IL6-gp80-gp130-JAK)2*-SHP2*-Grb2-SOS complex | [2] |
| k47f | 0.023 | (IL6-gp80-gp130-JAK)2*-SHP2*-Grb2-SOS-Ras-GTP complex dissociation | [2] |
| k47r | 0.00022 | (IL6-gp80-gp130-JAK)2*-SHP2*-Grb2-SOS-Ras-GTP complex formation | [2] |
| k48f | 0.47 | SHP2*-Grb2-SOS binding at (IL6-gp80-gp130-JAK)2* complex | [2] |
| k48r | 0.000245 | SHP2*-Grb2-SOS dissociation from (IL6-gp80-gp130-JAK)2* complex | [2] |
| k49f | 0.3 | SHP2* dissociation from Grb2-SOS | [2] |

| | | | |
|---|---|---|---|
| k49r | 0.021 | SHP2* binding to Grb2-SOS | [2] |
| k50f | 0.0015 | Grb2-SOS complex dissociation | [2] |
| k50r | 0.0045 | Grb2-SOS complex formation | [2] |
| k51f | 1.7 | Max rate of SHP2* deactivation | [2] |
| k51r | 340 | Km of SHP2* deactivation | [2] |
| k52f | 0.3 | SHP2* dissociation from (IL6-gp80-gp130-JAK)2* complex | [2] |
| k52r | 0.0009 | SHP2* binding to (IL6-gp80-gp130-JAK)2* complex | [2] |
| k53f | 0.01 | SHP2* binding to Grb2 | [2] |
| k53r | 0.55 | SHP2* dissociation from Grb2 | [2] |
| k54f | 0.3 | SHP2*-Grb2 dissociation from (IL6-gp80-gp130-JAK)2* complex | [2] |
| k54r | 0.0009 | SHP2*-Grb2 binding to (IL6-gp80-gp130-JAK)2* complex | [2] |
| k55f | 0.03 | SOS dissociation from SHP2*-Grb2 complex | [2] |
| k55r | 0.064 | SOS binding to SHP2*-Grb2 complex | [2] |
| k56f | 0.03 | Grb2-SOS binding to (IL6-gp80-gp130-JAK)2*-SHP2 complex | [2] |
| k56r | 0.0429 | Grb2-SOS dissociation from (IL6-gp80-gp130-JAK)2*-SHP2 complex | [2] |
| k57f | 0.0717 | Raf* combination with Phosp1 | [2] |
| k57r | 0.2 | Raf* dissociation from Phosp1 | [2] |
| k58 | 1 | Raf deactivation by Phosp1 | [2] |
| k59f | 0.011 | MEK combination with Raf* | [2] |
| k59r | 0.001833 | MEK dissociation from Raf* | [2] |
| k60 | 3.5 | MEK activation by Raf* | [2] |
| k61f | 0.011 | MEK-P combination with Raf* | [2] |
| k61r | 0.001833 | MEK-P dissociation from Raf* | [2] |
| k62 | 2.9 | MEK-P activation by Raf* | [2] |
| k63f | 0.0143 | MEK-PP combination with Phosp2 | [2] |
| k63r | 0.8 | MEK-PP dissociation from Phosp2 | [2] |
| k64 | 0.058 | MEK-PP deactivation by Phosp2 | [2] |
| k65f | 0.00025 | MEK-P combination with Phosp2 | [2] |
| k65r | 0.5 | MEK-P dissociation from Phosp2 | [2] |
| k66 | 0.058 | MEK-P deactivation by Phosp2 | [2] |
| k67f | 0.00011 | ERK combination with MEK-PP | [2] |
| k67r | 0.033 | ERK dissociation from MEK-PP | [2] |
| k68 | 16 | ERK activation by MEK-PP | [2] |
| k69f | 0.00011 | ERK-P combination with MEK-PP | [2] |
| k69r | 0.033 | ERK-P dissociation from MEK-PP | [2] |
| k70 | 6.7 | ERK-P activation by MEK-PP | [2] |
| k71f | 0.014 | ERK-PP combination with Phosp3 | [2] |

| | | | |
|---|---|---|---|
| k71r | 0.6 | ERK-PP dissociation from Phosp3 | [2] |
| k72 | 0.27 | ERK-PP deactivation by Phosp3 | [2] |
| k73f | 0.005 | ERK-P combination with Phosp3 | [2] |
| k73r | 0.5 | ERK-P dissociation from Phosp3 | [2] |
| k74 | 0.3 | ERK-P deactivation by Phosp3 | [2] |
| k75f | 0.2335 | Max rate of CEBPi activation by ERK-PP | [2] |
| k75r | 20000 | Km of CEBPi activation by ERK-PP | [2] |
| k76 | 0.0388 | CEBP deactivation | [2] |
| k77f | 0.9854 | CEBPn formation | [2] |
| k77r | 0.0009 | CEBPn dissociation | [2] |

First order rate constants are in units of $s^{-1}$ and second order rate constants are expressed in $nM^{-1}s^{-1}$. Michaelis constants are in nM.

**Table S4. State variables of the crosstalk model and their initial values**

| Species | Initial values (nM） |
|---|---|
| gp80 | 8 |
| IL6-gp80 | 0 |
| gp130 | 0.8 |
| JAK(IL-6) | 12 |
| gp130-JAK | 0 |
| IL6-gp80-gp130-JAK | 0 |
| (IL6-gp80-gp130-JAK)2 | 0 |
| (IL6-gp80-gp130-JAK)2* | 0 |
| STAT3C | 1000 |
| (IL6-gp80-gp130-JAK)2*-STAT3C | 0 |
| STAT3C* | 0 |
| (IL6-gp80-gp130-JAK)2*-STAT3C* | 0 |
| (STAT3C*)2 | 0 |
| SHP2 | 100 |
| (IL6-gp80-gp130-JAK)2*-SHP2 | 0 |
| PP1 | 50 |
| PP1-STAT3C* | 0 |
| PP1-(STAT3C*)2 | 0 |
| STAT3C-STAT3C* | 0 |
| (STAT3N*)2 | 0 |
| STAT3N* | 0 |
| PP2 | 60 |
| PP2-STAT3N* | 0 |
| STAT3N | 0 |
| PP2-(STAT3N*)2 | 0 |

| | |
|---|---|
| STAT3N-STAT3N* | 0 |
| mRNA-SOCS3N | 0 |
| mRNA-SOCS3C | 0 |
| SOCS3 | 0 |
| (IL6-gp80-gp130-JAK)2*-SOCS3 | 0 |
| (IL6-gp80-gp130-JAK)2*-SPH2* | 0 |
| Grb2 | 85 |
| (IL6-gp80-gp130-JAK)2*-SPH2*-Grb2 | 0 |
| SOS | 34 |
| (IL6-gp80-gp130-JAK)2*-SPH2*-Grb2-SOS | 0 |
| Ras-GDP | 19000 |
| (IL6-gp80-gp130-JAK)2*-SPH2*-Grb2-SOS-Ras-GDP | 0 |
| Ras-GTP | 0 |
| Raf | 67 |
| Raf-Ras-GTP | 0 |
| Raf* | 0 |
| Ras-GTP* | 0 |
| (IL6-gp80-gp130-JAK)2*-SPH2*-Grb2-SOS-Ras-GTP | 0 |
| SHP2-Grb2-SOS | 0 |
| Grb2-SOS | 0 |
| SHP2* | 0 |
| SHP2*-Grb2 | 0 |
| Phosp1 | 0 |
| Raf*-Phosp1 | 0 |
| MEK | 41667 |
| MEK-Raf* | 0 |
| MEK-P | 0 |
| MEK-P-Raf* | 0 |
| MEK-PP | 0 |
| Phosp2 | 67 |
| MEK-PP-Phosp2 | 0 |
| MEK-P-Phosp2 | 0 |
| ERK | 35000 |
| ERK-MEK-PP | 0 |
| ERK-P | 0 |
| ERK-P-MEK-PP | 0 |
| ERK-PP | 0 |
| Phosp3 | 16667 |
| ERK-PP-Phosp3 | 0 |
| ERK-P-Phosp3 | 0 |
| CEBPi | 40493 |
| CEBP | 0 |

| | |
|---|---|
| CEBPn | 0 |
| IL-6 | 0.1 |
| IFN | 0.1 |
| R: receptor for IFN | 12 |
| JAK(IFN) | 12 |
| R-JAK | 0 |
| IFN-R-JAK | 0 |
| (IFN-R-JAK)2 | 0 |
| (IFN-R-JAK)2* | 0 |
| STAT1C | 1000 |
| (IFN-R-JAK)2*-STAT1C | 0 |
| STAT1C* | 0 |
| (IFN-R-JAK)2*-STAT1C* | 0 |
| (STAT1C*)2 | 0 |
| PP1-STAT1C* | 0 |
| PP1-(STAT1C*)2 | 0 |
| STAT1C-STAT1C* | 0 |
| (STAT1N*)2 | 0 |
| STAT1N* | 0 |
| PP2-STAT1N* | 0 |
| STAT1N | 0 |
| PP2-(STAT1N*)2 | 0 |
| STAT1N-STAT1N* | 0 |
| mRNA-SOCS1N | 0 |
| mRNA-SOCS1C | 0 |
| SOCS1 | 0 |
| (IFN-R-JAK)2*-SOCS1 | 0 |
| (IFN-R-JAK)2*-SHP2 | 0 |
| (IFN-R-JAK)2*-STAT1C-SOCS1 | 0 |
| (IFN-R-JAK)2*-STAT1C-SHP2-SOCS1 | 0 |
| (IFN-R-JAK)2*-STAT1C-SHP2 | 0 |
| (IL6-gp80-gp130-JAK)2*-STAT1C | 0 |
| (IL6-gp80-gp130-JAK)2*-STAT1C* | 0 |
| (IFN-R-JAK)2*-STAT3C | 0 |
| (IFN-R-JAK)2*-STAT3C* | 0 |
| STAT1C*-STAT3C* | 0 |
| STAT1N*-STAT3N* | 0 |
| PP1-STAT1C*-STAT3C* | 0 |
| PP2-STAT1N*-STAT3N* | 0 |
| STAT1* | 0 |
| STAT3* | 0 |

**Table S5. Re-estimated parameters of the non-competitive model**

| Parameter | Value | Description | Reference |
|---|---|---|---|
| n_kf1 | 0.002 | STAT3 binding at IFNR sites | Estimated |
| n_kr1 | 2 | STAT3 dissociation from IFNR sites | Estimated |
| n_k2 | 0.2 | STAT3 activation rate at IFNR sites | Estimated |
| n_kf3 | 0.005 | STAT3C* binding at IFNR sites | Estimated |
| n_kr3 | 0.5 | STAT3C* dissociation from IFNR sites | Estimated |
| n_kf4 | 0.002 | STAT1 binding at gp130 sites | Estimated |
| n_kr4 | 2 | STAT1 dissociation from gp130 sites | Estimated |
| n_k5 | 0.2 | STAT1 activation rate at gp130 sites | Estimated |
| n_kf6 | 0.005 | STAT1C* binding at gp130 sites | Estimated |
| n_kr6 | 0.5 | STAT1C* dissociation from gp130 sites | Estimated |
| n_kf17 | 0.008 | STAT1 binding at IFNR sites | [1] |
| n_kr17 | 0.8 | STAT1 dissociation from IFNR sites | [1] |
| n_kf18 | 0.002 | STAT3 binding at IFNR sites | Estimated |
| n_kr18 | 2 | STAT3 dissociation from IFNR sites | Estimated |
| n_kf19 | 0.002 | STAT1 binding at gp130 sites | Estimated |
| n_kr19 | 2 | STAT1 dissociation from gp130 sites | Estimated |
| n_kf20 | 0.008 | STAT3 binding at gp130 sites | [2] |
| n_kr20 | 0.8 | STAT3 dissociation from gp130 sites | [2] |
| n_k21 | 0.4 | STAT1 activation rate at IFNR sites | [1] |
| n_k22 | 0.2 | STAT3 activation rate at IFNR sites | Estimated |
| n_k23 | 0.2 | STAT1 activation rate at gp130 sites | Estimated |
| n_k24 | 0.4 | STAT3 activation rate at gp130 sites | [2] |

First order rate constants are in units of $s^{-1}$ and second order rate constants are expressed in $nM^{-1}s^{-1}$. Michaelis constants are in nM.

**Table S6. Results of sensitivity analysis with respect to variations in the concentrations of pathway components for the competition model**

| Parameter | IFN | IL-6 |
|---|---|---|
| PP2 | -1.10702 | -1.538 |
| PP1 | -0.05275 | -0.07177 |
| SHP2 | -0.52562 | -0.5025 |
| STAT3C | 0.000918 | 1.18097 |
| STAT1C | 0.499321 | 0.103269 |
| R | 0.529619 | 0 |
| gp80 | 0 | 0.121868 |
| gp130 | 0 | 0.055231 |
| JAK(IFN) | 0.529618 | 0 |

| | | |
|---|---|---|
| JAK(IL-6) | 0 | 1.67086 |
| IL-6 | 1.08949 | 0 |
| IFN | 0 | 0.121868 |

The definition of the parameter sensitivity can refer to the "Methods" section in the main text. The positive (or negative) sensitivity values indicate consistent (or opposite) percentage changes in output to the perturbation in the parameter compared to the nominal solution.

**Table S7. Results of sensitivity analysis with respect to variations in the kinetic parameter for the competition model**

| Parameter | IFN | IL-6 | Description |
|---|---|---|---|
| k1f | 0 | 0.121868 | IL6 combination with gp80 |
| k1r | 0 | -0.191126 | IL6 dissociation from gp80 |
| k2f | 0 | 0.0552303 | gp130 combination with JAK |
| k2r | 0 | -0.072901 | gp130 dissociation from JAK |
| k3f | 0 | 0.146778 | IL6-gp80-gp130-JAK formation |
| k3r | 0 | -0.195713 | IL6-gp80-gp130-JAK dissociation |
| k6f | 0 | 0.15858 | (IL6-gp80-gp130-JAK)2 complex dimerization |
| k6r | 1.58E-07 | -0.172858 | (IL6-gp80-gp130-JAK)2 complex dissociation |
| k7 | 1.82E-07 | 0.24868 | (IL6-gp80-gp130-JAK)2 complex activation |
| k8f | 1.36E-07 | 0.765515 | STAT3 binding at gp130 sites |
| k8r | -4.14E-07 | -0.442549 | STAT3 dissociation from gp130 sites |
| k9 | -9.52E-10 | 0.529317 | STAT3 activation rate at gp130 sites |
| k10f | -2.10E-06 | -0.0021417 | STAT3C* binding at gp130 sites |
| k10r | 1.57E-07 | 0.00166223 | STAT3C* dissociation from gp130 sites |
| k16f | 0.00134494 | -0.00961244 | STAT3 homodimers formation in cytosol |
| k16r | -0.00112481 | 0.00920069 | STAT3 homodimers dissociation in cytosol |
| k17f | -4.16E-07 | -0.459035 | SHP2 binding at (IL6-gp80-gp130-JAK)2* complex |
| k17r | 2.59E-07 | 0.0197143 | SHP2 dissociation from (IL6-gp80-gp130-JAK)2* complex |
| k18 | 2.48E-07 | -0.000504302 | (IL6-gp80-gp130-JAK)2* complex inactivation of by SHP2 |
| k19f | 0.000936284 | -0.0392736 | PP1 combination with STAT3C* |
| k19r | -0.000763889 | 0.0312984 | PP1 dissociation from STAT3C* |
| k20 | 0.00224987 | -0.0523803 | STAT3 inactivation by PP1 |
| k21f | -0.00067499 | -0.0120521 | PP1 combination with (STAT3C*)2 |
| k21r | 0.000525229 | 0.00936552 | PP1 dissociation from (STAT3C*)2 |

| | | | |
|---|---|---|---|
| k22 | 0.000900784 | -0.0598852 | STAT3 inactivation by PP1 within (STAT3C*)2 |
| k23f | -8.69E-06 | 4.08E-05 | STAT3C combination with STAT3C* |
| k23r | 1.55E-05 | -0.000246455 | STAT3C dissociation from STAT3C* |
| k24 | 0.00974621 | -0.184408 | STAT3 homodimers nuclear import |
| k25f | -0.00543954 | -0.152308 | STAT1 homodimers dissociation in nuclear |
| k25r | 0.00705188 | 0.144074 | STAT1 homodimers formation in nuclear |
| k26f | 0.0174087 | -0.330483 | PP1 combination with STAT3C* |
| k26r | -0.0136058 | 0.268419 | PP1 dissociation from STAT3C* |
| k27 | 0.00810629 | -0.431082 | STAT1 inactivation by PP1 |
| k28f | 0.0099286 | -0.826581 | PP1 combination with (STAT3C*)2 |
| k28r | -0.00784331 | 0.936416 | PP1 dissociation from (STAT3C*)2 |
| k29 | 0.00526295 | -1.15251 | STAT3 inactivation by PP1 within (STAT3C*)2 |
| k30f | 3.84E-06 | -0.000773945 | STAT3N dissociation from STAT3N* |
| k30r | -5.41E-07 | 7.60E-08 | STAT3N combination with STAT3N* |
| k31 | -1.61E-05 | 0.00166878 | STAT3 nuclear export |
| k32f | 1.58E-07 | -0.47458 | Max rate of (STAT3N*)2 inducing mRNA of SOCS3 |
| k32r | 1.20E-10 | 0.494908 | Km of (STAT3N*)2 inducing mRNA of SOCS3 |
| k33 | -1.17E-06 | -0.327549 | mRNA of SOCS3 nuclear export |
| k34 | -2.87E-07 | -0.475239 | Translation of SOCS3 |
| k35f | 1.55E-07 | -0.206762 | SOCS3 binding at (IL6-gp80-gp130-JAK)2* complex |
| k35r | 1.56E-07 | 0.242485 | SOCS3 dissociation from (IL6-gp80-gp130-JAK)2* complex |
| k36 | 4.65E-12 | 0.10735 | mRNA of SOCS3 degrading rate |
| k37 | 2.44E-07 | 0.0598051 | SOCS3 degrading rate |
| k38 | 1.56E-07 | -0.227934 | (IL6-gp80-gp130-JAK)2* complex inactivation of by SHP2 |
| k39f | 3.76E-10 | -0.014523 | SHP2 activation within (IL6-gp80-gp130-JAK)2*-SHP2 complex |
| k39r | 2.44E-07 | 0.000925971 | SHP2 deactivation within (IL6-gp80-gp130-JAK)2*-SHP2 complex |

| | | | |
|---|---|---|---|
| k40f | 1.56E-07 | 0.0909505 | Grb2 binding at (IL6-gp80-gp130-JAK)2*-SHP2* complex |
| k40r | -3.14E-07 | -0.0551323 | Grb2 dissociation from (IL6-gp80-gp130-JAK)2*-SHP2 complex |
| k41f | 2.44E-07 | -0.00252796 | SOS binding at (IL6-gp80-gp130-JAK)2*-SHP2*-Grb2 complex |
| k41r | 2.44E-07 | 0.0177295 | SOS dissociation from (IL6-gp80-gp130-JAK)2*-SHP2-Grb2 complex |
| k42f | 2.76E-07 | -0.483011 | Ras-GDP binding at (IL6-gp80-gp130-JAK)2*-SHP2*-Grb2-SOS complex |
| k42r | 4.04E-10 | 0.407438 | Ras-GDP dissociation from (IL6-gp80-gp130-JAK)2*-SHP2-Grb2-SOS complex |
| k43f | 2.44E-07 | 0.119607 | Ras-GDP activation by (IL6-gp80-gp130-JAK)2*-SHP2*-Grb2-SOS complex |
| k43r | 0 | -5.07E-06 | Ras-GTP deactivation by (IL6-gp80-gp130-JAK)2*-SHP2*-Grb2-SOS complex |
| k44f | 0 | -0.0014107 | Raf combination with Ras-GTP |
| k44r | 0 | 1.15E-05 | Raf dissociation from Ras-GTP |
| k45f | 4.64E-10 | -0.000132014 | Raf activation by Ras-GTP |
| k45r | 0 | 2.60E-05 | Raf* deactivation by Ras-GTP |
| k46f | 0 | -0.0760325 | Ras-GTP* binding at (IL6-gp80-gp130-JAK)2*-SHP2*-Grb2-SOS complex |
| k46r | 5.25E-10 | 0.0881827 | Ras-GTP* dissociation from (IL6-gp80-gp130-JAK)2*-SHP2*-Grb2-SOS complex |
| k47f | 1.82E-07 | 0.00638043 | (IL6-gp80-gp130-JAK)2*-SHP2*-Grb2-SOS -Ras-GTP complex dissociation |
| k47r | 1.58E-07 | -0.0361897 | (IL6-gp80-gp130-JAK)2*-SHP2*-Grb2-SOS -Ras-GTP complex formation |
| k48f | 2.62E-07 | 0.647503 | SHP2*-Grb2-SOS binding at (IL6-gp80-gp130-JAK)2* complex |
| k48r | 0 | -0.00781241 | SHP2*-Grb2-SOS dissociation from (IL6-gp80-gp130-JAK)2* complex |
| k49f | 1.56E-07 | -0.0205943 | SHP2* dissociation from Grb2-SOS |

| | | | |
|---|---|---|---|
| k49r | 4.78E-15 | 0.0267126 | SHP2* binding to Grb2-SOS |
| k50f | 4.32E-07 | 0.00123088 | Grb2-SOS complex dissociation |
| k50r | 4.36E-07 | -0.00430478 | Grb2-SOS complex formation |
| k51f | 1.56E-07 | -0.0175449 | Max rate of SHP2* deactivation |
| k51r | 1.56E-07 | 0.0167897 | Km of SHP2* deactivation |
| k52f | 9.08E-11 | 0.160398 | SHP2* dissociation from (IL6-gp80-gp130-JAK)2* complex |
| k52r | 0 | -0.0109974 | SHP2* binding to (IL6-gp80-gp130-JAK)2* complex |
| k53f | 1.58E-07 | -0.00351982 | SHP2* binding to Grb2 |
| k53r | 1.58E-07 | 0.00338257 | SHP2* dissociation from Grb2 |
| k54f | 1.58E-07 | 0.062672 | SHP2*-Grb2 dissociation from (IL6-gp80-gp130-JAK)2* complex |
| k54r | 0 | -0.00768864 | SHP2*-Grb2 binding to (IL6-gp80-gp130-JAK)2* complex |
| k55f | 0 | 0.000118197 | SOS dissociation from SHP2*-Grb2 complex |
| k55r | 4.64E-10 | -0.000569644 | SOS binding to SHP2*-Grb2 complex |
| k56f | 1.56E-07 | -0.195653 | Grb2-SOS binding to (IL6-gp80-gp130-JAK)2*-SHP2 complex |
| k56r | 2.76E-07 | 0.0222085 | Grb2-SOS dissociation from (IL6-gp80-gp130-JAK)2*-SHP2 complex |
| k57f | 0 | -8.37E-05 | Raf* combination with Phosp1 |
| k57r | 0 | 7.71E-06 | Raf* dissociation from Phosp1 |
| k58 | 0 | -5.07E-05 | Raf deactivation by Phosp1 |
| k59f | 0 | -7.07E-05 | MEK combination with Raf* |
| k59r | 0 | -6.15E-07 | MEK dissociation from Raf* |
| k60 | 0 | -0.00021936 | MEK activation by Raf* |
| k61f | 0 | 4.85E-05 | MEK-P combination with Raf* |
| k61r | 0 | 1.32E-07 | MEK-P dissociation from Raf* |
| k62 | 0 | -0.000388358 | MEK-P activation by Raf* |
| k63f | 0 | 1.03E-06 | MEK-PP combination with Phosp2 |
| k63r | 0 | -1.60E-06 | MEK-PP dissociation from Phosp2 |
| k64 | 0 | 4.73E-05 | MEK-PP deactivation by Phosp2 |
| k65f | 0 | 9.47E-07 | MEK-P combination with Phosp2 |

| | | | |
|---|---|---|---|
| k65r | 0 | -1.04E-06 | MEK-P dissociation from Phosp2 |
| k66 | 0 | 5.21E-06 | MEK-P deactivation by Phosp2 |
| k67f | 0 | -4.82E-07 | ERK combination with MEK-PP |
| k67r | 0 | 3.90E-07 | ERK dissociation from MEK-PP |
| k68 | 0 | 4.95E-07 | ERK activation by MEK-PP |
| k69f | 0 | -4.01E-07 | ERK-P combination with MEK-PP |
| k69r | 0 | -1.72E-07 | ERK-P dissociation from MEK-PP |
| k70 | 0 | -3.31E-07 | ERK-P activation by MEK-PP |
| k71f | 0 | 4.35E-08 | ERK-PP combination with Phosp3 |
| k71r | 0 | -1.09E-07 | ERK-PP dissociation from Phosp3 |
| k72 | 0 | -5.56E-09 | ERK-PP deactivation by Phosp3 |
| k73f | 0 | -5.10E-07 | ERK-P combination with Phosp3 |
| k73r | 0 | -6.49E-07 | ERK-P dissociation from Phosp3 |
| k74 | 0 | -4.61E-08 | ERK-P deactivation by Phosp3 |
| k75f | 0 | -1.45E-07 | Max rate of CEBPi activation by ERK-PP |
| k75r | 0 | 1.61E-07 | Km of CEBPi activation by ERK-PP |
| k76 | 0 | 3.91E-07 | CEBP deactivation |
| k77f | 0 | -6.04E-07 | CEBPn formation |
| k77r | 0 | -6.10E-07 | CEBPn dissociation |
| kf1 | 0.108106 | -5.76E-08 | IFNR combination with JAK |
| kb1 | -0.118735 | 7.64E-08 | IFNR dissociation from JAK |
| kf2 | 1.08949 | 0 | IFN combination with R-JAK |
| kb2 | -0.860051 | 0 | IFN dissociation from R-JAK |
| kf3 | 0.561679 | 0 | (IFN-R-JAK)2 complex dimerization |
| kb3 | -0.485481 | 2.59E-07 | (IFN-R-JAK)2 complex dissociation |
| kf4 | 0.579146 | -1.81E-07 | (IFN-R-JAK)2 complex activation |
| kf5 | 0.920281 | 3.73E-08 | STAT1 binding at IFNR sites |
| kb5 | -0.527806 | -7.59E-07 | STAT1 dissociation from IFNR sites |
| kf6 | 0.494715 | -1.71E-07 | STAT1 activation rate at IFNR sites |
| kf7 | -0.00191204 | -2.31E-07 | STAT1C* binding at IFNR sites |
| kb7 | 0.00150782 | -6.54E-07 | STAT1C* dissociation from IFNR sites |

| | | | |
|---|---|---|---|
| kf8 | -0.0126352 | 0.002968 | STAT1 homodimers formation in cytosol |
| kb8 | 0.0126982 | -0.00273999 | STAT1 homodimers dissociation in cytosol |
| kf9 | -0.200213 | 5.17E-08 | SHP2 binding at (IFN-R-JAK)2* complex |
| kb9 | 0.173514 | 3.03E-07 | SHP2 dissociation from (IFN-R-JAK)2* complex |
| kf10 | -0.197613 | -4.03E-07 | (IFN-R-JAK)2* complex inactivation of by SHP2 |
| kf11 | -0.0290778 | -0.000975343 | PP1 combination with STAT1C* |
| kb11 | 0.022967 | 0.000590942 | PP1 dissociation from STAT1C* |
| kf12 | -0.0416347 | 0.000488961 | STAT1 inactivation by PP1 |
| kf13 | 4.18E-05 | -1.10E-05 | STAT1C combination with STAT1C* |
| kb13 | -0.000292798 | 2.71E-05 | STAT1C dissociation from STAT1C* |
| kf14 | -0.190609 | 0.0201524 | STAT1 homodimers nuclear import |
| kf15 | -0.382591 | 0.110933 | PP2 combination with STAT1N* |
| kb15 | 0.35352 | -0.10356 | PP2 dissociation from STAT1N* |
| kf17 | 0.00121986 | 9.73E-06 | STAT1 inactivation by PP2 |
| kf16 | -0.67097 | 0.0575866 | STAT1 nuclear export |
| k18a | -0.646078 | 9.01E-08 | Max rate of (STAT1N*)2 inducing mRNA-SOCS1 |
| k18b | 0.684174 | 1.04E-07 | Km of (STAT1N*)2 inducing mRNA -SOCS1 |
| kf19 | -0.373617 | -1.42E-07 | mRNA of SOCS1 nuclear export |
| kf20 | -0.646079 | 1.74E-07 | Translation of SOCS1 |
| kf21 | -0.59167 | 2.12E-07 | SOCS1 binding at (IFN-R-JAK)2* complex |
| kb21 | 0.576228 | -7.30E-07 | SOCS1 dissociation from (IFN-R-JAK)2* complex |
| kf22 | 0.199141 | -2.63E-07 | mRNA of SOCS1 degrading rate |
| kf23 | 0.179613 | 1.48E-07 | SOCS1 degrading rate |
| kf24 | -0.0140464 | -0.00367923 | PP1 combination with (STAT1C*)2 |
| kb24 | 0.0107448 | 0.00288126 | PP1 dissociation from (STAT1C*)2 |
| kf25 | -0.0639015 | -0.00108704 | STAT1 inactivation by PP1 within (STAT1C*)2 |
| kf26 | 0.121735 | -0.00220328 | STAT1 homodimers formation in nuclear |
| kb26 | -0.118656 | 0.00212399 | STAT1 homodimers dissociation in nuclear |

| | | | |
|---|---|---|---|
| kf27 | -0.314663 | 0.00989138 | PP2 combination with (STAT1N*)2 |
| kb27 | 0.297118 | -0.0078173 | PP2 dissociation from (STAT1N*)2 |
| kf28 | -0.537823 | 0.00530863 | STAT1 deactivation by PP2 within (STAT1N*)2 |
| kf29 | 8.67E-07 | -3.84E-07 | STAT1N combination with STAT1N* |
| kb29 | -0.00022888 | 1.85E-05 | STAT1N dissociation from STAT1N* |
| kf30 | -0.474515 | -6.65E-07 | STAT1C binding at (IFN-R-JAK)2*-SOCS1 complex |
| kb30 | 0.543759 | -8.42E-08 | STAT1C dissociation from (IFN-R-JAK)2*-SOCS1 complex |
| kf31 | -0.349744 | -4.44E-07 | SHP2 binding at (IFN-R-JAK)2*-STAT1C-SOCS1 complex |
| kb31 | 0.34494 | -3.07E-07 | SHP2 dissociation from (IFN-R-JAK)2*-STAT1C-SOCS1 complex |
| kf32 | -0.229267 | -8.59E-08 | (IFN-R-JAK)2*-STAT1C-SHP2-SOCS1 complex dissociation |
| kf33 | -0.0576678 | -4.44E-07 | SOCS1 dissociation from (IFN-R-JAK)2*-STAT1C-SHP2-SOCS1 complex |
| n_kf1 | 0.00590598 | 1.85E-07 | STAT3 binding at IFNR sites |
| n_kr1 | -0.00416891 | -3.92E-07 | STAT3 dissociation from IFNR sites |
| n_k2 | 0.00402307 | -6.10E-07 | STAT3 activation rate at IFNR sites |
| n_kf3 | -6.42E-06 | -3.55E-07 | STAT3C* binding at IFNR sites |
| n_kr3 | 6.53E-06 | -8.21E-08 | STAT3C* dissociation from IFNR sites |
| n_kf4 | 2.76E-07 | 0.100181 | STAT1 binding at gp130 sites |
| n_kr4 | 2.76E-07 | -0.0591942 | STAT1 dissociation from gp130 sites |
| n_k5 | 2.42E-07 | 0.0640334 | STAT1 activation rate at gp130 sites |
| n_kf6 | -2.42E-07 | -9.89E-06 | STAT1C* binding at gp130 sites |
| n_kr6 | 1.79E-11 | 7.80E-06 | STAT1C* dissociation from gp130 sites |
| n_kf7 | 1.46E-07 | -0.00103274 | Max rate of (STAT1N*)2 inducing mRNA-SOCS3 |
| n_kr7 | 2.59E-07 | 0.000793487 | Km of (STAT1N*)2 inducing mRNA -SOCS3 |
| n_kf8 | 0.00461257 | 0.00504897 | STAT1/3 dimers formation in cytosol |
| n_kr8 | -0.0042064 | -0.00436441 | STAT1/3 dimers dissociation in cytosol |
| n_kf9 | -0.021741 | -0.0671042 | STAT1/3 dimers formation in nucleus |

| | | | |
|---|---|---|---|
| n_kr9 | 0.0264869 | 0.0613915 | STAT1/3 dimers dissociation in nucleus |
| n_k10 | 0.00187114 | -0.00882142 | STAT1/3 dimers nuclear import |
| n_kf11 | -0.0052467 | -0.0085852 | PP1 combination with STAT1/3 dimers |
| n_kr11 | 0.00408078 | 0.00669567 | PP1 dissociation from STAT1/3 dimers |
| n_kf12 | 0.0244101 | -0.103754 | PP2 combination with STAT1/3 dimers |
| n_kr12 | -0.0223063 | 0.101852 | PP2 dissociation from STAT1/3 dimers |
| n_k13 | -0.00882717 | -0.00158213 | STAT1 inactivation by PP1 within STAT1/3 dimers |
| n_k14 | 0.00130904 | -0.012887 | STAT3 inactivation by PP1 within STAT1/3 dimers |
| n_k15 | -0.196276 | 0.082933 | STAT1 inactivation by PP2 within STAT1/3 dimers |
| n_k16 | 0.0742326 | -0.423821 | STAT3 inactivation by PP2 within STAT1/3 dimers |

The definition of the parameter sensitivity can refer to the "Methods" section in the main text. The positive (or negative) sensitivity values indicate consistent (or opposite) percentage changes in output to the perturbation in the parameter compared to the nominal solution.

**Table S8. Results of sensitivity analysis with respect to variations in the concentrations of pathway components for the non-competitive model**

| Parameter | IFN | IL-6 |
|---|---|---|
| PP2 | -0.86819 | -1.49525 |
| PP1 | -0.05413 | -0.06777 |
| SHP2 | -0.42032 | -0.44196 |
| STAT3C | 0.307906 | 1.36415 |
| STAT1C | 0.498613 | 0.398571 |
| R | 0.487952 | 0 |
| gp80 | 0 | 0.126754 |
| gp130 | 0 | 0.055787 |
| JAK(IFN) | 0.487951 | 0 |
| JAK(IL-6) | 0 | 1.46179 |
| IL-6 | 0.964033 | 0 |
| IFN | 0 | 0.126754 |

The definition of the parameter sensitivity can refer to the "Methods" section in the main text. The positive (or negative) sensitivity values indicate consistent (or opposite) percentage changes in output to the perturbation in the parameter compared to the nominal solution.

**Table S9. Results of sensitivity analysis with respect to variations in the kinetic parameter for the non-competitive model**

| Parameter | IFN | IL-6 | Description |
|---|---|---|---|
| k1f | 0 | 0.121868 | IL6 combination with gp80 |
| k1r | 0 | -0.191126 | IL6 dissociation from gp80 |
| k2f | 0 | 0.0552303 | gp130 combination with JAK |
| k2r | 0 | -0.072901 | gp130 dissociation from JAK |
| k3f | 0 | 0.146778 | IL6-gp80-gp130-JAK formation |
| k3r | 0 | -0.195713 | IL6-gp80-gp130-JAK dissociation |
| k6f | 0 | 0.15858 | (IL6-gp80-gp130-JAK)2 complex dimerization |
| k6r | 1.58E-07 | -0.172858 | (IL6-gp80-gp130-JAK)2 complex dissociation |
| k7 | 1.82E-07 | 0.24868 | (IL6-gp80-gp130-JAK)2 complex activation |
| k8f | 1.36E-07 | 0.765515 | STAT3 binding at gp130 sites |
| k8r | -4.14E-07 | -0.442549 | STAT3 dissociation from gp130 sites |
| k9 | -9.52E-10 | 0.529317 | STAT3 activation rate at gp130 sites |
| k10f | -2.10E-06 | -0.0021417 | STAT3C* binding at gp130 sites |
| k10r | 1.57E-07 | 0.00166223 | STAT3C* dissociation from gp130 sites |
| k16f | 0.00134494 | -0.00961244 | STAT3 homodimers formation in cytosol |
| k16r | -0.00112481 | 0.00920069 | STAT3 homodimers dissociation in cytosol |
| k17f | -4.16E-07 | -0.459035 | SHP2 binding at (IL6-gp80-gp130-JAK)2* complex |
| k17r | 2.59E-07 | 0.0197143 | SHP2 dissociation from (IL6-gp80-gp130-JAK)2* complex |
| k18 | 2.48E-07 | -0.000504302 | (IL6-gp80-gp130-JAK)2* complex inactivation of by SHP2 |
| k19f | 0.000936284 | -0.0392736 | PP1 combination with STAT3C* |
| k19r | -0.000763889 | 0.0312984 | PP1 dissociation from STAT3C* |
| k20 | 0.00224987 | -0.0523803 | STAT3 inactivation by PP1 |
| k21f | -0.00067499 | -0.0120521 | PP1 combination with (STAT3C*)2 |
| k21r | 0.000525229 | 0.00936552 | PP1 dissociation from (STAT3C*)2 |
| k22 | 0.000900784 | -0.0598852 | STAT3 inactivation by PP1 within (STAT3C*)2 |
| k23f | -8.69E-06 | 4.08E-05 | STAT3C combination with STAT3C* |
| k23r | 1.55E-05 | -0.000246455 | STAT3C dissociation from STAT3C* |
| k24 | 0.00974621 | -0.184408 | STAT3 homodimers nuclear import |
| k25f | -0.00543954 | -0.152308 | STAT1 homodimers dissociation in nuclear |
| k25r | 0.00705188 | 0.144074 | STAT1 homodimers formation in nuclear |

| | | | |
|---|---|---|---|
| k26f | 0.0174087 | -0.330483 | PP1 combination with STAT3C* |
| k26r | -0.0136058 | 0.268419 | PP1 dissociation from STAT3C* |
| k27 | 0.00810629 | -0.431082 | STAT1 inactivation by PP1 |
| k28f | 0.0099286 | -0.826581 | PP1 combination with (STAT3C*)2 |
| k28r | -0.00784331 | 0.936416 | PP1 dissociation from (STAT3C*)2 |
| k29 | 0.00526295 | -1.15251 | STAT3 inactivation by PP1 within (STAT3C*)2 |
| k30f | 3.84E-06 | -0.000773945 | STAT3N dissociation from STAT3N* |
| k30r | -5.41E-07 | 7.60E-08 | STAT3N combination with STAT3N* |
| k31 | -1.61E-05 | 0.00166878 | STAT3 nuclear export |
| k32f | 1.58E-07 | -0.47458 | Max rate of (STAT3N*)2 inducing mRNA of SOCS3 |
| k32r | 1.20E-10 | 0.494908 | Km of (STAT3N*)2 inducing mRNA of SOCS3 |
| k33 | -1.17E-06 | -0.327549 | mRNA of SOCS3 nuclear export |
| k34 | -2.87E-07 | -0.475239 | Translation of SOCS3 |
| k35f | 1.55E-07 | -0.206762 | SOCS3 binding at (IL6-gp80-gp130-JAK)2* complex |
| k35r | 1.56E-07 | 0.242485 | SOCS3 dissociation from (IL6-gp80-gp130-JAK)2* complex |
| k36 | 4.65E-12 | 0.10735 | mRNA of SOCS3 degrading rate |
| k37 | 2.44E-07 | 0.0598051 | SOCS3 degrading rate |
| k38 | 1.56E-07 | -0.227934 | (IL6-gp80-gp130-JAK)2* complex inactivation of by SHP2 |
| k39f | 3.76E-10 | -0.014523 | SHP2 activation within (IL6-gp80-gp130-JAK)2*-SHP2 complex |
| k39r | 2.44E-07 | 0.000925971 | SHP2 deactivation within (IL6-gp80-gp130-JAK)2*-SHP2 complex |
| k40f | 1.56E-07 | 0.0909505 | Grb2 binding at (IL6-gp80-gp130-JAK)2*-SHP2* complex |
| k40r | -3.14E-07 | -0.0551323 | Grb2 dissociation from (IL6-gp80-gp130-JAK)2*-SHP2 complex |
| k41f | 2.44E-07 | -0.00252796 | SOS binding at (IL6-gp80-gp130-JAK)2*-SHP2*-Grb2 complex |
| k41r | 2.44E-07 | 0.0177295 | SOS dissociation from (IL6-gp80-gp130-JAK)2*-SHP2-Grb2 complex |

| | | | |
|---|---|---|---|
| k42f | 2.76E-07 | -0.483011 | Ras-GDP binding at (IL6-gp80-gp130-JAK)2*-SHP2*-Grb2-SOS complex |
| k42r | 4.04E-10 | 0.407438 | Ras-GDP dissociation from (IL6-gp80-gp130-JAK)2*-SHP2-Grb2-SOS complex |
| k43f | 2.44E-07 | 0.119607 | Ras-GDP activation by (IL6-gp80-gp130-JAK)2*-SHP2*-Grb2-SOS complex |
| k43r | 0 | -5.07E-06 | Ras-GTP deactivation by (IL6-gp80-gp130-JAK)2*-SHP2*-Grb2-SOS complex |
| k44f | 0 | -0.0014107 | Raf combination with Ras-GTP |
| k44r | 0 | 1.15E-05 | Raf dissociation from Ras-GTP |
| k45f | 4.64E-10 | -0.000132014 | Raf activation by Ras-GTP |
| k45r | 0 | 2.60E-05 | Raf* deactivation by Ras-GTP |
| k46f | 0 | -0.0760325 | Ras-GTP* binding at (IL6-gp80-gp130-JAK)2*-SHP2*-Grb2-SOS complex |
| k46r | 5.25E-10 | 0.0881827 | Ras-GTP* dissociation from (IL6-gp80-gp130-JAK)2*-SHP2*-Grb2-SOS complex |
| k47f | 1.82E-07 | 0.00638043 | (IL6-gp80-gp130-JAK)2*-SHP2*-Grb2-SOS-Ras-GTP complex dissociation |
| k47r | 1.58E-07 | -0.0361897 | (IL6-gp80-gp130-JAK)2*-SHP2*-Grb2-SOS-Ras-GTP complex formation |
| k48f | 2.62E-07 | 0.647503 | SHP2*-Grb2-SOS binding at (IL6-gp80-gp130-JAK)2* complex |
| k48r | 0 | -0.00781241 | SHP2*-Grb2-SOS dissociation from (IL6-gp80-gp130-JAK)2* complex |
| k49f | 1.56E-07 | -0.0205943 | SHP2* dissociation from Grb2-SOS |
| k49r | 4.78E-15 | 0.0267126 | SHP2* binding to Grb2-SOS |
| k50f | 4.32E-07 | 0.00123088 | Grb2-SOS complex dissociation |
| k50r | 4.36E-07 | -0.00430478 | Grb2-SOS complex formation |
| k51f | 1.56E-07 | -0.0175449 | Max rate of SHP2* deactivation |
| k51r | 1.56E-07 | 0.0167897 | Km of SHP2* deactivation |
| k52f | 9.08E-11 | 0.160398 | SHP2* dissociation from (IL6-gp80-gp130-JAK)2* complex |

| | | | |
|---|---|---|---|
| k52r | 0 | -0.0109974 | SHP2* binding to (IL6-gp80-gp130-JAK)2* complex |
| k53f | 1.58E-07 | -0.00351982 | SHP2* binding to Grb2 |
| k53r | 1.58E-07 | 0.00338257 | SHP2* dissociation from Grb2 |
| k54f | 1.58E-07 | 0.062672 | SHP2*-Grb2 dissociation from (IL6-gp80-gp130-JAK)2* complex |
| k54r | 0 | -0.00768864 | SHP2*-Grb2 binding to (IL6-gp80-gp130-JAK)2* complex |
| k55f | 0 | 0.000118197 | SOS dissociation from SHP2*-Grb2 complex |
| k55r | 4.64E-10 | -0.000569644 | SOS binding to SHP2*-Grb2 complex |
| k56f | 1.56E-07 | -0.195653 | Grb2-SOS binding to (IL6-gp80-gp130-JAK)2*-SHP2 complex |
| k56r | 2.76E-07 | 0.0222085 | Grb2-SOS dissociation from (IL6-gp80-gp130-JAK)2*-SHP2 complex |
| k57f | 0 | -8.37E-05 | Raf* combination with Phosp1 |
| k57r | 0 | 7.71E-06 | Raf* dissociation from Phosp1 |
| k58 | 0 | -5.07E-05 | Raf deactivation by Phosp1 |
| k59f | 0 | -7.07E-05 | MEK combination with Raf* |
| k59r | 0 | -6.15E-07 | MEK dissociation from Raf* |
| k60 | 0 | -0.00021936 | MEK activation by Raf* |
| k61f | 0 | 4.85E-05 | MEK-P combination with Raf* |
| k61r | 0 | 1.32E-07 | MEK-P dissociation from Raf* |
| k62 | 0 | -0.000388358 | MEK-P activation by Raf* |
| k63f | 0 | 1.03E-06 | MEK-PP combination with Phosp2 |
| k63r | 0 | -1.60E-06 | MEK-PP dissociation from Phosp2 |
| k64 | 0 | 4.73E-05 | MEK-PP deactivation by Phosp2 |
| k65f | 0 | 9.47E-07 | MEK-P combination with Phosp2 |
| k65r | 0 | -1.04E-06 | MEK-P dissociation from Phosp2 |
| k66 | 0 | 5.21E-06 | MEK-P deactivation by Phosp2 |
| k67f | 0 | -4.82E-07 | ERK combination with MEK-PP |
| k67r | 0 | 3.90E-07 | ERK dissociation from MEK-PP |
| k68 | 0 | 4.95E-07 | ERK activation by MEK-PP |
| k69f | 0 | -4.01E-07 | ERK-P combination with MEK-PP |

| | | | |
|---|---|---|---|
| k69r | 0 | -1.72E-07 | ERK-P dissociation from MEK-PP |
| k70 | 0 | -3.31E-07 | ERK-P activation by MEK-PP |
| k71f | 0 | 4.35E-08 | ERK-PP combination with Phosp3 |
| k71r | 0 | -1.09E-07 | ERK-PP dissociation from Phosp3 |
| k72 | 0 | -5.56E-09 | ERK-PP deactivation by Phosp3 |
| k73f | 0 | -5.10E-07 | ERK-P combination with Phosp3 |
| k73r | 0 | -6.49E-07 | ERK-P dissociation from Phosp3 |
| k74 | 0 | -4.61E-08 | ERK-P deactivation by Phosp3 |
| k75f | 0 | -1.45E-07 | Max rate of CEBPi activation by ERK-PP |
| k75r | 0 | 1.61E-07 | Km of CEBPi activation by ERK-PP |
| k76 | 0 | 3.91E-07 | CEBP deactivation |
| k77f | 0 | -6.04E-07 | CEBPn formation |
| k77r | 0 | -6.10E-07 | CEBPn dissociation |
| kf1 | 0.108106 | -5.76E-08 | IFNR combination with JAK |
| kb1 | -0.118735 | 7.64E-08 | IFNR dissociation from JAK |
| kf2 | 1.08949 | 0 | IFN combination with R-JAK |
| kb2 | -0.860051 | 0 | IFN dissociation from R-JAK |
| kf3 | 0.561679 | 0 | (IFN-R-JAK)2 complex dimerization |
| kb3 | -0.485481 | 2.59E-07 | (IFN-R-JAK)2 complex dissociation |
| kf4 | 0.579146 | -1.81E-07 | (IFN-R-JAK)2 complex activation |
| kf5 | 0.920281 | 3.73E-08 | STAT1 binding at IFNR sites |
| kb5 | -0.527806 | -7.59E-07 | STAT1 dissociation from IFNR sites |
| kf6 | 0.494715 | -1.71E-07 | STAT1 activation rate at IFNR sites |
| kf7 | -0.00191204 | -2.31E-07 | STAT1C* binding at IFNR sites |
| kb7 | 0.00150782 | -6.54E-07 | STAT1C* dissociation from IFNR sites |
| kf8 | -0.0126352 | 0.002968 | STAT1 homodimers formation in cytosol |
| kb8 | 0.0126982 | -0.00273999 | STAT1 homodimers dissociation in cytosol |
| kf9 | -0.200213 | 5.17E-08 | SHP2 binding at (IFN-R-JAK)2* complex |
| kb9 | 0.173514 | 3.03E-07 | SHP2 dissociation from (IFN-R-JAK)2* complex |
| kf10 | -0.197613 | -4.03E-07 | (IFN-R-JAK)2* complex inactivation of by SHP2 |

| | | | |
|---|---|---|---|
| kf11 | -0.0290778 | -0.000975343 | PP1 combination with STAT1C* |
| kb11 | 0.022967 | 0.000590942 | PP1 dissociation from STAT1C* |
| kf12 | -0.0416347 | 0.000488961 | STAT1 inactivation by PP1 |
| kf13 | 4.18E-05 | -1.10E-05 | STAT1C combination with STAT1C* |
| kb13 | -0.000292798 | 2.71E-05 | STAT1C dissociation from STAT1C* |
| kf14 | -0.190609 | 0.0201524 | STAT1 homodimers nuclear import |
| kf15 | -0.382591 | 0.110933 | PP2 combination with STAT1N* |
| kb15 | 0.35352 | -0.10356 | PP2 dissociation from STAT1N* |
| kf17 | 0.00121986 | 9.73E-06 | STAT1 inactivation by PP2 |
| kf16 | -0.67097 | 0.0575866 | STAT1 nuclear export |
| k18a | -0.646078 | 9.01E-08 | Max rate of (STAT1N*)2 inducing mRNA-SOCS1 |
| k18b | 0.684174 | 1.04E-07 | Km of (STAT1N*)2 inducing mRNA -SOCS1 |
| kf19 | -0.373617 | -1.42E-07 | mRNA of SOCS1 nuclear export |
| kf20 | -0.646079 | 1.74E-07 | Translation of SOCS1 |
| kf21 | -0.59167 | 2.12E-07 | SOCS1 binding at (IFN-R-JAK)2* complex |
| kb21 | 0.576228 | -7.30E-07 | SOCS1 dissociation from (IFN-R-JAK)2* complex |
| kf22 | 0.199141 | -2.63E-07 | mRNA of SOCS1 degrading rate |
| kf23 | 0.179613 | 1.48E-07 | SOCS1 degrading rate |
| kf24 | -0.0140464 | -0.00367923 | PP1 combination with (STAT1C*)2 |
| kb24 | 0.0107448 | 0.00288126 | PP1 dissociation from (STAT1C*)2 |
| kf25 | -0.0639015 | -0.00108704 | STAT1 inactivation by PP1 within (STAT1C*)2 |
| kf26 | 0.121735 | -0.00220328 | STAT1 homodimers formation in nuclear |
| kb26 | -0.118656 | 0.00212399 | STAT1 homodimers dissociation in nuclear |
| kf27 | -0.314663 | 0.00989138 | PP2 combination with (STAT1N*)2 |
| kb27 | 0.297118 | -0.0078173 | PP2 dissociation from (STAT1N*)2 |
| kf28 | -0.537823 | 0.00530863 | STAT1 deactivation by PP2 within (STAT1N*)2 |
| kf29 | 8.67E-07 | -3.84E-07 | STAT1N combination with STAT1N* |
| kb29 | -0.00022888 | 1.85E-05 | STAT1N dissociation from STAT1N* |

| | | | |
|---|---|---|---|
| kf30 | -0.474515 | -6.65E-07 | STAT1C binding at (IFN-R-JAK)2*-SOCS1 complex |
| kb30 | 0.543759 | -8.42E-08 | STAT1C dissociation from (IFN-R-JAK)2*-SOCS1 complex |
| kf31 | -0.349744 | -4.44E-07 | SHP2 binding at (IFN-R-JAK)2*-STAT1C-SOCS1 complex |
| kb31 | 0.34494 | -3.07E-07 | SHP2 dissociation from (IFN-R-JAK)2*-STAT1C-SOCS1 complex |
| kf32 | -0.229267 | -8.59E-08 | (IFN-R-JAK)2*-STAT1C-SHP2-SOCS1 complex dissociation |
| kf33 | -0.0576678 | -4.44E-07 | SOCS1 dissociation from (IFN-R-JAK)2*-STAT1C-SHP2-SOCS1 complex |
| n_kf1 | 0.00590598 | 1.85E-07 | STAT3 binding at IFNR sites |
| n_kr1 | -0.00416891 | -3.92E-07 | STAT3 dissociation from IFNR sites |
| n_k2 | 0.00402307 | -6.10E-07 | STAT3 activation rate at IFNR sites |
| n_kf3 | -6.42E-06 | -3.55E-07 | STAT3C* binding at IFNR sites |
| n_kr3 | 6.53E-06 | -8.21E-08 | STAT3C* dissociation from IFNR sites |
| n_kf4 | 2.76E-07 | 0.100181 | STAT1 binding at gp130 sites |
| n_kr4 | 2.76E-07 | -0.0591942 | STAT1 dissociation from gp130 sites |
| n_k5 | 2.42E-07 | 0.0640334 | STAT1 activation rate at gp130 sites |
| n_kf6 | -2.42E-07 | -9.89E-06 | STAT1C* binding at gp130 sites |
| n_kr6 | 1.79E-11 | 7.80E-06 | STAT1C* dissociation from gp130 sites |
| n_kf7 | 1.46E-07 | -0.00103274 | Max rate of (STAT1N*)2 inducing mRNA-SOCS3 |
| n_kr7 | 2.59E-07 | 0.000793487 | Km of (STAT1N*)2 inducing mRNA -SOCS3 |
| n_kf8 | 0.00461257 | 0.00504897 | STAT1/3 dimers formation in cytosol |
| n_kr8 | -0.0042064 | -0.00436441 | STAT1/3 dimers dissociation in cytosol |
| n_kf9 | -0.021741 | -0.0671042 | STAT1/3 dimers formation in nucleus |
| n_kr9 | 0.0264869 | 0.0613915 | STAT1/3 dimers dissociation in nucleus |
| n_k10 | 0.00187114 | -0.00882142 | STAT1/3 dimers nuclear import |
| n_kf11 | -0.0052467 | -0.0085852 | PP1 combination with STAT1/3 dimers |
| n_kr11 | 0.00408078 | 0.00669567 | PP1 dissociation from STAT1/3 dimers |
| n_kf12 | 0.0244101 | -0.103754 | PP2 combination with STAT1/3 dimers |
| n_kr12 | -0.0223063 | 0.101852 | PP2 dissociation from STAT1/3 dimers |

| | | | |
|---|---|---|---|
| n_k13 | -0.00882717 | -0.00158213 | STAT1 inactivation by PP1 within STAT1/3 dimers |
| n_k14 | 0.00130904 | -0.012887 | STAT3 inactivation by PP1 within STAT1/3 dimers |
| n_k15 | -0.196276 | 0.082933 | STAT1 inactivation by PP2 within STAT1/3 dimers |
| n_k16 | 0.0742326 | -0.423821 | STAT3 inactivation by PP2 within STAT1/3 dimers |
| n_kf17 | 0.175374 | 3.28E-09 | STAT1 binding at IFNR sites |
| n_kr17 | -0.12568 | 0 | STAT1 dissociation from IFNR sites |
| n_kf18 | 0.117156 | 0 | STAT3 binding at IFNR sites |
| n_kr18 | -0.10681 | 0 | STAT3 dissociation from IFNR sites |
| n_k19 | 0.316427 | 0 | STAT1 binding at gp130 sites |
| n_k20 | -0.05966 | 0 | STAT1 dissociation from gp130 sites |
| n_kf21 | 1.70E-06 | 0.36268 | STAT3 binding at gp130 sites |
| n_kr21 | 1.70E-06 | -0.27986 | STAT3 dissociation from gp130 sites |
| n_kf22 | 1.16E-06 | 0.010229 | STAT1 activation rate at IFNR sites |
| n_kr22 | 0 | -0.00879 | STAT3 activation rate at IFNR sites |
| n_k23 | 3.38E-11 | 0.019239 | STAT1 activation rate at gp130 sites |
| n_k24 | 3.22E-07 | 0.365773 | STAT3 activation rate at gp130 sites |

The definition of the parameter sensitivity can refer to the "Methods" section in the main text. The positive (or negative) sensitivity values indicate consistent (or opposite) percentage changes in output to the perturbation in the parameter compared to the nominal solution.

**New biochemical reactions added to the crosstalk model**

$$(IFN\text{-}R\text{-}JAK)2^{*} + STAT3C \underset{n\_kr1}{\overset{n\_kf1}{\rightleftarrows}} (IFN\text{-}R\text{-}JAK)2^{*}\text{-}STAT3C \quad \text{(N1)}$$

$$(IFN\text{-}R\text{-}JAK)2^{*}\text{-}STAT3C \xrightarrow{n\_k2} (IFN\text{-}R\text{-}JAK)2^{*} + STAT3C^{*} \quad \text{(N2)}$$

$$(IFN\text{-}R\text{-}JAK)2^{*} + STAT3C^{*} \underset{n\_kr3}{\overset{n\_kf3}{\rightleftarrows}} (IFN\text{-}R\text{-}JAK)2^{*}\text{-}STAT3C^{*} \quad \text{(N3)}$$

$$(IL6\text{-}gp80\text{-}gp130\text{-}JAK)2^{*} + STAT1C \underset{n\_kr4}{\overset{n\_kf4}{\rightleftarrows}} (IL6\text{-}gp80\text{-}gp130\text{-}JAK)2^{*}\text{-}STAT1C \quad \text{(N4)}$$

$$(IL6\text{-}gp80\text{-}gp130\text{-}JAK)2^{*}\text{-}STAT1C \xrightarrow{n\_k5} (IL6\text{-}gp80\text{-}gp130\text{-}JAK)2^{*} + STAT1C^{*} \quad \text{(N5)}$$

$$(IL6\text{-}gp80\text{-}gp130\text{-}JAK)2^{*} + STAT1C^{*} \underset{n\_kr6}{\overset{n\_kf6}{\rightleftarrows}} (IL6\text{-}gp80\text{-}gp130\text{-}JAK)2^{*}\text{-}STAT1C^{*} \quad \text{(N6)}$$

$$d\left[mRNA\text{-}SOCS3N\right]/dt = V\max\left(STAT1N^{*}\right)2/\left[\left(STAT1N^{*}\right)2 + Km\right] \quad \text{(N7)}$$

$$STAT1C^{*} + STAT3C^{*} \underset{n\_kr8}{\overset{n\_kf8}{\rightleftarrows}} STAT1C^{*}\text{-}STAT3C^{*} \quad \text{(N8)}$$

$$STAT1N^{*} + STAT3N^{*} \underset{n\_kr9}{\overset{n\_kf9}{\rightleftarrows}} STAT1N^{*}\text{-}STAT3N^{*} \quad \text{(N9)}$$

$$STAT1C^{*}\text{-}STAT3C^{*} \xrightarrow{n\_k10} STAT1N^{*}\text{-}STAT3N^{*} \quad \text{(N10)}$$

$$PP1 + STAT1C^{*}\text{-}STAT3C^{*} \underset{n\_kr11}{\overset{n\_kf11}{\rightleftarrows}} PP1\text{-}STAT1C^{*}\text{-}STAT3C^{*} \quad \text{(N11)}$$

$$PP2 + STAT1N^{*}\text{-}STAT3N^{*} \underset{n\_kr12}{\overset{n\_kf12}{\rightleftarrows}} PP2\text{-}STAT1N^{*}\text{-}STAT3N^{*} \quad \text{(N12)}$$

$$PP1\text{-}STAT1C^{*}\text{-}STAT3C^{*} \xrightarrow{n\_k13} PP1 + STAT1C + STAT3C^{*} \quad \text{(N13)}$$

$$PP1\text{-}STAT1C^{*}\text{-}STAT3C^{*} \xrightarrow{n\_k14} PP1 + STAT1C^{*} + STAT3C \quad \text{(N14)}$$

$$PP2\text{-}STAT1N^{*}\text{-}STAT3N^{*} \xrightarrow{n\_k15} PP2 + STAT1N + STAT3N^{*} \quad \text{(N15)}$$

$$PP2\text{-}STAT1N^{*}\text{-}STAT3N^{*} \xrightarrow{n\_k16} PP2 + STAT1N^{*} + STAT3N \quad \text{(N16)}$$

Where *R* represents receptor; *C* represents species within cytoplasm; *N* represents species within nuclei; 2 represents dimers; and * represents activation state. The *mRNA-SOCS3N* represents SOCS3 mRNA in the nucleus; *(STAT1N*)2* represents phosphorylated STAT1 homodimers in the nucleus; $V_{max}$ represents maximum reaction velocity of the SOCS3-mRNA transcription; $K_m$ represents half of substrate concentration when enzymatic reaction gets the maximum reaction velocity.

**New biochemical reactions added to the non-competitive model**

$$\left(IFN\text{-}R\text{-}JAK\right)2^{*}\text{-}STAT3C + STAT1C \underset{n\_kr17}{\overset{n\_kf17}{\rightleftarrows}} \left(IFN\text{-}R\text{-}JAK\right)2^{*}\text{-}STAT1C\text{-}STAT3C \quad \text{(N17)}$$

$$\left(IFN\text{-}R\text{-}JAK\right)2^{*}\text{-}STAT1C + STAT3C \underset{n\_kr18}{\overset{n\_kf18}{\rightleftarrows}} \left(IFN\text{-}R\text{-}JAK\right)2^{*}\text{-}STAT1C\text{-}STAT3C \quad \text{(N18)}$$

$$\left(IL6\text{-}gp80\text{-}gp130\text{-}JAK\right)2^{*}\text{-}STAT3C + STAT1C \underset{n\_kr19}{\overset{n\_kf19}{\rightleftarrows}} \left(IL6\text{-}gp80\text{-}gp130\text{-}JAK\right)2^{*}\text{-}STAT1C\text{-}STAT3C \quad \text{(N19)}$$

$$\left(IL6\text{-}gp80\text{-}gp130\text{-}JAK\right)2^{*}\text{-}STAT1C + STAT3C \underset{n\_kr20}{\overset{n\_kf20}{\rightleftarrows}} \left(IL6\text{-}gp80\text{-}gp130\text{-}JAK\right)2^{*}\text{-}STAT1C\text{-}STAT3C \quad \text{(N20)}$$

$$\left(IFN\text{-}R\text{-}JAK\right)2^{*}\text{-}STAT1C\text{-}STAT3C \xrightarrow{n\_k21} \left(IFN\text{-}R\text{-}JAK\right)2^{*}\text{-}STAT3C + STAT1C^{*} \quad \text{(N21)}$$

$$\left(IFN\text{-}R\text{-}JAK\right)2^{*}\text{-}STAT1C\text{-}STAT3C \xrightarrow{n\_k22} \left(IFN\text{-}R\text{-}JAK\right)2^{*}\text{-}STAT1C + STAT3C^{*} \quad \text{(N22)}$$

$$\left(IL6\text{-}gp80\text{-}gp130\text{-}JAK\right)2^{*}\text{-}STAT1C\text{-}STAT3C \xrightarrow{n\_k23} \left(IFN\text{-}R\text{-}JAK\right)2^{*}\text{-}STAT3C + STAT1C^{*} \quad \text{(N23)}$$

$$\left(IL6\text{-}gp80\text{-}gp130\text{-}JAK\right)2^{*}\text{-}STAT1C\text{-}STAT3C \xrightarrow{n\_k24} \left(IFN\text{-}R\text{-}JAK\right)2^{*}\text{-}STAT1C + STAT3C^{*} \quad \text{(N24)}$$

**Biochemical reactions of IFNγ signalling part of the crosstalk model**

$$R + JAK_{(IFN)} \underset{kb1}{\overset{kf1}{\rightleftarrows}} R\text{-}JAK \quad \text{(V1)}$$

$$IFN + R\text{-}JAK \underset{kb2}{\overset{kf2}{\rightleftarrows}} IFN\text{-}R\text{-}JAK \quad \text{(V2)}$$

$$(IFN\text{-}R\text{-}JAK) + (IFN\text{-}R\text{-}JAK) \underset{kb3}{\overset{kf3}{\rightleftarrows}} (IFN\text{-}R\text{-}JAK)2 \quad \text{(V3)}$$

$$(IFN\text{-}R\text{-}JAK)2 \xrightarrow{kf4} (IFN\text{-}R\text{-}JAK)2^* \quad \text{(V4)}$$

$$(IFN\text{-}R\text{-}JAK)2^* + STAT1C \underset{kb5}{\overset{kf5}{\rightleftarrows}} (IFN\text{-}R\text{-}JAK)2^*\text{-}STAT1C \quad \text{(V5)}$$

$$(IFN\text{-}R\text{-}JAK)2^*\text{-}STAT1C \xrightarrow{kf6} (IFN\text{-}R\text{-}JAK)2^* + STAT1C^* \quad \text{(V6)}$$

$$(IFN\text{-}R\text{-}JAK)2^* + STAT1C^* \underset{kb7}{\overset{kf7}{\rightleftarrows}} (IFN\text{-}R\text{-}JAK)2^*\text{-}STAT1C^* \quad \text{(V7)}$$

$$STAT1C^* + STAT1C^* \underset{kb8}{\overset{kf8}{\rightleftarrows}} (STAT1C^*)2 \quad \text{(V8)}$$

$$(IFN\text{-}R\text{-}JAK)2^* + SHP2 \underset{kb9}{\overset{kf9}{\rightleftarrows}} (IFN\text{-}R\text{-}JAK)2^*\text{-}SHP2 \quad \text{(V9)}$$

$$(IFN\text{-}R\text{-}JAK)2^*\text{-}SHP2 \xrightarrow{kf10} (IFN\text{-}R - JAK)2 + SHP2 \quad \text{(V10)}$$

$$PP1 + STAT1C^* \underset{kb11}{\overset{kf11}{\rightleftarrows}} PP1\text{-}STAT1C^* \quad \text{(V11)}$$

$$PP1\text{-}STAT1C^* \xrightarrow{kf12} PP1 + STAT1C \quad \text{(V12)}$$

$$STAT1C + STAT1C^* \underset{kb13}{\overset{kf13}{\rightleftarrows}} STAT1C\text{-}STAT1C^* \quad \text{(V13)}$$

$$(STAT1C^*)2 \underset{}{\overset{kf14}{\rightleftarrows}} (STAT1N^*)2 \quad \text{(V14)}$$

$$PP2 + STAT1N^* \underset{kb15}{\overset{kf15}{\rightleftarrows}} PP2\text{-}STAT1N^* \quad \text{(V15)}$$

$$PP2\text{-}STAT1N^* \xrightarrow{kf16} PP2 + STAT1N \quad \text{(V16)}$$

$$STAT1N \xrightarrow{kf17} STAT1C \quad \text{(V17)}$$

$$d[mRNA\text{-}SOCS1N]/dt = k18a * (STAT1N^*)2/[(STAT1N^*)2 + k18b] \quad \text{(V18)}$$

$$mRNA\text{-}SOCS1N \xrightarrow{kf19} mRNA\text{-}SOCS1C \quad \text{(V19)}$$

$$d[SOCS1]/dt = kf20 * mRNA\text{-}SOCS1C \quad \text{(V20)}$$

$$(IFN\text{-}R\text{-}JAK)2^* + SOCS1 \underset{kb21}{\overset{kf21}{\rightleftarrows}} (IFN\text{-}R\text{-}JAK)2^*\text{-}SOCS1 \quad \text{(V21)}$$

$$d[mRNA\text{-}SOCS1C]/dt = -kf22 * mRNA\text{-}SOCS1C \quad \text{(V22)}$$

$$d[SOCS1C]/dt = -kf23 * SOCS1C \quad \text{(V23)}$$

$$PP1 + (STAT1C*)2 \underset{kb24}{\overset{kf24}{\rightleftarrows}} PP1\text{-}(STAT1C*)2 \quad \text{(V24)}$$

$$PP1\text{-}(STAT1C*)2 \xrightarrow{kf25} PP1 + STAT1C\text{-}STAT1C* \quad \text{(V25)}$$

$$STAT1N* + STAT1N* \underset{kb26}{\overset{kf26}{\rightleftarrows}} (STAT1N*)2 \quad \text{(V26)}$$

$$PP2 + (STAT1N*)2 \underset{kb27}{\overset{kf27}{\rightleftarrows}} PP2\text{-}(STAT1N*)2 \quad \text{(V27)}$$

$$PP2\text{-}(STAT1N*)2 \xrightarrow{kf28} PP2 + STAT1N\text{-}STAT1N* \quad \text{(V28)}$$

$$STAT1N + STAT1N* \underset{kb29}{\overset{kf29}{\rightleftarrows}} STAT1N\text{-}STAT1N* \quad \text{(V29)}$$

$$(IFN\text{-}R\text{-}JAK)2*\text{-}SOCS1 + STAT1C \underset{kb30}{\overset{kf30}{\rightleftarrows}} (IFN\text{-}R\text{-}JAK)2*\text{-}STAT1C\text{-}SOCS1 \quad \text{(V30)}$$

$$(IFN\text{-}R\text{-}JAK)2*\text{-}STAT1C\text{-}SOCS1 + SHP2 \underset{kb31}{\overset{kf31}{\rightleftarrows}} (IFN\text{-}R\text{-}JAK)2*\text{-}STAT1C\text{-}SHP2\text{-}SOCS1 \quad \text{(V31)}$$

$$(IFN\text{-}R\text{-}JAK)2*\text{-}STAT1C\text{-}SHP2\text{-}SOCS1 \xrightarrow{kf32} (IFN\text{-}R\text{-}JAK)2* + SOCS1 + STAT1C + SHP2 \quad \text{(V32)}$$

$$(IFN\text{-}R\text{-}JAK)2*\text{-}SOCS1\text{-}STAT1C\text{-}SHP2 \xrightarrow{kf33} (IFN\text{-}R\text{-}JAK)2*\text{-}STAT1C\text{-}SHP2 + SOCS1 \quad \text{(V33)}$$

**Biochemical reactions of IL-6 signalling part of the crosstalk model**

$$IL6 + gp80 \underset{k1r}{\overset{k1f}{\rightleftarrows}} IL6\text{-}gp80 \quad (1)$$

$$gp130 + JAK_{(IL\text{-}6)} \underset{k2r}{\overset{k2f}{\rightleftarrows}} gp130\text{-}JAK \quad (2)$$

$$IL6\text{-}gp80 + gp130\text{-}JAK \underset{k3r}{\overset{k3f}{\rightleftarrows}} IL6\text{-}gp80\text{-}gp130\text{-}JAK \quad (3)$$

$$(IL6\text{-}gp80\text{-}gp130\text{-}JAK) + (IL6\text{-}gp80\text{-}gp130\text{-}JAK) \underset{k6r}{\overset{k6f}{\rightleftarrows}} (IL6\text{-}gp80\text{-}gp130\text{-}JAK)2 \quad (6)$$

$$(IL6\text{-}gp80\text{-}gp130\text{-}JAK)2 \xrightarrow{k7} (IL6\text{-}gp80\text{-}gp130\text{-}JAK)2* \quad (7)$$

$$(IL6\text{-}gp80\text{-}gp130\text{-}JAK)2* + STAT3C \underset{k8r}{\overset{k8f}{\rightleftarrows}} (IL6\text{-}gp80\text{-}gp130\text{-}JAK)2*\text{-}STAT3C \quad (8)$$

$$(IL6\text{-}gp80\text{-}gp130\text{-}JAK)2*\text{-}STAT3C \xrightarrow[k9r]{k9f} (IL6\text{-}gp80\text{-}gp130\text{-}JAK)2* + STAT3C* \quad (9)$$

$$(IL6\text{-}gp80\text{-}gp130\text{-}JAK)2* + STAT3C* \underset{k10r}{\overset{k10f}{\rightleftarrows}} (IL6\text{-}gp80\text{-}gp130\text{-}JAK)2*\text{-}STAT3C* \quad (10)$$

$$STAT3C* + STAT3C* \underset{k16r}{\overset{k16f}{\rightleftarrows}} (STAT3C*)2 \quad (16)$$

$$(IL6\text{-}gp80\text{-}gp130\text{-}JAK)2* + SHP2 \underset{k17r}{\overset{k17f}{\rightleftarrows}} (IL6\text{-}gp80\text{-}gp130\text{-}JAK)2*\text{-}SHP2 \quad (17)$$

$$(IL6\text{-}gp80\text{-}gp130\text{-}JAK)2^{*}\text{-}SHP2 \xrightarrow{k18} (IL6\text{-}gp80\text{-}gp130\text{-}JAK)2 + SHP2 \quad (18)$$

$$PP1 + STAT3C^{*} \underset{k19r}{\overset{k19f}{\rightleftarrows}} PP1\text{-}STAT3C^{*} \quad (19)$$

$$PP1\text{-}STAT3C^{*} \xrightarrow{k20} PP1 + STAT3C \quad (20)$$

$$PP1 + (STAT3C^{*})2 \underset{k21r}{\overset{k21f}{\rightleftarrows}} PP1\text{-}(STAT3C^{*})2 \quad (21)$$

$$PP1\text{-}(STAT3C^{*})2 \underset{k22r}{\overset{k22f}{\rightleftarrows}} PP1 + STAT3C\text{-}STAT3C^{*} \quad (22)$$

$$STAT3C + STAT3C^{*} \underset{k23r}{\overset{k23f}{\rightleftarrows}} STAT3C\text{-}STAT3C^{*} \quad (23)$$

$$(STAT3C^{*})2 \xrightarrow{k24} (STAT3N^{*})2 \quad (24)$$

$$(STAT3N^{*})2 \underset{k25r}{\overset{k25f}{\rightleftarrows}} STAT3N^{*} + STAT3N^{*} \quad (25)$$

$$PP2 + STAT3N^{*} \underset{k26r}{\overset{k26f}{\rightleftarrows}} PP1\text{-}STAT3N^{*} \quad (26)$$

$$PP2\text{-}STAT3N^{*} \xrightarrow{k27} PP2 + STAT3N \quad (27)$$

$$PP2 + (STAT3N^{*})2 \underset{k28r}{\overset{k28f}{\rightleftarrows}} PP2\text{-}(STAT3N^{*})2 \quad (28)$$

$$PP2\text{-}(STAT3N^{*})2 \xrightarrow[k29r]{k29f} PP2 + STAT3N\text{-}STAT3N^{*} \quad (29)$$

$$STAT3N\text{-}STAT3N^{*} \underset{k30r}{\overset{k30f}{\rightleftarrows}} STAT3N + STAT3N^{*} \quad (30)$$

$$STAT3N \xrightarrow{k31} STAT3C \quad (31)$$

$$d[mRNA\text{-}SOCS3N]/dt = k32f * (STAT3N^{*})2/[(STAT3N^{*})2 + k32r] \quad (32)$$

$$mRNA-SOCS3N \xrightarrow{k33} mRNA-SOCS3C \quad (33)$$

$$d[SOCS3]/dt = k34 * mRNA\text{-}SOCS3C \quad (34)$$

$$(IL6\text{-}gp80\text{-}gp130\text{-}JAK)2^{*} + SOCS3 \underset{k35r}{\overset{k35f}{\rightleftarrows}} (IL6\text{-}gp80\text{-}gp130\text{-}JAK)2^{*}\text{-}SOCS3 \quad (35)$$

$$d[mRNA\text{-}SOCS3C]/dt = -k36 * mRNA\text{-}SOCS3C \quad (36)$$

$$d[SOCS3C]/dt = -k37 * SOCS3C \quad (37)$$

$$(IL6\text{-}gp80\text{-}gp130\text{-}JAK)2^{*}\text{-}SOCS3 \xrightarrow{k38} (IL6\text{-}gp80\text{-}gp130\text{-}JAK)2 + SOCS3 \quad (38)$$

$$(IL6\text{-}gp80\text{-}gp130\text{-}JAK)2^{*}\text{-}SHP2 \underset{k39r}{\overset{k39f}{\rightleftarrows}} (IL6\text{-}gp80\text{-}gp130\text{-}JAK)2^{*}\text{-}SHP2^{*} \quad (39)$$

$$\left(IL6\text{-}gp80\text{-}gp130\text{-}JAK\right)2^{*}\text{-}SHP2^{*} + Grb2 \underset{k40r}{\overset{k40f}{\rightleftarrows}} \left(IL6\text{-}gp80\text{-}gp130\text{-}JAK\right)2^{*}\text{-}SHP2^{*}\text{-}Grb2 \quad (40)$$

$$\left(IL6\text{-}gp80\text{-}gp130\text{-}JAK\right)2^{*}\text{-}SHP2^{*}\text{-}Grb2 + SOS \underset{k41r}{\overset{k41f}{\rightleftarrows}} \left(IL6\text{-}gp80\text{-}gp130\text{-}JAK\right)2^{*}\text{-}SHP2^{*}\text{-}Grb2\text{-}SOS \quad (41)$$

$$\left(IL6\text{-}gp80\text{-}gp130\text{-}JAK\right)2^{*}\text{-}SHP2^{*}\text{-}Grb2\text{-}SOS + Ras\text{-}GDP \underset{k42r}{\overset{k42f}{\rightleftarrows}} \left(IL6\text{-}gp80\text{-}gp130\text{-}JAK\right)2^{*}\text{-}SHP2^{*}\text{-}Grb2\text{-}SOS\text{-}Ras\text{-}GDP \quad (42)$$

$$\left(IL6\text{-}gp80\text{-}gp130\text{-}JAK\right)2^{*}\text{-}SHP2^{*}\text{-}Grb2\text{-}SOS\text{-}Ras\text{-}GDP \underset{k43r}{\overset{k43f}{\rightleftarrows}} \left(IL6\text{-}gp80\text{-}gp130\text{-}JAK\right)2^{*}\text{-}SHP2^{*}\text{-}Grb2\text{-}SOS + Ras\text{-}GTP \quad (43)$$

$$Ras\text{-}GTP + Raf \xrightarrow{k44} Raf\text{-}Ras\text{-}GTP \quad (44)$$

$$Raf\text{-}Ras\text{-}GTP \xrightarrow{k45} Ras\text{-}GTP^{*} + Raf^{*} \quad (45)$$

$$\left(IL6\text{-}gp80\text{-}gp130\text{-}JAK\right)2^{*}\text{-}SHP2^{*}\text{-}Grb2\text{-}SOS + Ras\text{-}GTP^{*} \underset{k46r}{\overset{k46f}{\rightleftarrows}} \left(IL6\text{-}gp80\text{-}gp130\text{-}JAK\right)2^{*}\text{-}SHP2^{*}\text{-}Grb2\text{-}SOS\text{-}Ras\text{-}GTP \quad (46)$$

$$\left(IL6\text{-}gp80\text{-}gp130\text{-}JAK\right)2^{*}\text{-}SHP2^{*}\text{-}Grb2\text{-}SOS\text{-}Ras\text{-}GTP \underset{k47r}{\overset{k47f}{\rightleftarrows}} \left(IL6\text{-}gp80\text{-}gp130\text{-}JAK\right)2^{*}\text{-}SHP2^{*}\text{-}Grb2\text{-}SOS + Ras\text{-}GDP \quad (47)$$

$$\left(IL6\text{-}gp80\text{-}gp130\text{-}JAK\right)2^{*}\text{-}SHP2^{*}\text{-}Grb2\text{-}SOS \underset{k48r}{\overset{k48f}{\rightleftarrows}} \left(IL6\text{-}gp80\text{-}gp130\text{-}JAK\right)2^{*} + SHP2^{*}\text{-}Grb2\text{-}SOS \quad (48)$$

$$SHP2^{*}\text{-}Grb2\text{-}SOS \underset{k49r}{\overset{k49f}{\rightleftarrows}} Grb2\text{-}SOS + SHP2^{*} \quad (49)$$

$$Grb2\text{-}SOS \underset{k50r}{\overset{k50f}{\rightleftarrows}} Grb2 + SOS \quad (50)$$

$$SHP2^{*} \xrightarrow{k51} SHP2 \quad (51)$$

$$\left(IL6\text{-}gp80\text{-}gp130\text{-}JAK\right)2^{*}\text{-}SHP2^{*} \underset{k52r}{\overset{k52f}{\rightleftarrows}} \left(IL6\text{-}gp80\text{-}gp130\text{-}JAK\right)2^{*} + SHP2^{*} \quad (52)$$

$$Grb2 + SHP2^{*} \underset{k53r}{\overset{k53f}{\rightleftarrows}} SHP2^{*}\text{-}Grb2 \quad (53)$$

$$\left(IL6\text{-}gp80\text{-}gp130\text{-}JAK^{*}\right)2\text{-}SHP2^{*}\text{-}Grb2 \underset{k54r}{\overset{k54f}{\rightleftarrows}} \left(IL6\text{-}gp80\text{-}gp130\text{-}JAK^{*}\right)2 + SHP2^{*}\text{-}Grb2 \quad (54)$$

$$SOS + SHP2^{*}\text{-}Grb2 \underset{k55r}{\overset{k55f}{\rightleftarrows}} SHP2^{*}\text{-}Grb2\text{-}SOS \quad (55)$$

$$\left(IL6\text{-}gp80\text{-}gp130\text{-}JAK\right)2^{*}\text{-}SHP2^{*} + Grb2\text{-}SOS \underset{k56r}{\overset{k56f}{\rightleftarrows}} \left(IL6\text{-}gp80\text{-}gp130\text{-}JAK\right)2^{*}\text{-}SHP2^{*}\text{-}Grb2\text{-}SOS \quad (56)$$

$$Phosp1 + Raf^{*} \underset{k57r}{\overset{k57f}{\rightleftarrows}} Raf^{*}\text{-}Phosp1 \quad (57)$$

$$Raf^{*}\text{-}Phosp1 \xrightarrow{k58} Raf + Phosp1 \quad (58)$$

$$Raf^{*} + MEK \underset{k59r}{\overset{k59f}{\rightleftarrows}} MEK\text{-}Raf^{*} \quad (59)$$

$$MEK\text{-}Raf^{*} \xrightarrow{k60} MEK\text{-}P + Raf^{*} \quad (60)$$

$$MEK\text{-}P + Raf^{*} \underset{k61r}{\overset{k61f}{\rightleftarrows}} MEK\text{-}P\text{-}Raf^{*} \quad (61)$$

$$MEK\text{-}P\text{-}Raf* \xrightarrow{k62} MEK\text{-}PP + Raf* \quad (62)$$

$$MEK\text{-}PP + Phosp2 \underset{k63r}{\overset{k63f}{\rightleftarrows}} MEK\text{-}PP\text{-}Phosp2 \quad (63)$$

$$MEK\text{-}PP\text{-}Phosp2 \xrightarrow{k64} MEK\text{-}P + Phosp2 \quad (64)$$

$$MEK\text{-}P + Phosp2 \underset{k65r}{\overset{k65f}{\rightleftarrows}} MEK\text{-}P\text{-}Phosp2 \quad (65)$$

$$MEK\text{-}P\text{-}Phosp2 \xrightarrow{k66} MEK + Phosp2 \quad (66)$$

$$MEK\text{-}PP + ERK \underset{k67r}{\overset{k67f}{\rightleftarrows}} ERK\text{-}MEK\text{-}PP \quad (67)$$

$$ERK - MEK - PP \xrightarrow{k68} ERK - P + MEK - PP \quad (68)$$

$$ERK\text{-}P + MEK\text{-}PP \underset{k69r}{\overset{k69f}{\rightleftarrows}} ERK\text{-}P\text{-}MEK\text{-}PP \quad (69)$$

$$ERK\text{-}P\text{-}MEK\text{-}PP \xrightarrow{k70} ERK\text{-}PP + MEK\text{-}PP \quad (70)$$

$$ERK\text{-}PP + Phosp3 \underset{k71r}{\overset{k71f}{\rightleftarrows}} ERK\text{-}PP\text{-}Phosp3 \quad (71)$$

$$ERK\text{-}PP\text{-}Phosp3 \xrightarrow{k72} ERK\text{-}P + Phosp3 \quad (72)$$

$$ERK\text{-}P + Phosp3 \underset{k73r}{\overset{k73f}{\rightleftarrows}} ERK\text{-}P\text{-}Phosp3 \quad (73)$$

$$ERK\text{-}P\text{-}Phosp3 \xrightarrow{k74} ERK + Phosp3 \quad (74)$$

$$d[CEBP]/dt = k75f * CEBPi * ERK\text{-}PP/(CEBPi + k75r) \quad (75)$$

$$CEBP \xrightarrow{k76} CEBPi \quad (76)$$

$$CEBP + CEBP \underset{k77r}{\overset{k77f}{\rightleftarrows}} CEBPn \quad (77)$$

# Reference


1. Yamada S, Shiono S, Joo A, Yoshimura A: **Control mechanism of JAK/STAT signal transduction pathway**. *FEBS Lett* 2003, **534**(1-3):190-196.
2. Moya C, Huang Z, Cheng P, Jayaraman A, Hahn J: **Investigation of IL-6 and IL-10 signalling via mathematical modelling**. *IET Syst Biol* 2011, **5**(1):15.