

Process 0 on cabernet out of 1

BIOCHAM 3.4

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| **load\_biocham('tgf\_andrieux\_ovidiu.bc')**.

volume(PM,1).

volume(Endosome,1).

volume(nucleus,1).

volume(cytosol,1).

parameter(PM,1).

parameter(Endosome,1).

parameter(nucleus,1).

parameter(cytosol,1).

parameter(PPase,1).

parameter(TGFb,10).

parameter(ka,1).

parameter(kcd,0.000468).

parameter(klid,0.00416).

parameter(ki,0.00555).

parameter(pRI,9.75e-05).

parameter(kr,0.000555).

parameter(pRII,4.87e-05).

parameter(kin,0.0026).

parameter(kex,0.056).

parameter(kphos,0.000404).

parameter(kdephos,0.0071).

parameter(kin\_CIF,0.0148).

parameter(kon,0.002).

parameter(koff,0.016).

present(RI::PM,2.9).

present(RII::PM,2.7).

present(S2c::cytosol,170.3).

present(S2n::nucleus,7.9).

present(S4c::cytosol,50.8).

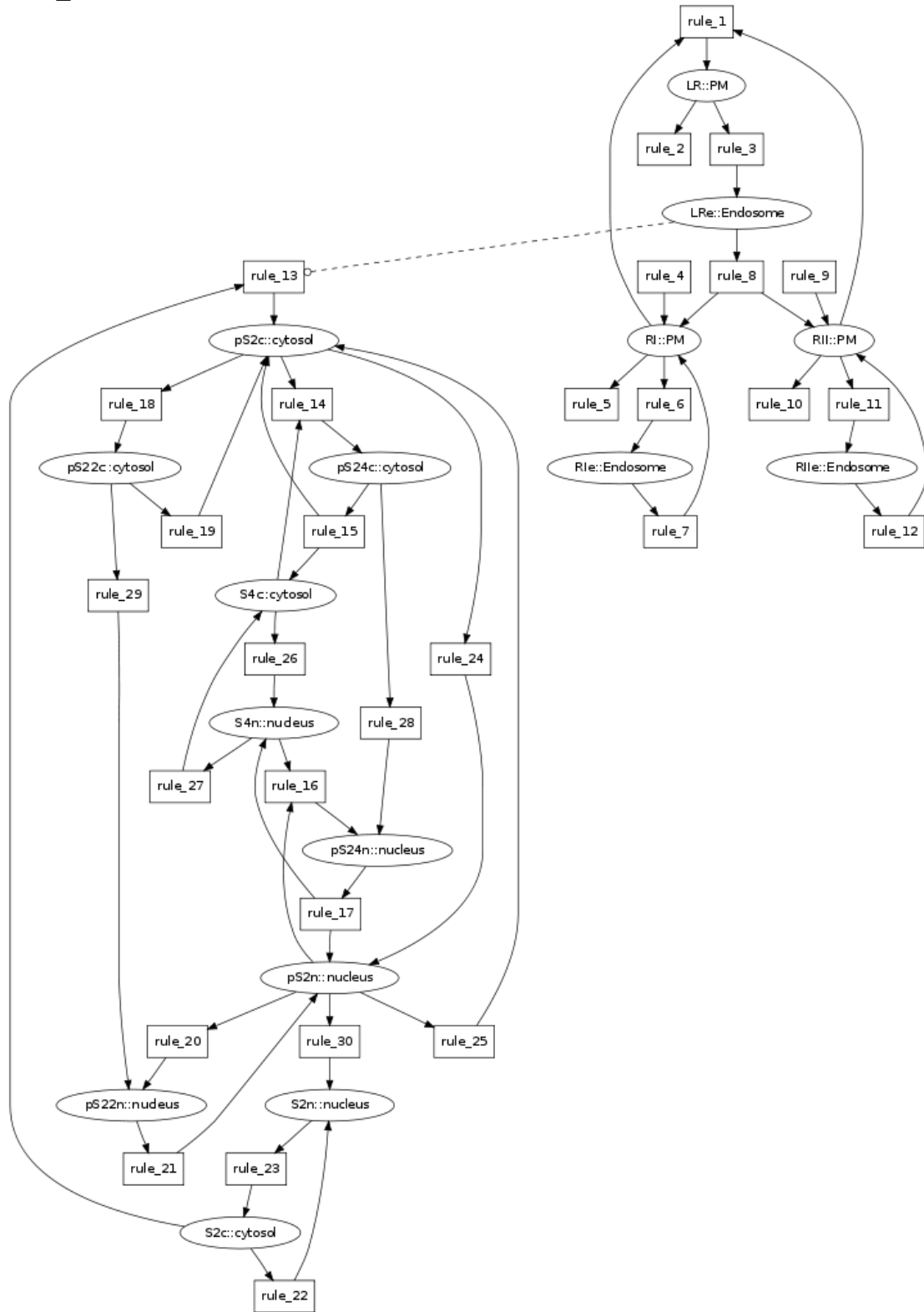
present(S4n::nucleus,50.8).  
 absent(LR::PM).  
 absent(LRe::Endosome).  
 absent(RIle::Endosome).  
 absent(Rle::Endosome).  
 absent(pS2c::cytosol).  
 absent(pS2n::nucleus).  
 absent(pS22c::cytosol).  
 absent(pS22n::nucleus).  
 absent(pS24c::cytosol).  
 absent(pS24n::nucleus).

**| list \_ rules.**

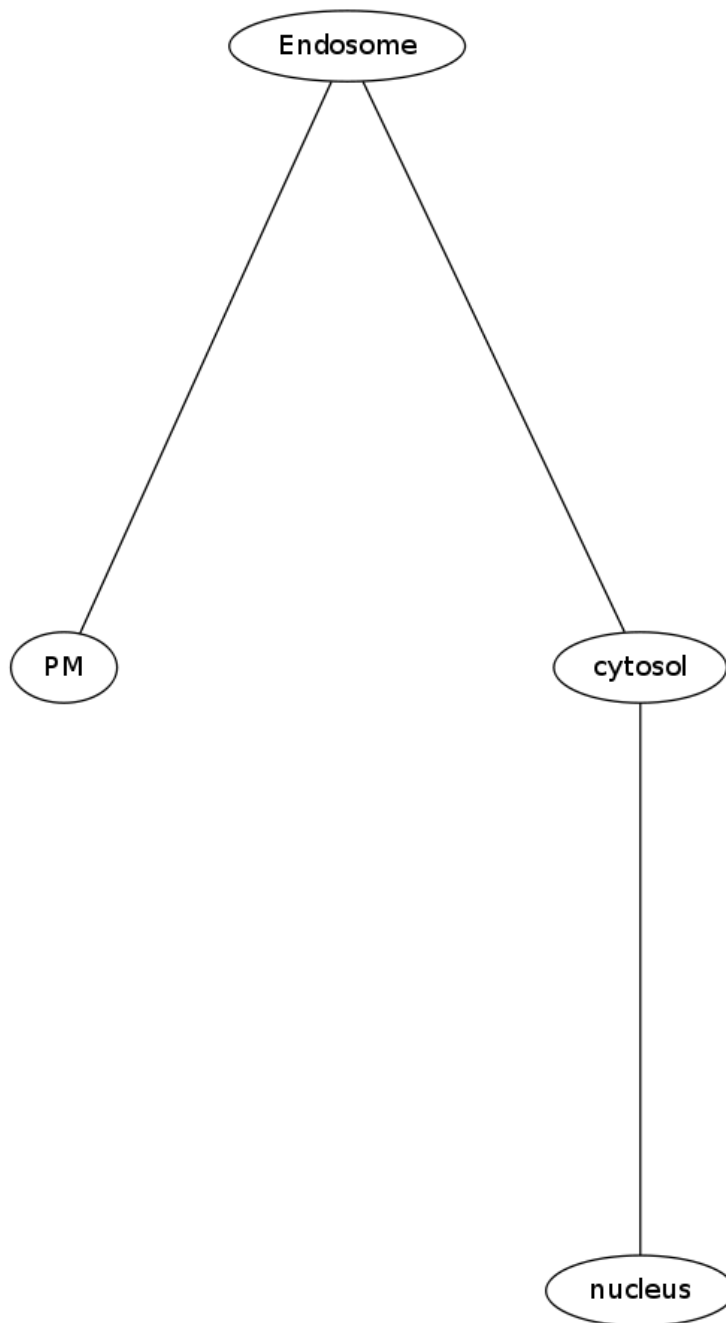
reaction\_1:ka\*TGFb\*[RI::PM]\*[RII::PM] for RI::PM+(RII::PM)=>LR::PM.  
 reaction\_2:kcd\*[LR::PM]+klid\*[LR::PM] for LR::PM=>\_.  
 reaction\_4:ki\*[LR::PM] for LR::PM=>LRe::Endosome.  
 reaction\_5:pRI for \_=>RI::PM.  
 reaction\_6:kcd\*[RI::PM] for RI::PM=>\_.  
 reaction\_7:ki\*[RI::PM] for RI::PM=>Rle::Endosome.  
 reaction\_8:kr\*[Rle::Endosome] for Rle::Endosome=>RI::PM.  
 reaction\_9:kr\*[LRe::Endosome] for LRe::Endosome=>RII::PM+(RI::PM).  
 reaction\_10:pRII for \_=>RII::PM.  
 reaction\_11:kcd\*[RII::PM] for RII::PM=>\_.  
 reaction\_12:ki\*[RII::PM] for RII::PM=>RIle::Endosome.  
 reaction\_13:kr\*[RIle::Endosome] for RIle::Endosome=>RII::PM.  
 reaction\_14:kphos\*[LRe::Endosome]\*[S2c::cytosol] for S2c::cytosol+(LRe::Endosome)=>pS2c::cyto  
 sol+(LRe::Endosome).  
 reaction\_15:(kon\*[pS2c::cytosol]\*[S4c::cytosol],koff\*[pS24c::cytosol]) for S4c::cytosol+(pS2c::cyto  
 sol)<=>pS24c::cytosol.  
 reaction\_16:(kon\*[pS2n::nucleus]\*[S4n::nucleus],koff\*[pS24n::nucleus]) for S4n::nucleus+(pS2n::nu  
 cleus)<=>pS24n::nucleus.  
 reaction\_17:(kon\*[pS2c::cytosol]\*[pS2c::cytosol],koff\*[pS22c::cytosol]) for 2\*(pS2c::cytosol)<=>p  
 S22c::cytosol.  
 reaction\_18:(kon\*[pS2n::nucleus]\*[pS2n::nucleus],koff\*[pS22n::nucleus]) for 2\*(pS2n::nucleus)<=>  
 pS22n::nucleus.  
 reaction\_19:(kin\*[S2c::cytosol],kex\*[S2n::nucleus]) for S2c::cytosol<=>S2n::nucleus.  
 reaction\_20:(kin\*[pS2c::cytosol],kex\*[pS2n::nucleus]) for pS2c::cytosol<=>pS2n::nucleus.  
 reaction\_21:(kin\*[S4c::cytosol],kin\*[S4n::nucleus]) for S4c::cytosol<=>S4n::nucleus.  
 reaction\_22:kin\_CIF\*[pS24c::cytosol] for pS24c::cytosol=>pS24n::nucleus.  
 reaction\_23:kin\_CIF\*[pS22c::cytosol] for pS22c::cytosol=>pS22n::nucleus.

reaction\_24:kdephos\*[pS2n::nucleus]\*PPase for pS2n::nucleus=>S2n::nucleus.

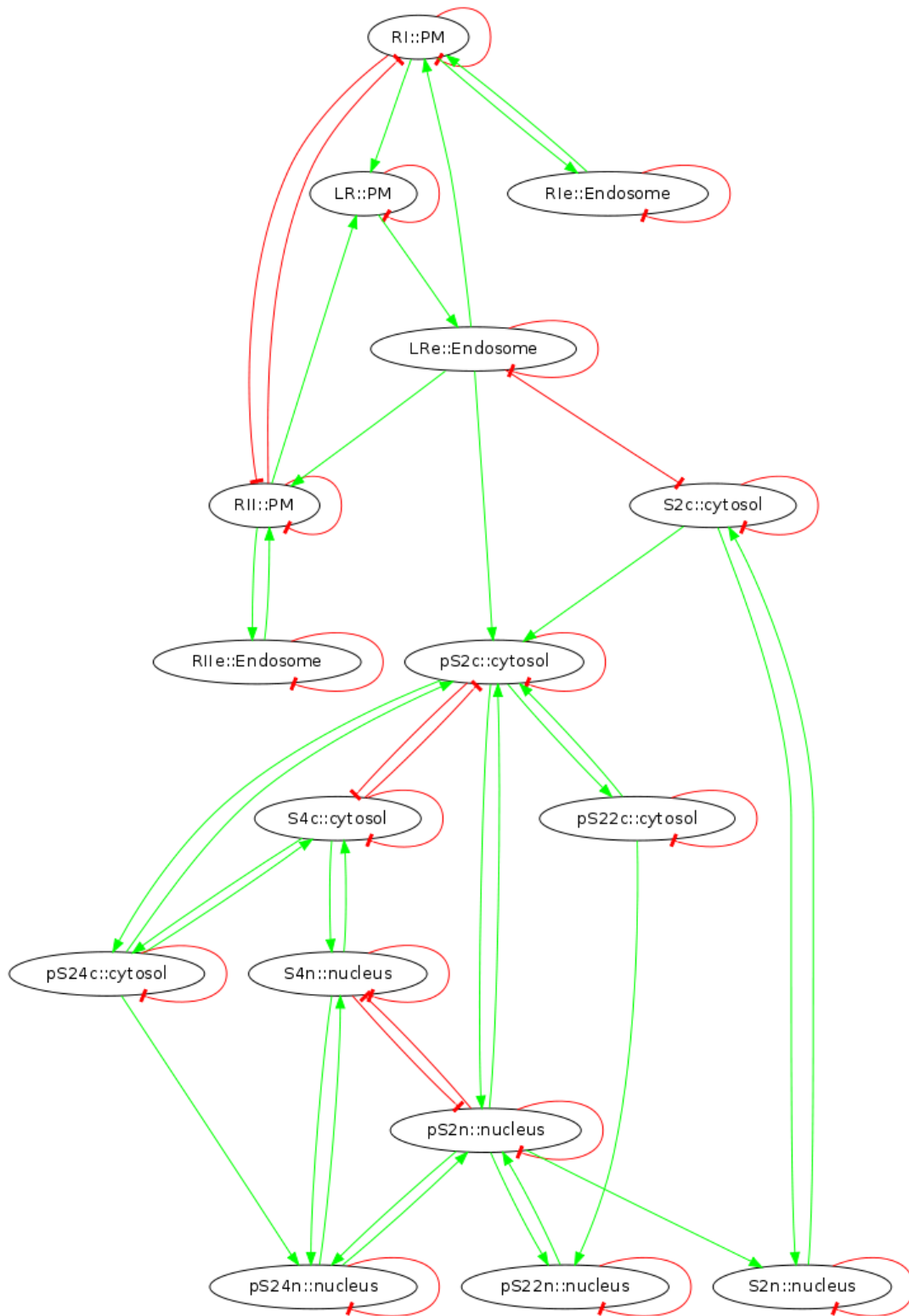
| draw\_reactions.



| draw\_neighborhood.



| draw\_influences.



## | list\_kinetics

..

Init ODE

2.9  $d[RI::PM]/dt = pRI + (kr*[RIe::Endosome] + kr*[LRe::Endosome] - ki*[RI::PM] - kcd*[RI::PM]) - ka*TGFb*[RI::PM]*[RII::PM]$

2.7  $d[RII::PM]/dt = kr*[LRe::Endosome] + pRII + kr*[RIIe::Endosome] - ki*[RII::PM] - kcd*[RII::PM] - ka*TGFb*[RI::PM]*[RII::PM]$

170.3  $d[S2c::cytosol]/dt = kex*[S2n::nucleus] - kin*[S2c::cytosol] - kphos*[LRe::Endosome]*[S2c::cytosol]$

7.9  $d[S2n::nucleus]/dt = kin*[S2c::cytosol] + kdephos*[pS2n::nucleus]*PPase - kex*[S2n::nucleus]$

50.8  $d[S4c::cytosol]/dt = koff*[pS24c::cytosol] + kin*[S4n::nucleus] - kin*[S4c::cytosol] - kon*[pS2c::cytosol]*[S4c::cytosol]$

50.8  $d[S4n::nucleus]/dt = koff*[pS24n::nucleus] + kin*[S4c::cytosol] - kin*[S4n::nucleus] - kon*[pS2n::nucleus]*[S4n::nucleus]$

0  $d[LR::PM]/dt = ka*TGFb*[RI::PM]*[RII::PM] - (kcd + klid + ki)*[LR::PM]$

0  $d[LRe::Endosome]/dt = ki*[LR::PM] - kr*[LRe::Endosome]$

0  $d[RIIe::Endosome]/dt = ki*[RII::PM] - kr*[RIIe::Endosome]$

0  $d[RIe::Endosome]/dt = ki*[RI::PM] - kr*[RIe::Endosome]$

0  $d[pS2c::cytosol]/dt = kphos*[LRe::Endosome]*[S2c::cytosol] + koff*[pS24c::cytosol] + (2*koff*[pS22c::cytosol] + kex*[pS2n::nucleus] - kin*[pS2c::cytosol] - 2*kon*[pS2c::cytosol]*[pS2c::cytosol] - kon*[pS2c::cytosol]*[S4c::cytosol])$

0  $d[pS2n::nucleus]/dt = koff*[pS24n::nucleus] + (2*koff*[pS22n::nucleus] + kin*[pS2c::cytosol] - kex*[pS2n::nucleus] - kdephos*[pS2n::nucleus]*PPase - 2*kon*[pS2n::nucleus]*[pS2n::nucleus] - kon*[pS2n::nucleus]*[S4n::nucleus])$

0  $d[pS22c::cytosol]/dt = kon*[pS2c::cytosol]*[pS2c::cytosol] - (koff + kin\_CIF)*[pS22c::cytosol]$

0  $d[pS22n::nucleus]/dt = kon*[pS2n::nucleus]*[pS2n::nucleus] + kin\_CIF*[pS22c::cytosol] - koff*[pS22n::nucleus]$

0  $d[pS24c::cytosol]/dt = kon*[pS2c::cytosol]*[S4c::cytosol] - (koff + kin\_CIF)*[pS24c::cytosol]$

0  $d[pS24n::nucleus]/dt = kon*[pS2n::nucleus]*[S4n::nucleus] + kin\_CIF*[pS24c::cytosol] - koff*[pS24n::nucleus]$

## | search\_conservations.

[S4c::cytosol,S4n::nucleus,pS24c::cytosol,pS24n::nucleus].

[2\*(pS22c::cytosol),2\*(pS22n::nucleus),S2c::cytosol,S2n::nucleus,pS24c::cytosol,pS24n::nucleus,pS2c::cytosol,pS2n::nucleus].

## | list\_dimensions.

cytosol has unknown dimension

nucleus has unknown dimension

Endosome has unknown dimension

PM has unknown dimension

ka has unknown dimension

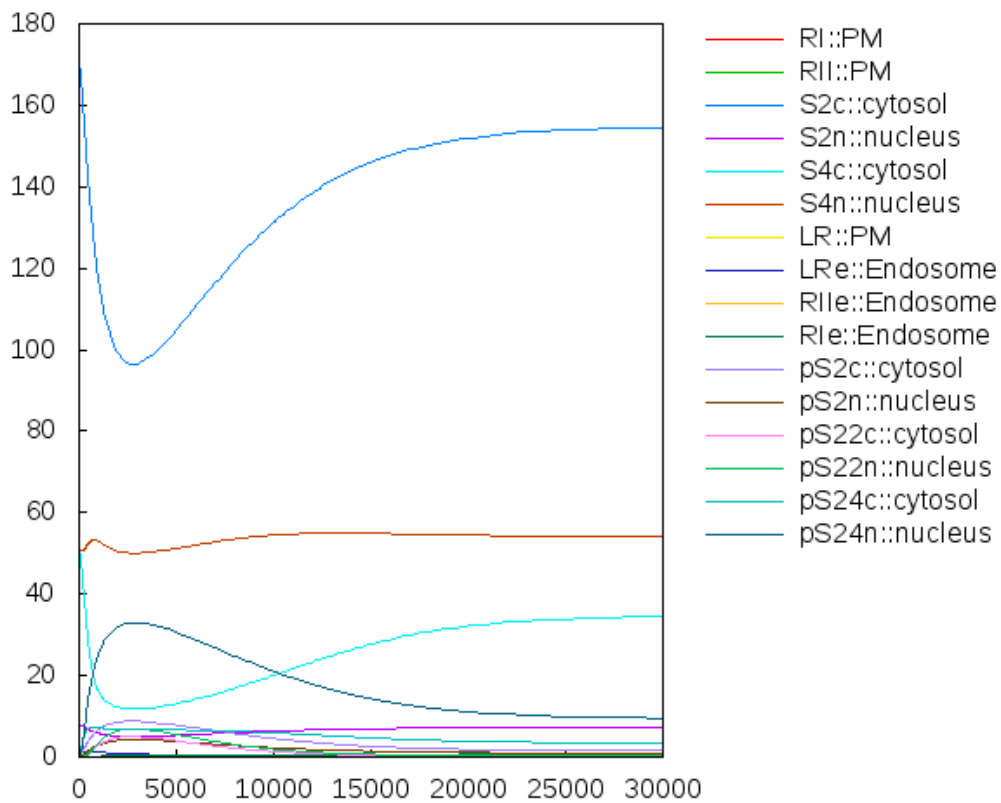
TGFb has unknown dimension

kdepshos has unknown dimension  
 PPase has unknown dimension  
 kcd has dimension  $\text{time}^{-1}$   
 klid has dimension  $\text{time}^{-1}$   
 ki has dimension  $\text{time}^{-1}$   
 pRI has dimension  $\text{time}^{-1}$   
 kr has dimension  $\text{time}^{-1}$   
 pRII has dimension  $\text{time}^{-1}$   
 kin has dimension  $\text{time}^{-1}$   
 kex has dimension  $\text{time}^{-1}$   
 kphos has dimension  $\text{time}^{-1}$   
 kin\_CIF has dimension  $\text{time}^{-1}$   
 kon has dimension  $\text{time}^{-1}$   
 koff has dimension  $\text{time}^{-1}$

| **numerical\_simulation(30000).**

Simulation time: 0.55s

| **plot.**





| **check\_ttl(G([S2c::cytosol]>80)).**

G([S2c::cytosol]>80) is true.

| **check\_ttl(G([S2c::cytosol]>100)).**

G([S2c::cytosol]>100) is false.

| **domains(G([S2c::cytosol]>V)).**

V < 96.4354

time elapsed : 0 ms

| **search\_parameters\_cmaes([kphos,kon,koff,kin,kex],  
[(0.00001,0.001),(0.0001,0.01),(0.001,0.1),(0.001,0.01),(0.001,0.1)],  
G([S2c::cytosol]>V), [V], [100], 30000).**

Simulation time: 0.54s

Simulation time: 0.53s

Initial Parameters :

parameter(kphos,0.000404).

parameter(kon,0.002).

parameter(koff,0.016).

parameter(kin,0.0026).

parameter(kex,0.056).

Initial Cost : 3.5646

dim: 5; multi: 0; maxevals\_b: 300; stopfitness\_b: 0.010000; cseed: 0; std: 0.100000

(4,8)-CMA-ES(mu\_eff=2.8), Ver="3.02.03.beta", dimension=5, randomSeed=808888772 (Thu Apr 18 12:30:47 2013)

Simulation time: 0.51s

Simulation time: 0.55s

Simulation time: 0.55s

Simulation time: 0.51s

Simulation time: 0.53s

Simulation time: 0.53s

Simulation time: 0.52s

Simulation time: 0.53s

1 generations, 8 fevals (0.0 sec): f(x)=0

(axis-ratio=1.00e+00, max/min-stddev=8.56e-02/8.27e-02)

Stop (run 1):

Fitness: function value 0.00e+00 <= stopFitness (1.00e-02)

Simulation time: 0.52s

Final cost : 0

Simulation time: 0.54s

Found Parameters :

parameter(kphos,0.000356805724).

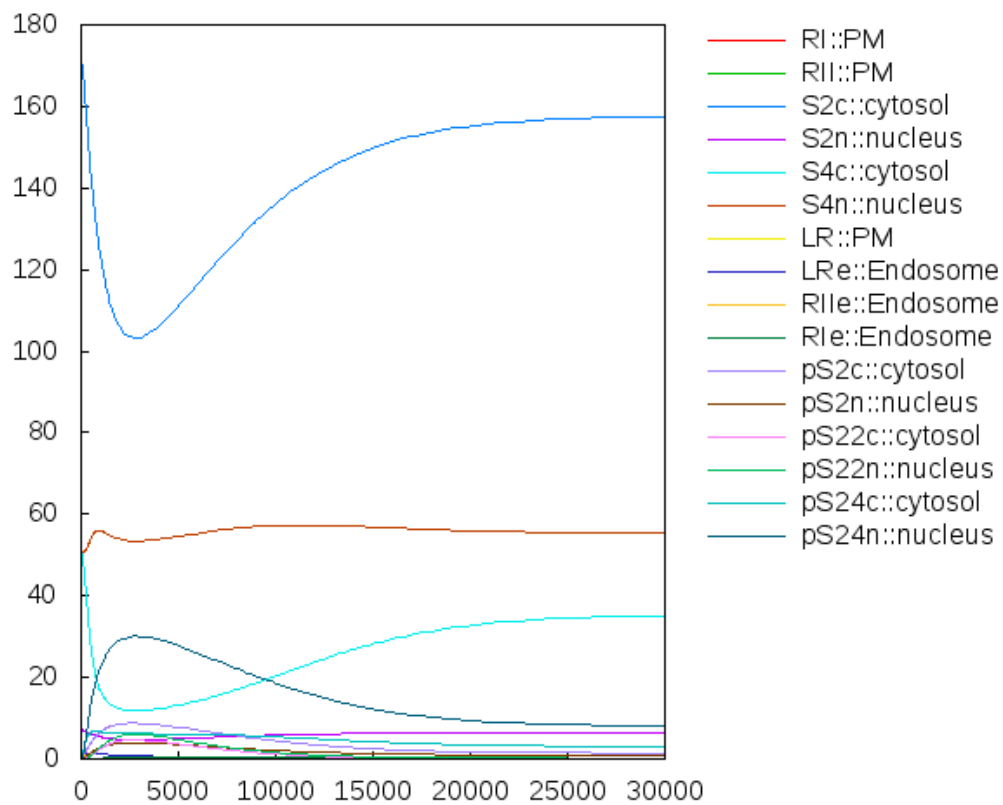
```

parameter(kon,0.00188201839).
parameter(koff,0.0165358208).
parameter(kin,0.002218906).
parameter(kex,0.0543609711).

```

Time elapsed 6.49 s

| **plot.**



| **list\_parameters.**

```

parameter(PM,1).
parameter(Endosome,1).
parameter(nucleus,1).
parameter(cytosol,1).
parameter(PPase,1).
parameter(TGFb,10).
parameter(ka,1).
parameter(kcd,0.000468).
parameter(klid,0.00416).
parameter(ki,0.00555).

```

parameter(pRI,9.75e-05).  
 parameter(kr,0.000555).  
 parameter(pRII,4.87e-05).  
 parameter(kdephos,0.0071).  
 parameter(kin\_CIF,0.0148).  
 parameter(kphos,0.000404).  
 parameter(kon,0.002).  
 parameter(koff,0.016).  
 parameter(kin,0.0026).  
 parameter(kex,0.056).

**| boolean\_simulation(100).**

All molecules not explicitly present are considered absent.

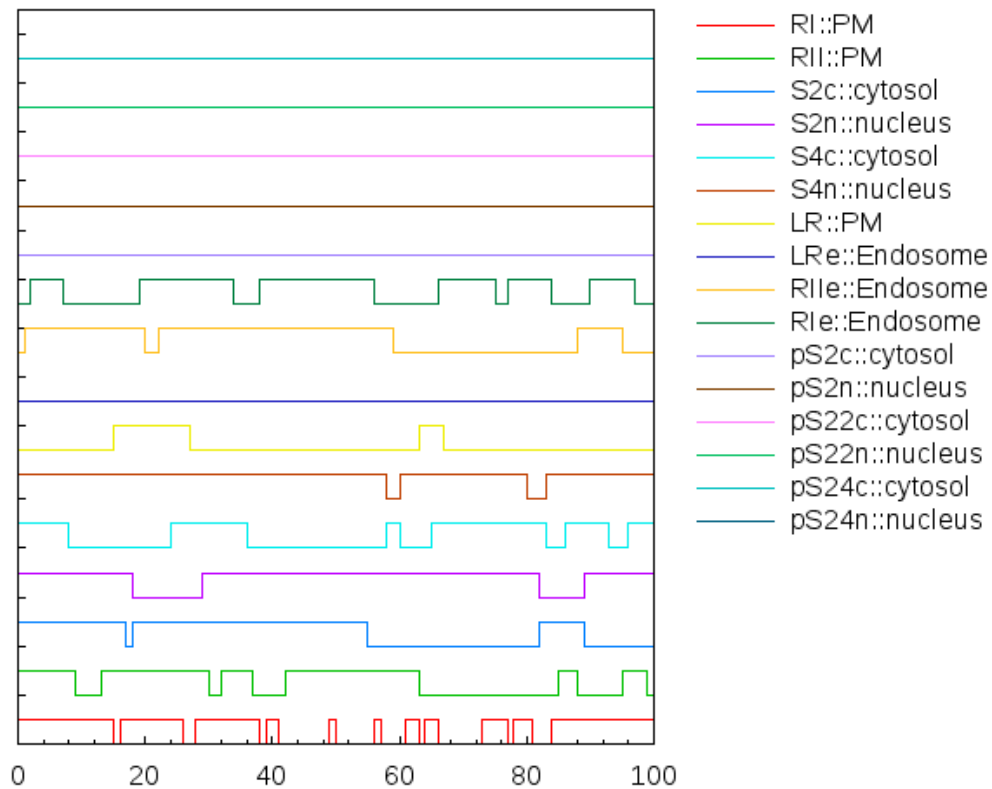
0: RI::PM RII::PM S2c::cytosol S2n::nucleus S4c::cytosol S4n::nucleus  
 1 reaction\_12: RI::PM RII::PM S2c::cytosol S2n::nucleus S4c::cytosol S4n::nucleus RIIe::Endosome  
 2 reaction\_7: RI::PM RII::PM S2c::cytosol S2n::nucleus S4c::cytosol S4n::nucleus RIIe::Endosome RIIe::Endosome  
 3 reaction\_10: RI::PM RII::PM S2c::cytosol S2n::nucleus S4c::cytosol S4n::nucleus RIIe::Endosome RIIe::Endosome  
 4 reaction\_21: RI::PM RII::PM S2c::cytosol S2n::nucleus S4c::cytosol S4n::nucleus RIIe::Endosome RIIe::Endosome  
 5 reaction\_5: RI::PM RII::PM S2c::cytosol S2n::nucleus S4c::cytosol S4n::nucleus RIIe::Endosome RIIe::Endosome  
 6 reaction\_8: RI::PM RII::PM S2c::cytosol S2n::nucleus S4c::cytosol S4n::nucleus RIIe::Endosome RIIe::Endosome  
 7 reaction\_8: RI::PM RII::PM S2c::cytosol S2n::nucleus S4c::cytosol S4n::nucleus RIIe::Endosome  
 8 reaction\_21: RI::PM RII::PM S2c::cytosol S2n::nucleus S4n::nucleus RIIe::Endosome  
 9 reaction\_11: RI::PM S2c::cytosol S2n::nucleus S4n::nucleus RIIe::Endosome  
 10 reaction\_19: RI::PM S2c::cytosol S2n::nucleus S4n::nucleus RIIe::Endosome  
 11 reaction\_19: RI::PM S2c::cytosol S2n::nucleus S4n::nucleus RIIe::Endosome  
 12 reaction\_19: RI::PM S2c::cytosol S2n::nucleus S4n::nucleus RIIe::Endosome  
 13 reaction\_10: RI::PM RII::PM S2c::cytosol S2n::nucleus S4n::nucleus RIIe::Endosome  
 14 reaction\_11: RI::PM RII::PM S2c::cytosol S2n::nucleus S4n::nucleus RIIe::Endosome  
 15 reaction\_1: RII::PM S2c::cytosol S2n::nucleus S4n::nucleus LR::PM RIIe::Endosome  
 16 reaction\_5: RI::PM RII::PM S2c::cytosol S2n::nucleus S4n::nucleus LR::PM RIIe::Endosome  
 17 reaction\_19: RI::PM RII::PM S2n::nucleus S4n::nucleus LR::PM RIIe::Endosome  
 18 reaction\_19: RI::PM RII::PM S2c::cytosol S4n::nucleus LR::PM RIIe::Endosome  
 19 reaction\_7: RI::PM RII::PM S2c::cytosol S4n::nucleus LR::PM RIIe::Endosome RIIe::Endosome

20 reaction\_13: RI::PM RII::PM S2c::cytosol S4n::nucleus LR::PM Rle::Endosome  
 21 reaction\_2: RI::PM RII::PM S2c::cytosol S4n::nucleus LR::PM Rle::Endosome  
 22 reaction\_12: RI::PM RII::PM S2c::cytosol S4n::nucleus LR::PM RIIe::Endosome Rle::Endosome  
 23 reaction\_5: RI::PM RII::PM S2c::cytosol S4n::nucleus LR::PM RIIe::Endosome Rle::Endosome  
 24 reaction\_21: RI::PM RII::PM S2c::cytosol S4c::cytosol S4n::nucleus LR::PM RIIe::Endosome Rle::Endosome  
 25 reaction\_11: RI::PM RII::PM S2c::cytosol S4c::cytosol S4n::nucleus LR::PM RIIe::Endosome Rle::Endosome  
 26 reaction\_6: RII::PM S2c::cytosol S4c::cytosol S4n::nucleus LR::PM RIIe::Endosome Rle::Endosome  
 27 reaction\_2: RII::PM S2c::cytosol S4c::cytosol S4n::nucleus RIIe::Endosome Rle::Endosome  
 28 reaction\_5: RI::PM RII::PM S2c::cytosol S4c::cytosol S4n::nucleus RIIe::Endosome Rle::Endosome  
 29 reaction\_19: RI::PM RII::PM S2c::cytosol S2n::nucleus S4c::cytosol S4n::nucleus RIIe::Endosome Rle::Endosome  
 30 reaction\_12: RI::PM S2c::cytosol S2n::nucleus S4c::cytosol S4n::nucleus RIIe::Endosome Rle::Endosome  
 31 reaction\_19: RI::PM S2c::cytosol S2n::nucleus S4c::cytosol S4n::nucleus RIIe::Endosome Rle::Endosome  
 32 reaction\_10: RI::PM RII::PM S2c::cytosol S2n::nucleus S4c::cytosol S4n::nucleus RIIe::Endosome Rle::Endosome  
 33 reaction\_6: RI::PM RII::PM S2c::cytosol S2n::nucleus S4c::cytosol S4n::nucleus RIIe::Endosome Rle::Endosome  
 34 reaction\_8: RI::PM RII::PM S2c::cytosol S2n::nucleus S4c::cytosol S4n::nucleus RIIe::Endosome Rle::Endosome  
 35 reaction\_19: RI::PM RII::PM S2c::cytosol S2n::nucleus S4c::cytosol S4n::nucleus RIIe::Endosome Rle::Endosome  
 36 reaction\_21: RI::PM RII::PM S2c::cytosol S2n::nucleus S4n::nucleus RIIe::Endosome Rle::Endosome  
 37 reaction\_11: RI::PM S2c::cytosol S2n::nucleus S4n::nucleus RIIe::Endosome Rle::Endosome  
 38 reaction\_7: S2c::cytosol S2n::nucleus S4n::nucleus RIIe::Endosome Rle::Endosome  
 39 reaction\_5: RI::PM S2c::cytosol S2n::nucleus S4n::nucleus RIIe::Endosome Rle::Endosome  
 40 reaction\_7: RI::PM S2c::cytosol S2n::nucleus S4n::nucleus RIIe::Endosome Rle::Endosome  
 41 reaction\_6: S2c::cytosol S2n::nucleus S4n::nucleus RIIe::Endosome Rle::Endosome  
 42 reaction\_10: RII::PM S2c::cytosol S2n::nucleus S4n::nucleus RIIe::Endosome Rle::Endosome  
 43 reaction\_13: RII::PM S2c::cytosol S2n::nucleus S4n::nucleus RIIe::Endosome Rle::Endosome

44 reaction\_19: RII::PM S2c::cytosol S2n::nucleus S4n::nucleus RIIe::Endosome Rle::Endosome  
 45 reaction\_19: RII::PM S2c::cytosol S2n::nucleus S4n::nucleus RIIe::Endosome Rle::Endosome  
 46 reaction\_12: RII::PM S2c::cytosol S2n::nucleus S4n::nucleus RIIe::Endosome Rle::Endosome  
 47 reaction\_12: RII::PM S2c::cytosol S2n::nucleus S4n::nucleus RIIe::Endosome Rle::Endosome  
 48 reaction\_10: RII::PM S2c::cytosol S2n::nucleus S4n::nucleus RIIe::Endosome Rle::Endosome  
 49 reaction\_5: RI::PM RII::PM S2c::cytosol S2n::nucleus S4n::nucleus RIIe::Endosome Rle::Endosome  
 50 reaction\_7: RII::PM S2c::cytosol S2n::nucleus S4n::nucleus RIIe::Endosome Rle::Endosome  
 51 reaction\_19: RII::PM S2c::cytosol S2n::nucleus S4n::nucleus RIIe::Endosome Rle::Endosome  
 52 reaction\_19: RII::PM S2c::cytosol S2n::nucleus S4n::nucleus RIIe::Endosome Rle::Endosome  
 53 reaction\_10: RII::PM S2c::cytosol S2n::nucleus S4n::nucleus RIIe::Endosome Rle::Endosome  
 54 reaction\_19: RII::PM S2c::cytosol S2n::nucleus S4n::nucleus RIIe::Endosome Rle::Endosome  
 55 reaction\_19: RII::PM S2n::nucleus S4n::nucleus RIIe::Endosome Rle::Endosome  
 56 reaction\_8: RI::PM RII::PM S2n::nucleus S4n::nucleus RIIe::Endosome  
 57 reaction\_6: RII::PM S2n::nucleus S4n::nucleus RIIe::Endosome  
 58 reaction\_21: RII::PM S2n::nucleus S4c::cytosol RIIe::Endosome  
 59 reaction\_13: RII::PM S2n::nucleus S4c::cytosol  
 60 reaction\_21: RII::PM S2n::nucleus S4n::nucleus  
 61 reaction\_5: RI::PM RII::PM S2n::nucleus S4n::nucleus  
 62 reaction\_11: RI::PM RII::PM S2n::nucleus S4n::nucleus  
 63 reaction\_1: S2n::nucleus S4n::nucleus LR::PM  
 64 reaction\_5: RI::PM S2n::nucleus S4n::nucleus LR::PM  
 65 reaction\_21: RI::PM S2n::nucleus S4c::cytosol S4n::nucleus LR::PM  
 66 reaction\_7: S2n::nucleus S4c::cytosol S4n::nucleus LR::PM Rle::Endosome  
 67 reaction\_2: S2n::nucleus S4c::cytosol S4n::nucleus Rle::Endosome  
 68 reaction\_21: S2n::nucleus S4c::cytosol S4n::nucleus Rle::Endosome  
 69 reaction\_21: S2n::nucleus S4c::cytosol S4n::nucleus Rle::Endosome  
 70 reaction\_21: S2n::nucleus S4c::cytosol S4n::nucleus Rle::Endosome  
 71 reaction\_21: S2n::nucleus S4c::cytosol S4n::nucleus Rle::Endosome  
 72 reaction\_21: S2n::nucleus S4c::cytosol S4n::nucleus Rle::Endosome  
 73 reaction\_5: RI::PM S2n::nucleus S4c::cytosol S4n::nucleus Rle::Endosome  
 74 reaction\_8: RI::PM S2n::nucleus S4c::cytosol S4n::nucleus Rle::Endosome

75 reaction\_8: RI::PM S2n::nucleus S4c::cytosol S4n::nucleus  
 76 reaction\_5: RI::PM S2n::nucleus S4c::cytosol S4n::nucleus  
 77 reaction\_7: S2n::nucleus S4c::cytosol S4n::nucleus Rle::Endosome  
 78 reaction\_5: RI::PM S2n::nucleus S4c::cytosol S4n::nucleus Rle::Endosome  
 79 reaction\_5: RI::PM S2n::nucleus S4c::cytosol S4n::nucleus Rle::Endosome  
 80 reaction\_21: RI::PM S2n::nucleus S4c::cytosol Rle::Endosome  
 81 reaction\_6: S2n::nucleus S4c::cytosol Rle::Endosome  
 82 reaction\_19: S2c::cytosol S4c::cytosol Rle::Endosome  
 83 reaction\_21: S2c::cytosol S4n::nucleus Rle::Endosome  
 84 reaction\_8: RI::PM S2c::cytosol S4n::nucleus  
 85 reaction\_10: RI::PM RII::PM S2c::cytosol S4n::nucleus  
 86 reaction\_21: RI::PM RII::PM S2c::cytosol S4c::cytosol S4n::nucleus  
 87 reaction\_11: RI::PM RII::PM S2c::cytosol S4c::cytosol S4n::nucleus  
 88 reaction\_12: RI::PM S2c::cytosol S4c::cytosol S4n::nucleus RIIe::Endosome  
 89 reaction\_19: RI::PM S2n::nucleus S4c::cytosol S4n::nucleus RIIe::Endosome  
 90 reaction\_7: RI::PM S2n::nucleus S4c::cytosol S4n::nucleus RIIe::Endosome Rle::Endosome  
 91 reaction\_8: RI::PM S2n::nucleus S4c::cytosol S4n::nucleus RIIe::Endosome Rle::Endosome  
 92 reaction\_8: RI::PM S2n::nucleus S4c::cytosol S4n::nucleus RIIe::Endosome Rle::Endosome  
 93 reaction\_21: RI::PM S2n::nucleus S4n::nucleus RIIe::Endosome Rle::Endosome  
 94 reaction\_6: RI::PM S2n::nucleus S4n::nucleus RIIe::Endosome Rle::Endosome  
 95 reaction\_13: RI::PM RII::PM S2n::nucleus S4n::nucleus Rle::Endosome  
 96 reaction\_21: RI::PM RII::PM S2n::nucleus S4c::cytosol S4n::nucleus Rle::Endosome  
 97 reaction\_8: RI::PM RII::PM S2n::nucleus S4c::cytosol S4n::nucleus  
 98 reaction\_10: RI::PM RII::PM S2n::nucleus S4c::cytosol S4n::nucleus  
 99 reaction\_11: RI::PM S2n::nucleus S4c::cytosol S4n::nucleus  
 100 reaction\_19: RI::PM S2c::cytosol S2n::nucleus S4c::cytosol S4n::nucleus

| plot.



**| add\_genCTL.**

Time: 3.00 s

**| list\_spec.**

Ei(reachable(RI::PM)).  
 Ei(reachable(!(RI::PM))).  
 Ai(oscil(RI::PM)).  
 Ei(steady(RI::PM)).  
 Ei(reachable(RII::PM)).  
 Ei(reachable(!(RII::PM))).  
 Ai(oscil(RII::PM)).  
 Ei(steady(RII::PM)).  
 Ei(reachable(LR::PM)).  
 Ei(reachable(!(LR::PM))).  
 Ai(oscil(LR::PM)).  
 Ei(steady(!(LR::PM))).  
 Ai(AG(!(LR::PM)->checkpoint(RI::PM,LR::PM))).  
 Ai(AG(!(LR::PM)->checkpoint(RII::PM,LR::PM))).

Ei(reachable(LRe::Endosome)).  
 Ei(reachable(!(LRe::Endosome))).  
 Ai(oscil(LRe::Endosome)).  
 Ei(steady(!(LRe::Endosome))).  
 Ai(AG(!(LRe::Endosome)->checkpoint(LR::PM,LRe::Endosome))).  
 Ei(reachable(Rle::Endosome)).  
 Ei(reachable(!(Rle::Endosome))).  
 Ai(oscil(Rle::Endosome)).  
 Ei(steady(!(Rle::Endosome))).  
 Ai(AG(!(Rle::Endosome)->checkpoint(RI::PM,Rle::Endosome))).  
 Ei(reachable(RIle::Endosome)).  
 Ei(reachable(!(RIle::Endosome))).  
 Ai(oscil(RIle::Endosome)).  
 Ei(steady(!(RIle::Endosome))).  
 Ai(AG(!(RIle::Endosome)->checkpoint(RII::PM,RIle::Endosome))).  
 Ei(reachable(S2c::cytosol)).  
 Ei(reachable(!(S2c::cytosol))).  
 Ai(oscil(S2c::cytosol)).  
 Ei(steady(S2c::cytosol)).  
 Ai(AG(!(S2c::cytosol)->checkpoint(S2n::nucleus,S2c::cytosol))).  
 Ei(reachable(pS2c::cytosol)).  
 Ei(reachable(!(pS2c::cytosol))).  
 Ai(oscil(pS2c::cytosol)).  
 Ei(steady(!(pS2c::cytosol))).  
 Ei(reachable(S4c::cytosol)).  
 Ei(reachable(!(S4c::cytosol))).  
 Ai(oscil(S4c::cytosol)).  
 Ei(steady(S4c::cytosol)).  
 Ei(reachable(pS24c::cytosol)).  
 Ei(reachable(!(pS24c::cytosol))).  
 Ai(oscil(pS24c::cytosol)).  
 Ei(steady(!(pS24c::cytosol))).  
 Ai(AG(!(pS24c::cytosol)->checkpoint(S4c::cytosol,pS24c::cytosol))).  
 Ai(AG(!(pS24c::cytosol)->checkpoint(pS2c::cytosol,pS24c::cytosol))).  
 Ei(reachable(S4n::nucleus)).  
 Ei(reachable(!(S4n::nucleus))).  
 Ai(oscil(S4n::nucleus)).  
 Ei(steady(S4n::nucleus)).  
 Ei(reachable(pS2n::nucleus)).  
 Ei(reachable(!(pS2n::nucleus))).



Ai(oscil(pS2n::nucleus)).  
 Ei(steady(!(pS2n::nucleus))).  
 Ei(reachable(pS24n::nucleus)).  
 Ei(reachable(!(pS24n::nucleus))).  
 Ai(oscil(pS24n::nucleus)).  
 Ei(steady(!(pS24n::nucleus))).  
 Ei(reachable(pS22c::cytosol)).  
 Ei(reachable(!(pS22c::cytosol))).  
 Ai(oscil(pS22c::cytosol)).  
 Ei(steady(!(pS22c::cytosol))).  
 Ai(AG(!(pS22c::cytosol)->checkpoint(pS2c::cytosol,pS22c::cytosol))).  
 Ei(reachable(pS22n::nucleus)).  
 Ei(reachable(!(pS22n::nucleus))).  
 Ai(oscil(pS22n::nucleus)).  
 Ei(steady(!(pS22n::nucleus))).  
 Ei(reachable(S2n::nucleus)).  
 Ei(reachable(!(S2n::nucleus))).  
 Ai(oscil(S2n::nucleus)).  
 Ei(steady(S2n::nucleus)).

**| reduce\_model.**

- 1: deleting LR::PM=>\_
- 2: deleting RI::PM=>\_
- 3: deleting RII::PM=>\_
- 4: deleting pS24c::cytosol=>S4c::cytosol+(pS2c::cytosol)
- 5: deleting S4n::nucleus+(pS2n::nucleus)=>pS24n::nucleus
- 6: deleting pS22c::cytosol=>2\*(pS2c::cytosol)
- 7: deleting 2\*(pS2n::nucleus)=>pS22n::nucleus
- 8: deleting S2c::cytosol=>S2n::nucleus
- 9: deleting pS2c::cytosol=>pS2n::nucleus
- 10: deleting S4c::cytosol=>S4n::nucleus
- 11: deleting \_=>RI::PM
- 12: deleting \_=>RII::PM
- 13: deleting pS2n::nucleus=>pS2c::cytosol

After reduction, 17 rules remain corresponding to the bias ? => ?

Deletion(s):

- [GUI] checkCTL LR::PM=>\_
- [GUI] checkCTL RI::PM=>\_
- [GUI] checkCTL RII::PM=>\_
- [GUI] checkCTL pS24c::cytosol=>S4c::cytosol+(pS2c::cytosol)

[GUI] checkCTL S4n::nucleus+(pS2n::nucleus)=>pS24n::nucleus  
 [GUI] checkCTL pS22c::cytosol=>2\*(pS2c::cytosol)  
 [GUI] checkCTL 2\*(pS2n::nucleus)=>pS22n::nucleus  
 [GUI] checkCTL S2c::cytosol=>S2n::nucleus  
 [GUI] checkCTL pS2c::cytosol=>pS2n::nucleus  
 [GUI] checkCTL S4c::cytosol=>S4n::nucleus  
 [GUI] checkCTL \_=>RI::PM  
 [GUI] checkCTL \_=>RII::PM  
 [GUI] checkCTL pS2n::nucleus=>pS2c::cytosol

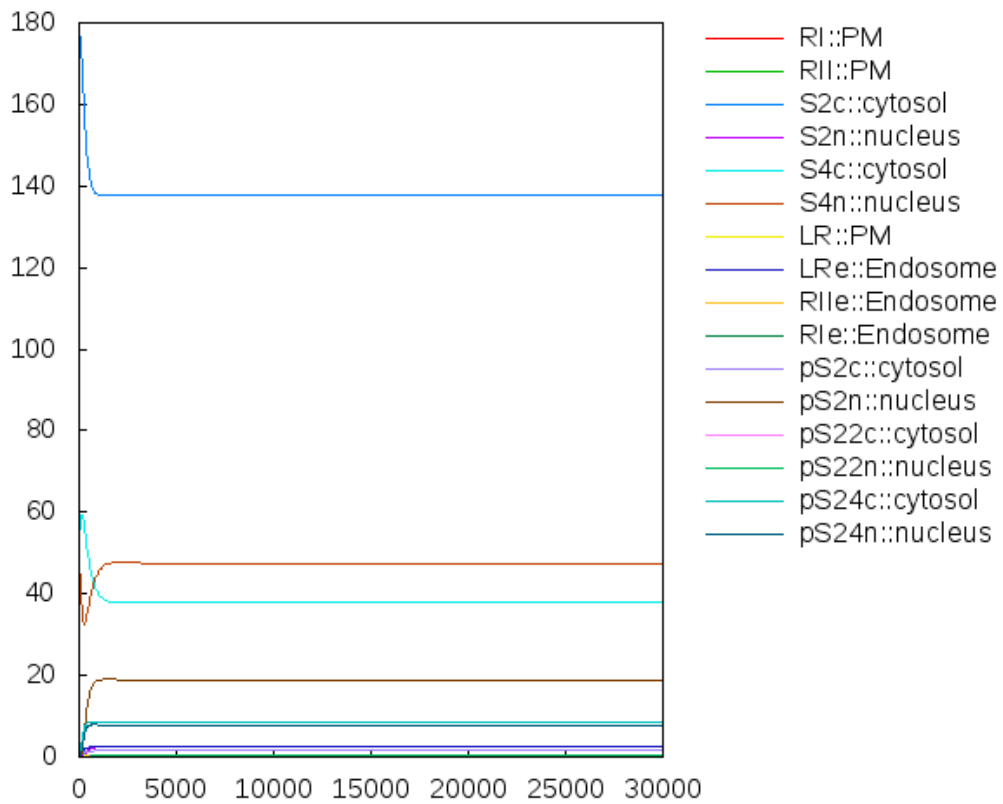
**| list \_rules.**

S4n::nucleus=>S4c::cytosol.  
 reaction\_22:kin\_CIF\*[pS24c::cytosol] for pS24c::cytosol=>pS24n::nucleus.  
 reaction\_23:kin\_CIF\*[pS22c::cytosol] for pS22c::cytosol=>pS22n::nucleus.  
 reaction\_24:kdephos\*[pS2n::nucleus]\*PPase for pS2n::nucleus=>S2n::nucleus.  
 reaction\_1:ka\*TGFb\*[RI::PM]\*[RII::PM] for RI::PM+(RII::PM)=>LR::PM.  
 reaction\_4:ki\*[LR::PM] for LR::PM=>LRe::Endosome.  
 reaction\_7:ki\*[RI::PM] for RI::PM=>RIe::Endosome.  
 reaction\_8:kr\*[RIe::Endosome] for RIe::Endosome=>RI::PM.  
 reaction\_9:kr\*[LRe::Endosome] for LRe::Endosome=>RII::PM+(RI::PM).  
 reaction\_12:ki\*[RII::PM] for RII::PM=>RIIe::Endosome.  
 reaction\_13:kr\*[RIIe::Endosome] for RIIe::Endosome=>RII::PM.  
 reaction\_14:kphos\*[LRe::Endosome]\*[S2c::cytosol] for S2c::cytosol+(LRe::Endosome)=>pS2c::cyto  
 sol+(LRe::Endosome).  
 S4c::cytosol+(pS2c::cytosol)=>pS24c::cytosol.  
 pS24n::nucleus=>S4n::nucleus+(pS2n::nucleus).  
 2\*(pS2c::cytosol)=>pS22c::cytosol.  
 pS22n::nucleus=>2\*(pS2n::nucleus).  
 S2n::nucleus=>S2c::cytosol.

**| numerical\_simulation(30000).**

Simulation time: 0.26s

**| plot.**



Process 0 on cabernet out of 1

BIOCHAM 3.4

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