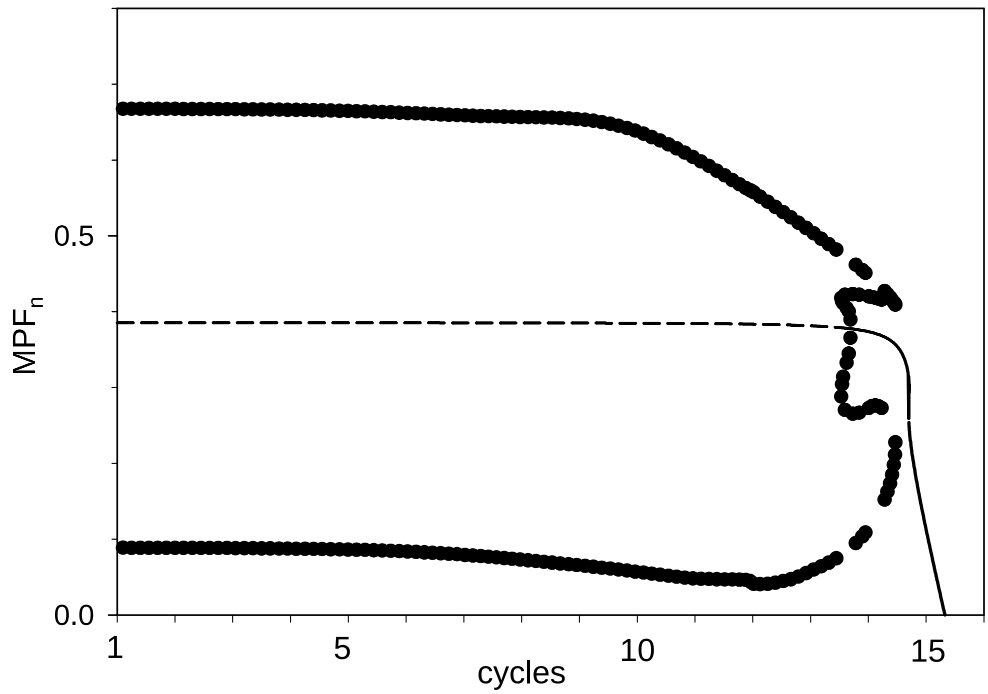
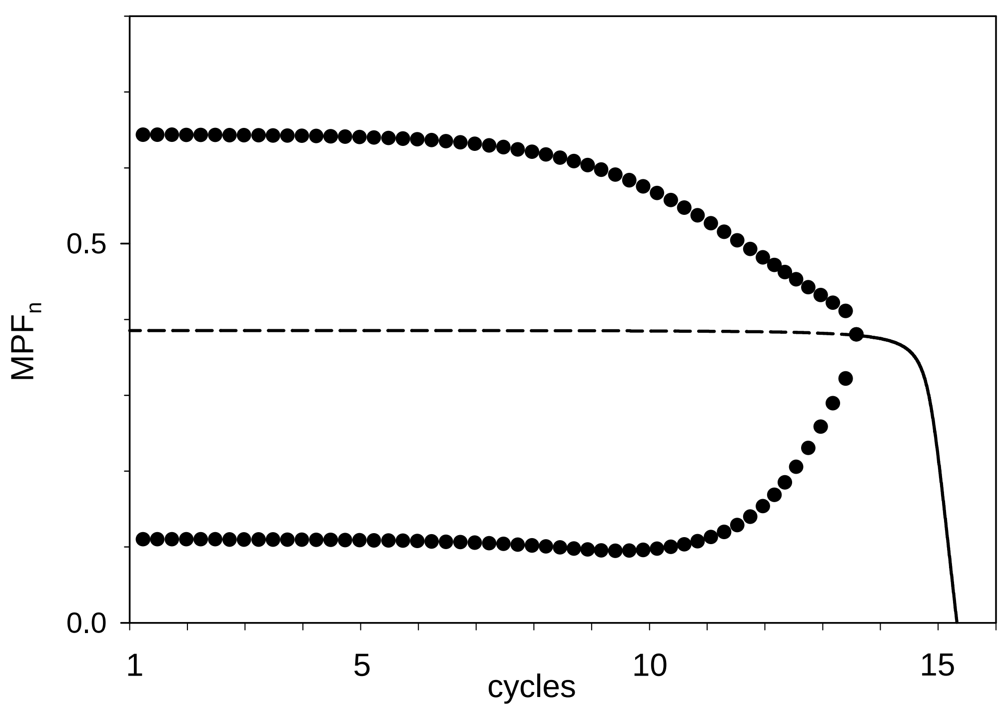
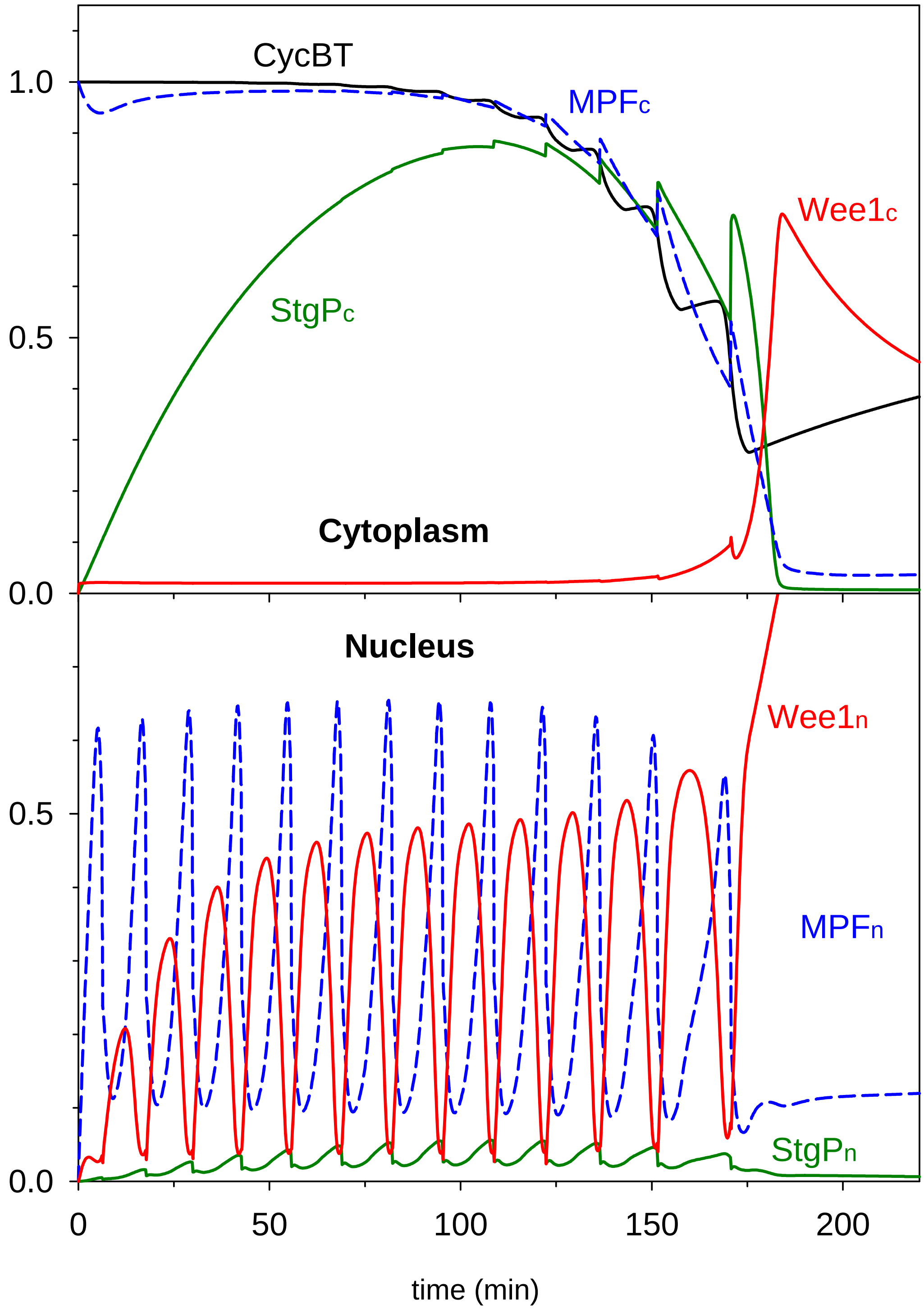


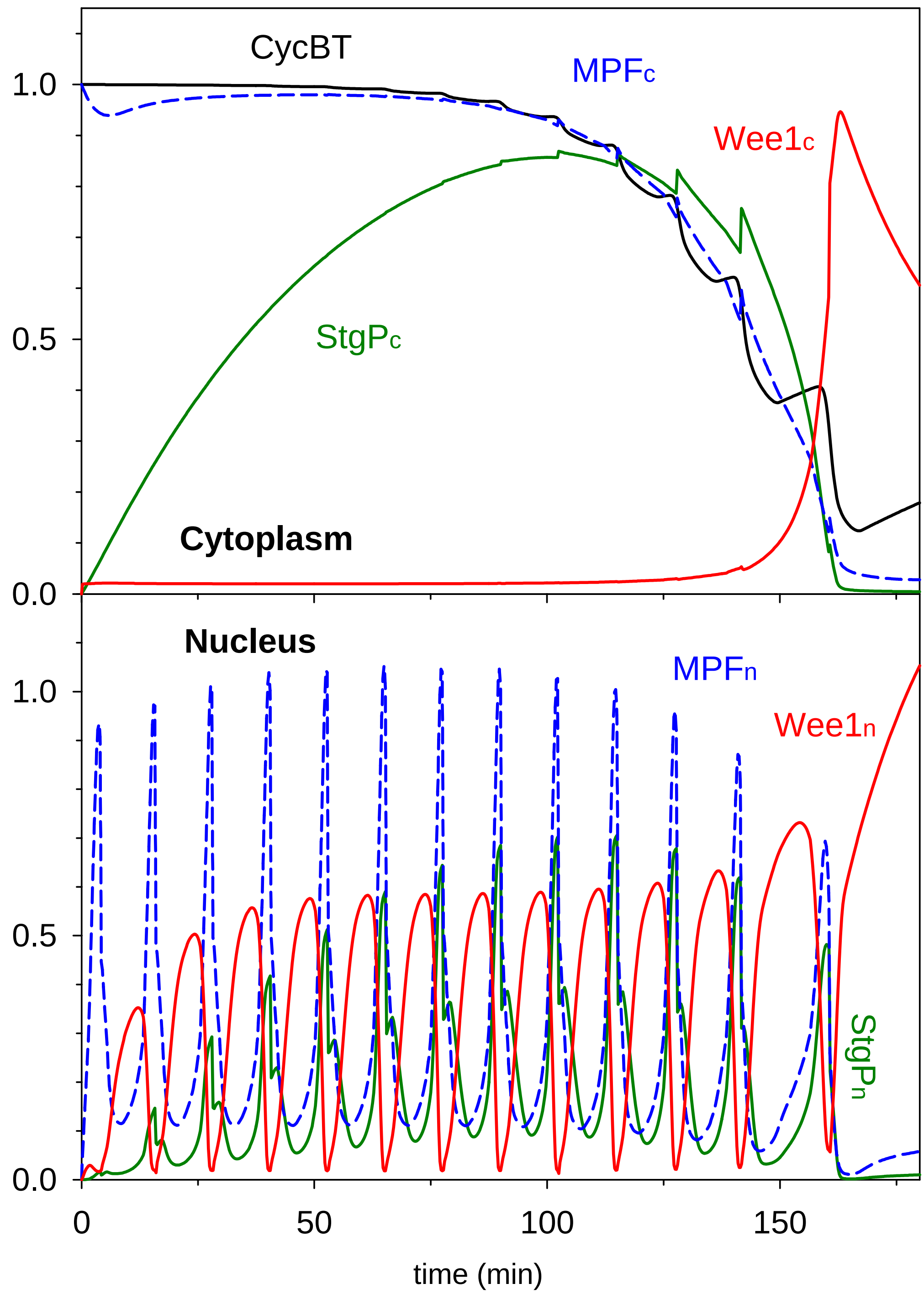

Suppl. FigS1: One parameter bifurcation diagram for *Drosophila* embryos which over-express twine $k_{stg}$' = 0.8 (see Table III for the other parameter values).




Suppl. FigS2: One parameter bifurcation diagram for *Drosophila* Wee1 mutants with $k_{wee}$" = 0 (see Table III for the other parameter values).




Suppl. FigS3: The early cell cycle in *Drosophila* embryos in which DNA replication is inhibited and the checkpoint is activated ($k_{outs}$=1 instead of 0.02; see Table III for the other parameter values).




Suppl. FigS4: Drosophila early embryonic cell cycles simulated with the nuclear envelope breakdown model. Here we assume that the transport coefficients for nuclear 'import' of MPF, String and Wee1 are increased (doubled) when MPF is above the value of 0.3 (during mitosis). The transport coefficients of String and Wee1 for the nuclear 'export' are also increased during mitosis and made equal to the value of the 'import' rate. The rate of nuclear 'export' of MPF is kept zero both during interphase and mitosis (see drosophila_model.ode for details).

```
Drosophila_model.ode

#  Dynamical modeling of syncytial mitotic
#        cycles in Drosophila embryos
#
#     Laurence Calzone, Denis Thieffry,
#      John J. Tyson, and Bela Novak
#
#  Run this file as is to get Fig 3 in paper.
#
#  To simulate Figure 1 (StringTot not regulated)
#  set ksstg=0, kdstg=0 and init Stgc=0.8
#
#  To simulate the model when nuclear envelope
#  breakdown (NEB) increases the transport rates,
#  follow the instructions below for 'commenting'
#  and 'uncommenting' specific lines


#### Initial concentrations ####

init MPFn=0, preMPFn=0
init MPFc=1, preMPFc=0
init IE=0, FZY=0, N=1
init Stgm=1, Xm=0, Xp=0
init StgPn=0, Stgn=0, StgPc=0
init Wee1Pn=0, Wee1n=0, Wee1c=0

# Uncomment these initial values to simulate
# the NEB hypothesis
#init kin=0.2, kins=0.1, kinw=0.05
#init kout=0, kouts=0.1, koutw=0.01

# Uncomment these definitions to simulate
# the NEB hypothesis
#!kin_l = kin_s*ftm
#!kins_l = kins_s*fts
#!kinw_l = kinw_s*ftw
#!kout_l = kout_s
#!kouts_l = kins_s*fts
#!koutw_l = kinw_s*ftw

#### Set of ordinary differential equations ####

# Index 'n' for nuclear species,
#   and 'c' for cytoplasmic species

# CycB/CDK Kinetics

dMPFn/dt    = kin*MPFc-kout*MPFn-(kdn'+kdn"*FZY)*MPFn-
(kwee'+kwee"*Wee1n)*MPFn+(kstg'+kstg"*StgPn)*preMPFn

dpreMPFn/dt = kin*preMPFc-kout*preMPFn-
(kdn'+kdn"*FZY)*preMPFn+(kwee'+kwee"*Wee1n)*MPFn-(kstg'+kstg"*StgPn)*preMPFn

dMPFc/dt    = ksc-(E*N*kin*MPFc-E*N*kout*MPFn)/(1-N*E)-
kdc'*MPFc+(kstg'+kstg"*StgPc)*preMPFc-(kwee'+kwee"*Wee1c)*MPFc

dpreMPFc/dt = -(E*N*kin*preMPFc-E*N*kout*preMPFn)/(1-N*E)-kdc'*preMPFc-
(kstg'+kstg"*StgPc)*preMPFc+(kwee'+kwee"*Wee1c)*MPFc
```

```
# Degradation of the cyclins in the nuclei
# IE = Intermediary Enzyme

dIE/dt    = kaie*(1-IE)*MPFn/(Jaie+1-IE)-kiie*IE/(Jiie+IE)

dFZY/dt   = kafz*IE*(1-FZY)/(Jafz+1-FZY)-kifz*FZY/(Jifz+FZY)


# Degradation of maternal String mRNA
# and zygotic factor-X kinetics

dStgm/dt  = -(kdm'/(Jm+Stgm)+kdm"*Xp)*Stgm

dXm/dt    = ksxm*N

dXp/dt    = ksxp*Xm


# String kinetics

dStgPn/dt  = kins*StgPc-kouts*StgPn+(kastg'+kastg"*MPFn)*Stgn/(jastg+Stgn)-
kistg*StgPn/(jistg+StgPn)-kdstg*stgPn

dStgn/dt   = kins*Stgc-kouts*Stgn-
(kastg'+kastg"*MPFn)*Stgn/(jastg+Stgn)+kistg*StgPn/(jistg+StgPn)-kdstg*stgn

dstgPc/dt  = -kdstg*stgPc-(E*N*kins*stgPc-E*N*kouts*StgPn)/(1-
N*E)+(kastg'+kastg"*MPFc)*stgc/(jastg+stgc)-kistg*stgPc/(jistg+stgPc)

dstgc/dt   = ksstg*Stgm-kdstg*stgc-(E*N*kins*stgc-E*N*kouts*Stgn)/(1-N*E)-
(kastg'+kastg"*MPFc)*stgc/(jastg+stgc)+kistg*stgPc/(jistg+stgPc)


# Wee1 kinetics

dWee1n/dt  = kinw*Wee1c-koutw*Wee1n+kawee*Wee1Pn/(jawee+Wee1Pn)-
(kiwee'+kiwee"*MPFn)*Wee1n/(jiwee+Wee1n)

dWee1c/dt  = -(kinw*Wee1c-koutw*Wee1n)*N*E/(1-N*E)+kawee*Wee1Pc/(jawee+Wee1Pc)-
(kiwee'+kiwee"*MPFc)*Wee1c/(jiwee+Wee1c)

dWee1Pn/dt = kinw*Wee1Pc-koutw*Wee1Pn-
kawee*Wee1Pn/(jawee+Wee1Pn)+(kiwee'+kiwee"*MPFn)*Wee1n/(jiwee+Wee1n)


# We compute Wee1Pc from the total Wee1 amount

Wee1Pc=(Wee1Tot-N*E*(Wee1n+Wee1Pn))/(1-N*E)-Wee1c



# The following differential equation...
dN/dt     = 0
# ... is a trick to declare N (number of nuclei)
# as a variable, so that N can be increased by
# 1.95-fold each time the nuclei divide.
# The approx doubling of N is accomplished by
# the following global statement:

global +1 {FZY-kez} {N=factor*N}
```

```
# Uncomment these differential equations to
# simulate the NEB hypothesis
#dkin/dt   = 0
#dkins/dt  = 0
#dkinw/dt  = 0
#dkout/dt  = 0
#dkouts/dt = 0
#dkoutw/dt = 0


#### Other conditional events ####


# Rescaling of the variables at division

global +1 {FZY-kez} {MPFn=MPFn/1.95; preMPFn=preMPFn/1.95; Wee1n=Wee1n/1.95;
Wee1Pn=Wee1Pn/1.95; Wee1c=(1-N*E)/(1-1.95*N*E)*Wee1c; Wee1Pc=(1-N*E)/(1-
1.95*N*E)*Wee1Pc}

global +1 {FZY-kez} {Stgn=Stgn/1.95; StgPn=StgPn/1.95; Stgc=(1-N*E)/(1-
1.95*N*E)*Stgc; StgPc=(1-N*E)/(1-1.95*N*E)*StgPc; MPFc=(1-N*E)/(1-
1.95*N*E)*MPFc; preMPFc=(1-N*E)/(1-1.95*N*E)*preMPFc}


# Uncomment these global statements to simulate
# the NEB hypothesis
# (index 'l' for large, and 's' for small)

#global +1 {MPFn-kez1} {kin=kin_l; kins=kins_l; kinw=kinw_l; kout=kout_l;
kouts=kouts_l; koutw=koutw_l}

#global -1 {MPFn-kez2} {kin=kin_s; kins=kins_s; kinw=kinw_s; kout=kout_s;
kouts=kouts_s; koutw=koutw_s}


#### Auxiliary functions for plotting ####

# Total CyclinB
CycBT=(1-N*E)*(MPFc+preMPFc)+N*E*(MPFn+preMPFn)



# Total String
StgTot=(1-N*E)*(Stgc+StgPc)+N*E*(Stgn+StgPn)

# Total String Phosphorylated
StgPT=(1-N*E)*stgPc+N*E*stgPn

aux CycBT=CycBT
aux StgTot=StgTot
aux StgPT=StgPT
aux Wee1Pc=Wee1Pc


#### Parameter values ####

p ksc=0.01, kdc'=0.01, kdn'=0.01, kdn"=1.5
p kafz=1, kifz=0.2, Jafz=0.01, Jifz=0.01
p kaie=1, kiie=0.4, Jaie=0.01, Jiie=0.01
```

```
p kwee'=0.005, kwee"=1, kawee=0.3, kiwee'=0.01
p kiwee"=1, Jawee=0.05, Jiwee=0.05
p kstg'=0.2, kstg"=2, kastg'=0, kastg"=1
p kistg=0.3, Jastg=0.05, Jistg=0.05
p Wee1Tot=0.8, E=0.00007
p ksstg=0.02, kdstg=0.015
p kdm'=0.002, Jm=0.05, kdm"=0.2
p ksxm=0.0005, ksxp=0.001
p kez=0.5, factor=1.95

# Comment-out these parameters to simulate
# the NEB hypothesis
p kouts=0.02, koutw=0.01
p kins=0.08, kinw=0.04
p kin=0.15, kout=0

# Uncomment these parameters to simulate
# the NEB hypothesis
#p kouts_s=0.1, koutw_s=0.01, kout_s=0
#p kins_s=0.1,  kinw_s=0.05, kin_s=0.2
#p fts=2, ftw=2, ftm=2
#p kez1=0.3, kez2=0.3

@ Total=300, METH=stiff
@ XLO=0, XHI=300, YLO=0, YHI=1
@ BOUND=50000, dt=0.1, NPLOT=4
@ YP=Stgtot, YP2=StgPn, YP3=Wee1n, YP4=MPFn

done
```

```
drosophila_bifurcation.ode

#  Dynamical modeling of syncytial mitotic
#        cycles in Drosophila embryos
#
#     Laurence Calzone, Denis Thieffry,
#      John J. Tyson, and Bela Novak
#
#  Run this file as is to get Fig 2 in paper.
#



init MPFn=1, preMPFn=0
init MPFc=0, CyclinBT=1
init IE=0, FZY=0
init StgPn=0, Stgn=0, StgPc=0
init Wee1Pn=0, Wee1n=0.8, Wee1c=0


dMPFn/dt    = kin*MPFc-(kdn'+kdn"*FZY)*MPFn-
(kwee'+kwee"*Wee1n)*MPFn+(kstg'+kstg"*StgPn)*preMPFn

dpreMPFn/dt = kin*preMPFc-(kdn'+kdn"*FZY)*preMPFn+(kwee'+kwee"*Wee1n)*MPFn-
(kstg'+kstg"*StgPn)*preMPFn

dMPFc/dt    = ksc-(E*N*kin*MPFc)/(1-N*E)-kdc'*MPFc+(kstg'+kstg"*StgPc)*preMPFc-
(kwee'+kwee"*Wee1c)*MPFc

dCyclinBT/dt = (1-N*E)*ksc - (1-N*E)*kdc'*(MPFc+preMPFc) -
N*E*(kdn'+kdn"*FZY)*(MPFn+preMPFn)

dIE/dt    = kaie*(1-IE)*MPFn/(Jaie+1-IE)-kiie*IE/(Jiie+IE)

dFZY/dt   = kafz*IE*(1-FZY)/(Jafz+1-FZY)-kifz*FZY/(Jifz+FZY)

dStgPn/dt  = kins*StgPc-kouts*StgPn+(kastg'+kastg"*MPFn)*Stgn/(jastg+Stgn)-
kistg*StgPn/(jistg+StgPn)

dStgn/dt   = kins*Stgc-kouts*Stgn-
(kastg'+kastg"*MPFn)*Stgn/(jastg+Stgn)+kistg*StgPn/(jistg+StgPn)

dstgPc/dt  = -(E*N*kins*stgPc-E*N*kouts*StgPn)/(1-
N*E)+(kastg'+kastg"*MPFc)*stgc/(jastg+stgc)-kistg*stgPc/(jistg+stgPc)

dWee1n/dt  = kinw*Wee1c-koutw*Wee1n+kawee*Wee1Pn/(jawee+Wee1Pn)-
(kiwee'+kiwee"*MPFn)*Wee1n/(jiwee+Wee1n)

dWee1c/dt  = -(kinw*Wee1c-koutw*Wee1n)*N*E/(1-N*E)+kawee*Wee1Pc/(jawee+Wee1Pc)-
(kiwee'+kiwee"*MPFc)*Wee1c/(jiwee+Wee1c)

dWee1Pn/dt = kinw*Wee1Pc-koutw*Wee1Pn-
kawee*Wee1Pn/(jawee+Wee1Pn)+(kiwee'+kiwee"*MPFn)*Wee1n/(jiwee+Wee1n)

N=1.95^(Cycle-1)

preMPFc=(CyclinBT-N*E*(preMPFn+MPFn))/(1-N*E)-MPFc

stgc=(StringTot-N*E*(stgPn+stgn))/(1-N*E)-stgPc

StgTot=(1-N*E)*(Stgc+StgPc)+N*E*(Stgn+StgPn)
```

```
StgPT=(1-N*E)*stgPc+N*E*stgPn

Wee1Pc=(Wee1Tot-N*E*(Wee1n+Wee1Pn))/(1-N*E)-Wee1c

aux preMPFc=preMPFc
aux Stgc=Stgc
aux StgPT=StgPT
aux Wee1Pc=Wee1Pc


p Cycle=15
p StringTot=0.8, Wee1Tot=0.8
p ksc=0.01, kdc'=0.01, kdn'=0.01, kdn"=1.5
p kafz=1, kifz=0.2, Jafz=0.01, Jifz=0.01
p kaie=1, kiie=0.4, Jaie=0.01, Jiie=0.01
p kwee'=0.005, kwee"=1, kawee=0.3, kiwee'=0.01
p kiwee"=1, Jawee=0.05, Jiwee=0.05
p kstg'=0.2, kstg"=2, kastg'=0, kastg"=1, kistg=0.3
p Jastg=0.05, Jistg=0.05
p kouts=0.02, koutw=0.01
p kins=0.08, kinw=0.04
p kin=0.15, E=0.00007

@ YP=MPFn, Total=300, METH=stiff, XLO=0, XHI=300, YLO=0, YHI=2
@ BOUND=50000, dt=0.5

done
```