Models of the Tyson Lab

Models used by the Tyson Lab are characterized by their use of differential equations and an additional set of rules that specify when to perform actions upon sets of variables. A typical rule is that the mass of the cell is multiplied by a certain fraction when cell division occurs. Cell division occurrences can be recognized by the decrease of a certain protein (in the case of budding yeast, Clb2 falling below a concentration of 0.3). The rule for cell division specifies that the quantity (Clb2 – 0.3) must have gone from positive to negative for the actions to be triggered.

The Tyson Lab has typically used diagrams that are subsequently converted by hand to differential equations to develop their models. These differential equations are written in the XPP ode file format for the purposes of simulation in the program XPP.

Currently, the Tyson Lab is in the process of entering previous models into the JigCell Model Builder, a chemical reaction centered spreadsheet interface for specifying models. From this interface models may be output into XPP format or saved in the JigCell Model Builder's native spreadsheet format.

This document provides two models in different formats: a frog egg extract model and a budding yeast cell cycle model. The frog egg extract model is given in JigCell Model Builder format, XPP ode file format, and SBML format. The budding yeast model is given in JigCell Model Builder format and XPP ode file format. The budding yeast model has seven times more differential equations than the frog egg extract model.

The budding yeast model cannot be represented in SBML because of its use of rules, for which SBML has no current support. A further limitation on the expressiveness of SBML in the budding yeast model is that it uses Goldbeter-Koshland functions. SBML does not support user-defined functions, which requires that these functions be inlined in the kinetic law for a reaction. This is not a problem for a modeling language, but is for the translation of SBML into human readable form, since a program cannot deduce what kinetic laws are inlined functions or contain inlined functions.

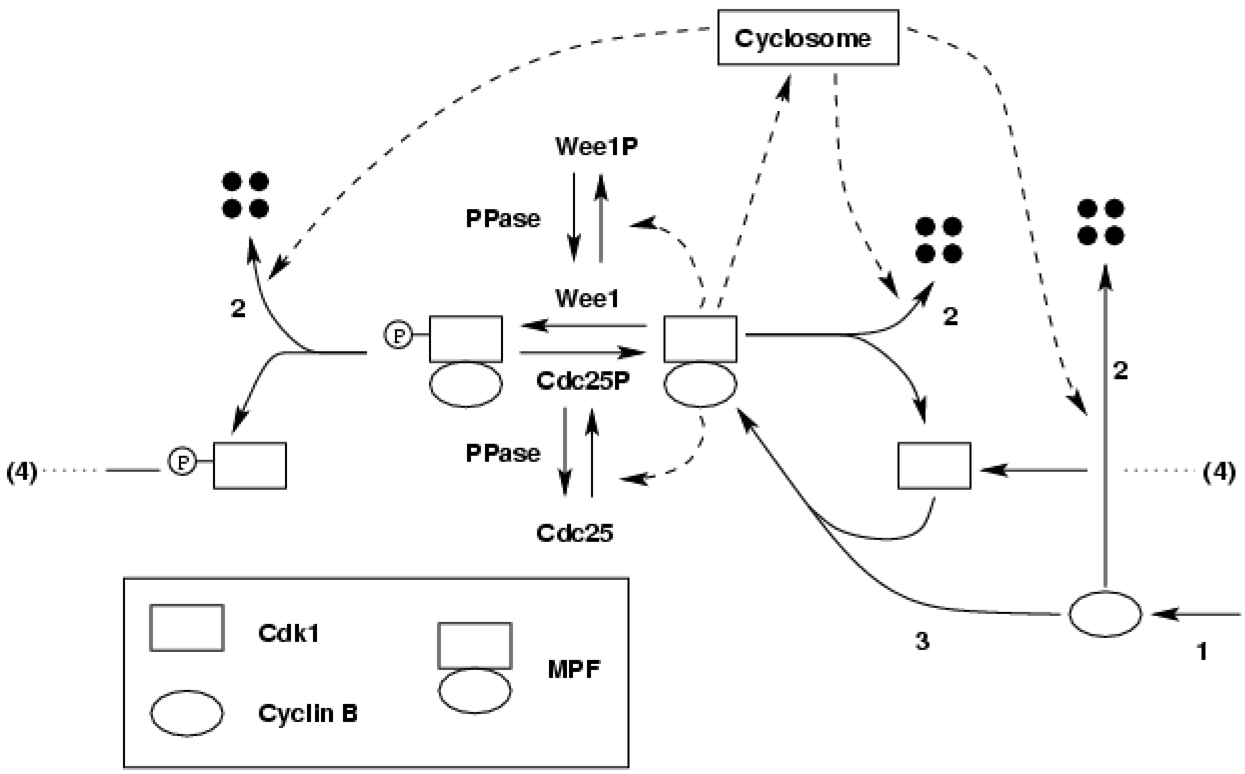
Frog Egg Extract Model

Description:

This is a model based on the biochemistry of M-phase promoting factor (MPF) in Xenopus oocyte extracts. It is a simpler model based on an earlier work - Marlovits, G., Tyson, C.J., Novák, B. & Tyson, J.J. (1998), *Modeling M-phase control in Xenopus oocyte extracts: the surveillance mechanism for unreplicated DNA*. Biophy. Chem. **72**: 169-184. This model contains five differential equations, eighteen parameters, and eight initial conditions.

This paper is available at http://cellcycle.mkt.bme.hu/articles/xeno/biophys/marlovits.pdf

Diagram:



Differential Equations:

$$\frac{\partial}{\partial t}\mathrm{Ca}(t) = -\frac{vcppp\_\ vc\_\ Ca}{kmcr\_ + Ca} + \frac{vc\_\ \mathrm{Ci}\ Ma}{kmc\_ + \mathrm{Ci}}$$

$$\frac{\partial}{\partial t}\mathrm{Wa}(t) = -\frac{vw\_\ Wa\ Ma}{kmw\_ + Wa} + \frac{vw\_\ vwppp\_\ Wi}{kmwr\_ + Wi}$$

$$\frac{\partial}{\partial t}\mathrm{Ma}(t) = -kw\ Ma + kc\ Mi$$

$$\frac{\partial}{\partial t}\mathrm{L}(t) = -kc\ L$$

$$\frac{\partial}{\partial t}\mathrm{L2}(t) = kw\ (1 - L2)$$

$$\mathrm{Ci} = CTotal - Ca$$

$$Wi = WTotal - Wa$$

$$Mi = TotalCyclin - Ma$$

$$kc = vcp\_\ \mathrm{Ci} + vcpp\_\ Ca$$

$$kw = vwp\_\ Wi + vwpp\_\ Wa$$

$$vcp\_ = vcp\ Cdc25Total\_$$

$$vcpp\_ = vcpp\ Cdc25Total\_$$

$$vcppp\_ = \frac{vcppp}{Cdc25Total\_}$$

$$vwp\_ = vwp\ Wee1Total\_$$

$$vwpp\_ = vwpp\ Wee1Total\_$$

$$vwppp\_ = \frac{vwppp}{Wee1Total\_}$$

$$kmc\_ = \frac{kmc}{Cdc25Total\_}$$

$$kmcr\_ = \frac{kmcr}{Cdc25Total\_}$$

$$kmw\_ = \frac{kmw}{Wee1Total\_}$$

$$kmwr\_ = \frac{kmwr}{Wee1Total\_}$$

$$vc\_ = \frac{vc\ Cdc2Total\_}{Cdc25Total\_}$$

$$vw\_ = \frac{vw\ Cdc2Total\_}{Wee1Total\_}$$

$$Cdc25Total\_ = Cdc25Total\ Dilution$$

$$Wee1Total\_ = Wee1Total\ Dilution$$

$$Cdc2Total\_ = Dilution$$

JigCell Model Builder Representation:

Model Spreadsheet (Name column removed for space)

Reaction	Type	Equation	Modifiers and Constants
Ma->Mi	Mass Action	kw*Ma	Kf=kw
Mi->Ma	Mass Action	kc*Mi	Kf=kc
Ca->Ci	Michaelis-Menten	(vcppp_*vc_*Ca*1)/(kmcr_+Ca)	k1=vcppp_*vc_; M1=1; J1=kmcr_
Ci->Ca	Michaelis-Menten	(vc_*Ci*Ma)/(kmc_+Ci)	k1=vc_; M1=Ma; J1=kmc_
Wa->Wi	Michaelis-Menten	(vw_*Wa*Ma)/(kmw_+Wa)	k1=vw_; M1=Ma; J1=kmw_
Wi->Wa	Michaelis-Menten	(vw_*vwppp_*Wi*1)/(kmwr_+Wi)	k1=vw_*vwppp_; M1=1; J1=kmwr_
L->	Mass Action	kc*L	Kf=kc
->L2	Local	kw*(1-L2)	
kc	Species	vcp*Ci+vcpp*Ca	vcp=vcp_; vcpp=vcpp_
kw	Species	vwp*Wi+vwpp*Wa	vwp=vwp_; vwpp=vwpp_
vcp_	Species	vcp*Cdc25Total	vcp=vcp; Cdc25Total=Cdc25Total_
vcpp_	Species	vcpp*Cdc25Total	vcpp=vcpp; Cdc25Total=Cdc25Total_
vcppp_	Species	vcppp/Cdc25Total	vcppp=vcppp; Cdc25Total=Cdc25Total_
vwp_	Species	vwp*Wee1Total	vwp=vwp; Wee1Total=Wee1Total_
vwpp_	Species	vwpp*Wee1Total	vwpp=vwpp; Wee1Total=Wee1Total_
vwppp_	Species	vwppp/Wee1Total	vwppp=vwppp; Wee1Total=Wee1Total_
kmc_	Species	kmc/Cdc25Total	kmc=kmc; Cdc25Total=Cdc25Total_
kmcr_	Species	kmcr/Cdc25Total	kmcr=kmcr; Cdc25Total=Cdc25Total_
kmw_	Species	kmw/Wee1Total	kmw=kmw; Wee1Total=Wee1Total_
kmwr_	Species	kmwr/Wee1Total	kmwr=kmwr; Wee1Total=Wee1Total_
vc_	Species	vc*Cdc2Total/Cdc25Total	vc=vc; Cdc2Total=Cdc2Total_; Cdc25Total=Cdc25Total_
vw_	Species	vw*Cdc2Total/Wee1Total	vw=vw; Cdc2Total=Cdc2Total_; Wee1Total=Wee1Total_
Cdc25Total_	Species	Cdc25Total	Cdc25Total=Cdc25Total*Dilution
Wee1Total_	Species	Wee1Total	Wee1Total=Wee1Total*Dilution
Cdc2Total_	Species	Cdc2Total	Cdc2Total=Dilution

Constants Spreadsheet

Name	Value
WTotal	1
TotalCyclin	1
CTotal	1
Dilution	1
vcp	0.0165
vcpp	0.182
vcppp	0.0709
vwp	0.0000003
vwpp	0.763
vwppp	0.0709
kmc	0.1
kmcr	1

kmw	0.1
kmwr	1
vc	1
vw	1
Cdc25Total	1
Wee1Total	1

Species Spreadsheet

Name	Initial Condition
Mi	1
Ci	1
Wi	0
Ca	0
Wa	1
Ma	0
L	1
L2	0

Conservation Relations Spreadsheet

Conservation Relation	Constant Total Name	Dependent Species
Ci + Ca	CTotal	Ci
Wi + Wa	WTotal	Wi
Mi + Ma	TotalCyclin	Mi

XPP Ode File (Differential Equations)

```
#  C:\JigCell\models\model.odef  Generated by JigCell


#Functions


#Dependent species

Ci=(CTotal - Ca)
Wi=(WTotal - Wa)
Mi=(TotalCy_2 - Ma)

#Species

kc=(vcp_)*Ci+(vcpp_)*Ca
aux kc=kc
kw=(vwp_)*Wi+(vwpp_)*Wa
aux kw=kw
vcp_=(vcp)*(Cdc25T_49)
aux vcp_=vcp_
vcpp_=(vcpp)*(Cdc25T_49)
aux vcpp_=vcpp_
vcppp_=(vcppp)/(Cdc25T_49)
aux vcppp_=vcppp_
vwp_=(vwp)*(Wee1To_50)
aux vwp_=vwp_
vwpp_=(vwpp)*(Wee1To_50)
aux vwpp_=vwpp_
vwppp_=(vwppp)/(Wee1To_50)
aux vwppp_=vwppp_
kmc_=(kmc)/(Cdc25T_49)
aux kmc_=kmc_
kmcr_=(kmcr)/(Cdc25T_49)
aux kmcr_=kmcr_
kmw_=(kmw)/(Wee1To_50)
aux kmw_=kmw_
kmwr_=(kmwr)/(Wee1To_50)
aux kmwr_=kmwr_
vc_=(vc)*(Cdc2To_51)/(Cdc25T_49)
aux vc_=vc_
vw_=(vw)*(Cdc2To_51)/(Wee1To_50)
aux vw_=vw_
Cdc25T_49=(Cdc25T_17*Dilution)
aux Cdc25T_49=Cdc25T_49
Wee1To_50=(Wee1Total*Dilution)
aux Wee1To_50=Wee1To_50
Cdc2To_51=(Dilution)
aux Cdc2To_51=Cdc2To_51

#Independent Species

dCa/dt= - (vcppp_*vc_*Ca*1)/(kmcr_+Ca) + (vc_*Ci*Ma)/(kmc_+Ci)
dWa/dt= - (vw_*Wa*Ma)/(kmw_+Wa) + (vw_*vwppp_*Wi*1)/(kmwr_+Wi)
```

```
dMa/dt= - kw*Ma + kc*Mi
dL/dt= - kc*L
dL2/dt=kw*(1-L2)

#Globals


#Initial Conditions

init Ca=0, Wa=1, Ma=0, L=1
init L2=0

#Constants

param WTotal=1, TotalCy_2=1, CTotal=1, Dilution=1
param vcp=0.0165, vcpp=0.182, vcppp=0.0709, vwp=0.0000003
param vwpp=0.763, vwppp=0.0709, kmc=0.1, kmcr=1
param kmw=0.1, kmwr=1, vc=1, vw=1
param Cdc25T_17=1, Wee1Total=1

#Plot dependent species

aux Ci=Ci
aux Wi=Wi
aux Mi=Mi

done
```

SBML File


```
<sbml level="1" version="1">
     <model name="Frog Egg Extract">
        <listOfCompartments>
            <compartment name="cell" volume="1"/>
        </listOfCompartments>
        <listOfSpecies>
            <specie name="Mi" compartment="cell" initialAmount="1"/>
            <specie name="Ci" compartment="cell" initialAmount="1"/>
            <specie name="Wi" compartment="cell" initialAmount="0"/>
            <specie name="Ca" compartment="cell" initialAmount="0"/>
            <specie name="Wa" compartment="cell" initialAmount="1"/>
            <specie name="Ma" compartment="cell" initialAmount="0"/>
            <specie name="L"  compartment="cell" initialAmount="1"/>
            <specie name="L2" compartment="cell" initialAmount="0"/>
     </listOfSpecies>
     <listOfParameters>
            <parameter name="WTotal" value="1"/>
            <parameter name="TotalCyclin" value="1"/>
            <parameter name="CTotal" value="1"/>
            <parameter name="Dilution" value="1"/>
            <parameter name="vcp" value="0.0165"/>
            <parameter name="vcpp" value="0.182"/>
            <parameter name="vcppp" value="0.0709"/>
            <parameter name="vwp" value="0.0000003"/>
            <parameter name="vwpp" value="0.763"/>
            <parameter name="vwppp" value="0.0709"/>
            <parameter name="kmc" value="0.1"/>
            <parameter name="kmcr" value="1"/>
            <parameter name="kmw" value="0.1"/>
            <parameter name="kmwr" value="1"/>
            <parameter name="vc" value="1"/>
            <parameter name="vw" value="1"/>
            <parameter name="Cdc25Total" value="1"/>
            <parameter name="Wee1Total" value="1"/>
     </listOfParameters>
     <listOfRules>
```

```
    <parameterRule name="kc" formula="vcp_*Ci+vcpp_*Ca"/>
    <parameterRule name="kw" formula="vwp_*Wi+vwpp_*Wa"/>
    <parameterRule name="vcp_" formula="vcp*Cdc25Total_"/>
    <parameterRule name="vcpp_" formula="vcpp*Cdc25Total_"/>
    <parameterRule name="vcppp_" formula="vcppp/Cdc25Total_"/>
    <parameterRule name="vwp_" formula="vwp*Wee1Total_"/>
    <parameterRule name="vwpp_" formula="vwpp*Wee1Total_"/>
    <parameterRule name="vwppp_" formula="vwppp/Wee1Total_"/>
    <parameterRule name="kmc_" formula="kmc/Cdc25Total_"/>
    <parameterRule name="kmcr_" formula="kmcr/Cdc25Total_"/>
    <parameterRule name="kmw_" formula="kmw/Wee1Total_"/>
    <parameterRule name="kmwr_" formula="kmwr/Wee1Total_"/>
    <parameterRule name="vc_" formula="vc*Cdc2Total_/Cdc25Total_"/>
    <parameterRule name="vw_" formula="vw*Cdc2Total_/Wee1Total_"/>
    <parameterRule name="Cdc25Total_" formula="Cdc25Total*Dilution"/>
    <parameterRule name="Wee1Total_" formula="Wee1Total*Dilution"/>
    <parameterRule name="Cdc2Total_" formula="Dilution"/>
    <specieConcentrationRule specie="Ci" formula="CTotal - Ca"/>
    <specieConcentrationRule specie="Wi" formula="WTotal - Wa"/>
    <specieConcentrationRule specie="Mi" formula="TotalCyclin - Ma"/>
</listOfRules>
<listOfReactions>
    <reaction name="MPF inactivation">
      <listOfReactants>
          <specieReference specie="Ma"/>
      </listOfReactants>
      <listOfProducts>
          <specieReference specie="Mi"/>
      </listOfProducts>
      <kineticLaw formula="massi">
          <listOfParameters>
              <parameter name="k" value="kw"/>
          </listOfParameters>
      </kineticLaw>
    </reaction>
    <reaction name="MPF activation">
      <listOfReactants>
```

```
      <specieReference specie="Mi"/>
   </listOfReactants>
   <listOfProducts>
      <specieReference specie="Ma"/>
   </listOfProducts>
   <kineticLaw formula="massi">
      <listOfParameters>
           <parameter name="k" value="kc"/>
      </listOfParameters>
    </kineticLaw>
</reaction>
<reaction name="Cdc25 inactivation">
   <listOfReactants>
      <specieReference specie="Ca"/>
   </listOfReactants>
   <listOfProducts>
      <specieReference specie="Ci"/>
   </listOfProducts>
   <kineticLaw formula="uui">
      <listOfParameters>
           <parameter name="Vm" value="vcppp_*vc_"/>
           <parameter name="Km" value="kmcr_"/>
      </listOfParameters>
    </kineticLaw>
</reaction>
<reaction name="Cdc25 activation">
  <listOfReactants>
      <specieReference specie="Ci"/>
  </listOfReactants>
  <listOfProducts>
      <specieReference specie="Ca"/>
  </listOfProducts>
  <kineticLaw formula="uui">
      <listOfParameters>
            <parameter name="Vm" value="vc_*Ma"/>
            <parameter name="Km" value="kmc_"/>
      </listOfParameters>
```

```
   </kineticLaw>
</reaction>
<reaction name="Wee1 inactivation">
  <listOfReactants>
      <specieReference specie="Wa"/>
  </listOfReactants>
  <listOfProducts>
      <specieReference specie="Wi"/>
  </listOfProducts>
  <kineticLaw formula="uui">
      <listOfParameters>
          <parameter name="Vm" value="vw_*Ma"/>
          <parameter name="Km" value="kmw_"/>
      </listOfParameters>
  </kineticLaw>
</reaction>
<reaction name="Wee1 activation">
  <listOfReactants>
      <specieReference specie="Wi"/>
  </listOfReactants>
  <listOfProducts>
      <specieReference specie="Wa"/>
  </listOfProducts>
  <kineticLaw formula="uui">
      <listOfParameters>
          <parameter name="Vm" value="vw_*vwppp_"/>
          <parameter name="Km" value="kmwr_"/>
      </listOfParameters>
  </kineticLaw>
</reaction>
<reaction name="Labelled inactive MPF affected by Cdc25">
  <listOfReactants>
      <specieReference specie="L"/>
  </listOfReactants>
  <listOfProducts>
  </listOfProducts>
  <kineticLaw formula="massi">
```

```
              <listOfParameters>
                <parameter name="k" value="kc"/>
              </listOfParameters>
           </kineticLaw>
        </reaction>
        <reaction name="Labelled inactive MPF affected by Wee1">
          <listOfReactants>
          </listOfReactants>
          <listOfProducts>
               <specieReference specie="L2"/>
          </listOfProducts>
          <kineticLaw formula="kw*(1-L2)"/>
        </reaction>
    </listOfReactions>
  </model>
</sbml>
```

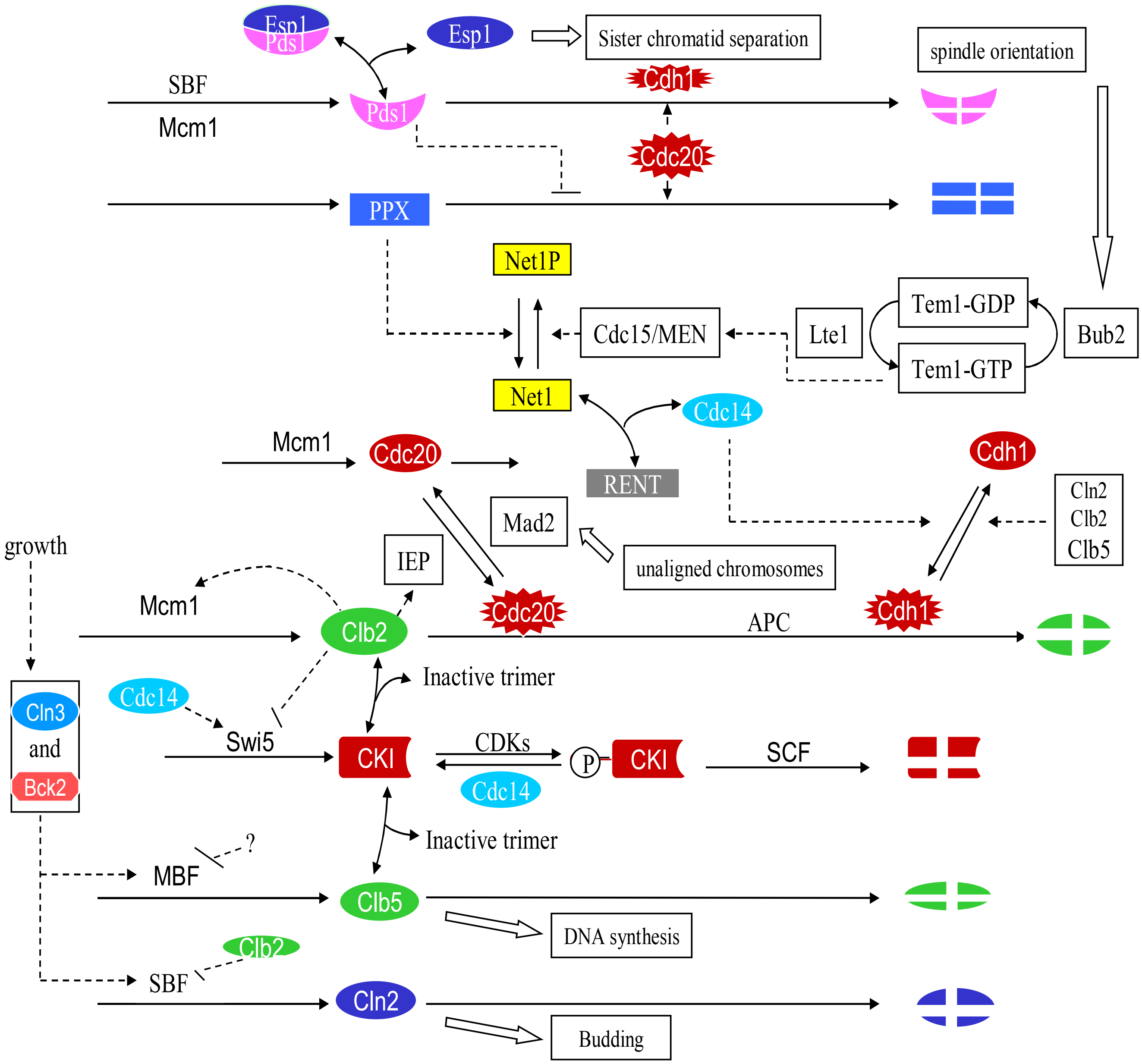
Budding Yeast Model

Description:

This is a model of the budding yeast cell cycle of Saccharomyces cerevisiae based on its known molecular machinery. This model is an extended version of earlier work, with the most recently published being: Chen, C.K., Csikász-Nagy, A., Győrffy, B., Val, J., Novák, B., & Tyson, J.J. (2000) Kinetic Analysis of a Molecular Model of the Budding Yeast Cell Cycle. *Molecular Biology of the Cell* **11,** 369–391. This model contains 37 differential equations and 141 parameters.

This paper is available at http://cellcycle.mkt.bme.hu/articles/budding/chen/full.pdf

Diagram:



Esp1
Pds1
Esp1
Sister chromatid separation
spindle orientation
SBF
Mcm1
Pds1
Cdh1
Cdc20
PPX
Net1P
Cdc15/MEN
Lte1
Tem1-GDP
Tem1-GTP
Bub2
Net1
Cdc14
Mcm1
Cdc20
RENT
Cdh1
Cln2
Clb2
Clb5
Mad2
unaligned chromosomes
growth
IEP
Mcm1
Clb2
Cdc20
APC
Cdh1
Inactive trimer
Cdc14
Cln3
and
Bck2
Swi5
CKI
CDKs
P
CKI
SCF
Cdc14
Inactive trimer
?
MBF
Clb5
DNA synthesis
Clb2
SBF
Cln2
Budding

Differential Equations:

$$\frac{\partial}{\partial t}\mathrm{CLB2}(t) = -Vdb2\ CLB2 - kasb2\ CLB2\ SIC1 - kasf2\ CLB2\ CDC6 + (ksb2p + ksb2pp\ MCM1)\ MASS + kdib2\ C2 + kd3c1\ C2P + kdif2\ F2 + kd3f6\ F2P$$

$$\frac{\partial}{\partial t}\mathrm{CLB5}(t) = -Vdb5\ CLB5 - kasb5\ CLB5\ SIC1 - kasf5\ CLB5\ CDC6 + (ksb5p + ksb5pp\ SBF)\ MASS + kdib5\ C5 + kd3c1\ C5P + kdif5\ F5 + kd3f6\ F5P$$

$$\frac{\partial}{\partial t}\mathrm{SIC1P}(t) = -kppc1\ CDC14\ SIC1P - kd3c1\ SIC1P + Vkpc1\ SIC1 + Vdb2\ C2P + Vdb5\ C5P$$

$$\frac{\partial}{\partial t}\mathrm{C5}(t) = -kdib5\ C5 - Vkpc1\ C5 - Vdb5\ C5 + kasb5\ CLB5\ SIC1 + kppc1\ CDC14\ C5P$$

$$\frac{\partial}{\partial t}\mathrm{C2P}(t) = -kppc1\ CDC14\ C2P - kd3c1\ C2P - Vdb2\ C2P + Vkpc1\ C2$$

$$\frac{\partial}{\partial t}\mathrm{SWI5P}(t) = -kaswi5\ CDC14\ SWI5P - kdswi5\ SWI5P + kiswi5\ CLB2\ SWI5$$

$$\frac{\partial}{\partial t}\mathrm{IEP}(t) = -\frac{kiiep\ IEP}{jiiep + IEP} + \frac{kaiep\ CLB2\ IE}{jaiep + IE}$$

$$\frac{\partial}{\partial t}\mathrm{CDC20}(t) = -MAD2\ CDC20 - kd20\ CDC20 + (ka20p + ka20pp\ IEP)\ CDC20i$$

$$\frac{\partial}{\partial t}\mathrm{CDH1}(t) = -\frac{Vicdh\ CDH1}{Jicdh + CDH1} + \frac{(kacdhp + kacdhpp\ CDC14)\ CDH1i}{Jacdh + CDH1i}$$

$$\frac{\partial}{\partial t}\mathrm{NET1}(t) = -kasrent\ CDC14\ NET1 - Vkpnet\ NET1 + kdirent\ RENT + Vppnet\ NET1P$$

$$\frac{\partial}{\partial t}\mathrm{PPX}(t) = -Vdppx\ PPX + ksppx$$

$$\frac{\partial}{\partial t}\mathrm{ESP1}(t) = -kasesp\ PDS1\ ESP1 + Vdpds\ PE + kdiesp\ PE$$

$$\frac{\partial}{\partial t}\mathrm{ORI}(t) = -kdori\ ORI + ksori\ (eorib5\ CLB5 + eorib2\ CLB2)$$

$$\frac{\partial}{\partial t}\mathrm{SPN}(t) = -kdspn\ SPN + \frac{ksspn\ (FRAC + (1 - FRAC)\ MORPHO)\ CLB2}{Jspn + CLB2}$$

$$\frac{\partial}{\partial t}\mathrm{C2}(t) = -kdib2\ C2 - Vkpc1\ C2 - Vdb2\ C2 + kasb2\ CLB2\ SIC1 + kppc1\ CDC14\ C2P$$

$$\frac{\partial}{\partial t}\mathrm{SWI5}(t) = -kiswi5\ CLB2\ SWI5 - kdswi5\ SWI5 + ksswi5p + ksswi5pp\ MCM1 + kaswi5\ CDC14\ SWI5P$$

$$\frac{\partial}{\partial t}\mathrm{CDC20i}(t) = -(ka20p + ka20pp\ IEP)\ CDC20i - kd20\ CDC20i + ks20p + ks20pp\ MCM1 + MAD2\ CDC20$$

$$\frac{\partial}{\partial t}\mathrm{CDC14}(t) = -kasrent\ CDC14\ NET1 - kasrentp\ CDC14\ NET1P + kdirent\ RENT + kdirentp\ RENTP$$

$$\frac{\partial}{\partial t}\mathrm{CDC15}(t) = -ki15\ CDC15 + (ka15p\ TEM1GDP + ka15pp\ TEM1GTP)\ CDC15i$$

$$\frac{\partial}{\partial t}\mathrm{CLN2}(t) = -kdn2\ CLN2 + (ksn2p + ksn2pp\ SBF)\ MASS$$

$$\frac{\partial}{\partial t}\mathrm{C5P}(t) = -kppc1\ CDC14\ C5P - kd3c1\ C5P - Vdb5\ C5P + Vkpc1\ C5$$

$$\frac{\partial}{\partial t}\mathrm{TEM1GTP}(t) = -\frac{bub2\ TEM1GTP}{Jitem + TEM1GTP} + \frac{lte1\ TEM1GDP}{Jatem + TEM1GDP}$$

$$\frac{\partial}{\partial t}\mathrm{BUD}(t) = -kdbud\ BUD + ksbud\ (ebudn2\ CLN2 + ebudn3\ CLN3 + ebudb5\ CLB5)$$

$$\frac{\partial}{\partial t}\mathrm{SIC1}(t) = -Vkpc1\ SIC1 - kasb2\ CLB2\ SIC1 - kasb5\ CLB5\ SIC1 + ksc1p + ksc1pp\ SWI5 + kppc1\ CDC14\ SIC1P + kdib2\ C2 + kdib5\ C5 + Vdb2\ C2 + Vdb5\ C5$$

$$\frac{\partial}{\partial t}\mathrm{RENT}(t) = -kdirent\ RENT - Vkpnet\ RENT + kasrent\ CDC14\ NET1 + Vppnet\ RENTP$$

$$\frac{\partial}{\partial t}\mathrm{PDS1}(t) = -Vdpds\ PDS1 - kasesp\ PDS1\ ESP1 + ks1pds + ks2pds\ SBF + ks3pds\ MCM1 + kdiesp\ PE$$

$$\frac{\partial}{\partial t}\mathrm{CDC6}(t) = -Vkpf6\ CDC6 - kasf2\ CLB2\ CDC6 - kasf5\ CLB5\ CDC6 + ksf6p + ksf6pp\ SWI5 + ksf6ppp\ SBF + Vppf6\ CDC6P + kdif2\ F2 + kdif5\ F5 + Vdb2\ F2 + Vdb5\ F5$$

$$\frac{\partial}{\partial t}\mathrm{CDC6P}(t) = -Vppf6\ CDC6P - kd3f6\ CDC6P + Vkpf6\ CDC6 + Vdb5\ F5P + Vdb2\ F2P$$

$$\frac{\partial}{\partial t}\mathrm{F2}(t) = -kdif2\ F2 - Vkpf6\ F2 - Vdb2\ F2 + kasf2\ CLB2\ CDC6 + Vppf6\ F2P$$

$$\frac{\partial}{\partial t}\mathrm{F5}(t) = -kdif5\ F5 - Vkpf6\ F5 - Vdb5\ F5 + kasf5\ CLB5\ CDC6 + Vppf6\ F5P$$

$$\frac{\partial}{\partial t}\mathrm{F5P}(t) = -Vppf6\ F5P - kd3f6\ F5P - Vdb5\ F5P + Vkpf6\ F5$$

$$\frac{\partial}{\partial t}\mathrm{F2P}(t) = -Vppf6\ F2P - kd3f6\ F2P - Vdb2\ F2P + Vkpf6\ F2$$

$$\frac{\partial}{\partial t}\mathrm{MAD2}(t) = 0$$

$$\frac{\partial}{\partial t}\mathrm{lte1}(t) = 0$$

$$\frac{\partial}{\partial t}\mathrm{bub2}(t) = 0$$

$$\frac{\partial}{\partial t}\mathrm{MORPHO}(t) = 0$$

$$\frac{\partial}{\partial t}\mathrm{MASS}(t) = \mu\, MASS$$

$$NET1P = NCDC14 + NET1 - CDC14$$

$$CDC15i = CDC15T - CDC15$$

$$PE = ESP1T - ESP1$$

$$CDH1i = CDH1T - CDH1$$

$$TEM1GDP = TEM1T - TEM1GTP \quad RENTP = NET1T - NET1 - NET1P - RENT$$

$$IE = IET - IEP$$

$$Vdb2 = kdb2p\,(1 - CDH1) + kdb2pp\, CDH1 + kdb2p\, CDC20$$
$$Vasbf = kasbf\,(esbfn2\, CLN2 + esbfn3\,(CLN3 + BCK2) + esbfb5\, CLB5)$$
$$SBF = \mathrm{GK}(Vasbf, kisbfp + kisbfpp\, CLB2, Jasbf, Jisbf)$$
$$MCM1 = \mathrm{GK}(kamcm\, CLB2, kimcm, Jamcm, Jimcm)$$

$$Vdb5 = kdb5p + kdb5pp\, CDC20 \quad Vsic1 = kasb2\, CLB2 + kasb5\, CLB5 + Vkpc1$$

$$Vkpc1 = kd1c1 + \frac{Vd2c1}{Jd2c1 + SIC1T}$$
$$Vd2c1 = kd2c1\,(ec1n3\, CLN3 + ec1n2\, CLN2 + ec1k2\, BCK2 + ec1b2\, CLB2 + ec1b5\, CLB5)$$
$$Vkpf6 = kd1f6 + \frac{kd2f6\,(ef6n3\, CLN3 + ef6k2\, BCK2 + ef6n2\, CLN2 + ef6b2\, CLB2 + ef6b5\, CLB5)}{Jd2f6 + CDC6T}$$
$$Vppf6 = kppf6\, CDC14$$
$$Vicdh = kicdhp + kicdhpp\,(eicdhn3\, CLN3 + eicdhn2\, CLN2 + eicdhb5\, CLB5 + eicdhb2\, CLB2)$$
$$Vkpnet = (kkpnetp + kkpnetpp\, CDC15)\, MASS$$

$$Vppnet = kppnetp + kppnetpp\, PPX$$

$$Vdppx = kdppxp + \frac{kdppxpp\,(eps20ppx + CDC20)\, Kmpds}{Kmpds + PDS1}$$
$$Vdpds = kd1pds + kd2pds\, CDC20 + kd3pds\, CDH1$$

$$BCK2 = bck0\, MASS$$

$$CLN3 = \frac{CLN3MAX\, Dn3\, MASS}{Jn3 + Dn3\, MASS}$$

$$CLB5T = C5 + C5P + CLB5$$

$$CLB2T = C2P + C2 + CLB2$$

$$SIC1T = SIC1 + SIC1P + C2 + C5 + C2P + C5P$$

$$CDC6T = CDC6 + CDC6P + F2 + F5 + F2P + F5P$$

JigCell Model Builder Representation:

Model Spreadsheet

Reaction	Name	Type	Equation	Modifiers and Constants
->CLN2		Mass Action	((ksn2' + ksn2''*SBF)*MASS)	Kf=(ksn2' + ksn2''*SBF)*MASS
CLN2->		Mass Action	kdn2*CLN2	Kf=kdn2
->CLB2		Mass Action	((ksb2'+ksb2''*MCM1)*MASS)	Kf=(ksb2'+ksb2''*MCM1)*MASS
CLB2->		Mass Action	Vdb2*CLB2	Kf=Vdb2
	BB	Function	A2-A1+A3*A2+A4*A1	
	GK	Function	2*A4*A1/(BB(A1,A2,A3,A4)+sqrt(BB(A1,A2,A3,A4)^2-4*(A2-A1)*A4*A1))	
Vdb2		Species	kdb2'*(1-CDH1)+kdb2''*CDH1+kdb2p*CDC20	kdb2'=kdb2'; kdb2''=kdb2''; kdb2p=kdb2p
Vasbf		Species	kasbf*(esbfn2*CLN2+esbfn3*(CLN3+BCK2)+esbfb5*CLB5)	kasbf=kasbf; esbfn2=esbfn2; esbfn3=esbfn3; esbfb5=esbfb5
SBF		Species	GK(Vasbf,kisbf'+kisbf''*CLB2,Jasbf,Jisbf)	kisbf'=kisbf'; kisbf''=kisbf''; Jasbf=Jasbf; Jisbf=Jisbf
MCM1		Species	GK(kamcm*CLB2,kimcm,Jamcm,Jimcm)	kamcm=kamcm; kimcm=kimcm; Jamcm=Jamcm; Jimcm=Jimcm
->MAD2		Mass Action	0	Kf=0
->CLB5		Mass Action	((ksb5'+ksb5''*SBF)*MASS)	Kf=(ksb5'+ksb5''*SBF)*MASS
CLB5->		Mass Action	Vdb5*CLB5	Kf=Vdb5
Vdb5		Species	kdb5'+kdb5''*CDC20	kdb5'=kdb5'; kdb5''=kdb5''
->SIC1		Mass Action	(ksc1'+ksc1''*SWI5)	Kf=ksc1'+ksc1''*SWI5
SIC1->SIC1P		Mass Action	Vkpc1*SIC1	Kf=Vkpc1
SIC1P->SIC1		Mass Action	kppc1*CDC14*SIC1P	Kf=kppc1*CDC14
SIC1P->		Mass Action	kd3c1*SIC1P	Kf=kd3c1
Vsic1		Species	kasb2*CLB2+kasb5*CLB5+Vkpc1	kasb2=kasb2; kasb5=kasb5
Vkpc1		Species	kd1c1+Vd2c1/(Jd2c1+SIC1T)	kd1c1=kd1c1; Jd2c1=Jd2c1
Vd2c1		Species	kd2c1*(ec1n3*CLN3+ec1n2*CLN2+ec1k2*BCK2+ec1b2*CLB2+ec1b5*CLB5)	kd2c1=kd2c1; ec1n3=ec1n3; ec1n2=ec1n2; ec1k2=ec1k2; ec1b2=ec1b2; ec1b5=ec1b5
CLB2+SIC1->C2		Mass Action	kasb2*CLB2*SIC1	Kf=kasb2
C2->CLB2+SIC1		Mass Action	kdib2*C2	Kf=kdib2

CLB5+SIC1->C5		Mass Action	kasb5*CLB5*SIC1	Kf=kasb5
C5->CLB5+SIC1		Mass Action	kdib5*C5	Kf=kdib5
C5P->C5		Mass Action	kppc1*CDC14*C5P	Kf=kppc1*CDC14
C5->C5P		Mass Action	Vkpc1*C5	Kf=Vkpc1
C2P->C2		Mass Action	kppc1*CDC14*C2P	Kf=kppc1*CDC14
C2->C2P		Mass Action	Vkpc1*C2	Kf=Vkpc1
C2P->CLB2		Mass Action	kd3c1*C2P	Kf=kd3c1
C5P->CLB5		Mass Action	kd3c1*C5P	Kf=kd3c1
C2->SIC1		Mass Action	Vdb2*C2	Kf=Vdb2
C5->SIC1		Mass Action	Vdb5*C5	Kf=Vdb5
C2P->SIC1P		Mass Action	Vdb2*C2P	Kf=Vdb2
C5P->SIC1P		Mass Action	Vdb5*C5P	Kf=Vdb5
->CDC6		Mass Action	(ksf6'+ksf6''*SWI5+ksf6'''*SBF)	Kf=ksf6'+ksf6''*SWI5+ksf6'''*SBF
CDC6->CDC6P		Mass Action	Vkpf6*CDC6	Kf=Vkpf6
CDC6P->CDC6		Mass Action	Vppf6*CDC6P	Kf=Vppf6
CDC6P->		Mass Action	kd3f6*CDC6P	Kf=kd3f6
Vkpf6		Species	kd1f6+kd2f6*(ef6n3*CLN3+ef6k2*BCK2+ef6n2*CLN2+ef6b2*CLB2+ef6b5*CLB5)/(Jd2f6+CDC6T)	kd1f6=kd1f6; kd2f6=kd2f6; ef6n3=ef6n3; ef6k2=ef6k2; ef6n2=ef6n2; ef6b2=ef6b2; ef6b5=ef6b5; Jd2f6=Jd2f6
Vppf6		Species	kppf6*CDC14	kppf6=kppf6
CLB2+CDC6->F2		Mass Action	kasf2*CLB2*CDC6	Kf=kasf2
F2->CLB2+CDC6		Mass Action	kdif2*F2	Kf=kdif2
CLB5+CDC6->F5		Mass Action	kasf5*CLB5*CDC6	Kf=kasf5
F5->CLB5+CDC6		Mass Action	kdif5*F5	Kf=kdif5
F5->F5P		Mass Action	Vkpf6*F5	Kf=Vkpf6
F5P->F5		Mass Action	Vppf6*F5P	Kf=Vppf6
F2->F2P		Mass Action	Vkpf6*F2	Kf=Vkpf6
F2P->F2		Mass	Vppf6*F2P	Kf=Vppf6

		Action		
F2P->CLB2		Mass Action	kd3f6*F2P	Kf=kd3f6
F5P->CLB5		Mass Action	kd3f6*F5P	Kf=kd3f6
F2->CDC6		Mass Action	Vdb2*F2	Kf=Vdb2
F5->CDC6		Mass Action	Vdb5*F5	Kf=Vdb5
F5P->CDC6P		Mass Action	Vdb5*F5P	Kf=Vdb5
F2P->CDC6P		Mass Action	Vdb2*F2P	Kf=Vdb2
->SWI5		Mass Action	(ksswi5'+ksswi5''*MCM1)	Kf=ksswi5'+ksswi5''*MCM1
SWI5->SWI5P		Mass Action	kiswi5*CLB2*SWI5	Kf=kiswi5*CLB2
SWI5P->SWI5		Mass Action	kaswi5*CDC14*SWI5P	Kf=kaswi5*CDC14
SWI5->		Mass Action	kdswi5*SWI5	Kf=kdswi5
SWI5P->		Mass Action	kdswi5*SWI5P	Kf=kdswi5
IE->IEP		Mass Action	(kaiep*CLB2/(jaiep+IE))*IE	Kf=kaiep*CLB2/(jaiep+IE)
IEP->IE		Mass Action	(kiiep/(jiiep+IEP))*IEP	Kf=kiiep/(jiiep+IEP)
->CDC20i		Mass Action	(ks20'+ks20''*MCM1)	Kf=ks20'+ks20''*MCM1
CDC20i->CDC20		Mass Action	(ka20'+ka20''*IEP)*CDC20i	Kf=ka20'+ka20''*IEP
CDC20->CDC20i		Mass Action	MAD2*CDC20	Kf=MAD2
CDC20->		Mass Action	kd20*CDC20	Kf=kd20
CDC20i->		Mass Action	kd20*CDC20i	Kf=kd20
CDH1i->CDH1		Mass Action	((kacdh'+kacdh''*CDC14)/(Jacdh+CDH1i))*CDH1i	Kf=(kacdh'+kacdh''*CDC14)/(Jacdh+CDH1i)
CDH1->CDH1i		Mass Action	(Vicdh/(Jicdh+CDH1))*CDH1	Kf=Vicdh/(Jicdh+CDH1)
Vicdh		Species	kicdh'+kicdh''*(eicdhn3*CLN3+eicdhn2*CLN2+eicdhb5*CLB5+eicdhb2*CLB2)	kicdh'=kicdh'; kicdh''=kicdh''; eicdhn3=eicdhn3; eicdhn2=eicdhn2; eicdhb5=eicdhb5; eicdhb2=eicdhb2
CDC14+NET1->RENT		Mass Action	kasrent*CDC14*NET1	Kf=kasrent
RENT->NET1+CDC14		Mass Action	kdirent*RENT	Kf=kdirent
CDC14+NET1P->RENTP		Mass Action	kasrentp*CDC14*NET1P	Kf=kasrentp
RENTP->CDC14		Mass Action	kdirentp*RENTP	Kf=kdirentp

+NET1P				
NET1->NET1P		Mass Action	Vkpnet*NET1	Kf=Vkpnet
Vkpnet		Species	(kkpnet'+kkpnet"*CDC15)*MASS	kkpnet'=kkpnet'; kkpnet"=kkpnet"
Vppnet		Species	kppnet'+kppnet"*PPX	kppnet'=kppnet'; kppnet"=kppnet"
NET1P->NET1		Mass Action	Vppnet*NET1P	Kf=Vppnet
RENT->RENTP		Mass Action	Vkpnet*RENT	Kf=Vkpnet
RENTP->RENT		Mass Action	Vppnet*RENTP	Kf=Vppnet
TEM1GDP->TEM1GTP		Mass Action	(lte1/(Jatem+TEM1GDP))*TEM1GDP	Kf=lte1/(Jatem+TEM1GDP)
TEM1GTP->TEM1GDP		Mass Action	(bub2/(Jitem+TEM1GTP))*TEM1GTP	Kf=bub2/(Jitem+TEM1GTP)
CDC15i->CDC15		Mass Action	(ka15'*TEM1GDP+ka15"*TEM1GTP)*CDC15i	Kf=ka15'*TEM1GDP+ka15"*TEM1GTP
CDC15->CDC15i		Mass Action	ki15*CDC15	Kf=ki15
->PPX		Mass Action	ksppx	Kf=ksppx
PPX->		Mass Action	Vdppx*PPX	Kf=Vdppx
Vdppx		Species	kdppx'+kdppx"*(eps20ppx+CDC20)*Kmpds/(Kmpds+PDS1)	kdppx'=kdppx'; kdppx"=kdppx"; eps20ppx=eps20ppx; Kmpds=Kmpds
->PDS1		Mass Action	(ks1pds+ks2pds*SBF+ks3pds*MCM1)	Kf=ks1pds+ks2pds*SBF+ks3pds*MCM1
PDS1->		Mass Action	Vdpds*PDS1	Kf=Vdpds
Vdpds		Species	kd1pds+kd2pds*CDC20+kd3pds*CDH1	kd1pds=kd1pds; kd2pds=kd2pds; kd3pds=kd3pds
PDS1+ESP1->PE		Mass Action	kasesp*PDS1*ESP1	Kf=kasesp
PE->ESP1		Mass Action	Vdpds*PE	Kf=Vdpds
PE->PDS1+ESP1		Mass Action	kdiesp*PE	Kf=kdiesp
->ORI		Mass Action	(ksori*(eorib5*CLB5+eorib2*CLB2))	Kf=ksori*(eorib5*CLB5+eorib2*CLB2)
ORI->		Mass Action	kdori*ORI	Kf=kdori
->BUD		Mass Action	(ksbud*(ebudn2*CLN2+ebudn3*CLN3+ebudb5*CLB5))	Kf=ksbud*(ebudn2*CLN2+ebudn3*CLN3+ebudb5*CLB5)
BUD->		Mass Action	kdbud*BUD	Kf=kdbud
->SPN		Mass Action	(ksspn*(FRAC+(1-FRAC)*MORPHO)*CLB2/(Jspn+CLB2))	Kf=ksspn*(FRAC+(1-FRAC)*MORPHO)*CLB2/(Jspn+CLB2)

SPN->		Mass Action	kdspn*SPN	Kf=kdspn
->lte1		Mass Action	0	Kf=0
->bub2		Mass Action	0	Kf=0
->MORPHO		Mass Action	0	Kf=0
->MASS		Mass Action	mu*MASS	Kf=mu*MASS
BCK2		Species	bck0*MASS	bck0=bck0
CLN3		Species	CLN3MAX*Dn3*MASS/(Jn3+Dn3*MASS)	CLN3MAX=CLN3MAX; Dn3=Dn3; Jn3=Jn3
CLB5T		Species	C5+C5P+CLB5	
CLB2T		Species	C2P+C2+CLB2	
SIC1T		Species	SIC1+SIC1P+C2+C5+C2P+C5P	
CDC6T		Species	CDC6+CDC6P+F2+F5+F2P+F5P	

Constants Spreadsheet

Name	Value
kasb5	50
kd3c1	1
kdswi5	0.1
ksswi5'	0.005
kiswi5	0.05
kaiep	0.1
kiiep	0.15
ks20'	0.006
ka20'	0.1
kacdh'	0.01
Jacdh	0.05
kicdh'	0.001
eicdhn3	0.25
eicdhb5	7
kasrent	200
kasrentp	1
kkpnet'	0.09
kppnet'	0.5
Jatem	0.1
ka15'	0.002
ki15	0.5
kdppx'	0.1
eps20ppx	0.15
ks1pds	0

ks3pds	0.06
kd2pds	0.12
kasesp	50
ksori	1.7
eorib2	0.4
ksbud	0.38
ebudn3	0.05
kdbud	0.06
FRAC	1
kdspn	0.06
bck0	0.054
Dn3	1
NCDC14	-0.8
ESP1T	1
TEM1T	1
IET	1
lte1h	1
KEZ	0.3
lte1l	0.1
Mad2h	8
kasb2	50
kd3f6	1
ksswi5''	0.1
jaiep	0.1
ks20''	0.6
kacdh''	0.8
kicdh''	0.08
eicdhb2	1
kdirentp	2
kppnet''	5
ka15''	1
kdppx''	2
ks2pds	0.03
kd3pds	0.04
eorib5	0.9
ebudn2	0.16
ksspn	0.08
mu	0.005776
Jn3	6
CDH1T	1
Mad2l	0.01
f	0.433
bub2h	1
kd20	0.3
kaswi5	1.8
ka20''	0.2
eicdhn2	0.25
kkpnet''	3

ksppx	0.1
kd1pds	0.005
kdori	0.08
Jspn	0.2
CDC15T	1
bub2l	0.2
kppc1	4
jiiep	0.1
kdirent	1
Kmpds	0.02
ebudb5	1
NET1T	2.8
Jicdh	0.05
kdiesp	1
KEZ2	0.15
CLN3MAX	0.4
Jitem	0.1
ksn2'	0
ksn2''	0.32
kdn2	0.12
ksb2'	0.0015
ksb2''	0.05
kdb2'	0.003
kdb2''	0.2
kdb2p	0.07
kasbf	0.38
esbfn2	1.25
esbfn3	10
esbfb5	8
kisbf'	0.6
kisbf''	8
Jasbf	0.01
Jisbf	0.01
kamcm	1
kimcm	0.15
Jamcm	0.1
Jimcm	0.1
ksb5'	0.0015
ksb5''	0.005
kdb5'	0.01
kdb5''	0.15
ksc1'	0.014
ksc1''	0.13
kd1c1	0.01
Jd2c1	0.05
kd2c1	1
ec1n3	0.3
ec1n2	0.038

ec1k2	0.03
ec1b2	0.4
ec1b5	0.25
kdib2	0.05
kdib5	0.05
ksf6'	0.026
ksf6''	0.13
ksf6'''	0
kd1f6	0.01
kd2f6	1
ef6n3	0.3
ef6k2	0.03
ef6n2	0.038
ef6b2	0.35
ef6b5	0.13
Jd2f6	0.05
kppf6	4
kasf2	15
kdif2	0.5
kasf5	0.01
kdif5	0.01

Species Spreadsheet

Name	Initial Condition
CLB2	0.27
CLB5	0.013397
SIC1P	0.003471
C5	0.002982
C2P	0.02797
CDC6P	0.004572
F5	0.001593
F2P	0.03599
SWI5P	0.032929
IEP	0.683371
CDC20	0.730576
CDH1	0.998514
NET1	0.908319
NET1P	0.970271
TEM1GDP	0.02287
CDC15i	0.338325
PPX	0.1032
ESP1	0.537416
ORI	29.57
SPN	0.000241
bub2	0.2
MASS	0.812198
C2	0.194241

CDC6	0.019517
F5P	0.000099
IE	0.311663
CDH1i	0.001486
RENT	0.571302
TEM1GTP	0.977013
PDS1	0.018061
BUD	0.000055
MORPHO	1
SIC1	0.00868
F2	0.535982
CDC20i	1.098074
RENTP	1.277698
PE	0.555477
CLN2	0.107497
SWI5	0.950772
CDC15	0.661675
C5P	0.764078
lte1	0.1
CDC14	0.495952
MAD2	0.01

Conservation Relations Spreadsheet

Conservation Relation	Constant Total Name	Dependent Species
IEP + IE	IET	IE
CDH1 + CDH1i	CDH1T	CDH1i
TEM1GDP + TEM1GTP	TEM1T	TEM1GDP
NET1 + NET1P + RENTP + RENT	NET1T	RENTP
ESP1 + PE	ESP1T	PE
CDC15i + CDC15	CDC15T	CDC15i
- NET1 - NET1P + CDC14	NCDC14	NET1P

Rules Spreadsheet

Sign	Condition	Actions
-1	CLB2-KEZ	MASS=f*MASS; BUD=0; SPN=0; lte1=lte1l; MORPHO=0
1	ORI-1	MAD2=Mad2h; bub2=bub2h
1	SPN-1	MAD2=Mad2l; lte1=lte1h; bub2=bub2l
-1	CLB2+CLB5-KEZ2	ORI=0
1	BUD-1	MORPHO=1

XPP Ode File (Differential Equations)

```
#  C:\Documents and Settings\laurence\Desktop\laurence\JigCell\0105.odef  Generated
by JigCell


#Functions

BB(A1,A2,A3,A4)=A2-A1+A3*A2+A4*A1
GK(A1,A2,A3,A4)=2*A4*A1/(BB(A1,A2,A3,A4)+(BB(A1,A2,A3,A4)^2-4*(A2-A1)*A4*A1)^.5)

#Dependent species

NET1P=(NCDC14 + NET1 - CDC14)/(-(1.0))
CDC15i=(CDC15T - CDC15)/(-(-1.0))
PE=(ESP1T - ESP1)
CDH1i=(CDH1T - CDH1)
TEM1GDP=(TEM1T - TEM1GTP)/(-(-1.0))
RENTP=(NET1T - NET1 - NET1P - RENT)/(-(-1.0))
IE=(IET - IEP)

#Species

Vdb2=(kdb2')*(1-CDH1)+(kdb2'')*CDH1+(kdb2p)*CDC20
aux Vdb2=Vdb2
Vasbf=(kasbf)*((esbfn2)*CLN2+(esbfn3)*(CLN3+BCK2)+(esbfb5)*CLB5)
aux Vasbf=Vasbf
SBF=GK(Vasbf,(kisbf')+(kisbf'')*CLB2,(Jasbf),(Jisbf))
aux SBF=SBF
MCM1=GK((kamcm)*CLB2,(kimcm),(Jamcm),(Jimcm))
aux MCM1=MCM1
Vdb5=(kdb5')+(kdb5'')*CDC20
aux Vdb5=Vdb5
Vsic1=(kasb2)*CLB2+(kasb5)*CLB5+Vkpc1
aux Vsic1=Vsic1
Vkpc1=(kd1c1)+Vd2c1/((Jd2c1)+SIC1T)
aux Vkpc1=Vkpc1
Vd2c1=(kd2c1)*((ec1n3)*CLN3+(ec1n2)*CLN2+(ec1k2)*BCK2+(ec1b2)*CLB2+(ec1b5)*CLB5)
aux Vd2c1=Vd2c1
Vkpf6=(kd1f6)+(kd2f6)*((ef6n3)*CLN3+(ef6k2)*BCK2+(ef6n2)*CLN2+(ef6b2)*CLB2+(ef6b5)*
CLB5)/((Jd2f6)+CDC6T)
aux Vkpf6=Vkpf6
Vppf6=(kppf6)*CDC14
aux Vppf6=Vppf6
Vicdh=(kicdh')+(kicdh'')*((eicdhn3)*CLN3+(eicdhn2)*CLN2+(eicdhb5)*CLB5+(eicdhb2)*CL
B2)
aux Vicdh=Vicdh
Vkpnet=((kkpnet')+(kkpnet'')*CDC15)*MASS
aux Vkpnet=Vkpnet
Vppnet=(kppnet')+(kppnet'')*PPX
aux Vppnet=Vppnet
Vdppx=(kdppx')+(kdppx'')*((eps20ppx)+CDC20)*(Kmpds)/((Kmpds)+PDS1)
aux Vdppx=Vdppx
Vdpds=(kd1pds)+(kd2pds)*CDC20+(kd3pds)*CDH1
aux Vdpds=Vdpds
BCK2=(bck0)*MASS
aux BCK2=BCK2
```

```
CLN3=(CLN3MAX)*(Dn3)*MASS/((Jn3)+(Dn3)*MASS)
aux CLN3=CLN3
CLB5T=C5+C5P+CLB5
aux CLB5T=CLB5T
CLB2T=C2P+C2+CLB2
aux CLB2T=CLB2T
SIC1T=SIC1+SIC1P+C2+C5+C2P+C5P
aux SIC1T=SIC1T
CDC6T=CDC6+CDC6P+F2+F5+F2P+F5P
aux CDC6T=CDC6T

#Independent Species

dCLB2/dt= - Vdb2*CLB2 - kasb2*CLB2*SIC1 - kasf2*CLB2*CDC6 +
((ksb2'+ksb2''*MCM1)*MASS) + kdib2*C2 + kd3c1*C2P + kdif2*F2 + kd3f6*F2P
dCLB5/dt= - Vdb5*CLB5 - kasb5*CLB5*SIC1 - kasf5*CLB5*CDC6 +
((ksb5'+ksb5''*SBF)*MASS) + kdib5*C5 + kd3c1*C5P + kdif5*F5 + kd3f6*F5P
dSIC1P/dt= - kppc1*CDC14*SIC1P - kd3c1*SIC1P + Vkpc1*SIC1 + Vdb2*C2P + Vdb5*C5P
dC5/dt= - kdib5*C5 - Vkpc1*C5 - Vdb5*C5 + kasb5*CLB5*SIC1 + kppc1*CDC14*C5P
dC2P/dt= - kppc1*CDC14*C2P - kd3c1*C2P - Vdb2*C2P + Vkpc1*C2
dSWI5P/dt= - kaswi5*CDC14*SWI5P - kdswi5*SWI5P + kiswi5*CLB2*SWI5
dIEP/dt= - (kiiep/(jiiep+IEP))*IEP + (kaiep*CLB2/(jaiep+IE))*IE
dCDC20/dt= - MAD2*CDC20 - kd20*CDC20 + (ka20'+ka20''*IEP)*CDC20i
dCDH1/dt= - (Vicdh/(Jicdh+CDH1))*CDH1 +
((kacdh'+kacdh''*CDC14)/(Jacdh+CDH1i))*CDH1i
dNET1/dt= - kasrent*CDC14*NET1 - Vkpnet*NET1 + kdirent*RENT + Vppnet*NET1P
dPPX/dt= - Vdppx*PPX + ksppx
dESP1/dt= - kasesp*PDS1*ESP1 + Vdpds*PE + kdiesp*PE
dORI/dt= - kdori*ORI + (ksori*(eorib5*CLB5+eorib2*CLB2))
dSPN/dt= - kdspn*SPN + (ksspn*(FRAC+(1-FRAC)*MORPHO)*CLB2/(Jspn+CLB2))
dC2/dt= - kdib2*C2 - Vkpc1*C2 - Vdb2*C2 + kasb2*CLB2*SIC1 + kppc1*CDC14*C2P
dSWI5/dt= - kiswi5*CLB2*SWI5 - kdswi5*SWI5 + (ksswi5'+ksswi5''*MCM1) +
kaswi5*CDC14*SWI5P
dCDC20i/dt= - (ka20'+ka20''*IEP)*CDC20i - kd20*CDC20i + (ks20'+ks20''*MCM1) +
MAD2*CDC20
dCDC14/dt= - kasrent*CDC14*NET1 - kasrentp*CDC14*NET1P + kdirent*RENT +
kdirentp*RENTP
dCDC15/dt= - ki15*CDC15 + (ka15'*TEM1GDP+ka15''*TEM1GTP)*CDC15i
dCLN2/dt= - kdn2*CLN2 + ((ksn2' + ksn2''*SBF)*MASS)
dC5P/dt= - kppc1*CDC14*C5P - kd3c1*C5P - Vdb5*C5P + Vkpc1*C5
dTEM1GTP/dt= - (bub2/(Jitem+TEM1GTP))*TEM1GTP + (lte1/(Jatem+TEM1GDP))*TEM1GDP
dBUD/dt= - kdbud*BUD + (ksbud*(ebudn2*CLN2+ebudn3*CLN3+ebudb5*CLB5))
dSIC1/dt= - Vkpc1*SIC1 - kasb2*CLB2*SIC1 - kasb5*CLB5*SIC1 + (ksc1'+ksc1''*SWI5) +
kppc1*CDC14*SIC1P + kdib2*C2 + kdib5*C5 + Vdb2*C2 + Vdb5*C5
dRENT/dt= - kdirent*RENT - Vkpnet*RENT + kasrent*CDC14*NET1 + Vppnet*RENTP
dPDS1/dt= - Vdpds*PDS1 - kasesp*PDS1*ESP1 + (ks1pds+ks2pds*SBF+ks3pds*MCM1) +
kdiesp*PE
dCDC6/dt= - Vkpf6*CDC6 - kasf2*CLB2*CDC6 - kasf5*CLB5*CDC6 +
(ksf6'+ksf6''*SWI5+ksf6'''*SBF) + Vppf6*CDC6P + kdif2*F2 + kdif5*F5 + Vdb2*F2 +
Vdb5*F5
dCDC6P/dt= - Vppf6*CDC6P - kd3f6*CDC6P + Vkpf6*CDC6 + Vdb5*F5P + Vdb2*F2P
dF2/dt= - kdif2*F2 - Vkpf6*F2 - Vdb2*F2 + kasf2*CLB2*CDC6 + Vppf6*F2P
dF5/dt= - kdif5*F5 - Vkpf6*F5 - Vdb5*F5 + kasf5*CLB5*CDC6 + Vppf6*F5P
dF5P/dt= - Vppf6*F5P - kd3f6*F5P - Vdb5*F5P + Vkpf6*F5
dF2P/dt= - Vppf6*F2P - kd3f6*F2P - Vdb2*F2P + Vkpf6*F2
dMAD2/dt=0
dlte1/dt=0
```

```
dbub2/dt=0
dMORPHO/dt=0
dMASS/dt=mu*MASS

#Globals

global 1 {SPN-1 } {MAD2=Mad2l; lte1=lte1h; bub2=bub2l }
global -1 {CLB2-KEZ } {MASS=f*MASS; BUD=0; SPN=0; lte1=lte1l; MORPHO=0 }
global -1 {CLB2+CLB5-KEZ2 } {ORI=0 }
global 1 {ORI-1 } {MAD2=Mad2h; bub2=bub2h }
global 1 {BUD-1 } {MORPHO=1 }

#Initial Conditions

init CLB2=0.27, CLB5=0.013397, SIC1P=0.003471, C5=0.002982
init C2P=0.027970, SWI5P=0.032929, IEP=0.683371, CDC20=0.730576
init CDH1=0.998514, NET1=0.908319, PPX=0.1032, ESP1=0.537416
init ORI=29.57, SPN=0.000241, C2=0.194241, SWI5=0.950772
init CDC20i=1.098074, CDC14=0.495952, CDC15=0.661675, CLN2=0.107497
init C5P=0.764078, TEM1GTP=0.977013, BUD=0.000055, SIC1=0.008680
init RENT=0.571302, PDS1=0.018061, CDC6=0.019517, CDC6P=0.004572
init F2=0.535982, F5=0.001593, F5P=0.000099, F2P=0.035990
init MAD2=0.01, lte1=0.1, bub2=0.2, MORPHO=1
init MASS=0.812198

#Constants

param kasb5=50, kd3c1=1, kd20=0.3, CDC15T=1
param CDH1T=1, NET1T=2.8, KEZ2=0.15, lte1h=1
param KEZ=0.3, lte1l=0.1, bub2h=1, kppc1=4
param ESP1T=1, IET=1, bub2l=0.2, Mad2h=8
param kdswi5=0.1, NCDC14=-0.8, Mad2l=0.01, kasb2=50
param TEM1T=1, f=0.433, kd3f6=1, ksn2'=0
param ksn2''=0.32, kdn2=0.12, ksb2'=0.0015, ksb2''=0.05
param kdb2'=0.003, kdb2''=0.2, kdb2p=0.07, kasbf=0.38
param esbfn2=1.25, esbfn3=10, esbfb5=8, kisbf'=0.6
param kisbf''=8, Jasbf=0.01, Jisbf=0.01, kamcm=1
param kimcm=0.15, Jamcm=0.1, Jimcm=0.1, ksb5'=0.0015
param ksb5''=0.005, kdb5'=0.01, kdb5''=0.15, ksc1'=0.014
param ksc1''=0.13, kd1c1=0.01, Jd2c1=0.05, kd2c1=1
param ec1n3=0.3, ec1n2=0.038, ec1k2=0.03, ec1b2=0.4
param ec1b5=0.25, kdib2=0.05, kdib5=0.05, ksf6'=0.026
param ksf6''=0.13, ksf6'''=0, kd1f6=0.01, kd2f6=1
param ef6n3=0.3, ef6k2=0.03, ef6n2=0.038, ef6b2=0.35
param ef6b5=0.13, Jd2f6=0.05, kppf6=4, kasf2=15
param kdif2=0.5, kasf5=0.01, kdif5=0.01, ksswi5'=0.005
param ksswi5''=0.1, kiswi5=0.05, kaswi5=1.8, kaiep=0.1
param jaiep=0.1, kiiep=0.15, jiiep=0.1, ks20'=0.006
param ks20''=0.6, ka20'=0.1, ka20''=0.2, kacdh'=0.01
param kacdh''=0.8, Jacdh=0.05, Jicdh=0.05, kicdh'=0.001
param kicdh''=0.08, eicdhn3=0.25, eicdhn2=0.25, eicdhb5=7
param eicdhb2=1, kasrent=200, kdirent=1, kasrentp=1
param kdirentp=2, kkpnet'=0.09, kkpnet''=3, kppnet'=0.5
param kppnet''=5, Jatem=0.1, Jitem=0.1, ka15'=0.002
param ka15''=1, ki15=0.5, ksppx=0.1, kdppx'=0.1
param kdppx''=2, eps20ppx=0.15, Kmpds=0.02, ks1pds=0
param ks2pds=0.03, ks3pds=0.06, kd1pds=0.005, kd2pds=0.12
```

```
param kd3pds=0.04, kasesp=50, kdiesp=1, ksori=1.7
param eorib5=0.9, eorib2=0.4, kdori=0.08, ksbud=0.38
param ebudn2=0.16, ebudn3=0.05, ebudb5=1, kdbud=0.06
param ksspn=0.08, FRAC=1, Jspn=0.2, kdspn=0.06
param mu=0.005776, bck0=0.054, CLN3MAX=0.4, Dn3=1
param Jn3=6

#Plot dependent species

aux NET1P=NET1P
aux CDC15i=CDC15i
aux PE=PE
aux CDH1i=CDH1i
aux TEM1GDP=TEM1GDP
aux RENTP=RENTP
aux IE=IE

done
```