

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.

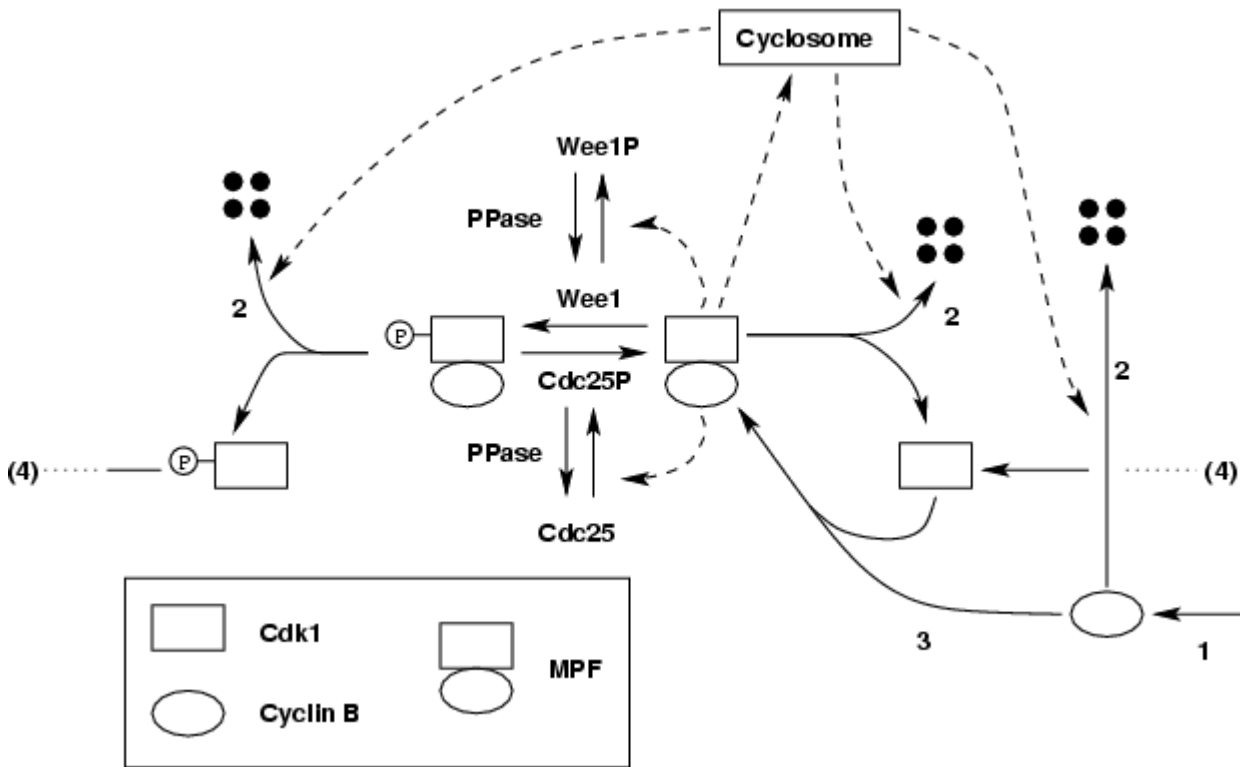
Frog Egg Extract Model

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*. *Biophys. 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:

$$\frac{\partial}{\partial t} Ca(t) = -\frac{vcppp_vc_Ca}{kmcr_+Ca} + \frac{vc_CiMa}{kmc_+Ci}$$

$$\frac{\partial}{\partial t} Wa(t) = -\frac{vw_WaMa}{kmw_+Wa} + \frac{vw_vwppp_Wi}{kmwr_+Wi}$$

$$\frac{\partial}{\partial t} Ma(t) = -kwMa + kcMi$$

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

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

$$Ci = CTotal - Ca$$

$$Wi = WTotal - Wa$$

$$Mi = TotalCyclin - Ma$$

$$kc = vcp_Ci + vcpp_Ca$$

$$kw = vwp_Wi + vwpp_Wa$$

$$vcp_ = vcp\ Cdc25Total_$$

$$vcpp_ = vcpp\ Cdc25Total_$$

$$vcppp_ = \frac{vcppp}{Cdc25Total_}$$

$$vwp_ = vwp\ WeelTotal_$$

$$vwpp_ = vwpp\ WeelTotal_$$

$$vwppp_ = \frac{vwppp}{WeelTotal_}$$

$$kmc_ = \frac{kmc}{Cdc25Total_}$$

$$kmcr_ = \frac{kmcr}{Cdc25Total_}$$

$$kmw_ = \frac{kmw}{WeelTotal_}$$

$$kmwr_{-} = \frac{kmwr}{WeelTotal_{-}}$$

$$vc_{-} = \frac{vc Cdc2Total_{-}}{Cdc25Total_{-}}$$

$$vw_{-} = \frac{vw Cdc2Total_{-}}{WeelTotal_{-}}$$

$$Cdc25Total_{-} = Cdc25Total \text{ Dilution}$$

$$WeelTotal_{-} = WeelTotal \text{ Dilution}$$

$$Cdc2Total_{-} = Dilution$$

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>

```

```

    </kineticLaw>
</reaction>
<reaction name="Weel 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="Weel 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>
```

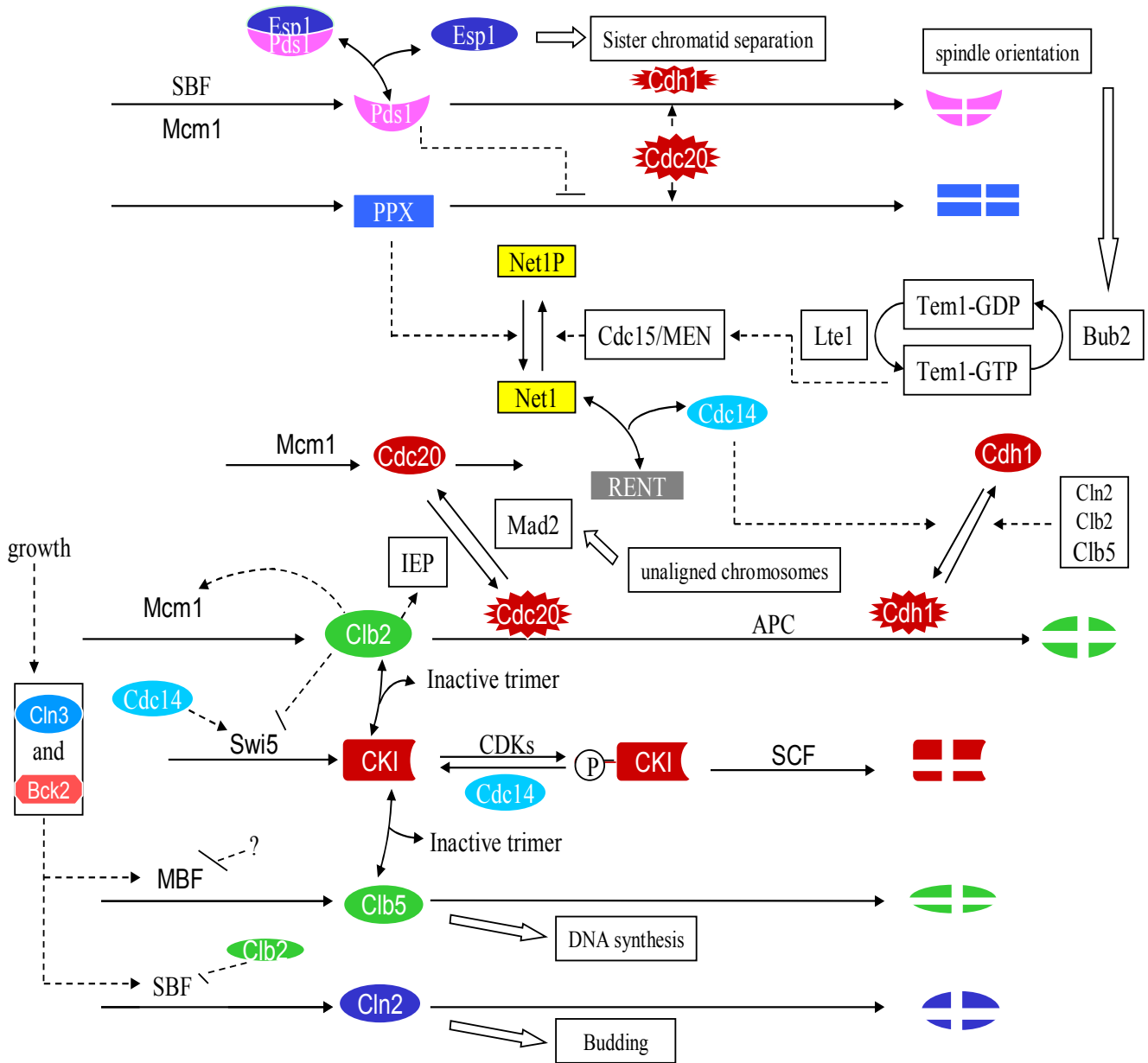
Budding Yeast Model

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., Gyórfy, 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:



Differential Equations:

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

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

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

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

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

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

$$\frac{\partial}{\partial t} \text{IEP}(t) = -\frac{kiiép \text{IEP}}{jiiép + \text{IEP}} + \frac{kaiep \text{CLB2 IE}}{jaiep + \text{IE}}$$

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

$$\frac{\partial}{\partial t} \text{CDH1}(t) = -\frac{Vidh \text{CDH1}}{Jidh + \text{CDH1}} + \frac{(kacdhp + kacdhpp \text{CDC14}) \text{CDH1i}}{Jacdh + \text{CDH1i}}$$

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

$$\text{NET1P} = \text{NCDC14} + \text{NET1} - \text{CDC14}$$

$$\text{CDC15i} = \text{CDC15T} - \text{CDC15}$$

$$\text{PE} = \text{ESP1T} - \text{ESP1}$$

$$\text{CDH1i} = \text{CDH1T} - \text{CDH1}$$

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

$$\text{IE} = \text{IET} - \text{IEP}$$

$$\text{Vdb2} = \text{kdb2p} (1 - \text{CDH1}) + \text{kdb2pp} \text{CDH1} + \text{kdb2p} \text{CDC20}$$

$$\text{Vasbf} = \text{kasbf} (\text{esbfn2} \text{CLN2} + \text{esbfn3} (\text{CLN3} + \text{BCK2}) + \text{esbfb5} \text{CLB5})$$

$$\text{SBF} = \text{GK}(\text{Vasbf}, \text{kisbfp} + \text{kisbfp} \text{CLB2}, \text{Jasbf}, \text{Jisbf})$$

$$\text{MCM1} = \text{GK}(\text{kamcm} \text{CLB2}, \text{kimcm}, \text{Jamcm}, \text{Jimcm})$$

$$\text{Vdb5} = \text{kdb5p} + \text{kdb5pp} \text{CDC20} \quad \text{Vsic1} = \text{kasb2} \text{CLB2} + \text{kasb5} \text{CLB5} + \text{Vkpc1}$$

$$\text{Vkpc1} = \text{kd1c1} + \frac{\text{Vd2c1}}{\text{Jd2c1} + \text{SIC1T}}$$

$$\text{Vd2c1} = \text{kd2c1} (\text{ec1n3} \text{CLN3} + \text{ec1n2} \text{CLN2} + \text{ec1k2} \text{BCK2} + \text{ec1b2} \text{CLB2} + \text{ec1b5} \text{CLB5})$$

$$\text{Vkpf6} = \text{kd1f6} + \frac{\text{kd2f6} (\text{ef6n3} \text{CLN3} + \text{ef6k2} \text{BCK2} + \text{ef6n2} \text{CLN2} + \text{ef6b2} \text{CLB2} + \text{ef6b5} \text{CLB5})}{\text{Jd2f6} + \text{CDC6T}}$$

$$\text{Vppf6} = \text{kppf6} \text{CDC14}$$

$$\text{Vidh} = \text{kicdhp} + \text{kicdhpp} (\text{eicdhn3} \text{CLN3} + \text{eicdhn2} \text{CLN2} + \text{eicdhn5} \text{CLB5} + \text{eicdhn2} \text{CLB2})$$

$$\text{Vkpnet} = (\text{kkpnetp} + \text{kkpnetpp} \text{CDC15}) \text{MASS}$$

$$\text{Vppnet} = \text{kppnetp} + \text{kppnetpp} \text{PPX}$$

$$\text{Vdppx} = \text{kdppxp} + \frac{\text{kdppxpp} (\text{eps20ppx} + \text{CDC20}) \text{Kmpds}}{\text{Kmpds} + \text{PDS1}}$$

$$\text{Vdps} = \text{kd1pds} + \text{kd2pds} \text{CDC20} + \text{kd3pds} \text{CDH1}$$

$$\text{BCK2} = \text{bck0} \text{MASS}$$

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

$$\text{CLB5T} = \text{C5} + \text{C5P} + \text{CLB5}$$

$$\text{CLB2T} = \text{C2P} + \text{C2} + \text{CLB2}$$

$$\text{SIC1T} = \text{SIC1} + \text{SIC1P} + \text{C2} + \text{C5} + \text{C2P} + \text{C5P}$$

$$\text{CDC6T} = \text{CDC6} + \text{CDC6P} + \text{F2} + \text{F5} + \text{F2P} + \text{F5P}$$

JigCell Model Builder Representation:

Model Spreadsheet

| Reaction | Name | Type | Equation | Modifiers and Constants |
|---------------|------|-------------|--|--|
| ->CLN2 | | Mass Action | $((k_{sn2}' + k_{sn2}'' * SBF) * MASS)$ | $K_f = (k_{sn2}' + k_{sn2}'' * SBF) * MASS$ |
| CLN2-> | | Mass Action | $k_{dn2} * CLN2$ | $K_f = k_{dn2}$ |
| ->CLB2 | | Mass Action | $((k_{sb2}' + k_{sb2}'' * MCM1) * MASS)$ | $K_f = (k_{sb2}' + k_{sb2}'' * MCM1) * MASS$ |
| CLB2-> | | Mass Action | $V_{db2} * CLB2$ | $K_f = V_{db2}$ |
| | 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 | $k_{db2}' * (1 - CDH1) + k_{db2}'' * CDH1 + k_{db2p} * CDC20$ | $k_{db2}' = k_{db2}'; k_{db2}'' = k_{db2}''; k_{db2p} = k_{db2p}$ |
| Vasbf | | Species | $k_{asbf}' * (esbfn2 * CLN2 + esbfn3 * (CLN3 + BCK2)) + esbfb5 * CLB5$ | $k_{asbf}' = k_{asbf}'; esbfn2 = esbfn2; esbfn3 = esbfn3; esbfb5 = esbfb5$ |
| 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 | $K_f = 0$ |
| ->CLB5 | | Mass Action | $((k_{sb5}' + k_{sb5}'' * SBF) * MASS)$ | $K_f = (k_{sb5}' + k_{sb5}'' * SBF) * MASS$ |
| CLB5-> | | Mass Action | $V_{db5} * CLB5$ | $K_f = V_{db5}$ |
| Vdb5 | | Species | $k_{db5}' + k_{db5}'' * CDC20$ | $k_{db5}' = k_{db5}'; k_{db5}'' = k_{db5}''$ |
| ->SIC1 | | Mass Action | $(k_{sc1}' + k_{sc1}'' * SWI5)$ | $K_f = k_{sc1}' + k_{sc1}'' * SWI5$ |
| SIC1->SIC1P | | Mass Action | $V_{kpc1} * SIC1$ | $K_f = V_{kpc1}$ |
| SIC1P->SIC1 | | Mass Action | $k_{ppc1} * CDC14 * SIC1P$ | $K_f = k_{ppc1} * CDC14$ |
| SIC1P-> | | Mass Action | $k_{d3c1} * SIC1P$ | $K_f = k_{d3c1}$ |
| Vsic1 | | Species | $k_{asb2} * CLB2 + k_{asb5} * CLB5 + V_{kpc1}$ | $k_{asb2} = k_{asb2}; k_{asb5} = k_{asb5}$ |
| Vkpc1 | | Species | $k_{d1c1} + V_{d2c1} / (J_{d2c1} + SIC1T)$ | $k_{d1c1} = k_{d1c1}; J_{d2c1} = J_{d2c1}$ |
| Vd2c1 | | Species | $k_{d2c1} * (ec1n3 * CLN3 + ec1n2 * CLN2 + ec1k2 * BCK2 + ec1b2 * CLB2 + ec1b5 * CLB5)$ | $k_{d2c1} = k_{d2c1}; ec1n3 = ec1n3; ec1n2 = ec1n2; ec1k2 = ec1k2; ec1b2 = ec1b2; ec1b5 = ec1b5$ |
| CLB2+SIC1->C2 | | Mass Action | $k_{asb2} * CLB2 * SIC1$ | $K_f = k_{asb2}$ |
| C2->CLB2+SIC1 | | Mass Action | $k_{dib2} * C2$ | $K_f = k_{dib2}$ |

| | | | | |
|---------------|--|-------------|--|--|
| 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 Action | 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 | (kiiiep/(jiiiep+IEP))*IEP | Kf=kiiiep/(jiiiep+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+eicdhn5*CLB5+eicdhn5*CLB2) | kicdh'=kicdh'; kicdh''=kicdh''; eicdhn3=eicdhn3; eicdhn2=eicdhn2; eicdhn5=eicdhn5; eicdhn5=eicdhn5; eicdhn2=eicdhn2 |
| 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*MC M1) | 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 | (kssp*(FRAC+(1-FRAC)*MORPHO)*CLB2/(Jspn+CLB2)) | Kf=kssp*(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 |
| jiiip | 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+(eicdhn5)*CLB5+(eicdhn2)*CLB2)

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 + Vkp6*CDC6 + Vdb5*F5P + Vdb2*F2P

dF2/dt= - kdif2*F2 - Vkp6*F2 - Vdb2*F2 + kasf2*CLB2*CDC6 + Vppf6*F2P

dF5/dt= - kdif5*F5 - Vkp6*F5 - Vdb5*F5 + kasf5*CLB5*CDC6 + Vppf6*F5P

dF5P/dt= - Vppf6*F5P - kd3f6*F5P - Vdb5*F5P + Vkp6*F5

dF2P/dt= - Vppf6*F2P - kd3f6*F2P - Vdb2*F2P + Vkp6*F2

dMAD2/dt=0

dlte1/dt=0

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

#Globals

```
global 1 {SPN-1 } {MAD2=Mad2l; ltel=lte1h; bub2=bub2l }
global -1 {CLB2-KEZ } {MASS=f*MASS; BUD=0; SPN=0; ltel=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, ltel=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, ltelh=1
param KEZ=0.3, ltel1=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, eicdhn5=7
param eicdhn2=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, kslpds=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 kssp=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
```