SBML Model Report

Model name: "Barrack2014 - Calcium/cell cycle coupling - Rs dependent ATP release"

May 6, 2016

1 General Overview

This is a document in SBML Level 2 Version 3 format. This model was created by the following two authors: Vijayalakshmi Chelliah[1] and Duncan Barrack[2] at January 30th 2014 at 3:57 p. m. and last time modified at February 28th 2014 at 4:35 p. m. Table 1 provides an overview of the quantities of all components of this model.

Table 1: Number of components in this model, which are described in the following sections.

Element	Quantity	Element	Quantity
compartment types	0	compartments	1
species types	0	species	16
events	0	constraints	0
reactions	0	function definitions	0
global parameters	48	unit definitions	0
rules	16	initial assignments	0

Model Notes

Barrack2014 - Calcium/cell cycle coupling - Rs dependent ATP release

This model is designed based on the hypothesis that cytoplasmic calcium accelerates entry into S phase of the cell cycle and/or acts to recruit otherwise quiescents cells onto the cell cy-

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cle. The model describes the ATP mediated calcium-cell cycle coupling via Rs (retinoblastoma tumour suppressor protein bound to the E2F transcription factor) in a single radial glial cell.

This model is described in the article:Modelling the coupling between intracellular calcium release and the cell cycle during cortical brain development.Barrack DS, Thul R, Owen MR.J Theor Biol. 2014 Jan 13;347C:17-32.

Abstract:

Most neocortical neurons formed during embryonic brain development arise from radial glial cells which communicate, in part, via ATP mediated calcium signals. Although the intercellular signalling mechanisms that regulate radial glia proliferation are not well understood, it has recently been demonstrated that ATP dependent intracellular calcium release leads to an increase of nearly 100% in overall cellular proliferation. It has been hypothesised that cytoplasmic calcium accelerates entry into S phase of the cell cycle and/or acts to recruit otherwise quiescent cells onto the cell cycle. In this paper we study this cell cycle acceleration and recruitment by forming a differential equation model for ATP mediated calcium-cell cycle coupling via Cyclin D in a single radial glial cell. Bifurcation analysis and numerical simulations suggest that the cell cycle period depends only weakly on cytoplasmic calcium. Therefore, the accelerative impact of calcium on the cell cycle can only account for a small fraction of the large increase in proliferation observed experimentally. Crucially however, our bifurcation analysis reveals that stable fixed point and stable limit cycle solutions can coexist, and that calcium dependent Cyclin D dynamics extend the oscillatory region to lower Cyclin D synthesis rates, thus rendering cells more susceptible to cycling. This supports the hypothesis that cycling glial cells recruit quiescent cells (in G0 phase) onto the cell cycle, via a calcium signalling mechanism, and that this may be the primary means by which calcium augments proliferation rates at the population scale. Numerical simulations of two coupled cells demonstrate that such a scenario is indeed feasible.

This model is hosted on BioModels Database and identifiedby: BIOMD0000000509 .

To cite BioModels Database, please use: BioModels Database: An enhanced, curated and annotated resourcefor published quantitative kinetic models .

2 Unit Definitions

This is an overview of five unit definitions which are all predefined by SBML and not mentioned in the model.

2.1 Unit `substance`

Notes Mole is the predefined SBML unit for `substance`.

Definition mol

2.2 Unit `volume`

Notes Litre is the predefined SBML unit for `volume`.

Definition l

2.3 Unit `area`

Notes Square metre is the predefined SBML unit for `area` since SBML Level 2 Version 1.

Definition m^2

2.4 Unit `length`

Notes Metre is the predefined SBML unit for `length` since SBML Level 2 Version 1.

Definition m

2.5 Unit `time`

Notes Second is the predefined SBML unit for `time`.

Definition s

3 Compartment

This model contains one compartment.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
`cell`			3	1	litre	☑	

3.1 Compartment `cell`

This is a three dimensional compartment with a constant size of one litre.

4 Species

This model contains 16 species. Section 7 provides further details and the derived rates of change of each species.

Table 3: Properties of each species.

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
d		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
ad		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
e		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
r		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
rs		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
x		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
ip3		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
kg		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
gstar		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
ro		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
ip3con		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
rscon		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
atp		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
y		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
delta		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐
ca		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☐	☐

5 Parameters

This model contains 48 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
addash			0.410		☑
vatp_s			50.000		☑
smoothness			0.010		☑
vdeg			2.000		☑
alpha			0.083		☑
gamma			1.000		☑
ae			0.160		☑
ax			0.080		☑
k			0.050		☑
qd			0.600		☑
qe			0.600		☑
qx			0.800		☑
f			0.200		☑
g			0.528		☑
ps			0.600		☑
pd			0.480		☑
pe			0.096		☑
px			0.480		☑
ddd			0.400		☑
dee			0.200		☑
dxx			1.040		☑
af			0.900		☑
rt			2.500		☑
yo			1.500		☑
gf			6.300		☑
kdeg			0.063		☑
kkdeg			50.000		☑
ka			0.017		☑
kd			0.150		☑
rhstar			0.600		☑
dip			280.000		☑
krel			10.000		☑
ip3min			0.012		☑
datpp			300.000		☑
kr			25.000		☑
scale			3600.000		☑
rscrit			1.000		☑

Id	Name	SBO	Value	Unit	Constant
ymax			500.000		☑
cabasil			0.021		☑
p1			0.016		☑
p2			0.515		☑
p3			1.313		☑
p4			0.332		☑
p5			0.788		☑
m			24.195		☑
n			9.792		☑
dist			50.000		☑
ip30			0.013		☑

6 Rules

This is an overview of 16 rules.

6.1 Rule d

Rule d is a rate rule for species d:

$$\frac{d}{dt}d = [ad] \cdot \frac{k \cdot gf}{1 + k \cdot gf} - ddd \cdot [e] \cdot [d] \tag{1}$$

6.2 Rule ad

Rule ad is an assignment rule for species ad:

$$ad = addash + gamma \cdot ([ca] - p1) \tag{2}$$

6.3 Rule e

Rule e is a rate rule for species e:

$$\frac{d}{dt}e = ae \cdot (1 + af \cdot (yo - [rs])) - dee \cdot [x] \cdot [e] \tag{3}$$

6.4 Rule r

Rule r is a rate rule for species r:

$$\frac{d}{dt}r = \frac{px \cdot (rt - [rs] - [r]) \cdot [x]}{qx + (rt - [rs] - [r]) + [x]} - ps \cdot (yo - [rs]) \cdot [r] \tag{4}$$

6.5 Rule `rs`

Rule `rs` is a rate rule for species `rs`:

$$\frac{d}{dt}\text{rs} = \text{ps} \cdot (\text{yo} - [\text{rs}]) \cdot [\text{r}] - \frac{\text{pd} \cdot [\text{rs}] \cdot [\text{d}]}{\text{qd} + [\text{rs}] + [\text{d}]} - \frac{\text{pe} \cdot [\text{rs}] \cdot [\text{e}]}{\text{qe} + [\text{rs}] + [\text{e}]} \tag{5}$$

6.6 Rule `x`

Rule `x` is a rate rule for species `x`:

$$\frac{d}{dt}\text{x} = \text{ax} \cdot [\text{e}] + \text{f} \cdot (\text{yo} - [\text{rs}]) + \text{g} \cdot [\text{x}]^2 \cdot [\text{e}] - \text{dxx} \cdot [\text{x}] \tag{6}$$

6.7 Rule `ip3`

Rule `ip3` is a rate rule for species `ip3`:

$$\frac{d}{dt}\text{ip3} = \text{scale} \cdot (\text{rhstar} \cdot [\text{gstar}] - \text{kdeg} \cdot [\text{ip3}]) \tag{7}$$

6.8 Rule `kg`

Rule `kg` is an assignment rule for species `kg`:

$$\text{kg} = \frac{\text{kd}}{\text{ka}} \tag{8}$$

6.9 Rule `gstar`

Rule `gstar` is an assignment rule for species `gstar`:

$$\text{gstar} = \frac{[\text{ro}] + [\text{delta}]}{[\text{kg}] + [\text{delta}] + [\text{ro}]} \tag{9}$$

Derived unit dimensionless

6.10 Rule `ro`

Rule `ro` is an assignment rule for species `ro`:

$$\text{ro} = \frac{[\text{atp}]}{\text{kr} + [\text{atp}]} \tag{10}$$

6.11 Rule `ip3con`

Rule `ip3con` is an assignment rule for species `ip3con`:

$$\text{ip3con} = \frac{\tanh\left(\frac{[\text{ip3}] - \text{ip3min}}{0.01}\right) + 1}{2} \tag{11}$$

6.12 Rule `rscon`

Rule `rscon` is an assignment rule for species `rscon`:

$$\text{rscon} = \frac{\tanh\left(\frac{\text{rscrit}-[\text{rs}]}{0.01}\right)+1}{2} \tag{12}$$

6.13 Rule `atp`

Rule `atp` is a rate rule for species `atp`:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{atp} = \text{scale}\cdot\left(\text{vatp\_s}\cdot([\text{y}]-[\text{atp}])\cdot[\text{rscon}]\cdot[\text{ip3con}]\cdot\frac{[\text{ip3}]-\text{ip3min}}{\text{krel}+[\text{ip3}]}-\frac{\text{vdeg}\cdot[\text{atp}]}{\text{kkdeg}+[\text{atp}]}\right) \tag{13}$$

6.14 Rule `y`

Rule `y` is a rate rule for species `y`:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{y} = \text{scale}\cdot\left(\text{alpha}\cdot(\text{ymax}-[\text{y}])-[\text{rscon}]\cdot[\text{ip3con}]\cdot\text{vatp\_s}\cdot([\text{y}]-[\text{atp}])\cdot\frac{[\text{ip3}]-\text{ip3min}}{\text{krel}+[\text{ip3}]}\right) \tag{14}$$

6.15 Rule `delta`

Rule `delta` is an assignment rule for species `delta`:

$$\text{delta} = \frac{[\text{kg}]\cdot\text{kdeg}\cdot\text{ip30}}{\text{rhstar}-\text{kdeg}\cdot\text{ip30}} \tag{15}$$

6.16 Rule `ca`

Rule `ca` is an assignment rule for species `ca`:

$$\text{ca} = \text{p1}+\frac{\text{p2}\cdot[\text{ip3}]^{\text{m}}}{\text{p3}^{\text{m}}+[\text{ip3}]^{\text{m}}}+\frac{\text{p4}\cdot[\text{ip3}]^{\text{n}}}{\text{p5}^{\text{n}}+[\text{ip3}]^{\text{n}}} \tag{16}$$

7 Derived Rate Equations

When interpreted as an ordinary differential equation framework, this model implies the following set of equations for the rates of change of each species.

7.1 Species `d`

Initial concentration $0\ \text{mol}\cdot\text{l}^{-1}$

Involved in rule `d`

One rule which determines this species' quantity.

7.2 Species ad

Initial concentration $0 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule ad

One rule which determines this species' quantity.

7.3 Species e

Initial concentration $1 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule e

One rule which determines this species' quantity.

7.4 Species r

Initial concentration $0 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule r

One rule which determines this species' quantity.

7.5 Species rs

Initial concentration $1.1 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule rs

One rule which determines this species' quantity.

7.6 Species x

Initial concentration $0 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule x

One rule which determines this species' quantity.

7.7 Species ip3

Initial concentration $0 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule ip3

One rule which determines this species' quantity.

7.8 Species kg

Initial concentration $0 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule kg

One rule which determines this species' quantity.

7.9 Species gstar

Initial concentration $0 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule gstar

One rule which determines this species' quantity.

7.10 Species ro

Initial concentration $0 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule ro

One rule which determines this species' quantity.

7.11 Species ip3con

Initial concentration $0 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule ip3con

One rule which determines this species' quantity.

7.12 Species rscon

Initial concentration $0 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule rscon

One rule which determines this species' quantity.

7.13 Species atp

Initial concentration $0 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule atp

One rule which determines this species' quantity.

7.14 Species y

Initial concentration $0 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule y

One rule which determines this species' quantity.

7.15 Species delta

Initial concentration $0 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule delta

One rule which determines this species' quantity.

7.16 Species ca

Initial concentration $0 \text{ mol} \cdot \text{l}^{-1}$

Involved in rule ca

One rule which determines this species' quantity.

SBML2LaTeX was developed by Andreas Dräger[a], Hannes Planatscher[a], Dieudonné M Wouamba[a], Adrian Schröder[a], Michael Hucka[b], Lukas Endler[c], Martin Golebiewski[d] and Andreas Zell[a]. Please see http://www.ra.cs.uni-tuebingen.de/software/SBML2LaTeX for more information.

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