SBML Model Report

Model name: "Del_Conte_Zerial2008_Rab5-_Rab7_cut_out_switch"

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: Perla Del Conte-Zerial[1] and Lukas Endler[2] at July 28th 2008 at 12:59 a. m. and last time modified at April 28th 2014 at 3:37 p. m. Table 1 gives 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	4
events	0	constraints	0
reactions	10	function definitions	5
global parameters	0	unit definitions	5
rules	0	initial assignments	0

Model Notes

Membrane identity and GTPase cascades regulated by toggle and cut-out switches
Perla Del Conte-Zerial, Lutz Brusch, Jochen C Rink, Claudio Collinet, Yannis Kalaidzidis,

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Marino Zerial, and Andreas Deutsch: Molecular Systems Biology4:206 15 July 2008, doi:10.1038/msb.2008.45

This is the cut-out switch model for the Rab5 - Rab7 transition, also referred to as model 2 in the original publication.
This model is not completely described in all details in the publication. Thanks go to Barbara Szomolay and Lutz Brusch for finding and clarifying this. According to Dr. Brusch this model represents the mechanism identified by the qualitative analysis in the article in the scenario deemed most useful by the authors. For the time-course simulations it was necessary to add a time dependency to one of the parameters, which is only verbally described in the article.
As argued in the publication the switch between early and late endosomes can be triggered by a parameter change. While with fixed parameter values each switch just converges to one steady state from its initial conditions and stays there, endosomes should switch between two different states. These changes would in reality of course depend on many different factors, such as cargo composition and amount in the specific endosome, its location and some additional cellular control mechanisms and encompass many different parameters. To keep the model simple the authors chose to add a time dependency to only one reaction - **ke** in the activation of RAB5 is multiplied with a term monotonously increasing over time from 0 to 1. They also hard coded a time dependence in this term, 100 minutes, to make the switch occur after several hundred minutes. As long as this modulating term remains monotonic all resulting time courses should look similar, with the switching behavior depending on the initial conditions and whether the term is increasing or decreasing. Monotonic increase is a reasonable assumption for the described mechanism of cargo accumulation.
Not explicitly described in the article:activation of Rab5 (time) : r*ke***time/(100+time)** /$(1+e^{(kg-R)*kf})$ instead of r*ke/$(1+e^{(kg-R)*kf})$

2 Unit Definitions

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

2.1 Unit `time`

Name sec

Definition s

2.2 Unit M

Name M

Definition $\mathrm{mol} \cdot \mathrm{l}^{-1}$

2.3 Unit ps

Name persec

Definition s^{-1}

2.4 Unit Mps

Name Mpers

Definition $\mathrm{mol} \cdot \mathrm{s}^{-1} \cdot \mathrm{l}^{-1}$

2.5 Unit lpmole

Name lpermole

Definition $\mathrm{l} \cdot \mathrm{mol}^{-1}$

2.6 Unit substance

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

Definition mol

2.7 Unit volume

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

Definition l

2.8 Unit area

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

Definition m^2

2.9 Unit length

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

Definition m

3 Compartment

This model contains one compartment.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
`endosome`	endosomal membrane		3	1	litre	☑	

3.1 Compartment `endosome`

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

Name endosomal membrane

4 Species

This model contains four 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
r5	Rab5-GDP	endosome	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
R5	Rab5-GTP	endosome	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
r7	Rab7-GDP	endosome	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
R7	Rab7-GTP	endosome	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟

5 Function definitions

This is an overview of five function definitions.

5.1 Function definition `hydrolysis`

Name hydrolysis

Arguments kh, R

Mathematical Expression

$$\mathrm{kh} \cdot \mathrm{R} \tag{1}$$

5.2 Function definition `sig_act`

Name Sigmoid Activation

Arguments ke, r, kg, R, kf

Mathematical Expression

$$\frac{\mathrm{ke} \cdot \mathrm{r}}{1 + \exp\left((\mathrm{kg} - \mathrm{R}) \cdot \mathrm{kf}\right)} \tag{2}$$

5.3 Function definition `hill_act`

Name Hills activation

Arguments r, ke, R, h, kg

Mathematical Expression

$$\frac{\mathrm{r} \cdot \mathrm{ke} \cdot \mathrm{R}^{\mathrm{h}}}{\mathrm{kg} + \mathrm{R}^{\mathrm{h}}} \tag{3}$$

5.4 Function definition `extraction`

Name extraction

Arguments kminus1, r

Mathematical Expression

$$\mathrm{kminus1} \cdot \mathrm{r} \tag{4}$$

5.5 Function definition sig_act_t

Name Sigmoid Activation 3 (t)

Arguments r, ke, t, kg, R, kf

Mathematical Expression

$$\frac{\mathrm{r} \cdot \frac{\mathrm{ke} \cdot \mathrm{t}}{100+\mathrm{t}}}{1+\exp\left((\mathrm{kg}-\mathrm{R}) \cdot \mathrm{kf}\right)} \tag{5}$$

6 Reactions

This model contains ten reactions. All reactions are listed in the following table and are subsequently described in detail. If a reaction is affected by a modifier, the identifier of this species is written above the reaction arrow.

Table 4: Overview of all reactions

№	Id	Name	Reaction Equation	SBO
1	`reaction_0`	recruitment of Rab5	$\emptyset \longrightarrow r5$	
2	`reaction_1`	activation of Rab5 (time)	$r5 \xrightarrow{R5} R5$	
3	`reaction_2`	extraction of Rab5	$r5 \longrightarrow \emptyset$	
4	`reaction_3`	recruitment of Rab7	$\emptyset \longrightarrow r7$	
5	`reaction_4`	activation of Rab7 by GEF7	$r7 \xrightarrow{R7} R7$	
6	`reaction_5`	activation of Rab7 by GEF5	$r7 \xrightarrow{R5} R7$	
7	`reaction_6`	hydrolysis of Rab5 by Rab7	$R5 \xrightarrow{R7} r5$	
8	`reaction_7`	extraction of rab7	$r7 \longrightarrow \emptyset$	
9	`reaction_8`	hydrolysis of Rab5 (intr.)	$R5 \longrightarrow r5$	
10	`reaction_9`	hydrolysis of Rab7 (intr.)	$R7 \longrightarrow r7$	

6.1 Reaction reaction_0

This is an irreversible reaction of no reactant forming one product.

Name recruitment of Rab5

Reaction equation

$$\emptyset \longrightarrow \mathrm{r5} \tag{6}$$

Product

Table 5: Properties of each product.

Id	Name	SBO
r5	Rab5-GDP	

Kinetic Law

Derived unit $\mathrm{mol} \cdot \mathrm{s}^{-1}$

$$v_1 = \mathrm{vol}\,(\mathrm{endosome}) \cdot \mathrm{K1} \tag{7}$$

Table 6: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
K1			1.0	$\mathrm{mol} \cdot \mathrm{s}^{-1} \cdot \mathrm{l}^{-1}$	☑

6.2 Reaction reaction_1

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name activation of Rab5 (time)

Reaction equation

$$\mathrm{r5} \xrightarrow{\mathrm{R5}} \mathrm{R5} \tag{8}$$

Reactant

Table 7: Properties of each reactant.

Id	Name	SBO
r5	Rab5-GDP	

Modifier

Table 8: Properties of each modifier.

Id	Name	SBO
R5	Rab5-GTP	

Product

Table 9: Properties of each product.

Id	Name	SBO
R5	Rab5-GTP	

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \mathrm{vol}\,(\mathrm{endosome}) \cdot \mathrm{sig\_act\_t}\,([\mathrm{r5}], \mathrm{ke}, \mathrm{time}, \mathrm{kg}, [\mathrm{R5}], \mathrm{kf}) \tag{9}$$

$$\mathrm{sig\_act\_t}\,(\mathrm{r}, \mathrm{ke}, \mathrm{t}, \mathrm{kg}, \mathrm{R}, \mathrm{kf}) = \frac{\mathrm{r} \cdot \frac{\mathrm{ke} \cdot \mathrm{t}}{100 + \mathrm{t}}}{1 + \exp\left((\mathrm{kg} - \mathrm{R}) \cdot \mathrm{kf}\right)} \tag{10}$$

$$\mathrm{sig\_act\_t}\,(\mathrm{r}, \mathrm{ke}, \mathrm{t}, \mathrm{kg}, \mathrm{R}, \mathrm{kf}) = \frac{\mathrm{r} \cdot \frac{\mathrm{ke} \cdot \mathrm{t}}{100 + \mathrm{t}}}{1 + \exp\left((\mathrm{kg} - \mathrm{R}) \cdot \mathrm{kf}\right)} \tag{11}$$

Table 10: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
ke			0.3	s^{-1}	☑
kg			0.1	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑
kf			2.5	$\mathrm{l} \cdot \mathrm{mol}^{-1}$	☑

6.3 Reaction `reaction_2`

This is an irreversible reaction of one reactant forming no product.

Name extraction of Rab5

Reaction equation

$$\mathrm{r5} \longrightarrow \emptyset \tag{12}$$

Reactant

Table 11: Properties of each reactant.

Id	Name	SBO
`r5`	Rab5-GDP	

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{mol}$

$$v_3 = \mathrm{vol}\left(\mathrm{endosome}\right) \cdot \mathrm{extraction}\left(\mathrm{kminus1}, [\mathrm{r5}]\right) \tag{13}$$

$$\mathrm{extraction}\left(\mathrm{kminus1}, \mathrm{r}\right) = \mathrm{kminus1} \cdot \mathrm{r} \tag{14}$$

$$\mathrm{extraction}\left(\mathrm{kminus1}, \mathrm{r}\right) = \mathrm{kminus1} \cdot \mathrm{r} \tag{15}$$

Table 12: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
`kminus1`			1.0	s^{-1}	☑

6.4 Reaction `reaction_3`

This is an irreversible reaction of no reactant forming one product.

Name recruitment of Rab7

Reaction equation

$$\emptyset \longrightarrow \mathrm{r7} \tag{16}$$

Product

Table 13: Properties of each product.

Id	Name	SBO
r7	Rab7-GDP	

Kinetic Law

Derived unit $\mathrm{mol} \cdot \mathrm{s}^{-1}$

$$v_4 = \mathrm{vol}\,(\mathrm{endosome}) \cdot \mathrm{K1} \tag{17}$$

Table 14: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
K1			0.483	$\mathrm{mol} \cdot \mathrm{s}^{-1} \cdot \mathrm{l}^{-1}$	☑

6.5 Reaction reaction_4

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name activation of Rab7 by GEF7

Reaction equation

$$\mathrm{r7} \xrightarrow{\mathrm{R7}} \mathrm{R7} \tag{18}$$

Reactant

Table 15: Properties of each reactant.

Id	Name	SBO
r7	Rab7-GDP	

Modifier

Table 16: Properties of each modifier.

Id	Name	SBO
R7	Rab7-GTP	

Id	Name	SBO

Product

Table 17: Properties of each product.

Id	Name	SBO
R7	Rab7-GTP	

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \text{vol}\,(\text{endosome}) \cdot \text{hill\_act}\,([\text{r7}], \text{ke}, [\text{R7}], \text{h}, \text{kg}) \tag{19}$$

$$\text{hill\_act}\,(\text{r}, \text{ke}, \text{R}, \text{h}, \text{kg}) = \frac{\text{r} \cdot \text{ke} \cdot \text{R}^{\text{h}}}{\text{kg} + \text{R}^{\text{h}}} \tag{20}$$

$$\text{hill\_act}\,(\text{r}, \text{ke}, \text{R}, \text{h}, \text{kg}) = \frac{\text{r} \cdot \text{ke} \cdot \text{R}^{\text{h}}}{\text{kg} + \text{R}^{\text{h}}} \tag{21}$$

Table 18: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
ke			0.21	s^{-1}	☑
h			3.00	dimensionless	☑
kg			0.10		☑

6.6 Reaction reaction_5

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name activation of Rab7 by GEF5

Reaction equation

$$\text{r7} \xrightarrow{\text{R5}} \text{R7} \tag{22}$$

Reactant

Table 19: Properties of each reactant.

Id	Name	SBO
r7	Rab7-GDP	

Modifier

Table 20: Properties of each modifier.

Id	Name	SBO
R5	Rab5-GTP	

Product

Table 21: Properties of each product.

Id	Name	SBO
R7	Rab7-GTP	

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \mathrm{vol}\,(\mathrm{endosome}) \cdot \mathrm{sig\_act}\,(\mathrm{ke}, [\mathrm{r7}], \mathrm{kg}, [\mathrm{R5}], \mathrm{kf}) \tag{23}$$

$$\mathrm{sig\_act}\,(\mathrm{ke}, \mathrm{r}, \mathrm{kg}, \mathrm{R}, \mathrm{kf}) = \frac{\mathrm{ke} \cdot \mathrm{r}}{1 + \exp\left((\mathrm{kg} - \mathrm{R}) \cdot \mathrm{kf}\right)} \tag{24}$$

$$\mathrm{sig\_act}\,(\mathrm{ke}, \mathrm{r}, \mathrm{kg}, \mathrm{R}, \mathrm{kf}) = \frac{\mathrm{ke} \cdot \mathrm{r}}{1 + \exp\left((\mathrm{kg} - \mathrm{R}) \cdot \mathrm{kf}\right)} \tag{25}$$

Table 22: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
ke			0.021	s^{-1}	☑
kg			1.000	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	☑
kf			3.000	$\mathrm{l} \cdot \mathrm{mol}^{-1}$	☑

6.7 Reaction reaction_6

This is an irreversible reaction of one reactant forming one product influenced by one modifier.

Name hydrolysis of Rab5 by Rab7

Reaction equation

$$\mathrm{R5} \xrightarrow{\mathrm{R7}} \mathrm{r5} \tag{26}$$

Reactant

Table 23: Properties of each reactant.

Id	Name	SBO
R5	Rab5-GTP	

Modifier

Table 24: Properties of each modifier.

Id	Name	SBO
R7	Rab7-GTP	

Product

Table 25: Properties of each product.

Id	Name	SBO
r5	Rab5-GDP	

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \mathrm{vol}\left(\mathrm{endosome}\right) \cdot \mathrm{sig\_act}\left(\mathrm{ke}, [\mathrm{R5}], \mathrm{kg}, [\mathrm{R7}], \mathrm{kf}\right) \tag{27}$$

$$\mathrm{sig\_act}\left(\mathrm{ke}, \mathrm{r}, \mathrm{kg}, \mathrm{R}, \mathrm{kf}\right) = \frac{\mathrm{ke} \cdot \mathrm{r}}{1 + \exp\left(\left(\mathrm{kg} - \mathrm{R}\right) \cdot \mathrm{kf}\right)} \tag{28}$$

$$\mathrm{sig\_act}\left(\mathrm{ke}, \mathrm{r}, \mathrm{kg}, \mathrm{R}, \mathrm{kf}\right) = \frac{\mathrm{ke} \cdot \mathrm{r}}{1 + \exp\left(\left(\mathrm{kg} - \mathrm{R}\right) \cdot \mathrm{kf}\right)} \tag{29}$$

Table 26: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
ke			0.31	s^{-1}	☑
kg			0.30	$mol \cdot l^{-1}$	☑
kf			3.00	$l \cdot mol^{-1}$	☑

6.8 Reaction reaction_7

This is an irreversible reaction of one reactant forming no product.

Name extraction of rab7

Reaction equation

$$r7 \longrightarrow \emptyset \tag{30}$$

Reactant

Table 27: Properties of each reactant.

Id	Name	SBO
r7	Rab7-GDP	

Kinetic Law

Derived unit $s^{-1} \cdot mol$

$$v_8 = \text{vol}(\text{endosome}) \cdot \text{extraction}(\text{kminus1}, [\text{r7}]) \tag{31}$$

$$\text{extraction}(\text{kminus1}, \text{r}) = \text{kminus1} \cdot \text{r} \tag{32}$$

$$\text{extraction}(\text{kminus1}, \text{r}) = \text{kminus1} \cdot \text{r} \tag{33}$$

Table 28: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
kminus1			0.483	s^{-1}	☑

6.9 Reaction reaction_8

This is an irreversible reaction of one reactant forming one product.

Name hydrolysis of Rab5 (intr.)

Reaction equation

$$\mathrm{R5} \longrightarrow \mathrm{r5} \tag{34}$$

Reactant

Table 29: Properties of each reactant.

Id	Name	SBO
R5	Rab5-GTP	

Product

Table 30: Properties of each product.

Id	Name	SBO
r5	Rab5-GDP	

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{mol}$

$$v_9 = \mathrm{vol}\left(\mathrm{endosome}\right) \cdot \mathrm{hydrolysis}\left(\mathrm{kh}, [\mathrm{R5}]\right) \tag{35}$$

$$\mathrm{hydrolysis}\left(\mathrm{kh}, \mathrm{R}\right) = \mathrm{kh} \cdot \mathrm{R} \tag{36}$$

$$\mathrm{hydrolysis}\left(\mathrm{kh}, \mathrm{R}\right) = \mathrm{kh} \cdot \mathrm{R} \tag{37}$$

Table 31: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
kh			0.06	s^{-1}	☑

6.10 Reaction reaction_9

This is an irreversible reaction of one reactant forming one product.

Name hydrolysis of Rab7 (intr.)

Reaction equation

$$\mathrm{R7} \longrightarrow \mathrm{r7} \tag{38}$$

Reactant

Table 32: Properties of each reactant.

Id	Name	SBO
R7	Rab7-GTP	

Product

Table 33: Properties of each product.

Id	Name	SBO
r7	Rab7-GDP	

Kinetic Law

Derived unit $\mathrm{s}^{-1} \cdot \mathrm{mol}$

$$v_{10} = \mathrm{vol}\left(\mathrm{endosome}\right) \cdot \mathrm{hydrolysis}\left(\mathrm{kh}, [\mathrm{R7}]\right) \tag{39}$$

$$\mathrm{hydrolysis}\left(\mathrm{kh}, \mathrm{R}\right) = \mathrm{kh} \cdot \mathrm{R} \tag{40}$$

$$\mathrm{hydrolysis}\left(\mathrm{kh}, \mathrm{R}\right) = \mathrm{kh} \cdot \mathrm{R} \tag{41}$$

Table 34: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
kh			0.15	s^{-1}	☑

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 r5

Name Rab5-GDP

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

This species takes part in five reactions (as a reactant in reaction_1, reaction_2 and as a product in reaction_0, reaction_6, reaction_8).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{r5} = v_1 + v_7 + v_9 - v_2 - v_3 \tag{42}$$

7.2 Species R5

Name Rab5-GTP

Initial concentration $0.0010\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in five reactions (as a reactant in reaction_6, reaction_8 and as a product in reaction_1 and as a modifier in reaction_1, reaction_5).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{R5} = v_2 - v_7 - v_9 \tag{43}$$

7.3 Species r7

Name Rab7-GDP

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

This species takes part in five reactions (as a reactant in reaction_4, reaction_5, reaction_7 and as a product in reaction_3, reaction_9).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{r7} = v_4 + v_{10} - v_5 - v_6 - v_8 \tag{44}$$

7.4 Species R7

Name Rab7-GTP

Initial concentration $0.0010\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in five reactions (as a reactant in reaction_9 and as a product in reaction_4, reaction_5 and as a modifier in reaction_4, reaction_6).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{R7} = v_5 + v_6 - v_{10} \tag{45}$$

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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