SBML Model Report

Model name: "Fujita2010_Akt_Signalling_EGFRinhib"

May 5, 2016

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following two authors: Lukas Endler[1] and Kazuhiro Fujita[2] at August 24th 2010 at 1:34 p. m. and last time modified at February 21st 2014 at 4:40 p. m. Table 1 shows 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	14
events	0	constraints	0
reactions	15	function definitions	0
global parameters	16	unit definitions	9
rules	4	initial assignments	2

Model Notes

Akt pathway model with EGFR inhibitor
made by Kazuhiro A. Fujita.
This is the Akt pathway model with an EGFR inhibitor described in:
Decoupling of receptor and downstream signals in the Akt pathway by its low-pass filter

[1]EMBL-EBI, lukas@ebi.ac.uk
[2]University of Tokyo, kazuhiro.fujita@gmail.com

characteristics.
Fujita KA, Toyoshima Y, Uda S, Ozaki Y, Kubota H, and Kuroda S. Sci Signal. 2010 Jul 27;3(132):ra56. PMID: 20664065 ; DOI: 10.1126/scisignal.2000810
Abstract:
In cellular signal transduction, the information in an external stimulus is encoded in temporal patterns in the activities of signaling molecules; for example, pulses of a stimulus may produce an increasing response or may produce pulsatile responses in the signaling molecules. Here, we show how the Akt pathway, which is involved in cell growth, specifically transmits temporal information contained in upstream signals to downstream effectors. We modeled the epidermal growth factor (EGF)dependent Akt pathway in PC12 cells on the basis of experimental results. We obtained counterintuitive results indicating that the sizes of the peak amplitudes of receptor and downstream effector phosphorylation were decoupled; weak, sustained EGF receptor (EGFR) phosphorylation, rather than strong, transient phosphorylation, strongly induced phosphorylation of the ribosomal protein S6, a molecule downstream of Akt. Using frequency response analysis, we found that a three-component Akt pathway exhibited the property of a low-pass filter and that this property could explain decoupling of the peak amplitudes of receptor phosphorylation and that of downstream effectors. Furthermore, we found that lapatinib, an EGFR inhibitor used as an anticancer drug, converted strong, transient Akt phosphorylation into weak, sustained Akt phosphorylation, and, because of the low-pass filter characteristics of the Akt pathway, this led to stronger S6 phosphorylation than occurred in the absence of the inhibitor. Thus, an EGFR inhibitor can potentially act as a downstream activator of some effectors.

The different versions of input, step, pulse and ramp, can be simulated using the parameters EGF_conc_pulse , EGF_conc_step and EGF_conc_ramp . Depending on which one is set unequal to 0, either a continous pulse with value EGF_conc_pulse , a 60 second step with EGF_conc_step or a signal increasing from 0 to EGF_conc_pulse over a time periode of 3600 seconds are used as input. In case more than one parameter are set to values greater than 0 these input profiles are added to each other. The pulse time and the time over which the ramp input increases can be set by pulse_time and ramp_time .

2 Unit Definitions

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

2.1 Unit substance

Name arbitrary_amount

Definition dimensionless

2.2 Unit conc

Name arbitrary_conc

Definition $\text{dimensionless} \cdot \text{ml}^{-1}$

2.3 Unit time

Name seconds

Definition s

2.4 Unit volume

Name ml

Definition ml

2.5 Unit per_sec

Name per second

Definition s^{-1}

2.6 Unit ng

Name ng

Definition ng

2.7 Unit ng_per_ml

Name ng_per_ml

Definition $\text{ng} \cdot \text{ml}^{-1}$

2.8 Unit ml_per_ng_per_sec

Name ml_per_ng_per_sec

Definition $\text{ml} \cdot \text{ng}^{-1} \cdot \text{s}^{-1}$

2.9 Unit per_conc_per_sec

Name per conc per second

Definition $\mathrm{ml} \cdot \mathrm{dimensionless} \cdot \mathrm{s}^{-1}$

2.10 Unit area

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

Definition m^2

2.11 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
Cell	Cell	0000290	3	1	litre	☑	

3.1 Compartment Cell

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

Name Cell

SBO:0000290 physical compartment

4 Species

This model contains 14 species. The boundary condition of three of these species is set to `true` so that these species' amount cannot be changed by any reaction. Section 9 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
EGF	EGF	Cell	$\mathrm{ng \cdot ml^{-1}}$	⊟	☑
EGFR	EGFR	Cell	dimensionless $\cdot$ $\mathrm{ml^{-1}}$	⊟	⊟
pEGFR	pEGFR	Cell	dimensionless $\cdot$ $\mathrm{ml^{-1}}$	⊟	⊟
pEGFR_Akt	pEGFR_Akt	Cell	dimensionless $\cdot$ $\mathrm{ml^{-1}}$	⊟	⊟
Akt	Akt	Cell	dimensionless $\cdot$ $\mathrm{ml^{-1}}$	⊟	⊟
pAkt	pAkt	Cell	dimensionless $\cdot$ $\mathrm{ml^{-1}}$	⊟	⊟
S6	S6	Cell	dimensionless $\cdot$ $\mathrm{ml^{-1}}$	⊟	⊟
pAkt_S6	pAkt_S6	Cell	dimensionless $\cdot$ $\mathrm{ml^{-1}}$	⊟	⊟
pS6	pS6	Cell	dimensionless $\cdot$ $\mathrm{ml^{-1}}$	⊟	⊟
pro_EGFR	pro_EGFR	Cell	dimensionless $\cdot$ $\mathrm{ml^{-1}}$	☑	☑
EGF_EGFR	EGF_EGFR	Cell	dimensionless $\cdot$ $\mathrm{ml^{-1}}$	⊟	⊟

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
EGFR_i	EGFR_i	Cell	dimensionless $\cdot$ ml^{-1}	$\boxminus$	$\boxminus$
EGF_EGFR_i	EGF_EGFR_i	Cell	dimensionless $\cdot$ ml^{-1}	$\boxminus$	$\boxminus$
Inhibitor	Inhibitor	Cell	dimensionless $\cdot$ ml^{-1}	☑	☑

5 Parameters

This model contains 16 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
pEGFR_total	pEGFR_total		0.000	$ng \cdot ml^{-1}$	⊟
pAkt_total	pAkt_total		0.000	$ng \cdot ml^{-1}$	⊟
pEGFR_scaleFactor	pEGFR_scaleFactor		$1.81735 \cdot 10^{-4}$	ng	☑
pAkt_scaleFactor	pAkt_scaleFactor		60.059	ng	☑
pS6_scaleFactor	pS6_scaleFactor		49886.200	ng	☑
pS6_total	pS6_total		0.000	$ng \cdot ml^{-1}$	⊟
EGF_conc_step	EGF_conc_step		30.000	$ng \cdot ml^{-1}$	☑
EGF_conc_pulse	EGF_conc_pulse		0.000	$ng \cdot ml^{-1}$	☑
EGF_conc_ramp	EGF_conc_ramp		0.000	$ng \cdot ml^{-1}$	☑
EGFR_turnover	EGFR_turnover		$1.06386 \cdot 10^{-4}$	s^{-1}	☑
EGF_binding_kf	EGF_binding_kf		0.007	$ml \cdot ng^{-1} \cdot s^{-1}$	☑
EGF_binding_kb	EGF_binding_kb		0.041	s^{-1}	☑
inhibitor_binding_kf	inhibitor_binding_kf		$2.43466029020655 \cdot 10^{-5}$	$ml \cdot dimensionless \cdot s^{-1}$	☑
inhibitor_binding_kb	inhibitor_binding_kb		$5.25096686262403 \cdot 10^{-5}$	s^{-1}	☑
pulse_time	pulse_time		60.000	s	☑
ramp_time	ramp_time		3600.000	s	☑

6 Initialassignments

This is an overview of two initialassignments.

6.1 Initialassignment EGFR

Derived unit contains undeclared units

Math $\frac{[\text{pro\_EGFR}]}{1+\frac{\text{inhibitor\_binding\_kf}\cdot[\text{Inhibitor}]}{\text{inhibitor\_binding\_kb}+\text{EGFR\_turnover}}}$

6.2 Initialassignment EGFR_i

Derived unit ml^{-1}

Math $[\text{pro\_EGFR}] - [\text{EGFR}]$

7 Rules

This is an overview of four rules.

7.1 Rule pAkt_total

Rule pAkt_total is an assignment rule for parameter pAkt_total:

$$\text{pAkt\_total} = ([\text{pAkt}] + [\text{pAkt\_S6}]) \cdot \text{pAkt\_scaleFactor} \tag{1}$$

Derived unit $\text{ml}^{-1} \cdot \text{ng}$

7.2 Rule pEGFR_total

Rule pEGFR_total is an assignment rule for parameter pEGFR_total:

$$\text{pEGFR\_total} = ([\text{pEGFR}] + [\text{pEGFR\_Akt}]) \cdot \text{pEGFR\_scaleFactor} \tag{2}$$

Derived unit $\text{ml}^{-1} \cdot \text{ng}$

7.3 Rule EGF

Rule EGF is an assignment rule for species EGF:

$$\text{EGF} = \text{EGF\_conc\_step} + \begin{cases} \text{EGF\_conc\_pulse} & \text{if time} \leq \text{pulse\_time} \\ 0 & \text{otherwise} \end{cases} + \frac{\text{EGF\_conc\_ramp} \cdot \text{time}}{\text{ramp\_time}} \tag{3}$$

7.4 Rule pS6_total

Rule pS6_total is an assignment rule for parameter pS6_total:

$$\text{pS6\_total} = [\text{pS6}] \cdot \text{pS6\_scaleFactor} \tag{4}$$

Derived unit $\text{ml}^{-1} \cdot \text{ng}$

8 Reactions

This model contains 15 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 5: Overview of all reactions

№	Id	Name	Reaction Equation	SBO
1	reaction_1	EGF+EGFR	$EGF + EGFR \rightleftharpoons EGF\_EGFR$	0000177
2	reaction_2	pEGFR+Akt	$pEGFR + Akt \rightleftharpoons pEGFR\_Akt$	0000177
3	reaction_3	Akt_phosphorylation	$pEGFR\_Akt \longrightarrow pEGFR + pAkt$	0000216
4	reaction_4	pEGFR_degradation	$pEGFR \longrightarrow \emptyset$	0000179
5	reaction_5	pAkt+S6	$pAkt + S6 \rightleftharpoons pAkt\_S6$	0000177
6	reaction_6	S6_phosphorylation	$pAkt\_S6 \longrightarrow pAkt + pS6$	0000216
7	reaction_7	pAkt_dephospho	$pAkt \longrightarrow Akt$	0000330
8	reaction_8	pS6_dephospho	$pS6 \longrightarrow S6$	0000330
9	reaction_9	EGFR_synthesis	$pro\_EGFR \longrightarrow EGFR$	0000184
10	reaction_10	EGFR_phosphorylation	$EGF\_EGFR \longrightarrow pEGFR$	0000216
11	reaction_11	EGFR_degradation	$EGFR \longrightarrow \emptyset$	0000179
12	reaction_12	EGFR+i	$Inhibitor + EGFR \rightleftharpoons EGFR\_i$	0000177
13	reaction_13	EGF_EGFR+i	$Inhibitor + EGF\_EGFR \rightleftharpoons EGF\_EGFR\_i$	0000177
14	reaction_14	EGF+EGFR_i	$EGF + EGFR\_i \rightleftharpoons EGF\_EGFR\_i$	0000177
15	reaction_15	EGFR_i_degradation	$EGFR\_i \longrightarrow \emptyset$	0000179

8.1 Reaction `reaction_1`

This is a reversible reaction of two reactants forming one product.

Name EGF+EGFR

SBO:0000177 non-covalent binding

Reaction equation

$$\mathrm{EGF} + \mathrm{EGFR} \rightleftharpoons \mathrm{EGF\_EGFR} \tag{5}$$

Reactants

Table 6: Properties of each reactant.

Id	Name	SBO
`EGF`	EGF	
`EGFR`	EGFR	

Product

Table 7: Properties of each product.

Id	Name	SBO
`EGF_EGFR`	EGF_EGFR	

Kinetic Law

Derived unit s^{-1}

$$v_1 = \mathrm{vol}\,(\mathrm{Cell}) \cdot (\mathrm{EGF\_binding\_kf} \cdot [\mathrm{EGF}] \cdot [\mathrm{EGFR}] - \mathrm{EGF\_binding\_kb} \cdot [\mathrm{EGF\_EGFR}]) \tag{6}$$

8.2 Reaction `reaction_2`

This is a reversible reaction of two reactants forming one product.

Name pEGFR+Akt

SBO:0000177 non-covalent binding

Reaction equation

$$\mathrm{pEGFR} + \mathrm{Akt} \rightleftharpoons \mathrm{pEGFR\_Akt} \tag{7}$$

Reactants

Table 8: Properties of each reactant.

Id	Name	SBO
pEGFR	pEGFR	
Akt	Akt	

Product

Table 9: Properties of each product.

Id	Name	SBO
pEGFR_Akt	pEGFR_Akt	

Kinetic Law

Derived unit s^{-1}

$$v_2 = \mathrm{vol}\,(\mathrm{Cell}) \cdot (\mathrm{k1} \cdot [\mathrm{pEGFR}] \cdot [\mathrm{Akt}] - \mathrm{k2} \cdot [\mathrm{pEGFR\_Akt}]) \tag{8}$$

Table 10: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		$1.5543 \cdot 10^{-5}$	$\mathrm{ml} \cdot \mathrm{dimensionless} \cdot \mathrm{s}^{-1}$	☑
k2	k2		0.005	s^{-1}	☑

8.3 Reaction reaction_3

This is an irreversible reaction of one reactant forming two products.

Name Akt_phosphorylation

SBO:0000216 phosphorylation

Reaction equation

$$\mathrm{pEGFR\_Akt} \longrightarrow \mathrm{pEGFR} + \mathrm{pAkt} \tag{9}$$

Reactant

Table 11: Properties of each reactant.

Id	Name	SBO
pEGFR_Akt	pEGFR_Akt	

Products

Table 12: Properties of each product.

Id	Name	SBO
pEGFR	pEGFR	
pAkt	pAkt	

Kinetic Law

Derived unit s^{-1}

$$v_3 = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{k1} \cdot [\mathrm{pEGFR\_Akt}] \tag{10}$$

Table 13: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.053	s^{-1}	☑

8.4 Reaction reaction_4

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

Name pEGFR_degradation

SBO:0000179 degradation

Reaction equation

$$\mathrm{pEGFR} \longrightarrow \emptyset \tag{11}$$

Reactant

Table 14: Properties of each reactant.

Id	Name	SBO
pEGFR	pEGFR	

Id	Name	SBO

Kinetic Law

Derived unit s^{-1}

$$v_4 = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{k1} \cdot [\mathrm{pEGFR}] \tag{12}$$

Table 15: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.100	s^{-1}	☑

8.5 Reaction reaction_5

This is a reversible reaction of two reactants forming one product.

Name pAkt+S6

SBO:0000177 non-covalent binding

Reaction equation

$$\mathrm{pAkt} + \mathrm{S6} \rightleftharpoons \mathrm{pAkt\_S6} \tag{13}$$

Reactants

Table 16: Properties of each reactant.

Id	Name	SBO
pAkt	pAkt	
S6	S6	

Product

Table 17: Properties of each product.

Id	Name	SBO
pAkt_S6	pAkt_S6	

Kinetic Law

Derived unit s^{-1}

$$v_5 = \mathrm{vol}\,(\mathrm{Cell}) \cdot (\mathrm{k1} \cdot [\mathrm{pAkt}] \cdot [\mathrm{S6}] - \mathrm{k2} \cdot [\mathrm{pAkt\_S6}]) \tag{14}$$

Table 18: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		$2.10189 \cdot 10^{-6}$	$\mathrm{ml} \cdot \mathrm{dimensionless} \cdot \mathrm{s}^{-1}$	☑
k2	k2		$5.1794 \cdot 10^{-15}$	s^{-1}	☑

8.6 Reaction reaction_6

This is an irreversible reaction of one reactant forming two products.

Name S6_phosphorylation

SBO:0000216 phosphorylation

Reaction equation

$$\mathrm{pAkt\_S6} \longrightarrow \mathrm{pAkt} + \mathrm{pS6} \tag{15}$$

Reactant

Table 19: Properties of each reactant.

Id	Name	SBO
pAkt_S6	pAkt_S6	

Products

Table 20: Properties of each product.

Id	Name	SBO
pAkt	pAkt	
pS6	pS6	

Kinetic Law

Derived unit s^{-1}

$$v_6 = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{k1} \cdot [\mathrm{pAkt\_S6}] \tag{16}$$

Table 21: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.001	s^{-1}	☑

8.7 Reaction reaction_7

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

Name pAkt_dephospho

SBO:0000330 dephosphorylation

Reaction equation

$$\mathrm{pAkt} \longrightarrow \mathrm{Akt} \tag{17}$$

Reactant

Table 22: Properties of each reactant.

Id	Name	SBO
pAkt	pAkt	

Product

Table 23: Properties of each product.

Id	Name	SBO
Akt	Akt	

Kinetic Law

Derived unit s^{-1}

$$v_7 = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{k1} \cdot [\mathrm{pAkt}] \tag{18}$$

Table 24: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.033	s^{-1}	☑

8.8 Reaction reaction_8

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

Name pS6_dephospho

SBO:0000330 dephosphorylation

Reaction equation

$$\text{pS6} \longrightarrow \text{S6} \tag{19}$$

Reactant

Table 25: Properties of each reactant.

Id	Name	SBO
pS6	pS6	

Product

Table 26: Properties of each product.

Id	Name	SBO
S6	S6	

Kinetic Law

Derived unit s^{-1}

$$v_8 = \text{vol}(\text{Cell}) \cdot \text{k1} \cdot [\text{pS6}] \tag{20}$$

Table 27: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.001	s^{-1}	☑

8.9 Reaction reaction_9

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

Name EGFR_synthesis

SBO:0000184 translation

Reaction equation

$$\text{pro\_EGFR} \longrightarrow \text{EGFR} \tag{21}$$

Reactant

Table 28: Properties of each reactant.

Id	Name	SBO
pro_EGFR	pro_EGFR	

Product

Table 29: Properties of each product.

Id	Name	SBO
EGFR	EGFR	

Kinetic Law

Derived unit s^{-1}

$$v_9 = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{EGFR\_turnover} \cdot [\mathrm{pro\_EGFR}] \tag{22}$$

8.10 Reaction reaction_10

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

Name EGFR_phosphorylation

SBO:0000216 phosphorylation

Reaction equation

$$\text{EGF\_EGFR} \longrightarrow \text{pEGFR} \tag{23}$$

Reactant

Table 30: Properties of each reactant.

Id	Name	SBO
EGF_EGFR	EGF_EGFR	

Product

Table 31: Properties of each product.

Id	Name	SBO
pEGFR	pEGFR	

Kinetic Law

Derived unit s^{-1}

$$v_{10} = \mathrm{vol}(\mathrm{Cell}) \cdot \mathrm{k1} \cdot [\mathrm{EGF\_EGFR}] \tag{24}$$

Table 32: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
k1	k1		0.019	s^{-1}	☑

8.11 Reaction reaction_11

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

Name EGFR_degradation

SBO:0000179 degradation

Reaction equation

$$\mathrm{EGFR} \longrightarrow \emptyset \tag{25}$$

Reactant

Table 33: Properties of each reactant.

Id	Name	SBO
EGFR	EGFR	

Kinetic Law

Derived unit s^{-1}

$$v_{11} = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{EGFR\_turnover} \cdot [\mathrm{EGFR}] \tag{26}$$

8.12 Reaction `reaction_12`

This is a reversible reaction of two reactants forming one product.

Name EGFR+i

SBO:0000177 non-covalent binding

Reaction equation

$$\mathrm{Inhibitor} + \mathrm{EGFR} \rightleftharpoons \mathrm{EGFR\_i} \tag{27}$$

Reactants

Table 34: Properties of each reactant.

Id	Name	SBO
`Inhibitor`	Inhibitor	
`EGFR`	EGFR	

Product

Table 35: Properties of each product.

Id	Name	SBO
`EGFR_i`	EGFR_i	

Kinetic Law

Derived unit s^{-1}

$$v_{12} = \mathrm{vol}\,(\mathrm{Cell}) \cdot (\mathrm{inhibitor\_binding\_kf} \cdot [\mathrm{Inhibitor}] \cdot [\mathrm{EGFR}] - \mathrm{inhibitor\_binding\_kb} \cdot [\mathrm{EGFR\_i}]) \tag{28}$$

8.13 Reaction `reaction_13`

This is a reversible reaction of two reactants forming one product.

Name EGF_EGFR+i

SBO:0000177 non-covalent binding

Reaction equation

$$\text{Inhibitor} + \text{EGF\_EGFR} \rightleftharpoons \text{EGF\_EGFR\_i} \tag{29}$$

Reactants

Table 36: Properties of each reactant.

Id	Name	SBO
`Inhibitor`	Inhibitor	
`EGF_EGFR`	EGF_EGFR	

Product

Table 37: Properties of each product.

Id	Name	SBO
`EGF_EGFR_i`	EGF_EGFR_i	

Kinetic Law

Derived unit s^{-1}

$$v_{13} = \text{vol}(\text{Cell}) \cdot (\text{inhibitor\_binding\_kf} \cdot [\text{Inhibitor}] \cdot [\text{EGF\_EGFR}] - \text{inhibitor\_binding\_kb} \cdot [\text{EGF\_EGFR\_i}]) \tag{30}$$

8.14 Reaction `reaction_14`

This is a reversible reaction of two reactants forming one product.

Name EGF+EGFR_i

SBO:0000177 non-covalent binding

Reaction equation

$$\text{EGF} + \text{EGFR\_i} \rightleftharpoons \text{EGF\_EGFR\_i} \tag{31}$$

Reactants

Table 38: Properties of each reactant.

Id	Name	SBO
EGF	EGF	
EGFR_i	EGFR_i	

Product

Table 39: Properties of each product.

Id	Name	SBO
EGF_EGFR_i	EGF_EGFR_i	

Kinetic Law

Derived unit s^{-1}

$$v_{14} = \mathrm{vol}\,(\mathrm{Cell}) \cdot (\mathrm{EGF\_binding\_kf} \cdot [\mathrm{EGF}] \cdot [\mathrm{EGFR\_i}] - \mathrm{EGF\_binding\_kb} \cdot [\mathrm{EGF\_EGFR\_i}]) \quad (32)$$

8.15 Reaction reaction_15

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

Name EGFR_i_degradation

SBO:0000179 degradation

Reaction equation

$$\mathrm{EGFR\_i} \longrightarrow \emptyset \quad (33)$$

Reactant

Table 40: Properties of each reactant.

Id	Name	SBO
EGFR_i	EGFR_i	

Kinetic Law

Derived unit s^{-1}

$$v_{15} = \mathrm{vol}\,(\mathrm{Cell}) \cdot \mathrm{EGFR\_turnover} \cdot [\mathrm{EGFR\_i}] \quad (34)$$

9 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.

Identifiers for kinetic laws highlighted in gray cannot be verified to evaluate to units of SBML `substance` per `time`. As a result, some SBML interpreters may not be able to verify the consistency of the units on quantities in the model. Please check if

- parameters without an unit definition are involved or
- volume correction is necessary because the `hasOnlySubstanceUnits` flag may be set to `false` and `spacialDimensions`> 0 for certain species.

9.1 Species EGF

Name EGF

SBO:0000252 polypeptide chain

Initial concentration $30\ \mathrm{ng} \cdot \mathrm{ml}^{-1}$

Involved in rule EGF

This species takes part in two reactions (as a reactant in reaction_1, reaction_14). Not these but one rule determines the species' quantity because this species is on the boundary of the reaction system.

9.2 Species EGFR

Name EGFR

SBO:0000297 protein complex

Initial concentration $68190.2000000002\ \mathrm{dimensionless} \cdot \mathrm{ml}^{-1}$

Initial assignment EGFR

This species takes part in four reactions (as a reactant in reaction_1, reaction_11, reaction_12 and as a product in reaction_9).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{EGFR} = v_9 - v_1 - v_{11} - v_{12} \tag{35}$$

9.3 Species pEGFR

Name pEGFR

SBO:0000297 protein complex

Initial concentration $0\ \text{dimensionless} \cdot \text{ml}^{-1}$

This species takes part in four reactions (as a reactant in reaction_2, reaction_4 and as a product in reaction_3, reaction_10).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{pEGFR} = v_3 + v_{10} - v_2 - v_4 \tag{36}$$

9.4 Species pEGFR_Akt

Name pEGFR_Akt

SBO:0000297 protein complex

Initial concentration $0\ \text{dimensionless} \cdot \text{ml}^{-1}$

This species takes part in two reactions (as a reactant in reaction_3 and as a product in reaction_2).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{pEGFR\_Akt} = v_2 - v_3 \tag{37}$$

9.5 Species Akt

Name Akt

SBO:0000252 polypeptide chain

Initial concentration $0.043309\ \text{dimensionless} \cdot \text{ml}^{-1}$

This species takes part in two reactions (as a reactant in reaction_2 and as a product in reaction_7).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{Akt} = v_7 - v_2 \tag{38}$$

9.6 Species pAkt

Name pAkt

SBO:0000252 polypeptide chain

Initial concentration $0\ \text{dimensionless} \cdot \text{ml}^{-1}$

This species takes part in four reactions (as a reactant in reaction_5, reaction_7 and as a product in reaction_3, reaction_6).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{pAkt} = v_3 + v_6 - v_5 - v_7 \tag{39}$$

9.7 Species S6

Name S6

SBO:0000252 polypeptide chain

Initial concentration 3.54317 dimensionless $\cdot$ ml^{-1}

This species takes part in two reactions (as a reactant in reaction_5 and as a product in reaction_8).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{S6} = v_8 - v_5 \tag{40}$$

9.8 Species pAkt_S6

Name pAkt_S6

SBO:0000297 protein complex

Initial concentration 0 dimensionless $\cdot$ ml^{-1}

This species takes part in two reactions (as a reactant in reaction_6 and as a product in reaction_5).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{pAkt\_S6} = v_5 - v_6 \tag{41}$$

9.9 Species pS6

Name pS6

SBO:0000252 polypeptide chain

Initial concentration 0 dimensionless $\cdot$ ml^{-1}

This species takes part in two reactions (as a reactant in reaction_8 and as a product in reaction_6).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{pS6} = v_6 - v_8 \tag{42}$$

9.10 Species pro_EGFR

Name pro_EGFR

SBO:0000252 polypeptide chain

Initial concentration 68190.2000000002 dimensionless $\cdot$ ml^{-1}

This species takes part in one reaction (as a reactant in reaction_9), which does not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{pro\_EGFR} = 0 \tag{43}$$

9.11 Species EGF_EGFR

Name EGF_EGFR

SBO:0000297 protein complex

Initial concentration $0\ \text{dimensionless} \cdot \text{ml}^{-1}$

This species takes part in three reactions (as a reactant in reaction_10, reaction_13 and as a product in reaction_1).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{EGF\_EGFR} = v_1 - v_{10} - v_{13} \tag{44}$$

9.12 Species EGFR_i

Name EGFR_i

SBO:0000297 protein complex

Initial concentration $0\ \text{dimensionless} \cdot \text{ml}^{-1}$

Initial assignment EGFR_i

This species takes part in three reactions (as a reactant in reaction_14, reaction_15 and as a product in reaction_12).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{EGFR\_i} = v_{12} - v_{14} - v_{15} \tag{45}$$

9.13 Species EGF_EGFR_i

Name EGF_EGFR_i

SBO:0000297 protein complex

Initial concentration $0\ \text{dimensionless} \cdot \text{ml}^{-1}$

This species takes part in two reactions (as a product in reaction_13, reaction_14).

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{EGF\_EGFR\_i} = v_{13} + v_{14} \tag{46}$$

9.14 Species Inhibitor

Name Inhibitor

SBO:0000247 simple chemical

Initial concentration $0\ \text{dimensionless} \cdot \text{ml}^{-1}$

This species takes part in two reactions (as a reactant in reaction_12, reaction_13), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{Inhibitor} = 0 \tag{47}$$

A Glossary of Systems Biology Ontology Terms

SBO:0000177 non-covalent binding: Interaction between several biochemical entities that results in the formation of a non-covalent comple

SBO:0000179 degradation: Complete disappearance of a physical entity

SBO:0000184 translation: Process in which a polypeptide chain is produced from a messenger RNA

SBO:0000216 phosphorylation: Addition of a phosphate group (-H2PO4) to a chemical entity

SBO:0000247 simple chemical: Simple, non-repetitive chemical entity

SBO:0000252 polypeptide chain: Naturally occurring macromolecule formed by the repetition of amino-acid residues linked by peptidic bonds. A polypeptide chain is synthesized by the ribosome. CHEBI:1654

SBO:0000290 physical compartment: Specific location of space, that can be bounded or not. A physical compartment can have 1, 2 or 3 dimensions

SBO:0000297 protein complex: Macromolecular complex containing one or more polypeptide chains possibly associated with simple chemicals. CHEBI:3608

SBO:0000330 dephosphorylation: Removal of a phosphate group (-H2PO4) from a chemical entity.

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.

[a]Center for Bioinformatics Tübingen (ZBIT), Germany
[b]California Institute of Technology, Beckman Institute BNMC, Pasadena, United States
[c]European Bioinformatics Institute, Wellcome Trust Genome Campus, Hinxton, United Kingdom
[d]EML Research gGmbH, Heidelberg, Germany