SBML Model Report

Model name: "Chickarmane2008 - Stem cell lineage determination"

May 6, 2016

1 General Overview

This is a document in SBML Level 2 Version 3 format. This model was created by the following three authors: Vijayalakshmi Chelliah[1], Carsten Peterson[2] and Vijay Chickarmane[3] at December fifth 2008 at 2:17 p. m. and last time modified at June fifth 2013 at 4:45 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	20
events	0	constraints	0
reactions	12	function definitions	0
global parameters	49	unit definitions	3
rules	0	initial assignments	0

Model Notes

Chickarmane2008 - Stem cell lineage determination

[1]EMBL-EBI, viji@ebi.ac.uk
[2]Lund Strategic Research Centre for Stem Cell Biology and Cell Therapy, Lund University, Sweden., carsten@thep.lu.se
[3]Keck Graduate Institute, California, vchickar@caltech.edu

In this work, a dynamical model of lineage determination based upon a minimal circuit, as discussed in PMID: 17215298 , which contains the Oct4/Sox2/Nanog core as well its interaction with a few other key genes is discussed.

This model is described in the article:A computational model for understanding stem cell, trophectoderm and endoderm lineage determination.Chickarmane V, Peterson CPloS one. 2008, 3(10):e3478

Abstract:

BACKGROUND: Recent studies have associated the transcription factors, Oct4, Sox2 and Nanog as parts of a self-regulating network which is responsible for maintaining embryonic stem cell properties: self renewal and pluripotency. In addition, mutual antagonism between two of these and other master regulators have been shown to regulate lineage determination. In particular, an excess of Cdx2 over Oct4 determines the trophectoderm lineage whereas an excess of Gata-6 over Nanog determines differentiation into the endoderm lineage. Also, under/over-expression studies of the master regulator Oct4 have revealed that some self-renewal/pluripotency as well as differentiation genes are expressed in a biphasic manner with respect to the concentration of Oct4. METHODOLOGY/

PRINCIPAL FINDINGS: We construct a dynamical model of a minimalistic network, extracted from ChIP-on-chip and microarray data as well as literature studies. The model is based upon differential equations and makes two plausible assumptions; activation of Gata-6 by Oct4 and repression of Nanog by an Oct4-Gata-6 heterodimer. With these assumptions, the results of simulations successfully describe the biphasic behavior as well as lineage commitment. The model also predicts that reprogramming the network from a differentiated state, in particular the endoderm state, into a stem cell state, is best achieved by over-expressing Nanog, rather than by suppression of differentiation genes such as Gata-6.

CONCLUSIONS: The computational model provides a mechanistic understanding of how different lineages arise from the dynamics of the underlying regulatory network. It provides a framework to explore strategies of reprogramming a cell from a differentiated state to a stem cell state through directed perturbations. Such an approach is highly relevant to regenerative medicine since it allows for a rapid search over the host of possibilities for reprogramming to a stem cell state.

This model is hosted on BioModels Database and identifiedby: MODEL8390025091 .

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 of which two are predefined by SBML and not mentioned in the model.

2.1 Unit `substance`

Name arb_substance

Definition dimensionless

2.2 Unit `volume`

Name arb_volume

Definition l

2.3 Unit `time`

Name arb_time

Definition dimensionless

2.4 Unit `area`

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

Definition m^2

2.5 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		3	1	litre	☑	

3.1 Compartment `cell`

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

Name cell

4 Species

This model contains 20 species. The boundary condition of twelve of these species is set to `true` so that these species' amount cannot be changed by any reaction. 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
`OCT4_Gene`		`cell`	$\mathrm{dimensionless} \cdot \mathrm{l}^{-1}$	⊟	☑
`NANOG_Gene`		`cell`	$\mathrm{dimensionless} \cdot \mathrm{l}^{-1}$	⊟	☑
`SOX2_Gene`		`cell`	$\mathrm{dimensionless} \cdot \mathrm{l}^{-1}$	⊟	☑
`GATA6_Gene`		`cell`	$\mathrm{dimensionless} \cdot \mathrm{l}^{-1}$	⊟	☑
`CDX2_Gene`		`cell`	$\mathrm{dimensionless} \cdot \mathrm{l}^{-1}$	⊟	☑
`GCNF_Gene`		`cell`	$\mathrm{dimensionless} \cdot \mathrm{l}^{-1}$	⊟	☑
`targetGene`		`cell`	$\mathrm{dimensionless} \cdot \mathrm{l}^{-1}$	⊟	☑
`degradation`		`cell`	$\mathrm{dimensionless} \cdot \mathrm{l}^{-1}$	⊟	☑
`p53`		`cell`	$\mathrm{dimensionless} \cdot \mathrm{l}^{-1}$	⊟	☑
`A`		`cell`	$\mathrm{dimensionless} \cdot \mathrm{l}^{-1}$	⊟	☑
`SG`		`cell`	$\mathrm{dimensionless} \cdot \mathrm{l}^{-1}$	⊟	☑
`SN`		`cell`	$\mathrm{dimensionless} \cdot \mathrm{l}^{-1}$	⊟	☑
`OCT4`		`cell`	$\mathrm{dimensionless} \cdot \mathrm{l}^{-1}$	⊟	⊟
`SOX2`		`cell`	$\mathrm{dimensionless} \cdot \mathrm{l}^{-1}$	⊟	⊟
`NANOG`		`cell`	$\mathrm{dimensionless} \cdot \mathrm{l}^{-1}$	⊟	⊟
`GATA6`		`cell`	$\mathrm{dimensionless} \cdot \mathrm{l}^{-1}$	⊟	⊟
`CDX2`		`cell`	$\mathrm{dimensionless} \cdot \mathrm{l}^{-1}$	⊟	⊟
`GCNF`		`cell`	$\mathrm{dimensionless} \cdot \mathrm{l}^{-1}$	⊟	⊟
`OCT4_SOX2`		`cell`	$\mathrm{dimensionless} \cdot \mathrm{l}^{-1}$	⊟	⊟
`Protein`		`cell`	$\mathrm{dimensionless} \cdot \mathrm{l}^{-1}$	⊟	⊟

5 Parameters

This model contains 49 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
a0	a0		0.001		☑
a1	a1		1.000		☑
a2	a2		0.005		☑
a3	a3		0.025		☑
b0	b0		1.000		☑
b1	b1		0.001		☑
b2	b2		0.005		☑
b3	b3		0.025		☑
b4	b4		10.000		☑
b5	b5		10.000		☑
gamma1	gamma1		0.100		☑
c0	c0		0.001		☑
c1	c1		0.005		☑
c2	c2		0.025		☑
d0	d0		0.001		☑
d1	d1		0.005		☑
d2	d2		0.025		☑
d3	d3		0.050		☑
gamma2	gamma2		0.100		☑
e0	e0		0.001		☑
e1	e1		0.100		☑
e2	e2		0.100		☑
e3	e3		1.000		☑
f0	f0		0.001		☑
f1	f1		0.100		☑
f2	f2		0.100		☑
f3	f3		10.000		☑
f4	f4		1.000		☑
gamma3	gamma3		0.100		☑
g0	g0		0.001		☑
g1	g1		2.000		☑
h0	h0		2.000		☑
h1	h1		5.000		☑
gamma4	gamma4		0.100		☑
i0	i0		0.001		☑
i1	i1		0.100		☑
i2	i2		0.100		☑

Id	Name	SBO	Value	Unit	Constant
j0	j0		0.100		☑
j1	j1		0.100		☑
gamma5	gamma5		0.100		☑
p0	p0		0.100		☑
p1	p1		1.000		☑
p2	p2		$2.5 \cdot 10^{-4}$		☑
q0	q0		1.000		☑
q1	q1		$2.5 \cdot 10^{-4}$		☑
q2	q2		15.000		☑
q3	q3		10.000		☑
gammag	gammag		0.100		☑
gamman	gamman		0.010		☑

6 Reactions

This model contains twelve 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	R1	R1	$\mathrm{OCT4\_Gene} \xrightarrow{\mathrm{A,\ SOX2,\ NANOG,\ CDX2,\ GCNF}} \mathrm{OCT4}$	
2	R2	R2	$\mathrm{OCT4} \longrightarrow \mathrm{degradation}$	
3	R3	R3	$\mathrm{SOX2\_Gene} \xrightarrow{\mathrm{OCT4,\ NANOG}} \mathrm{SOX2}$	
4	R4	R4	$\mathrm{SOX2} \longrightarrow \mathrm{degradation}$	
5	R5	R5	$\mathrm{NANOG\_Gene} \xrightarrow{\mathrm{OCT4,\ SOX2,\ GATA6,\ SN}} \mathrm{NANOG}$	
6	R6	R6	$\mathrm{NANOG} \longrightarrow \mathrm{degradation}$	
7	R7	R7	$\mathrm{CDX2\_Gene} \xrightarrow{\mathrm{OCT4}} \mathrm{CDX2}$	
8	R8	R8	$\mathrm{CDX2} \longrightarrow \mathrm{degradation}$	
9	R9	R9	$\mathrm{GCNF\_Gene} \xrightarrow{\mathrm{CDX2,\ GATA6}} \mathrm{GCNF}$	
10	R10	R10	$\mathrm{GCNF} \longrightarrow \mathrm{degradation}$	
11	R11	R11	$\mathrm{GATA6\_Gene} \xrightarrow{\mathrm{OCT4,\ NANOG,\ SG}} \mathrm{GATA6}$	
12	R12	R12	$\mathrm{GATA6} \longrightarrow \mathrm{degradation}$	

6.1 Reaction R1

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

Name R1

Reaction equation

$$\text{OCT4\_Gene} \xrightarrow{\text{A, SOX2, NANOG, CDX2, GCNF}} \text{OCT4} \tag{1}$$

Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
OCT4_Gene		

Modifiers

Table 7: Properties of each modifier.

Id	Name	SBO
A		
SOX2		
NANOG		
CDX2		
GCNF		

Product

Table 8: Properties of each product.

Id	Name	SBO
OCT4		

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \frac{\mathrm{a0} + \mathrm{a1} \cdot [\mathrm{A}] + \mathrm{a2} \cdot [\mathrm{OCT4}] \cdot [\mathrm{SOX2}] + \mathrm{a3} \cdot [\mathrm{OCT4}] \cdot [\mathrm{SOX2}] \cdot [\mathrm{NANOG}]}{1 + \mathrm{b0} \cdot [\mathrm{A}] + \mathrm{b1} \cdot [\mathrm{OCT4}] + \mathrm{b2} \cdot [\mathrm{OCT4}] \cdot [\mathrm{SOX2}] + \mathrm{b3} \cdot [\mathrm{OCT4}] \cdot [\mathrm{SOX2}] \cdot [\mathrm{NANOG}] + \mathrm{b4} \cdot [\mathrm{CDX2}] \cdot [\mathrm{OCT4}] \cdot} \tag{2}$$

6.2 Reaction R2

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

Name R2

Reaction equation

$$\text{OCT4} \longrightarrow \text{degradation} \tag{3}$$

Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
OCT4		

Product

Table 10: Properties of each product.

Id	Name	SBO
degradation		

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \text{gamma1} \cdot [\text{OCT4}] \tag{4}$$

6.3 Reaction R3

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

Name R3

Reaction equation

$$\text{SOX2\_Gene} \xrightarrow{\text{OCT4, NANOG}} \text{SOX2} \tag{5}$$

Reactant

Table 11: Properties of each reactant.

Id	Name	SBO
SOX2_Gene		

Modifiers

Table 12: Properties of each modifier.

Id	Name	SBO
OCT4		
NANOG		

Product

Table 13: Properties of each product.

Id	Name	SBO
SOX2		

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \frac{\mathrm{c0} + \mathrm{c1} \cdot [\mathrm{OCT4}] \cdot [\mathrm{SOX2}] + \mathrm{c2} \cdot [\mathrm{OCT4}] \cdot [\mathrm{SOX2}] \cdot [\mathrm{NANOG}]}{1 + \mathrm{d0} \cdot [\mathrm{OCT4}] + \mathrm{d1} \cdot [\mathrm{OCT4}] \cdot [\mathrm{SOX2}] + \mathrm{d2} \cdot [\mathrm{OCT4}] \cdot [\mathrm{SOX2}] \cdot [\mathrm{NANOG}]} \tag{6}$$

6.4 Reaction R4

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

Name R4

Reaction equation

$$\mathrm{SOX2} \longrightarrow \mathrm{degradation} \tag{7}$$

Reactant

Table 14: Properties of each reactant.

Id	Name	SBO
SOX2		

Product

Table 15: Properties of each product.

Id	Name	SBO
degradation		

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \text{gamma2} \cdot [\text{SOX2}] \tag{8}$$

6.5 Reaction R5

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

Name R5

Reaction equation

$$\text{NANOG\_Gene} \xrightarrow{\text{OCT4, SOX2, GATA6, SN}} \text{NANOG} \tag{9}$$

Reactant

Table 16: Properties of each reactant.

Id	Name	SBO
NANOG_Gene		

Modifiers

Table 17: Properties of each modifier.

Id	Name	SBO
OCT4		

Id	Name	SBO
SOX2		
GATA6		
SN		

Product

Table 18: Properties of each product.

Id	Name	SBO
NANOG		

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \frac{e0 + e1 \cdot [OCT4] \cdot [SOX2] + e2 \cdot [OCT4] \cdot [SOX2] \cdot [NANOG] + e3 \cdot [SN]}{1 + f0 \cdot [OCT4] + f1 \cdot [OCT4] \cdot [SOX2] + f2 \cdot [OCT4] \cdot [SOX2] \cdot [NANOG] + f3 \cdot [OCT4] \cdot [GATA6] + f4 \cdot [SN]} \quad (10)$$

6.6 Reaction R6

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

Name R6

Reaction equation

$$\text{NANOG} \longrightarrow \text{degradation} \quad (11)$$

Reactant

Table 19: Properties of each reactant.

Id	Name	SBO
NANOG		

Product

Table 20: Properties of each product.

Id	Name	SBO
degradation		

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \mathrm{gamma3} \cdot [\mathrm{NANOG}] \tag{12}$$

6.7 Reaction R7

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

Name R7

Reaction equation

$$\mathrm{CDX2\_Gene} \xrightarrow{\mathrm{OCT4}} \mathrm{CDX2} \tag{13}$$

Reactant

Table 21: Properties of each reactant.

Id	Name	SBO
CDX2_Gene		

Modifier

Table 22: Properties of each modifier.

Id	Name	SBO
OCT4		

Product

Table 23: Properties of each product.

Id	Name	SBO
CDX2		

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \frac{\text{g0} + \text{g1} \cdot [\text{CDX2}]}{1 + \text{h0} \cdot [\text{CDX2}] + \text{h1} \cdot [\text{CDX2}] \cdot [\text{OCT4}]} \tag{14}$$

6.8 Reaction R8

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

Name R8

Reaction equation

$$\text{CDX2} \longrightarrow \text{degradation} \tag{15}$$

Reactant

Table 24: Properties of each reactant.

Id	Name	SBO
CDX2		

Product

Table 25: Properties of each product.

Id	Name	SBO
degradation		

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \text{gamma4} \cdot [\text{CDX2}] \tag{16}$$

6.9 Reaction R9

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

Name R9

Reaction equation

$$\text{GCNF\_Gene} \xrightarrow{\text{CDX2, GATA6}} \text{GCNF} \tag{17}$$

Reactant

Table 26: Properties of each reactant.

Id	Name	SBO
GCNF_Gene		

Modifiers

Table 27: Properties of each modifier.

Id	Name	SBO
CDX2		
GATA6		

Product

Table 28: Properties of each product.

Id	Name	SBO
GCNF		

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \frac{\mathrm{i0} + \mathrm{i1} \cdot [\mathrm{CDX2}] + \mathrm{i2} \cdot [\mathrm{GATA6}]}{1 + \mathrm{j0} \cdot [\mathrm{CDX2}] + \mathrm{j1} \cdot [\mathrm{GATA6}]} \tag{18}$$

6.10 Reaction R10

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

Name R10

Reaction equation

$$\text{GCNF} \longrightarrow \text{degradation} \tag{19}$$

Reactant

Table 29: Properties of each reactant.

Id	Name	SBO
GCNF		

Product

Table 30: Properties of each product.

Id	Name	SBO
degradation		

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = \text{gamma5} \cdot [\text{GCNF}] \tag{20}$$

6.11 Reaction R11

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

Name R11

Reaction equation

$$\text{GATA6\_Gene} \xrightarrow{\text{OCT4, NANOG, SG}} \text{GATA6} \tag{21}$$

Reactant

Table 31: Properties of each reactant.

Id	Name	SBO
GATA6_Gene		

Modifiers

Table 32: Properties of each modifier.

Id	Name	SBO
OCT4		
NANOG		
SG		

Product

Table 33: Properties of each product.

Id	Name	SBO
GATA6		

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \frac{p0 + p1 \cdot [OCT4] + p2 \cdot [GATA6]}{1 + q0 \cdot [OCT4] + q1 \cdot [GATA6] + q2 \cdot [NANOG] + q3 \cdot [SG]} \tag{22}$$

6.12 Reaction R12

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

Name R12

Reaction equation

$$\text{GATA6} \longrightarrow \text{degradation} \tag{23}$$

Reactant

Table 34: Properties of each reactant.

Id	Name	SBO
GATA6		

Product

Table 35: Properties of each product.

Id	Name	SBO
degradation		

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = \text{gammag} \cdot [\text{GATA6}] \tag{24}$$

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.

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.

7.1 Species OCT4_Gene

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

This species takes part in one reaction (as a reactant in R1), which does not influence its rate of change because this species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{OCT4\_Gene} = 0 \tag{25}$$

7.2 Species NANOG_Gene

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

This species takes part in one reaction (as a reactant in R5), which does not influence its rate of change because this species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{NANOG\_Gene} = 0 \tag{26}$$

7.3 Species SOX2_Gene

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

This species takes part in one reaction (as a reactant in R3), which does not influence its rate of change because this species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{SOX2\_Gene} = 0 \tag{27}$$

7.4 Species GATA6_Gene

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

This species takes part in one reaction (as a reactant in R11), which does not influence its rate of change because this species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{GATA6\_Gene} = 0 \tag{28}$$

7.5 Species CDX2_Gene

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

This species takes part in one reaction (as a reactant in R7), which does not influence its rate of change because this species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{CDX2\_Gene} = 0 \tag{29}$$

7.6 Species GCNF_Gene

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

This species takes part in one reaction (as a reactant in R9), which does not influence its rate of change because this species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{GCNF\_Gene} = 0 \tag{30}$$

7.7 Species targetGene

Initial concentration $0.01 \text{ dimensionless} \cdot \text{l}^{-1}$

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{targetGene} = 0 \tag{31}$$

7.8 Species degradation

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

This species takes part in six reactions (as a product in R2, R4, R6, R8, R10, R12), which do not influence its rate of change because this species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{degradation} = 0 \tag{32}$$

7.9 Species p53

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

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{p53} = 0 \tag{33}$$

7.10 Species A

Initial concentration $25 \text{ dimensionless} \cdot \text{l}^{-1}$

This species takes part in one reaction (as a modifier in R1), which does not influence its rate of change because this species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{A} = 0 \tag{34}$$

7.11 Species SG

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

This species takes part in one reaction (as a modifier in R11), which does not influence its rate of change because this species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{SG} = 0 \tag{35}$$

7.12 Species SN

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

This species takes part in one reaction (as a modifier in R5), which does not influence its rate of change because this species is on the boundary of the reaction system:

$$\frac{\mathrm{d}}{\mathrm{d}t}\text{SN} = 0 \tag{36}$$

7.13 Species OCT4

Initial concentration $0.01 \text{ dimensionless} \cdot \text{l}^{-1}$

This species takes part in six reactions (as a reactant in R2 and as a product in R1 and as a modifier in R3, R5, R7, R11).

$$\frac{d}{dt}\text{OCT4} = v_1 - v_2 \tag{37}$$

7.14 Species SOX2

Initial concentration $0.01 \text{ dimensionless} \cdot \text{l}^{-1}$

This species takes part in four reactions (as a reactant in R4 and as a product in R3 and as a modifier in R1, R5).

$$\frac{d}{dt}\text{SOX2} = v_3 - v_4 \tag{38}$$

7.15 Species NANOG

Initial concentration $0.01 \text{ dimensionless} \cdot \text{l}^{-1}$

This species takes part in five reactions (as a reactant in R6 and as a product in R5 and as a modifier in R1, R3, R11).

$$\frac{d}{dt}\text{NANOG} = v_5 - v_6 \tag{39}$$

7.16 Species GATA6

Initial concentration $0.01 \text{ dimensionless} \cdot \text{l}^{-1}$

This species takes part in four reactions (as a reactant in R12 and as a product in R11 and as a modifier in R5, R9).

$$\frac{d}{dt}\text{GATA6} = v_{11} - v_{12} \tag{40}$$

7.17 Species CDX2

Initial concentration $0.01 \text{ dimensionless} \cdot \text{l}^{-1}$

This species takes part in four reactions (as a reactant in R8 and as a product in R7 and as a modifier in R1, R9).

$$\frac{d}{dt}\text{CDX2} = v_7 - v_8 \tag{41}$$

7.18 Species GCNF

Initial concentration $0.01 \text{ dimensionless} \cdot \text{l}^{-1}$

This species takes part in three reactions (as a reactant in R10 and as a product in R9 and as a modifier in R1).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{GCNF} = v_9 - v_{10} \tag{42}$$

7.19 Species OCT4_SOX2

Initial concentration $0.1 \text{ dimensionless} \cdot \text{l}^{-1}$

This species does not take part in any reactions. Its quantity does hence not change over time:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{OCT4\_SOX2} = 0 \tag{43}$$

7.20 Species Protein

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

This species does not take part in any reactions. Its quantity does hence not change over time:

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Protein} = 0 \tag{44}$$

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