SBML Model Report

Model name: "Friedland2009_Ara_RTC3_counter"

May 6, 2016

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by Lukas Endler[1] at January 19th 2011 at 2:14 a. m. and last time modified at April eighth 2016 at 4:55 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	8
events	6	constraints	0
reactions	15	function definitions	0
global parameters	36	unit definitions	0
rules	2	initial assignments	0

Model Notes

This is the model of the RTC3 counter described in the article:
Synthetic gene networks that count.
Friedland AE, Lu TK, Wang X, Shi D, Church G, Collins JJ. Science. 2009 May 29;324(5931):1199-202. PMID:19478183, DOI:10.1126/science.1172005

Abstract:

Synthetic gene networks can be constructed to emulate digital circuits and devices, giving one

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the ability to program and design cells with some of the principles of modern computing, such as counting. A cellular counter would enable complex synthetic programming and a variety of biotechnology applications. Here, we report two complementary synthetic genetic counters in Escherichia coli that can count up to three induction events: the first, a riboregulated transcriptional cascade, and the second, a recombinase-based cascade of memory units. These modular devices permit counting of varied user-defined inputs over a range of frequencies and can be expanded to count higher numbers.

The 3 arabinose pulses are implemented using events, one for the start of pulses and one for the end. The variable pulse_flag changes arabinose consumption to fit behaviour during pulses and in between. To simulate two pulses only, set the pulse length of the third pulse to a negative value (though with an absolute value smaller than the pulse intervall length).

Originally created by libAntimony v1.4 (using libSBML 3.4.1)

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To cite BioModels Database, please use: Li C, Donizelli M, Rodriguez N, Dharuri H, Endler L, Chelliah V, Li L, He E, Henry A, Stefan MI, Snoep JL, Hucka M, Le Novre N, Laibe C (2010) BioModels Database: An enhanced, curated and annotated resource for published quantitative kinetic models. BMC Syst Biol., 4:92.

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`		0000290	3	1	litre	☑	

3.1 Compartment `cell`

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

SBO:0000290 physical compartment

4 Species

This model contains eight species. 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
taRNA		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
mT7cr		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
mGFPcr		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
pT7		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
pGFP		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
ara		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
pT3		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟
mT3cr		cell	$\mathrm{mol} \cdot \mathrm{l}^{-1}$	⊟	⊟

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5 Parameters

This model contains 36 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
cAra			$3 \cdot 10^{-4}$		☑
pulse_flag			0.000		⊟
dAra			0.120		☑
sT			0.847		☑
k_ara			0.057		☑
s0_taRNA			$8 \cdot 10^{-4}$		☑
d_taRNA			0.118		☑
s0_mT7cr			0.025		☑
d_mT7			0.071		☑
s0_mGFPcr			0.012		☑
k_pT3			3.006		☑
n3			0.889		☑
km3			7.908		☑
d_mGFP			0.070		☑
s0_pT7			$3 \cdot 10^{-4}$		☑
s_pT7k			0.077		☑
s0_pGFP			0.101		☑
s_pGFPk			0.992		☑
d_pT7			0.006		☑
d_pGFP			0.003		☑
s0_mT3cr			$3 \cdot 10^{-4}$		☑
k_pT7			3.801		☑
n7			2.602		☑
km7			3.046		☑
d_mT3			0.070		☑
s0_pT3			0.000		☑
s_pT3k			0.012		☑
d_pT3			0.007		☑
pulse-_interval			20.000		☑
pulse1_start			0.010		☑
pulse1-_length			11.000		☑
pulse_conc			0.010		☑
pulse2_start			0.000		⊟
pulse2-_length			11.000		☑

Id	Name	SBO	Value	Unit	Constant
pulse3_start			0.000		☐
pulse3-_length			22.000		☑

6 Rules

This is an overview of two rules.

6.1 Rule pulse2_start

Rule pulse2_start is an assignment rule for parameter pulse2_start:

$$\text{pulse2\_start} = \text{pulse1\_start} + \text{pulse1\_length} + \text{pulse\_interval} \tag{1}$$

6.2 Rule pulse3_start

Rule pulse3_start is an assignment rule for parameter pulse3_start:

$$\text{pulse3\_start} = \text{pulse2\_start} + \text{pulse2\_length} + \text{pulse\_interval} \tag{2}$$

7 Events

This is an overview of six events. Each event is initiated whenever its trigger condition switches from false to true. A delay function postpones the effects of an event to a later time point. At the time of execution, an event can assign values to species, parameters or compartments if these are not set to constant.

7.1 Event pulse_start1

Trigger condition

$$(\text{time} \geq \text{pulse1\_start}) \wedge (\text{time} \leq \text{pulse1\_start} + \text{pulse1\_length}) \tag{3}$$

Assignments

$$\text{pulse\_flag} = 1 \tag{4}$$

$$\text{ara} = \text{pulse\_conc} \tag{5}$$

7.2 Event pulse_start2

Trigger condition

$$(\text{time} \geq \text{pulse2\_start}) \wedge (\text{time} \leq \text{pulse2\_start} + \text{pulse2\_length}) \tag{6}$$

Assignments

$$\text{pulse\_flag} = 1 \tag{7}$$

$$\text{ara} = \text{pulse\_conc} \tag{8}$$

7.3 Event pulse_start3

Trigger condition

$$(\text{time} \geq \text{pulse3\_start}) \wedge (\text{time} \leq \text{pulse3\_start} + \text{pulse3\_length}) \tag{9}$$

Assignments

$$\text{pulse\_flag} = 1 \tag{10}$$

$$\text{ara} = \text{pulse\_conc} \tag{11}$$

7.4 Event pulse_end1

Trigger condition

$$(\text{time} < \text{pulse2\_start}) \wedge (\text{time} > \text{pulse1\_start} + \text{pulse1\_length}) \tag{12}$$

Assignment

$$\text{pulse\_flag} = 0 \tag{13}$$

7.5 Event pulse_end2

Trigger condition

$$(\text{time} < \text{pulse3\_start}) \wedge (\text{time} > \text{pulse2\_start} + \text{pulse2\_length}) \tag{14}$$

Assignment

$$\text{pulse\_flag} = 0 \tag{15}$$

7.6 Event pulse_end3

Trigger condition

$$\text{time} > \text{pulse3\_start} + \text{pulse3\_length} \tag{16}$$

Assignment

$$\text{pulse\_flag} = 0 \tag{17}$$

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	r0		ara $\longrightarrow \emptyset$	0000179
2	r1a		$\emptyset \xrightarrow{\text{ara}}$ taRNA	0000183
3	r1b		taRNA $\longrightarrow \emptyset$	0000179
4	r2a		$\emptyset \longrightarrow$ mT7cr	0000183
5	r2b		mT7cr $\longrightarrow \emptyset$	0000179
6	r3a		$\emptyset \xrightarrow{\text{pT3}}$ mGFPcr	0000183
7	r3b		mGFPcr $\longrightarrow \emptyset$	0000179
8	r6		$\emptyset \xrightarrow{\text{taRNA, mT7cr}}$ pT7	0000184
9	r7		$\emptyset \xrightarrow{\text{taRNA, mGFPcr}}$ pGFP	0000184
10	r8		pT7 $\longrightarrow \emptyset$	0000179
11	r9		pGFP $\longrightarrow \emptyset$	0000179
12	r10a		$\emptyset \xrightarrow{\text{pT7}}$ mT3cr	0000183
13	r10b		mT3cr $\longrightarrow \emptyset$	0000179
14	r11		$\emptyset \xrightarrow{\text{taRNA, mT3cr}}$ pT3	0000184
15	r12		pT3 $\longrightarrow \emptyset$	0000179

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8.1 Reaction r0

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

SBO:0000179 degradation

Reaction equation

$$\text{ara} \longrightarrow \emptyset \tag{18}$$

Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
ara		

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \text{vol}(\text{cell}) \cdot \begin{cases} \text{cAra} & \text{if } (\text{pulse\_flag} = 1) \wedge ([\text{ara}] > 0) \\ \text{dAra} \cdot [\text{ara}] & \text{otherwise} \end{cases} \tag{19}$$

8.2 Reaction r1a

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

SBO:0000183 transcription

Reaction equation

$$\emptyset \xrightarrow{\text{ara}} \text{taRNA} \tag{20}$$

Modifier

Table 7: Properties of each modifier.

Id	Name	SBO
ara		

Product

Table 8: Properties of each product.

Id	Name	SBO
taRNA		

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \mathrm{vol}\,(\mathrm{cell}) \cdot \left(\frac{\mathrm{sT} \cdot [\mathrm{ara}]}{[\mathrm{ara}] + \mathrm{k\_ara}} + \mathrm{s0\_taRNA} \right) \tag{21}$$

8.3 Reaction r1b

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

SBO:0000179 degradation

Reaction equation

$$\mathrm{taRNA} \longrightarrow \emptyset \tag{22}$$

Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
taRNA		

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{d\_taRNA} \cdot [\mathrm{taRNA}] \tag{23}$$

8.4 Reaction r2a

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

SBO:0000183 transcription

Reaction equation

$$\emptyset \longrightarrow \mathrm{mT7cr} \tag{24}$$

Product

Table 10: Properties of each product.

Id	Name	SBO
mT7cr		

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{s0\_mT7cr} \tag{25}$$

8.5 Reaction r2b

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

SBO:0000179 degradation

Reaction equation

$$\mathrm{mT7cr} \longrightarrow \emptyset \tag{26}$$

Reactant

Table 11: Properties of each reactant.

Id	Name	SBO
mT7cr		

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{d\_mT7} \cdot [\mathrm{mT7cr}] \tag{27}$$

8.6 Reaction r3a

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

SBO:0000183 transcription

Reaction equation

$$\emptyset \xrightarrow{\text{pT3}} \text{mGFPcr} \tag{28}$$

Modifier

Table 12: Properties of each modifier.

Id	Name	SBO
pT3		

Product

Table 13: Properties of each product.

Id	Name	SBO
mGFPcr		

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \text{vol}\,(\text{cell}) \cdot \left(\text{s0\_mGFPcr} + \frac{\text{k\_pT3} \cdot [\text{pT3}]^{\text{n3}}}{\text{km3}^{\text{n3}} + [\text{pT3}]^{\text{n3}}} \right) \tag{29}$$

8.7 Reaction r3b

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

SBO:0000179 degradation

Reaction equation

$$\text{mGFPcr} \longrightarrow \emptyset \tag{30}$$

Reactant

Table 14: Properties of each reactant.

Id	Name	SBO
mGFPcr		

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{d\_mGFP} \cdot [\mathrm{mGFPcr}] \tag{31}$$

8.8 Reaction r6

This is an irreversible reaction of no reactant forming one product influenced by two modifiers.

SBO:0000184 translation

Reaction equation

$$\emptyset \xrightarrow{\text{taRNA, mT7cr}} \mathrm{pT7} \tag{32}$$

Modifiers

Table 15: Properties of each modifier.

Id	Name	SBO
taRNA		
mT7cr		

Product

Table 16: Properties of each product.

Id	Name	SBO
pT7		

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \mathrm{vol}\,(\mathrm{cell}) \cdot (\mathrm{s0\_pT7} \cdot [\mathrm{mT7cr}] + \mathrm{s\_pT7k} \cdot [\mathrm{mT7cr}] \cdot [\mathrm{taRNA}]) \tag{33}$$

8.9 Reaction r7

This is an irreversible reaction of no reactant forming one product influenced by two modifiers.

SBO:0000184 translation

Reaction equation

$$\emptyset \xrightarrow{\text{taRNA, mGFPcr}} \text{pGFP} \tag{34}$$

Modifiers

Table 17: Properties of each modifier.

Id	Name	SBO
taRNA		
mGFPcr		

Product

Table 18: Properties of each product.

Id	Name	SBO
pGFP		

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \text{vol}\,(\text{cell}) \cdot (\text{s0\_pGFP} \cdot [\text{mGFPcr}] + \text{s\_pGFPk} \cdot [\text{mGFPcr}] \cdot [\text{taRNA}]) \tag{35}$$

8.10 Reaction r8

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

SBO:0000179 degradation

Reaction equation

$$\text{pT7} \longrightarrow \emptyset \tag{36}$$

Reactant

Table 19: Properties of each reactant.

Id	Name	SBO
pT7		

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{d\_pT7} \cdot [\mathrm{pT7}] \tag{37}$$

8.11 Reaction r9

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

SBO:0000179 degradation

Reaction equation

$$\mathrm{pGFP} \longrightarrow \emptyset \tag{38}$$

Reactant

Table 20: Properties of each reactant.

Id	Name	SBO
pGFP		

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{d\_pGFP} \cdot [\mathrm{pGFP}] \tag{39}$$

8.12 Reaction r10a

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

SBO:0000183 transcription

Reaction equation

$$\emptyset \xrightarrow{\mathrm{pT7}} \mathrm{mT3cr} \tag{40}$$

Modifier

Table 21: Properties of each modifier.

Id	Name	SBO
pT7		

Product

Table 22: Properties of each product.

Id	Name	SBO
mT3cr		

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = \mathrm{vol}\,(\mathrm{cell}) \cdot \left(\mathrm{s0\_mT3cr} + \frac{\mathrm{k\_pT7} \cdot [\mathrm{pT7}]^{\mathrm{n7}}}{\mathrm{km7}^{\mathrm{n7}} + [\mathrm{pT7}]^{\mathrm{n7}}} \right) \tag{41}$$

8.13 Reaction r10b

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

SBO:0000179 degradation

Reaction equation

$$\mathrm{mT3cr} \longrightarrow \emptyset \tag{42}$$

Reactant

Table 23: Properties of each reactant.

Id	Name	SBO
mT3cr		

Kinetic Law

Derived unit contains undeclared units

$$v_{13} = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{d\_mT3} \cdot [\mathrm{mT3cr}] \tag{43}$$

8.14 Reaction r11

This is an irreversible reaction of no reactant forming one product influenced by two modifiers.

SBO:0000184 translation

Reaction equation

$$\emptyset \xrightarrow{\text{taRNA, mT3cr}} \text{pT3} \tag{44}$$

Modifiers

Table 24: Properties of each modifier.

Id	Name	SBO
taRNA		
mT3cr		

Product

Table 25: Properties of each product.

Id	Name	SBO
pT3		

Kinetic Law

Derived unit contains undeclared units

$$v_{14} = \text{vol}(\text{cell}) \cdot (\text{s0\_pT3} \cdot [\text{mT3cr}] + \text{s\_pT3k} \cdot [\text{taRNA}] \cdot [\text{mT3cr}]) \tag{45}$$

8.15 Reaction r12

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

SBO:0000179 degradation

Reaction equation

$$\text{pT3} \longrightarrow \emptyset \tag{46}$$

Reactant

Table 26: Properties of each reactant.

Id	Name	SBO
pT3		

Kinetic Law

Derived unit contains undeclared units

$$v_{15} = \mathrm{vol}\,(\mathrm{cell}) \cdot \mathrm{d\_pT3} \cdot [\mathrm{pT3}] \tag{47}$$

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 `taRNA`

SBO:0000250 ribonucleic acid

Initial concentration $0.006796941377\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

This species takes part in five reactions (as a reactant in `r1b` and as a product in `r1a` and as a modifier in `r6`, `r7`, `r11`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{taRNA} = v_2 - v_3 \tag{48}$$

9.2 Species `mT7cr`

SBO:0000250 ribonucleic acid

Initial concentration $0.3569405099\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

This species takes part in three reactions (as a reactant in `r2b` and as a product in `r2a` and as a modifier in `r6`).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{mT7cr} = v_4 - v_5 \tag{49}$$

9.3 Species mGFPcr

SBO:0000250 ribonucleic acid

Initial concentration $0.176991329\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in three reactions (as a reactant in r3b and as a product in r3a and as a modifier in r7).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{mGFPcr} = v_6 - v_7 \tag{50}$$

9.4 Species pT7

SBO:0000252 polypeptide chain

Initial concentration $0.05230744612\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in three reactions (as a reactant in r8 and as a product in r6 and as a modifier in r10a).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{pT7} = v_8 - v_{10} \tag{51}$$

9.5 Species pGFP

SBO:0000252 polypeptide chain

Initial concentration $6.338921181\ \mathrm{mol}\cdot\mathrm{l}^{-1}$

This species takes part in two reactions (as a reactant in r9 and as a product in r7).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{pGFP} = v_9 - v_{11} \tag{52}$$

9.6 Species ara

SBO:0000247 simple chemical

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

Involved in events pulse_start1, pulse_start2, pulse_start3

This species takes part in two reactions (as a reactant in r0 and as a modifier in r1a).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{ara} = -v_1 \tag{53}$$

Furthermore, three events influence this species' rate of change.

9.7 Species pT3

SBO:0000252 polypeptide chain

Initial concentration $6.41674 \cdot 10^{-5}\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

This species takes part in three reactions (as a reactant in r12 and as a product in r11 and as a modifier in r3a).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{pT3} = v_{14} - v_{15} \tag{54}$$

9.8 Species mT3cr

SBO:0000250 ribonucleic acid

Initial concentration $0.00566438\ \mathrm{mol} \cdot \mathrm{l}^{-1}$

This species takes part in three reactions (as a reactant in r10b and as a product in r10a and as a modifier in r11).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{mT3cr} = v_{12} - v_{13} \tag{55}$$

A Glossary of Systems Biology Ontology Terms

SBO:0000179 **degradation:** Complete disappearance of a physical entity

SBO:0000183 **transcription:** Process through which a DNA sequence is copied to produce a complementary RNA

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

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

SBO:0000250 **ribonucleic acid:** Macromolecule formed by a repetition of ribonucleosides linked by phosphodiester bonds. CHEBI:3369

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

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