SBML Model Report

Model name: "Veening2008_DegU_Regulation"

May 6, 2016

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following three authors: Vijayalakshmi Chelliah[1], Jan-Willem Veening[2] and Oleg A Igoshin[3] at December second 2008 at 4:57 p. m. and last time modified at April fourth 2014 at 3:38 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	6
events	0	constraints	0
reactions	14	function definitions	0
global parameters	23	unit definitions	2
rules	3	initial assignments	0

Model Notes

This a model from the article:
Transient heterogeneity in extracellular protease production by Bacillus subtilis.
Veening JW, Igoshin OA, Eijlander RT, Nijland R, Hamoen LW, Kuipers OP Mol. Syst. Biol.

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2008 ; Volume: 4 : 184 18414485,
Abstract:
The most sophisticated survival strategy Bacillus subtilis employs is the differentiation of a subpopulation of cells into highly resistant endospores. To examine the expression patterns of non-sporulating cells within heterogeneous populations, we used buoyant density centrifugation to separate vegetative cells from endospore-containing cells and compared the transcriptome profiles of both subpopulations. This demonstrated the differential expression of various regulons. Subsequent single-cell analyses using promoter-gfp fusions confirmed our microarray results. Surprisingly, only part of the vegetative subpopulation highly and transiently expresses genes encoding the extracellular proteases Bpr (bacillopeptidase) and AprE (subtilisin), both of which are under the control of the DegU transcriptional regulator. As these proteases and their degradation products freely diffuse within the liquid growth medium, all cells within the clonal population are expected to benefit from their activities, suggesting that B. subtilis employs cooperative or even altruistic behavior. To unravel the mechanisms by which protease production heterogeneity within the non-sporulating subpopulation is established, we performed a series of genetic experiments combined with mathematical modeling. Simulations with our model yield valuable insights into how population heterogeneity may arise by the relatively long and variable response times within the DegU autoactivating pathway.

2 Unit Definitions

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

2.1 Unit `volume`

Name femtolitre

Definition fl

2.2 Unit `substance`

Name molecules

Definition item

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
univ		0000290	3	1	litre	☑	

3.1 Compartment univ

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

SBO:0000290 physical compartment

4 Species

This model contains six species. Section 8 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
AprE		univ	$\text{item} \cdot \text{fl}^{-1}$	⊟	⊟
DegU		univ	$\text{item} \cdot \text{fl}^{-1}$	⊟	⊟
DegUP		univ	$\text{item} \cdot \text{fl}^{-1}$	⊟	⊟
Dim		univ	$\text{item} \cdot \text{fl}^{-1}$	⊟	⊟
mAprE		univ	$\text{item} \cdot \text{fl}^{-1}$	⊟	⊟
mDegU		univ	$\text{item} \cdot \text{fl}^{-1}$	⊟	⊟

5 Parameters

This model contains 23 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Imax		0000186	0.048		☑
Io		0000186	0.004		☑
Irmax		0000186	0.400		☑
Iro		0000186	0.020		☑
K		0000281	7.000		☑
Kdim		0000281	12.000		☑
Kr		0000282	7.000		☑
Kr1		0000282	7.000		☑
R			7.000		☑
V			1.000		☑
ka		0000341	0.025		☑
kd		0000282	0.100		☑
kdeg		0000009	$4 \cdot 10^{-4}$		☑
kdegA		0000009	10^{-4}		☑
kdegm		0000009	0.010		☑
kdephos		0000009	0.000		☐
kphos		0000009	0.000		☐
ksyn		0000009	0.040		☑
ksyn1		0000009	0.040		☑
p			0.150		☑
q			0.004		☑
ratio	kphosratiokdephos		0.027		☑
DegU_Total	DegU_Total		0.000		☐

6 Rules

This is an overview of three rules.

6.1 Rule kphos

Rule kphos is an assignment rule for parameter kphos:

$$\text{kphos} = \text{ratio} \cdot \text{p} \tag{1}$$

6.2 Rule kdephos

Rule kdephos is an assignment rule for parameter kdephos:

$$\text{kdephos} = \frac{\text{q}}{\text{ratio}} \tag{2}$$

6.3 Rule DegU_Total

Rule DegU_Total is an assignment rule for parameter DegU_Total:

$$\text{DegU\_Total} = [\text{DegU}] + [\text{DegUP}] + 2 \cdot [\text{Dim}] \tag{3}$$

7 Reactions

This model contains 14 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	AprEdeg		$\mathrm{AprE} \longrightarrow \emptyset$	0000179
2	AprEsyn		$\emptyset \xrightarrow{\mathrm{mAprE}} \mathrm{AprE}$	0000184
3	DimerAss		$2\,\mathrm{DegUP} \longrightarrow \mathrm{Dim}$	0000412
4	DimerDis		$\mathrm{Dim} \longrightarrow 2\,\mathrm{DegUP}$	0000180
5	degradation1		$\mathrm{DegU} \longrightarrow \emptyset$	0000179
6	degradation2		$\mathrm{DegUP} \longrightarrow \emptyset$	0000179
7	degradation3		$\mathrm{Dim} \longrightarrow \emptyset$	0000179
8	degradationmRNA		$\mathrm{mDegU} \longrightarrow \emptyset$	0000179
9	dephosphorylation		$\mathrm{DegUP} \longrightarrow \mathrm{DegU}$	0000330
10	mRNAAprEdeg		$\mathrm{mAprE} \longrightarrow \emptyset$	0000179
11	mRNAAprEsyn		$\emptyset \xrightarrow{\mathrm{Dim}} \mathrm{mAprE}$	0000183
12	phosphorylation		$\mathrm{DegU} \longrightarrow \mathrm{DegUP}$	0000216
13	synthesisDegU		$\emptyset \xrightarrow{\mathrm{mDegU}} \mathrm{DegU}$	0000184
14	synthesismRNA		$\emptyset \xrightarrow{\mathrm{Dim}} \mathrm{mDegU}$	0000183

7.1 Reaction AprEdeg

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

SBO:0000179 degradation

Reaction equation

$$\text{AprE} \longrightarrow \emptyset \tag{4}$$

Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
AprE		

Kinetic Law

Derived unit contains undeclared units

$$v_1 = \text{kdeg} \cdot [\text{AprE}] \tag{5}$$

7.2 Reaction AprEsyn

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

SBO:0000184 translation

Reaction equation

$$\emptyset \xrightarrow{\text{mAprE}} \text{AprE} \tag{6}$$

Modifier

Table 7: Properties of each modifier.

Id	Name	SBO
mAprE		

Product

Table 8: Properties of each product.

Id	Name	SBO
AprE		

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \text{ksyn} \cdot [\text{mAprE}] \cdot \text{vol}(\text{univ}) \tag{7}$$

7.3 Reaction DimerAss

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

SBO:0000412 biological activity

Reaction equation

$$2\,\text{DegUP} \longrightarrow \text{Dim} \tag{8}$$

Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
DegUP		

Product

Table 10: Properties of each product.

Id	Name	SBO
Dim		

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \text{ka} \cdot [\text{DegUP}]^2 \tag{9}$$

7.4 Reaction `DimerDis`

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

SBO:0000180 dissociation

Reaction equation

$$\mathrm{Dim} \longrightarrow 2\,\mathrm{DegUP} \tag{10}$$

Reactant

Table 11: Properties of each reactant.

Id	Name	SBO
`Dim`		

Product

Table 12: Properties of each product.

Id	Name	SBO
`DegUP`		

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \mathrm{kd} \cdot [\mathrm{Dim}] \tag{11}$$

7.5 Reaction `degradation1`

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

SBO:0000179 degradation

Reaction equation

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

Reactant

Table 13: Properties of each reactant.

Id	Name	SBO
DegU		

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \text{kdeg} \cdot [\text{DegU}] \cdot \text{vol}(\text{univ}) \tag{13}$$

7.6 Reaction degradation2

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

SBO:0000179 degradation

Reaction equation

$$\text{DegUP} \longrightarrow \emptyset \tag{14}$$

Reactant

Table 14: Properties of each reactant.

Id	Name	SBO
DegUP		

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \text{kdeg} \cdot [\text{DegUP}] \cdot \text{vol}(\text{univ}) \tag{15}$$

7.7 Reaction degradation3

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

SBO:0000179 degradation

Reaction equation

$$\text{Dim} \longrightarrow \emptyset \tag{16}$$

Reactant

Table 15: Properties of each reactant.

Id	Name	SBO
Dim		

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \text{kdeg} \cdot [\text{Dim}] \cdot \text{vol}\,(\text{univ}) \tag{17}$$

7.8 Reaction degradationmRNA

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

SBO:0000179 degradation

Reaction equation

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

Reactant

Table 16: Properties of each reactant.

Id	Name	SBO
mDegU		

Kinetic Law

Derived unit contains undeclared units

$$v_8 = \text{kdegm} \cdot [\text{mDegU}] \tag{19}$$

7.9 Reaction dephosphorylation

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

SBO:0000330 dephosphorylation

Reaction equation

$$\text{DegUP} \longrightarrow \text{DegU} \tag{20}$$

Reactant

Table 17: Properties of each reactant.

Id	Name	SBO
DegUP		

Product

Table 18: Properties of each product.

Id	Name	SBO
DegU		

Kinetic Law

Derived unit contains undeclared units

$$v_9 = \text{kdephos} \cdot [\text{DegUP}] \tag{21}$$

7.10 Reaction mRNAAprEdeg

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

SBO:0000179 degradation

Reaction equation

$$\text{mAprE} \longrightarrow \emptyset \tag{22}$$

Reactant

Table 19: Properties of each reactant.

Id	Name	SBO
mAprE		

Kinetic Law

Derived unit contains undeclared units

$$v_{10} = \text{kdegm} \cdot [\text{mAprE}] \tag{23}$$

7.11 Reaction mRNAAprEsyn

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

SBO:0000183 transcription

Reaction equation

$$\emptyset \xrightarrow{\text{Dim}} \text{mAprE} \tag{24}$$

Modifier

Table 20: Properties of each modifier.

Id	Name	SBO
Dim		

Product

Table 21: Properties of each product.

Id	Name	SBO
mAprE		

Kinetic Law

Derived unit contains undeclared units

$$v_{11} = \frac{\text{Kr1}}{\text{R} + \text{Kr1}} \cdot \left(\frac{\text{Iro} \cdot \left(\frac{[\text{Dim}] \cdot \text{vol}(\text{univ})}{\text{Kdim}} + 1 \right)}{1 + \frac{[\text{Dim}] \cdot \text{vol}(\text{univ})}{\text{Kdim}} + \frac{([\text{Dim}] \cdot \text{vol}(\text{univ}))^2}{\text{Kdim}^2} + \frac{\text{R}}{\text{Kr}}} + \frac{\text{Irmax} \cdot ([\text{Dim}] \cdot \text{vol}(\text{univ}))^2}{\text{Kdim}^2 \cdot \left(1 + \frac{[\text{Dim}] \cdot \text{vol}(\text{univ})}{\text{Kdim}} + \frac{([\text{Dim}] \cdot \text{vol}(\text{univ}))^2}{\text{Kdim}^2} + \frac{\text{R}}{\text{Kr}} \right)} \right) \tag{25}$$

7.12 Reaction phosphorylation

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

SBO:0000216 phosphorylation

Reaction equation

$$\text{DegU} \longrightarrow \text{DegUP} \tag{26}$$

Reactant

Table 22: Properties of each reactant.

Id	Name	SBO
DegU		

Product

Table 23: Properties of each product.

Id	Name	SBO
DegUP		

Kinetic Law

Derived unit contains undeclared units

$$v_{12} = \text{kphos} \cdot [\text{DegU}] \tag{27}$$

7.13 Reaction synthesisDegU

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

SBO:0000184 translation

Reaction equation

$$\emptyset \xrightarrow{\text{mDegU}} \text{DegU} \tag{28}$$

Modifier

Table 24: Properties of each modifier.

Id	Name	SBO
mDegU		

Product

Table 25: Properties of each product.

Id	Name	SBO
DegU		

Kinetic Law

Derived unit contains undeclared units

$$v_{13} = \text{ksyn1} \cdot [\text{mDegU}] \cdot \text{vol}(\text{univ}) \tag{29}$$

7.14 Reaction synthesismRNA

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

SBO:0000183 transcription

Reaction equation

$$\emptyset \xrightarrow{\text{Dim}} \text{mDegU} \tag{30}$$

Modifier

Table 26: Properties of each modifier.

Id	Name	SBO
Dim		

Product

Table 27: Properties of each product.

Id	Name	SBO
mDegU		

Kinetic Law

Derived unit contains undeclared units

$$v_{14} = \frac{\text{Io} \cdot \text{K}}{[\text{Dim}] \cdot \text{vol}(\text{univ}) + \text{K}} + \frac{\text{Imax} \cdot [\text{Dim}] \cdot \text{vol}(\text{univ})}{[\text{Dim}] \cdot \text{vol}(\text{univ}) + \text{K}} \tag{31}$$

8 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.

8.1 Species AprE

SBO:0000245 macromolecule

Initial amount 0 item

This species takes part in two reactions (as a reactant in AprEdeg and as a product in AprEsyn).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{AprE} = v_2 - v_1 \tag{32}$$

8.2 Species DegU

SBO:0000245 macromolecule

Initial amount 10 item

This species takes part in four reactions (as a reactant in degradation1, phosphorylation and as a product in dephosphorylation, synthesisDegU).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{DegU} = v_9 + v_{13} - v_5 - v_{12} \tag{33}$$

8.3 Species DegUP

SBO:0000245 macromolecule

Initial amount 0 item

This species takes part in five reactions (as a reactant in DimerAss, degradation2, dephosphorylation and as a product in DimerDis, phosphorylation).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{DegUP} = 2\,v_4 + v_{12} - 2\,v_3 - v_6 - v_9 \tag{34}$$

8.4 Species Dim

SBO:0000420 multimer of macromolecules

Initial amount 0 item

This species takes part in five reactions (as a reactant in DimerDis, degradation3 and as a product in DimerAss and as a modifier in mRNAAprEsyn, synthesismRNA).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{Dim} = v_3 - v_4 - v_7 \tag{35}$$

8.5 Species mAprE

SBO:0000278 messenger RNA

Initial amount 0 item

This species takes part in three reactions (as a reactant in mRNAAprEdeg and as a product in mRNAAprEsyn and as a modifier in AprEsyn).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{mAprE} = v_{11} - v_{10} \tag{36}$$

8.6 Species mDegU

SBO:0000278 messenger RNA

Initial amount 0 item

This species takes part in three reactions (as a reactant in degradationmRNA and as a product in synthesismRNA and as a modifier in synthesisDegU).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{mDegU} = v_{14} - v_8 \tag{37}$$

A Glossary of Systems Biology Ontology Terms

SBO:0000009 kinetic constant: Numerical parameter that quantifies the velocity of a chemical reaction

SBO:0000179 degradation: Complete disappearance of a physical entity

SBO:0000180 dissociation: Transformation of a non-covalent complex that results in the formation of several independent biochemical entitie

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:0000186 maximal velocity: Limiting maximal velocity of an enzymatic reaction, reached when the substrate is in large excess and all the enzyme is complexed.

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

SBO:0000245 macromolecule: Molecular entity mainly built-up by the repetition of pseudo-identical units. CHEBI:3383

SBO:0000278 messenger RNA: A messenger RNA is a ribonucleic acid synthesized during the transcription of a gene, and that carries the information to encode one or several proteins

SBO:0000281 equilibrium constant: Quantity characterizing a chemical equilibrium in a chemical reaction, which is a useful tool to determine the concentration of various reactants or products in a system where chemical equilibrium occurs

SBO:0000282 dissociation constant: Equilibrium constant that measures the propensity of a larger object to separate (dissociate) reversibly into smaller components, as when a complex falls apart into its component molecules, or when a salt splits up into its component ions. The dissociation constant is usually denoted Kd and is the inverse of the affinity constant.

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

SBO:0000341 association rate constant: Rate with which components associate into a complex

SBO:0000412 biological activity: The potential action that a biological entity has on other entities. Example are enzymatic activity, binding activity etc

SBO:0000420 multimer of macromolecules: Non-covalent association between several macromolecule

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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