

SBML Model Report

Model name: “Smallbone2013 - Colon Crypt cycle - Version 3”



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: Vijayalakshmi Chelliah¹ and Kieran Smallbone² at December first 2011 at no o’ clock in the morning. and last time modified at February 28th 2014 at 4:52 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	4
events	0	constraints	0
reactions	9	function definitions	0
global parameters	20	unit definitions	6
rules	6	initial assignments	0

Model Notes

Smallbone2013 - Colon Crypt cycle - Version 3

This model is described in the article:[A mathematical model of the colon crypt capturing compositional dynamic interactions between cell types](#)Kieran Smallbone, Bernard M. CorfeInt J Exp Pathol. 2014 Feb;95(1):1-7.

¹EMBL-EBI, viji@ebi.ac.uk

²University of Manchester, kieran.smallbone@manchester.ac.uk

Abstract:

Models of the development and early progression of colorectal cancer are based upon understanding the cycle of stem cell turnover, proliferation, differentiation and death. Existing crypt compartmental models feature a linear pathway of cell types, with little regulatory mechanism. Previous work has shown that there are perturbations in the enteroendocrine cell population of macroscopically normal crypts, a compartment not included in existing models. We show that existing models do not adequately recapitulate the dynamics of cell fate pathways in the crypt. We report the progressive development, iterative testing and fitting of a developed compartmental model with additional cell types, and which includes feedback mechanisms and cross-regulatory mechanisms between cell types. The fitting of the model to existing data sets suggests a need to invoke cross-talk between cell types as a feature of colon crypt cycle models.

This model is hosted on [BioModels Database](#) and identified by: [MODEL1306190003](#).

To cite BioModels Database, please use: [BioModels Database: An enhanced, curated and annotated resource for published quantitative kinetic models](#).

To the extent possible under law, all copyright and related or neighbouring rights to this encoded model have been dedicated to the public domain worldwide. Please refer to [CC0 Public Domain Dedication](#) for more information.

2 Unit Definitions

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

2.1 Unit `substance`

Name cell

Definition item

2.2 Unit `time`

Name day

Definition 86400 s

2.3 Unit `volume`

Definition dimensionless

2.4 Unit `per_day`

Name per day

Definition $(86400\text{ s})^{-1}$

2.5 Unit `cell`

Name `cell`

Definition `item`

2.6 Unit `cell_per_day`

Name `cell_per_day`

Definition `item · (86400 s)-1`

2.7 Unit `area`

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

Definition `m2`

2.8 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
<code>compartment</code>	<code>crypt</code>		3	1	dimensionless	<input checked="" type="checkbox"/>	

3.1 Compartment `compartment`

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

Name `crypt`

4 Species

This model contains four 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
N0	N0	compartment	item dimensionless ⁻¹	· ⊖	⊖
N1	N1	compartment	item dimensionless ⁻¹	· ⊖	⊖
N2	N2	compartment	item dimensionless ⁻¹	· ⊖	⊖
N3	N3	compartment	item dimensionless ⁻¹	· ⊖	⊖

5 Parameters

This model contains 20 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
d0			0.020	$(86400 \text{ s})^{-1}$	<input checked="" type="checkbox"/>
d1			0.548	$(86400 \text{ s})^{-1}$	<input checked="" type="checkbox"/>
d2			1.889	$(86400 \text{ s})^{-1}$	<input checked="" type="checkbox"/>
T	cellularity		0.000	item	<input type="checkbox"/>
K	capacity		106.090	item	<input checked="" type="checkbox"/>
r0			1.999	$(86400 \text{ s})^{-1}$	<input checked="" type="checkbox"/>
f0	N0 division rate		0.000	$\text{item} \cdot (86400 \text{ s})^{-1}$	<input type="checkbox"/>
p00			0.000	dimensionless	<input type="checkbox"/>
p01			0.631	dimensionless	<input checked="" type="checkbox"/>
r1			10.586	$(86400 \text{ s})^{-1}$	<input checked="" type="checkbox"/>
f1	N1 division rate		0.000	$\text{item} \cdot (86400 \text{ s})^{-1}$	<input type="checkbox"/>
p11			0.000	dimensionless	<input type="checkbox"/>
p12			0.805	dimensionless	<input checked="" type="checkbox"/>
p03			0.000	dimensionless	<input type="checkbox"/>
q03			0.935	dimensionless	<input checked="" type="checkbox"/>
K03			0.784	item	<input checked="" type="checkbox"/>
d3			0.168	$(86400 \text{ s})^{-1}$	<input checked="" type="checkbox"/>
K0X			0.154	item	<input checked="" type="checkbox"/>
K1X			15.365	item	<input checked="" type="checkbox"/>
K2X			2.704	item	<input checked="" type="checkbox"/>

6 Rules

This is an overview of six rules.

6.1 Rule T

Rule T is an assignment rule for parameter T:

$$T = [N0] + [N1] + [N2] + [N3] \quad (1)$$

Derived unit item

6.2 Rule f0

Rule f0 is an assignment rule for parameter f0:

$$f0 = r0 \cdot [N0] \cdot \left(1 - \frac{T}{K}\right) \quad (2)$$

6.3 Rule p00

Rule p00 is an assignment rule for parameter p00:

$$p00 = 1 - p01 - p03 \quad (3)$$

6.4 Rule f1

Rule f1 is an assignment rule for parameter f1:

$$f1 = r1 \cdot [N1] \cdot \left(1 - \frac{T}{K}\right) \quad (4)$$

6.5 Rule p11

Rule p11 is an assignment rule for parameter p11:

$$p11 = 1 - p12 \quad (5)$$

6.6 Rule p03

Rule p03 is an assignment rule for parameter p03:

$$p03 = \frac{q03 \cdot K03}{[N3] + K03} \quad (6)$$

Derived unit dimensionless

7 Reactions

This model contains nine 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

Nº	Id	Name	Reaction Equation	SBO
1	R0X	N0 death	$N0 \xrightarrow{N3, N0, N3} \emptyset$	
2	R01	N0 differentiation to N1	$N0 \longrightarrow N0 + N1$	
3	R00	N0 renewal	$N0 \longrightarrow 2 N0$	
4	R1X	N1 death	$N1 \xrightarrow{N3, N1, N3} \emptyset$	
5	R12	N1 differentiation	$N1 \longrightarrow N1 + N2$	
6	R11	N1 renewal	$N1 \longrightarrow 2 N1$	
7	R2X	N2 death	$N2 \xrightarrow{N3, N2, N3} \emptyset$	
8	R03	N0 differentiation to N3	$N0 \longrightarrow N0 + N3$	
9	R3X	N3 death	$N3 \xrightarrow{N3} \emptyset$	

7.1 Reaction R0X

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

Name N0 death

Reaction equation



Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
N0	N0	

Modifiers

Table 7: Properties of each modifier.

Id	Name	SBO
N3	N3	
N0	N0	
N3	N3	

Kinetic Law

Derived unit $(86400 \text{ s})^{-1} \cdot \text{item}$

$$v_1 = \frac{d0 \cdot [\text{N0}] \cdot K0X}{[\text{N3}] + K0X} \quad (8)$$

7.2 Reaction R01

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

Name N0 differentiation to N1

Reaction equation



Reactant

Table 8: Properties of each reactant.

Id	Name	SBO
N0	N0	

Products

Table 9: Properties of each product.

Id	Name	SBO
N0	N0	
N1	N1	

Kinetic Law

Derived unit $\text{item} \cdot (86400 \text{ s})^{-1}$

$$v_2 = p01 \cdot f0 \quad (10)$$

7.3 Reaction R00

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

Name N0 renewal

Reaction equation



Reactant

Table 10: Properties of each reactant.

Id	Name	SBO
N0	N0	

Product

Table 11: Properties of each product.

Id	Name	SBO
N0	N0	

Id	Name	SBO
----	------	-----

Kinetic Law

Derived unit $\text{item} \cdot (86400 \text{ s})^{-1}$

$$v_3 = p00 \cdot f0 \quad (12)$$

7.4 Reaction R1X

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

Name N1 death

Reaction equation



Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
N1	N1	

Modifiers

Table 13: Properties of each modifier.

Id	Name	SBO
N3	N3	
N1	N1	
N3	N3	

Kinetic Law

Derived unit $(86400 \text{ s})^{-1} \cdot \text{item}$

$$v_4 = \frac{d1 \cdot [\text{N1}] \cdot K1X}{[\text{N3}] + K1X} \quad (14)$$

7.5 Reaction R12

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

Name N1 differentiation

Reaction equation



Reactant

Table 14: Properties of each reactant.

Id	Name	SBO
N1	N1	

Products

Table 15: Properties of each product.

Id	Name	SBO
N1	N1	
N2	N2	

Kinetic Law

Derived unit $\text{item} \cdot (86400 \text{ s})^{-1}$

$$v_5 = p_{12} \cdot f_1 \quad (16)$$

7.6 Reaction R11

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

Name N1 renewal

Reaction equation



Reactant

Table 16: Properties of each reactant.

Id	Name	SBO
N1	N1	

Product

Table 17: Properties of each product.

Id	Name	SBO
N1	N1	

Kinetic Law

Derived unit $\text{item} \cdot (86400 \text{ s})^{-1}$

$$v_6 = p11 \cdot f1 \tag{18}$$

7.7 Reaction R2X

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

Name N2 death

Reaction equation



Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
N2	N2	

Modifiers

Table 19: Properties of each modifier.

Id	Name	SBO
N3	N3	

Id	Name	SBO
N2	N2	
N3	N3	

Kinetic Law

Derived unit $(86400\text{ s})^{-1} \cdot \text{item}$

$$v_7 = \frac{d2 \cdot [\text{N2}] \cdot \text{K2X}}{[\text{N3}] + \text{K2X}} \quad (20)$$

7.8 Reaction R03

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

Name N0 differentiation to N3

Reaction equation



Reactant

Table 20: Properties of each reactant.

Id	Name	SBO
N0	N0	

Products

Table 21: Properties of each product.

Id	Name	SBO
N0	N0	
N3	N3	

Kinetic Law

Derived unit $\text{item} \cdot (86400\text{ s})^{-1}$

$$v_8 = p03 \cdot f0 \quad (22)$$

7.9 Reaction R3X

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

Name N3 death

Reaction equation



Reactant

Table 22: Properties of each reactant.

Id	Name	SBO
N3	N3	

Modifier

Table 23: Properties of each modifier.

Id	Name	SBO
N3	N3	

Kinetic Law

Derived unit $(86400 \text{ s})^{-1} \cdot \text{item}$

$$v_9 = d3 \cdot [\text{N3}] \quad (24)$$

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.

8.1 Species NO

Name NO

Initial amount 1.71589842441293 item

This species takes part in eight reactions (as a reactant in [R0X](#), [R01](#), [R00](#), [R03](#) and as a product in [R01](#), [R00](#), [R03](#) and as a modifier in [R0X](#)).

$$\frac{d}{dt}N0 = v_2 + 2v_3 + v_8 - v_1 - v_2 - v_3 - v_8 \quad (25)$$

8.2 Species N1

Name N1

Initial amount 26.8036712557471 item

This species takes part in seven reactions (as a reactant in [R1X](#), [R12](#), [R11](#) and as a product in [R01](#), [R12](#), [R11](#) and as a modifier in [R1X](#)).

$$\frac{d}{dt}N1 = v_2 + v_5 + 2v_6 - v_4 - v_5 - v_6 \quad (26)$$

8.3 Species N2

Name N2

Initial amount 44.6167755224769 item

This species takes part in three reactions (as a reactant in [R2X](#) and as a product in [R12](#) and as a modifier in [R2X](#)).

$$\frac{d}{dt}N2 = v_5 - v_7 \quad (27)$$

8.4 Species N3

Name N3

Initial amount 1.53646349229917 item

This species takes part in nine reactions (as a reactant in [R3X](#) and as a product in [R03](#) and as a modifier in [R0X](#), [R0X](#), [R1X](#), [R1X](#), [R2X](#), [R2X](#), [R3X](#)).

$$\frac{d}{dt}N3 = v_8 - v_9 \quad (28)$$

SBML²TeX 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.

^aCenter for Bioinformatics Tübingen (ZBIT), Germany

^bCalifornia Institute of Technology, Beckman Institute BNMC, Pasadena, United States

^cEuropean Bioinformatics Institute, Wellcome Trust Genome Campus, Hinxton, United Kingdom

^dEML Research gGmbH, Heidelberg, Germany