

## SBML Model Report

# Model name: “Hui2014 - Age-related changes in articular cartilage”



May 6, 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 Chelliah<sup>1</sup> and Carole Proctor<sup>2</sup> at December fifth 2014 at 5:02 p. m. and last time modified at April eighth 2016 at 5:51 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	4
species types	0	species	65
events	0	constraints	0
reactions	117	function definitions	0
global parameters	113	unit definitions	1
rules	0	initial assignments	0

## Model Notes

Hui2014 - Age-related changes in articularcartilage

This model is described in the article:[Oxidative changes and signalling pathways are pivotal in initiating age-related changes in articular cartilage](#)Wang Hui1, David A Young1, Andrew D Rowan1, Xin Xu2, Tim E Cawston1, Carole J Proctor1,3Annals of the Rheumatic Diseases

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Abstract:

**Objective:** To use a computational approach to investigate the cellular and extracellular matrix changes that occur with age in the knee joints of mice. **Methods:** Knee joints from an inbred C57/BL1/6 (ICRFa) mouse colony were harvested at 330 months of age. Sections were stained with H&E, Safranin-O, Picro-sirius red and antibodies to matrix metalloproteinase-13 (MMP-13), nitrotyrosine, LC-3B, Bcl-2, and cleaved type II collagen used for immunohistochemistry. Based on this and other data from the literature, a computer simulation model was built using the Systems Biology Markup Language using an iterative approach of data analysis and modelling. Individual parameters were subsequently altered to assess their effect on the model. **Results:** A progressive loss of cartilage matrix occurred with age. Nitrotyrosine, MMP-13 and anaplastic lymphoma kinase (ALK1) staining in cartilage increased with age with a concomitant decrease in LC-3B and Bcl-2. Stochastic simulations from the computational model showed a good agreement with these data, once transforming growth factor- $\beta$  signalling via ALK1/ALK5 receptors was included. Oxidative stress and the interleukin 1 pathway were identified as key factors in driving the cartilage breakdown associated with ageing. **Conclusions:** A progressive loss of cartilage matrix and cellularity occurs with age. This is accompanied with increased levels of oxidative stress, apoptosis and MMP-13 and a decrease in chondrocyte autophagy. These changes explain the marked predisposition of joints to develop osteoarthritis with age. Computational modelling provides useful insights into the underlying mechanisms involved in age-related changes in musculoskeletal tissues.

This model is hosted on [BioModels Database](#) and identified by: [BIOMD0000000560](#).

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

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## 2 Unit Definitions

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

### 2.1 Unit substance

**Definition** item

### 2.2 Unit volume

**Notes** Litre is the predefined SBML unit for volume.

**Definition** 1

### 2.3 Unit `area`

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

**Definition**  $\text{m}^2$

### 2.4 Unit `length`

**Notes** Metre is the predefined SBML unit for length since SBML Level 2 Version 1.

**Definition**  $\text{m}$

### 2.5 Unit `time`

**Notes** Second is the predefined SBML unit for time.

**Definition**  $\text{s}$

## 3 Compartments

This model contains four compartments.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
cell			3	1	litre	<input checked="" type="checkbox"/>	
nucleus			3	1	litre	<input checked="" type="checkbox"/>	
membrane			3	1	litre	<input checked="" type="checkbox"/>	
ecm			3	1	litre	<input checked="" type="checkbox"/>	

#### 3.1 Compartment `cell`

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

#### 3.2 Compartment `nucleus`

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

#### 3.3 Compartment `membrane`

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

### 3.4 Compartment $_{ecm}$

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

## 4 Species

This model contains 65 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 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 Condi- tion
	AcanmRNA	cell	item	<input type="checkbox"/>	<input type="checkbox"/>
	ADAMTS5	cell	item	<input type="checkbox"/>	<input type="checkbox"/>
	AGEprod	cell	item	<input type="checkbox"/>	<input type="checkbox"/>
	Alk1	cell	item	<input type="checkbox"/>	<input type="checkbox"/>
	Alk1_Alk5	cell	item	<input type="checkbox"/>	<input type="checkbox"/>
	Alk5	cell	item	<input type="checkbox"/>	<input type="checkbox"/>
	Alk5_dimer	cell	item	<input type="checkbox"/>	<input type="checkbox"/>
	Bax	cell	item	<input type="checkbox"/>	<input type="checkbox"/>
	Bax_Bcl2	cell	item	<input type="checkbox"/>	<input type="checkbox"/>
	Bax_Bcl2_Beclin	cell	item	<input type="checkbox"/>	<input type="checkbox"/>
	Bax_Bcl2_Beclin_I	cell	item	<input type="checkbox"/>	<input type="checkbox"/>
	Bcl2	cell	item	<input type="checkbox"/>	<input type="checkbox"/>
	Bcl2_Beclin	cell	item	<input type="checkbox"/>	<input type="checkbox"/>
	Bcl2_Beclin_I	cell	item	<input type="checkbox"/>	<input type="checkbox"/>
	Beclin	cell	item	<input type="checkbox"/>	<input type="checkbox"/>
	Beclin_I	cell	item	<input type="checkbox"/>	<input type="checkbox"/>
	Caspase_A	cell	item	<input type="checkbox"/>	<input type="checkbox"/>
	Caspase_I	cell	item	<input type="checkbox"/>	<input type="checkbox"/>
	Col2mRNA	cell	item	<input type="checkbox"/>	<input type="checkbox"/>
	DamP	cell	item	<input type="checkbox"/>	<input type="checkbox"/>
	IkB	cell	item	<input type="checkbox"/>	<input type="checkbox"/>

Id	Name	Compartment	Derived Unit	Constant	Boundary Condi- tion
IkB_NFkB		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
IL1		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
Lys_A		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
Lys_I		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
MMP13		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
MMP2		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
NatP		cell	item	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
NFkB		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
NFkB_P		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
p38		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
p38_P		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
proMMP13		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
proMMP2		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
RAGE		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
ROS		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
Runx2_A		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
Runx2_I		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
Smad1		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
Smad1_P		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
Smad1_P_Smad4		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
Smad2		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
Smad2_P		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
Smad2_P_Smad4		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
Smad4		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
Smad7		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
SOD		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
Sox9		cell	item	<input type="checkbox"/>	<input type="checkbox"/>

Id	Name	Compartment	Derived Unit	Constant	Boundary Condi- tion
Sox9_A		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
Sox9mRNA		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
Tgfb_A		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
Tgfb_Alk1_Alk5		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
Tgfb_Alk1_Alk5- _Smad7		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
Tgfb_Alk5_dimer		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
Tgfb_Alk5_dimer- _Smad7		cell	item	<input type="checkbox"/>	<input type="checkbox"/>
AggFrag		ecm	item	<input type="checkbox"/>	<input type="checkbox"/>
Aggrecan		ecm	item	<input type="checkbox"/>	<input type="checkbox"/>
Aggrecan- _Collagen2		ecm	item	<input type="checkbox"/>	<input type="checkbox"/>
ColFrag		ecm	item	<input type="checkbox"/>	<input type="checkbox"/>
Collagen2		ecm	item	<input type="checkbox"/>	<input type="checkbox"/>
Integrin		ecm	item	<input type="checkbox"/>	<input type="checkbox"/>
Tgfb_I		ecm	item	<input type="checkbox"/>	<input type="checkbox"/>
Sink		cell	item	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Source		cell	item	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
IntegrinCount		ecm	item	<input type="checkbox"/>	<input type="checkbox"/>

## 5 Parameters

This model contains 113 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
kactCasp			$10^{-7}$		✓
kactCaspBecI			$8.3 \cdot 10^{-7}$		✓
kactCaspp38			$8 \cdot 10^{-7}$		✓
kactIntegrin			$4 \cdot 10^{-7}$		✓
kactLys			$10^{-8}$		✓
kactMMP13			$10^{-4}$		✓
kactMMP2			$10^{-7}$		✓
kactNFkB			$10^{-4}$		✓
kactRAGE			0.001		✓
kactRunx2			0.001		✓
kactSox9			$5 \cdot 10^{-6}$		✓
kactTgfbIntegrin			0.001		✓
kactTgfbMMP2			$10^{-7}$		✓
kbinAggreCANCollagen2			$10^{-4}$		✓
kbinAlk1Alk5			$5 \cdot 10^{-5}$		✓
kbinBaxBcl2			1.670		✓
kbinBaxToBcl2Bec			$1.67 \cdot 10^{-4}$		✓
kbinBcl2Beclin			$7.5 \cdot 10^{-5}$		✓
kbinBecToBaxBcl2			$1.67 \cdot 10^{-5}$		✓
kbinSmad1Smad4			$5 \cdot 10^{-5}$		✓
kbinSmad2Smad4			$10^{-4}$		✓
kbinSmad7Alk1			0.500		✓
kbinSmad7Alk5			$2 \cdot 10^{-5}$		✓
kbinTgfbAlk1			$2 \cdot 10^{-5}$		✓
kbinTgfbAlk5			$3 \cdot 10^{-5}$		✓
kdamLys			$5 \cdot 10^{-6}$		✓
kdamNatP			$8 \cdot 10^{-6}$		✓
kdedimerAlk5			0.001		✓
kdegAcanmRNA			$9 \cdot 10^{-6}$		✓
kdegADAMTS5			$5 \cdot 10^{-5}$		✓
kdegAggreCAN			$10^{-9}$		✓
kdegAlk1			$1.2 \cdot 10^{-8}$		✓
kdegAlk5			$4 \cdot 10^{-7}$		✓
kdegBcl2			$1.67 \cdot 10^{-4}$		✓
kdegBcl2Casp			0.002		✓
kdegBcl2ROS			0.002		✓
kdegCol12mRNA			$1.07 \cdot 10^{-5}$		✓



Id	Name	SBO	Value	Unit	Constant
kdegCollagen			$10^{-8}$		<input checked="" type="checkbox"/>
kdegDamP			$4 \cdot 10^{-5}$		<input checked="" type="checkbox"/>
kdegIkB			$10^{-6}$		<input checked="" type="checkbox"/>
kdegIL1			0.005		<input checked="" type="checkbox"/>
kdegMMP13			$6.4 \cdot 10^{-6}$		<input checked="" type="checkbox"/>
kdegMMP2			$6.4 \cdot 10^{-6}$		<input checked="" type="checkbox"/>
kdegSmad7			0.005		<input checked="" type="checkbox"/>
kdegSmad7Alk1			$5 \cdot 10^{-6}$		<input checked="" type="checkbox"/>
kdegSmad7Alk5			$10^{-5}$		<input checked="" type="checkbox"/>
kdegSOD			0.001		<input checked="" type="checkbox"/>
kdegSox9			$4.8 \cdot 10^{-5}$		<input checked="" type="checkbox"/>
kdegSox9mRNA			$10^{-4}$		<input checked="" type="checkbox"/>
kdegTgfb			0.006		<input checked="" type="checkbox"/>
kdephosNFkB			0.010		<input checked="" type="checkbox"/>
kdephosp38			0.010		<input checked="" type="checkbox"/>
kdephosSmad1			$5 \cdot 10^{-4}$		<input checked="" type="checkbox"/>
kdephosSmad1Smad7			$6 \cdot 10^{-4}$		<input checked="" type="checkbox"/>
kdephosSmad2			0.006		<input checked="" type="checkbox"/>
kdimerAlk5			$2 \cdot 10^{-4}$		<input checked="" type="checkbox"/>
kgenROS			$5 \cdot 10^{-4}$		<input checked="" type="checkbox"/>
kgenROSbyDamP			$10^{-4}$		<input checked="" type="checkbox"/>
kgenROSbyp38			$10^{-4}$		<input checked="" type="checkbox"/>
kgenROSbyRAGE			$4 \cdot 10^{-4}$		<input checked="" type="checkbox"/>
kinactBec			$5 \cdot 10^{-10}$		<input checked="" type="checkbox"/>
kinactBecCasp			$10^{-8}$		<input checked="" type="checkbox"/>
kinactCasp			$3 \cdot 10^{-4}$		<input checked="" type="checkbox"/>
kinactCaspBcl2			$3 \cdot 10^{-4}$		<input checked="" type="checkbox"/>
kinactIntegrin			$5 \cdot 10^{-4}$		<input checked="" type="checkbox"/>
kinactNFkB			0.100		<input checked="" type="checkbox"/>
kinactRAGE			0.001		<input checked="" type="checkbox"/>
kinactRunx2			$5 \cdot 10^{-4}$		<input checked="" type="checkbox"/>
kinactSox9			0.002		<input checked="" type="checkbox"/>
kinactTgfb			0.050		<input checked="" type="checkbox"/>
kinhibLys			$7 \cdot 10^{-6}$		<input checked="" type="checkbox"/>
kphosNFkB			0.001		<input checked="" type="checkbox"/>
kphosp38			$10^{-7}$		<input checked="" type="checkbox"/>
kphosp38ROS			$10^{-4}$		<input checked="" type="checkbox"/>
kphosSmad1			$2 \cdot 10^{-5}$		<input checked="" type="checkbox"/>
kphosSmad2			$4 \cdot 10^{-5}$		<input checked="" type="checkbox"/>
kprodAGE			$10^{-6}$		<input checked="" type="checkbox"/>
krelAlk1Alk5			0.010		<input checked="" type="checkbox"/>
krelBaxBcl2			0.002		<input checked="" type="checkbox"/>

Id	Name	SBO	Value	Unit	Constant
krelBaxBcl2Bec			0.002		✓
krelBcl2BecIn			$5 \cdot 10^{-4}$		✓
krelBecBaxBcl2			0.017		✓
krelSmad1Smad4			0.017		✓
krelSmad2Smad4			0.017		✓
krelSmad7Alk1			0.001		✓
krelSmad7Alk5			$10^{-6}$		✓
krelTgfbAlk1			$10^{-6}$		✓
krelTgfbAlk5			$10^{-6}$		✓
kremROS			$3.83 \cdot 10^{-4}$		✓
kremROSBysOD			$10^{-4}$		✓
ksynAcanmRNA			0.000		✓
ksynAcanmRNASox9A			$4.6 \cdot 10^{-6}$		✓
ksynADAMTS5			$5 \cdot 10^{-4}$		✓
ksynAggreCAN			$10^{-6}$		✓
ksynAlk1			$5 \cdot 10^{-6}$		✓
ksynAlk5			$5 \cdot 10^{-6}$		✓
ksynBcl2			0.002		✓
ksynCol2			$10^{-7}$		✓
ksynCol2mRNA			0.000		✓
ksynCol2mRNASmad			$10^{-6}$		✓
ksynCol2mRNASox9A			$10^{-6}$		✓
ksynIkb			0.001		✓
ksynIL1			0.005		✓
ksynMMP13			$3.2 \cdot 10^{-5}$		✓
ksynMMP13Runx2			$1.5 \cdot 10^{-6}$		✓
ksynMMP2			$5 \cdot 10^{-6}$		✓
ksynNatP			0.000		✓
ksynRAGE			$10^{-4}$		✓
ksynSmad7			$10^{-5}$		✓
ksynSOD			0.002		✓
ksynSox9			$4.8 \cdot 10^{-4}$		✓
ksynSox9mRNA			$10^{-5}$		✓
ksynSox9mRNASox9A			$5 \cdot 10^{-6}$		✓

## 6 Reactions

This model contains 117 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	CaspaseActivation		$\text{Caspase\_I} + \text{Bax} \xrightarrow{\text{Caspase\_I, Bax}} \text{Caspase\_A} + \text{Bax}$	
2	CaspaseActivationByBeclin-I		$\text{Caspase\_I} + \text{Beclin\_I} \xrightarrow{\text{Caspase\_I, Beclin\_I}} \text{Caspase\_A} + \text{Beclin\_I}$	
3	CaspaseActivationBy-p38		$\text{Caspase\_I} + \text{p38\_P} \xrightarrow{\text{Caspase\_I, p38\_P}} \text{Caspase\_A} + \text{p38\_P}$	
4	CaspaseInactivation1		$\text{Caspase\_A} \xrightarrow{\text{Caspase\_A}} \text{Caspase\_I}$	
5	InhibitCaspase2		$\text{Caspase\_A} + \text{Bcl2\_Beclin} \xrightarrow{\text{Caspase\_A, Bcl2\_Beclin}} \text{Caspase\_I} + \text{Bcl2\_Beclin}$	
6	InhibitCaspase3		$\text{Caspase\_A} + \text{Bcl2} \xrightarrow{\text{Caspase\_A, Bcl2}} \text{Caspase\_I} + \text{Bcl2}$	
7	ActivateLysosome		$\text{Lys\_I} + \text{Beclin} \xrightarrow{\text{Lys\_I, Beclin}} \text{Lys\_A} + \text{Beclin}$	
8	InhibitLysosome		$\text{Lys\_A} \xrightarrow{\text{Lys\_A}} \text{Lys\_I}$	
9	Bcl2Synthesis		$\text{Source} \xrightarrow{\text{Source}} \text{Bcl2}$	
10	Bcl2Degradation		$\text{Bcl2} \xrightarrow{\text{Bcl2}} \text{Sink}$	
11	Bcl2DegradationStressInduced		$\text{Bcl2} + \text{ROS} \xrightarrow{\text{Bcl2, ROS}} \text{Sink} + \text{ROS}$	
12	Bcl2DegradationCaspaseInduced		$\text{Bcl2} + \text{Caspase\_A} \xrightarrow{\text{Bcl2, Caspase\_A}} \text{Sink} + \text{Caspase\_A}$	

Nº	Id	Name	Reaction Equation	SBO
13	Bax_Bcl2Binding		$\text{Bax} + \text{Bcl2} \xrightarrow{\text{Bax, Bcl2}} \text{Bax\_Bcl2}$	
14	Bax_Bcl2Release		$\text{Bax\_Bcl2} \xrightarrow{\text{Bax\_Bcl2}} \text{Bax} + \text{Bcl2}$	
15	Bcl2- _BeclinBinding		$\text{Bcl2} + \text{Beclin} \xrightarrow{\text{Bcl2, Beclin}} \text{Bcl2\_Beclin}$	
16	Bcl2- _BeclinRelease		$\text{Bcl2\_Beclin} \xrightarrow{\text{Bcl2\_Beclin}} \text{Bcl2} + \text{Beclin}$	
17	Bcl2_Beclin_I- _Binding		$\text{Bcl2} + \text{Beclin\_I} \xrightarrow{\text{Bcl2, Beclin\_I}} \text{Bcl2\_Beclin\_I}$	
18	Bcl2_Beclin_I- _Release		$\text{Bcl2\_Beclin\_I} \xrightarrow{\text{Bcl2\_Beclin\_I}} \text{Bcl2} + \text{Beclin\_I}$	
19	BeclinInactivation		$\text{Beclin} \xrightarrow{\text{Beclin}} \text{Beclin\_I}$	
20	BeclinInactivationByCaspase		$\text{Beclin} + \text{Caspase\_A} \xrightarrow{\text{Beclin, Caspase\_A}} \text{Beclin\_I} + \text{Caspase\_A}$	
21	BeclinBindingToBax- _Bcl2		$\text{Beclin} + \text{Bax\_Bcl2} \xrightarrow{\text{Beclin, Bax\_Bcl2}} \text{Bax\_Bcl2\_Beclin}$	
22	BeclinIBindingToBax- _Bcl2		$\text{Beclin\_I} + \text{Bax\_Bcl2} \xrightarrow{\text{Beclin\_I, Bax\_Bcl2}} \text{Bax\_Bcl2\_Beclin\_I}$	
23	BaxBindingToBcl2- _Beclin		$\text{Bax} + \text{Bcl2\_Beclin} \xrightarrow{\text{Bax, Bcl2\_Beclin}} \text{Bax\_Bcl2\_Beclin}$	
24	BaxBindingToBcl2- _BeclinI		$\text{Bax} + \text{Bcl2\_Beclin\_I} \xrightarrow{\text{Bax, Bcl2\_Beclin\_I}} \text{Bax\_Bcl2\_Beclin\_I}$	
25	BaxDissociation- _Bax_Bcl2- _Beclin		$\text{Bax\_Bcl2\_Beclin} \xrightarrow{\text{Bax\_Bcl2\_Beclin}} \text{Bax} + \text{Bcl2\_Beclin}$	

Nº	Id	Name	Reaction Equation	SBO
26	BaxDissociation- _Bax_Bcl2- _Beclin_I		$\text{Bax\_Bcl2\_Beclin\_I} \xrightarrow{\text{Bax\_Bcl2\_Beclin\_I}} \text{Bax} + \text{Bcl2\_Beclin\_I}$	+
27	BeclinDissociation- _Bax_Bcl2- _Beclin		$\text{Bax\_Bcl2\_Beclin} \xrightarrow{\text{Bax\_Bcl2\_Beclin}} \text{Beclin} + \text{Bax\_Bcl2}$	+
28	Beclin_I- _Dissociation- _Bax_Bcl2- _Beclin		$\text{Bax\_Bcl2\_Beclin\_I} \xrightarrow{\text{Bax\_Bcl2\_Beclin\_I}} \text{Beclin\_I} + \text{Bax\_Bcl2}$	+
29	ROS_generation		$\text{Source} \xrightarrow{\text{Source}} \text{ROS}$	
30	ROS_removal		$\text{ROS} \xrightarrow{\text{ROS}} \text{Sink}$	
31	Protein_Damage- _by_ROS		$\text{NatP} + \text{ROS} \xrightarrow{\text{NatP, ROS}} \text{DamP} + \text{ROS}$	
32	Removal_DamP- _by_Autophagy		$\text{DamP} + \text{Lys\_A} \xrightarrow{\text{DamP, Lys\_A}} \text{Lys\_A}$	
33	Production_of- _AGEproducts		$\text{Source} \xrightarrow{\text{Source}} \text{AGEprod}$	
34	RAGE_activation		$\text{AGEprod} \xrightarrow{\text{AGEprod}} \text{AGEprod} + \text{RAGE}$	
35	ROS_production- _by_RAGE		$\text{RAGE} \xrightarrow{\text{RAGE}} \text{RAGE} + \text{ROS}$	
36	IkB- _degradation- _via_ROS		$\text{ROS} + \text{IkB\_NFkB} \xrightarrow{\text{ROS, IkB\_NFkB}} \text{ROS} + \text{NFkB}$	

Nº	Id	Name	Reaction Equation	SBO
37	IkB- _degradation- _via_IL1		$IL1 + IkB\_NFkB \xrightarrow{IL1, IkB\_NFkB} IL1 + NFkB$	
38	NFkB- _inactivation		$NFkB + IkB \xrightarrow{NFkB, IkB} IkB\_NFkB$	
39	RAGE- _inactivation		$RAGE \xrightarrow{RAGE} Sink$	
40	RAGE- _upregulation- _byNFkB		$NFkB\_P \xrightarrow{NFkB\_P} NFkB\_P + RAGE$	
41	IL1_production		$NFkB\_P \xrightarrow{NFkB\_P} NFkB\_P + IL1$	
42	IL1_degradation		$IL1 \xrightarrow{IL1} Sink$	
43	IkB_production		$NFkB\_P \xrightarrow{NFkB\_P} NFkB\_P + IkB$	
44	MMP13- _production		$IL1 \xrightarrow{IL1} IL1 + proMMP13$	
45	MMP13_removal		$MMP13 \xrightarrow{MMP13} Sink$	
46	MMP2_production		$IL1 \xrightarrow{IL1} IL1 + proMMP2$	
47	MMP_activation		$proMMP2 \xrightarrow{proMMP2} MMP2$	
48	MMP2- _degradation		$MMP2 \xrightarrow{MMP2} Sink$	
49	ADAMTS5- _production		$IL1 \xrightarrow{IL1} IL1 + ADAMTS5$	
50	ADAMTS5_removal		$ADAMTS5 \xrightarrow{ADAMTS5} Sink$	

Nº	Id	Name	Reaction Equation	SBO
51	Aggrecan- _degradation		Aggrecan.Collagen2 + ADAMTS5 $\xrightarrow{\text{Aggrecan.Collagen2, ADAMTS5}}$ Collagen2 + ADAMTS5 + AggFrag	
52	Collagen- _degradation		Collagen2 + MMP13 $\xrightarrow{\text{Collagen2, MMP13}}$ MMP13 + ColFrag	
53	ROS_production- _by_DamP		DamP $\xrightarrow{\text{DamP}}$ DamP + ROS	
54	Protein- _synthesis		Source $\xrightarrow{\text{Source}}$ NatP	
55	SOD_synthesis		NFkB_P $\xrightarrow{\text{NFkB\_P}}$ NFkB_P + SOD	
56	SOD_degradation		SOD $\xrightarrow{\text{SOD}}$ Sink	
57	ROS_removal_by- _SOD		ROS + SOD $\xrightarrow{\text{SOD, ROS}}$ SOD	
58	p38- _phosphorylation		p38 + IL1 $\xrightarrow{\text{p38, IL1}}$ p38_P + IL1	
59	p38- _phosphorylation- _via_ROS		p38 + ROS $\xrightarrow{\text{p38, ROS}}$ p38_P + ROS	
60	p38- _dephosphorylation		p38_P $\xrightarrow{\text{p38\_P}}$ p38	
61	NFkB_activation		NFkB + p38_P $\xrightarrow{\text{NFkB, p38\_P}}$ NFkB_P + p38_P	
62	NFkB- _dephosphorylation		NFkB_P $\xrightarrow{\text{NFkB\_P}}$ NFkB	

Nº	Id	Name	Reaction Equation	SBO
63	ROS_production- _by_p38_P		$p38\_P \xrightarrow{p38\_P} p38\_P + ROS$	
64	Lysosome- _damage_by_ROS		$Lys\_A + ROS \xrightarrow{Lys\_A, ROS} Lys\_I + ROS$	
65	IntegrinActivationByMechanicalStress		$Source \xrightarrow{Source} Integrin + IntegrinCount$	
66	IntegrinInactivation		$Integrin \xrightarrow{Integrin} Sink$	
67	Alk5Synthesis		$Source \xrightarrow{Source} Alk5$	
68	TgfbActivationByIntegrin		$Tgfb\_I + Integrin \xrightarrow{Tgfb\_I, Integrin} Tgfb\_A + Integrin$	
69	TgfbActivationByMMP2		$Tgfb\_I + MMP2 \xrightarrow{Tgfb\_I, MMP2} Tgfb\_A + MMP2$	
70	TgfbInactivation		$Tgfb\_A \xrightarrow{Tgfb\_A} Tgfb\_I$	
71	Alk5Dimerisation		$2 Alk5 \xrightarrow{Alk5} Alk5\_dimer$	
72	Alk5Dedimerisation		$Alk5\_dimer \xrightarrow{Alk5\_dimer} 2 Alk5$	
73	Alk1Alk5Binding		$Alk1 + Alk5 \xrightarrow{Alk1, Alk5} Alk1\_Alk5$	
74	Alk1Alk5Release		$Alk1\_Alk5 \xrightarrow{Alk1\_Alk5} Alk1 + Alk5$	
75	TgfbReceptorBindingAlk5		$Tgfb\_A + Alk5\_dimer \xrightarrow{Tgfb\_A, Alk5\_dimer} Tgfb\_Alk5\_dimer$	
76	TgfbReceptorRelease		$Tgfb\_Alk5\_dimer \xrightarrow{Tgfb\_Alk5\_dimer} Tgfb\_A + Alk5\_dimer$	
77	Tgfb_Alk5- _BindingSmad7		$Tgfb\_Alk5\_dimer + Smad7 \xrightarrow{Tgfb\_Alk5\_dimer, Smad7} Tgfb\_Alk5\_dimer\_Smad7$	
78	Tgfb_Alk5- _Smad7Release		$Tgfb\_Alk5\_dimer\_Smad7 \xrightarrow{Tgfb\_Alk5\_dimer\_Smad7} Tgfb\_Alk5\_dimer + Smad7$	



Nº	Id	Name	Reaction Equation	SBO
79	Alk5-	Smad7Degradation	$\text{Tgfb\_Alk5\_dimer\_Smad7} \xrightarrow{\text{Tgfb\_Alk5\_dimer\_Smad7}} \text{Tgfb\_I}$	
80	TgfbReceptorBindingAlk1		$\text{Tgfb\_A} + \text{Alk1\_Alk5} \xrightarrow{\text{Tgfb\_A, Alk1\_Alk5}} \text{Tgfb\_Alk1\_Alk5}$	
81	TgfbAlk1Release		$\text{Tgfb\_Alk1\_Alk5} \xrightarrow{\text{Tgfb\_Alk1\_Alk5}} \text{Tgfb\_A} + \text{Alk1\_Alk5}$	
82	Smad2Phosphorylation		$\text{Tgfb\_Alk5\_dimer} + \text{Smad2} \xrightarrow{\text{Tgfb\_Alk5\_dimer, Smad2}} \text{Tgfb\_Alk5\_dimer} + \text{Smad2\_P}$	
83	Smad2Smad4Binding		$\text{Smad2\_P} + \text{Smad4} \xrightarrow{\text{Smad2\_P, Smad4}} \text{Smad2\_P\_Smad4}$	
84	Smad2PSmad4Release		$\text{Smad2\_P\_Smad4} \xrightarrow{\text{Smad2\_P\_Smad4}} \text{Smad2\_P} + \text{Smad4}$	
85	Smad2DephosphorylationNuc		$\text{Smad2\_P} \xrightarrow{\text{Smad2\_P}} \text{Smad2}$	
86	Smad7Synthesis		$\text{Smad2\_P\_Smad4} \xrightarrow{\text{Smad2\_P\_Smad4}} \text{Smad2\_P\_Smad4} + \text{Smad7}$	
87	Sox9Activation		$\text{Smad2\_P\_Smad4} + \text{Sox9} \xrightarrow{\text{Smad2\_P\_Smad4, Sox9}} \text{Smad2\_P\_Smad4} + \text{Sox9\_A}$	
88	Sox9Inactivation		$\text{Sox9\_A} \xrightarrow{\text{Sox9\_A}} \text{Sox9}$	
89	Sox9BasalTranscription		$\text{Source} \xrightarrow{\text{Source}} \text{Sox9mRNA}$	
90	Sox9EnhancedTranscription		$\text{Sox9\_A} \xrightarrow{\text{Sox9\_A}} \text{Sox9\_A} + \text{Sox9mRNA}$	
91	Sox9mRNA-	Degradation	$\text{Sox9mRNA} \xrightarrow{\text{Sox9mRNA}} \text{Sink}$	
92	Sox9Translation		$\text{Sox9mRNA} \xrightarrow{\text{Sox9mRNA}} \text{Sox9mRNA} + \text{Sox9}$	

Nº	Id	Name	Reaction Equation	SBO
93	Sox9Degradation		$\text{Sox9} \xrightarrow{\text{Sox9}} \text{Sink}$	
94	Collagen2EnhancedTranscriptionBySox9		$\text{Sox9\_A} \xrightarrow{\text{Sox9\_A}} \text{Sox9\_A} + \text{Col2mRNA}$	
95	Collagen2TranscriptionBySmad2Smad4		$\text{Smad2\_P\_Smad4} \xrightarrow{\text{Smad2\_P\_Smad4}} \text{Smad2\_P\_Smad4} + \text{Col2mRNA}$	
96	Col2mRNA-Degradation		$\text{Col2mRNA} \xrightarrow{\text{Col2mRNA}} \text{Sink}$	
97	Collagen2Translation		$\text{Col2mRNA} \xrightarrow{\text{Col2mRNA}} \text{Col2mRNA} + \text{Collagen2}$	
98	AggreCANEnhancedTranscription		$\text{Sox9\_A} \xrightarrow{\text{Sox9\_A}} \text{Sox9\_A} + \text{AcanmRNA}$	
99	AcanmRNA-Degradation		$\text{AcanmRNA} \xrightarrow{\text{AcanmRNA}} \text{Sink}$	
100	AggreCANTranslation		$\text{AcanmRNA} \xrightarrow{\text{AcanmRNA}} \text{AcanmRNA} + \text{AggreCAN}$	
101	AggreCANCollagen2Binding		$\text{AggreCAN} + \text{Collagen2} \xrightarrow{\text{AggreCAN, Collagen2}} \text{AggreCAN\_Collagen2}$	
102	Runx2-InhibitionBySmad2		$\text{Runx2\_A} + \text{Smad2\_P\_Smad4} \xrightarrow{\text{Runx2\_A, Smad2\_P\_Smad4}} \text{Runx2\_I} + \text{Smad2\_P\_Smad4}$	
103	Alk5Degradation		$\text{Alk5} \xrightarrow{\text{Alk5}} \text{Sink}$	
104	Smad1Activation		$\text{Tgfb\_Alk1\_Alk5} + \text{Smad1} \xrightarrow{\text{Tgfb\_Alk1\_Alk5, Smad1}} \text{Tgfb\_Alk1\_Alk5} + \text{Smad1\_P}$	
105	Smad1Dephosphorylation		$\text{Smad1\_P} \xrightarrow{\text{Smad1\_P}} \text{Smad1}$	
106	Smad1DephosphorylationViaSmad7		$\text{Smad1\_P} + \text{Smad7} \xrightarrow{\text{Smad1\_P, Smad7}} \text{Smad1} + \text{Smad7}$	
107	Smad1Smad4Binding		$\text{Smad1\_P} + \text{Smad4} \xrightarrow{\text{Smad1\_P, Smad4}} \text{Smad1\_P\_Smad4}$	

Nº	Id	Name	Reaction Equation	SBO
108	Smad1Smad4Release		$\text{Smad1\_P\_Smad4} \xrightarrow{\text{Smad1\_P\_Smad4}} \text{Smad1\_P} + \text{Smad4}$	
109	Runx2ActivationBySmad1		$\text{Runx2\_I} + \text{Smad1\_P\_Smad4} \xrightarrow{\text{Runx2\_I, Smad1\_P\_Smad4}} \text{Runx2\_A} + \text{Smad1\_P\_Smad4}$	
110	MMP13InductionByRunx2		$\text{Runx2\_A} \xrightarrow{\text{Runx2\_A}} \text{proMMP13} + \text{Runx2\_A}$	
111	Alk1Synthesis		$\text{Source} \xrightarrow{\text{Source}} \text{Alk1}$	
112	Alk1Degradation		$\text{Alk1} \xrightarrow{\text{Alk1}} \text{Sink}$	
113	MMP13Activation		$\text{proMMP13} \xrightarrow{\text{proMMP13}} \text{MMP13}$	
114	Tgfb_Alk1_Alk5- _BindingSmad7		$\text{Tgfb\_Alk1\_Alk5} + \text{Smad7} \xrightarrow{\text{Tgfb\_Alk1\_Alk5, Smad7}} \text{Tgfb\_Alk1\_Alk5\_Smad7}$	
115	Tgfb_Alk1_Alk5- _Smad7Release		$\text{Tgfb\_Alk1\_Alk5\_Smad7} \xrightarrow{\text{Tgfb\_Alk1\_Alk5\_Smad7}} \text{Tgfb\_Alk1\_Alk5} + \text{Smad7}$	
116	Alk1- _Smad7Degradation		$\text{Tgfb\_Alk1\_Alk5\_Smad7} \xrightarrow{\text{Tgfb\_Alk1\_Alk5\_Smad7}} \text{Tgfb\_I}$	
117	Smad7Degradation		$\text{Smad7} \xrightarrow{\text{Smad7}} \text{Sink}$	

## 6.1 Reaction `CaspaseActivation`

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

### Reaction equation



### Reactants

Table 6: Properties of each reactant.

Id	Name	SBO
Caspase_I		
Bax		

### Modifiers

Table 7: Properties of each modifier.

Id	Name	SBO
Caspase_I		
Bax		

### Products

Table 8: Properties of each product.

Id	Name	SBO
Caspase_A		
Bax		

### Kinetic Law

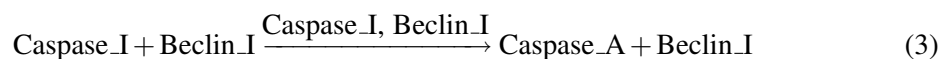
**Derived unit** contains undeclared units

$$v_1 = k_{\text{actCasp}} \cdot \text{Caspase\_I} \cdot \text{Bax} \quad (2)$$

## 6.2 Reaction `CaspaseActivationByBeclin_I`

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

### Reaction equation



### Reactants

Table 9: Properties of each reactant.

Id	Name	SBO
Caspase_I		
Beclin_I		

### Modifiers

Table 10: Properties of each modifier.

Id	Name	SBO
Caspase_I		
Beclin_I		

### Products

Table 11: Properties of each product.

Id	Name	SBO
Caspase_A		
Beclin_I		

### Kinetic Law

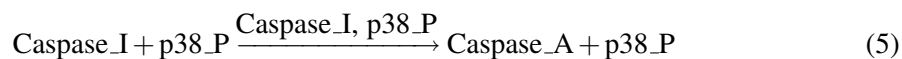
**Derived unit** contains undeclared units

$$v_2 = \text{kactCaspBecI} \cdot \text{Caspase\_I} \cdot \text{Beclin\_I} \quad (4)$$

### 6.3 Reaction `CaspaseActivationBy_p38`

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

#### Reaction equation



#### Reactants

Table 12: Properties of each reactant.

Id	Name	SBO
Caspase_I		
p38_P		

#### Modifiers

Table 13: Properties of each modifier.

Id	Name	SBO
Caspase_I		
p38_P		

#### Products

Table 14: Properties of each product.

Id	Name	SBO
Caspase_A		
p38_P		

#### Kinetic Law

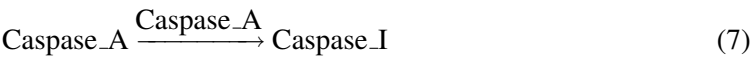
**Derived unit** contains undeclared units

$$v_3 = \text{kactCaspp38} \cdot \text{Caspase\_I} \cdot \text{p38\_P} \quad (6)$$

### 6.4 Reaction `CaspaseInactivation1`

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

Reaction equation



Reactant

Table 15: Properties of each reactant.

Id	Name	SBO
Caspase_A		

Modifier

Table 16: Properties of each modifier.

Id	Name	SBO
Caspase_A		

Product

Table 17: Properties of each product.

Id	Name	SBO
Caspase_I		

Kinetic Law

**Derived unit** contains undeclared units

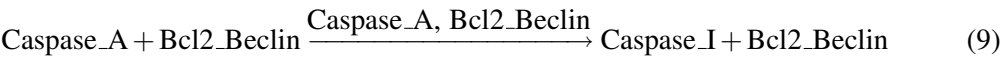
$$v_4 = \text{kinactCasp} \cdot \text{Caspase\_A}$$

(8)

6.5 Reaction `InhibitCaspase2`

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

Reaction equation



Reactants

Table 18: Properties of each reactant.

Id	Name	SBO
Caspase_A		
Bcl2_Beclin		

## Modifiers

Table 19: Properties of each modifier.

Id	Name	SBO
Caspase_A		
Bcl2_Beclin		

## Products

Table 20: Properties of each product.

Id	Name	SBO
Caspase_I		
Bcl2_Beclin		

## Kinetic Law

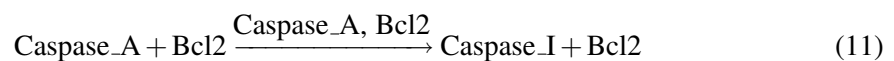
**Derived unit** contains undeclared units

$$v_5 = \text{kinactCaspBcl2} \cdot \text{Caspase\_A} \cdot \text{Bcl2\_Beclin} \quad (10)$$

### 6.6 Reaction `InhibitCaspase3`

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

#### Reaction equation



## Reactants



Table 21: Properties of each reactant.

Id	Name	SBO
Caspase_A		
Bcl2		

## Modifiers

Table 22: Properties of each modifier.

Id	Name	SBO
Caspase_A		
Bcl2		

## Products

Table 23: Properties of each product.

Id	Name	SBO
Caspase_I		
Bcl2		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_6 = \text{kinactCaspBcl2} \cdot \text{Caspase\_A} \cdot \text{Bcl2} \quad (12)$$

### 6.7 Reaction ActivateLysosome

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

#### Reaction equation



## Reactants

Table 24: Properties of each reactant.

Id	Name	SBO
Lys_I		
Beclin		

## Modifiers

Table 25: Properties of each modifier.

Id	Name	SBO
Lys_I		
Beclin		

## Products

Table 26: Properties of each product.

Id	Name	SBO
Lys_A		
Beclin		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_7 = k_{actLys} \cdot Lys\_I \cdot Beclin \quad (14)$$

## 6.8 Reaction `InhibitLysosome`

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

### Reaction equation



## Reactant

Table 27: Properties of each reactant.

Id	Name	SBO
Lys_A		

## Modifier

Table 28: Properties of each modifier.

Id	Name	SBO
Lys_A		

## Product

Table 29: Properties of each product.

Id	Name	SBO
Lys_I		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_8 = \text{kinhibLys} \cdot \text{Lys\_A} \quad (16)$$

## 6.9 Reaction Bcl2Synthesis

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

### Reaction equation



## Reactant

Table 30: Properties of each reactant.

Id	Name	SBO
Source		

## Modifier

Table 31: Properties of each modifier.

Id	Name	SBO
Source		

## Product

Table 32: Properties of each product.

Id	Name	SBO
Bc12		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_9 = k_{\text{synBc12}} \cdot \text{Source} \quad (18)$$

## 6.10 Reaction Bc12Degradation

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

### Reaction equation



## Reactant

Table 33: Properties of each reactant.

Id	Name	SBO
Bc12		

## Modifier

Table 34: Properties of each modifier.

Id	Name	SBO
Bc12		

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

## Product

Table 35: Properties of each product.

Id	Name	SBO
	Sink	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{10} = k_{degBcl2} \cdot Bcl2 \quad (20)$$

## 6.11 Reaction Bcl2DegradationStressInduced

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

## Reaction equation



## Reactants

Table 36: Properties of each reactant.

Id	Name	SBO
	Bcl2	
	ROS	

## Modifiers

Table 37: Properties of each modifier.

Id	Name	SBO
	Bcl2	
	ROS	

## Products

Table 38: Properties of each product.

Id	Name	SBO
	Sink	
	ROS	

## Kinetic Law

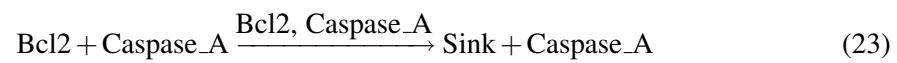
**Derived unit** contains undeclared units

$$v_{11} = kdegBcl2ROS \cdot Bcl2 \cdot ROS \quad (22)$$

### 6.12 Reaction `Bcl2DegradationCaspaseInduced`

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

## Reaction equation



## Reactants

Table 39: Properties of each reactant.

Id	Name	SBO
	Bcl2	
	Caspase_A	

## Modifiers

Table 40: Properties of each modifier.

Id	Name	SBO
	Bcl2	
	Caspase_A	

## Products

Table 41: Properties of each product.

Id	Name	SBO
Sink		
Caspase_A		

## Kinetic Law

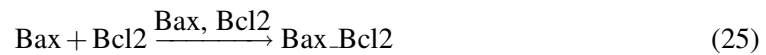
**Derived unit** contains undeclared units

$$v_{12} = kdegBcl2Casp \cdot Bcl2 \cdot Caspase\_A \quad (24)$$

## 6.13 Reaction `Bax_Bcl2Binding`

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

### Reaction equation



## Reactants

Table 42: Properties of each reactant.

Id	Name	SBO
Bax		
Bcl2		

## Modifiers

Table 43: Properties of each modifier.

Id	Name	SBO
Bax		
Bcl2		

## Product

Table 44: Properties of each product.

Id	Name	SBO
Bax_Bcl2		

## Kinetic Law

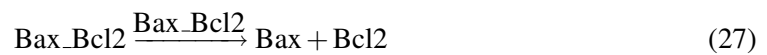
**Derived unit** contains undeclared units

$$v_{13} = k_{\text{binBaxBcl2}} \cdot \text{Bax} \cdot \text{Bcl2} \quad (26)$$

## 6.14 Reaction Bax\_Bcl2Release

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

## Reaction equation



## Reactant

Table 45: Properties of each reactant.

Id	Name	SBO
Bax_Bcl2		

## Modifier

Table 46: Properties of each modifier.

Id	Name	SBO
Bax_Bcl2		

## Products

Table 47: Properties of each product.

Id	Name	SBO
Bax		
Bcl2		



## Kinetic Law

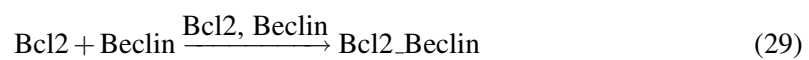
**Derived unit** contains undeclared units

$$v_{14} = k_{rel} B_{ax} B_{cl2} \cdot B_{ax\_Bcl2} \quad (28)$$

## 6.15 Reaction Bcl2\_BeclinBinding

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

### Reaction equation



### Reactants

Table 48: Properties of each reactant.

Id	Name	SBO
Bcl2		
Beclin		

### Modifiers

Table 49: Properties of each modifier.

Id	Name	SBO
Bcl2		
Beclin		

### Product

Table 50: Properties of each product.

Id	Name	SBO
Bcl2_Beclin		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{15} = k_{bin} B_{cl2} B_{eclin} \cdot B_{cl2} \cdot B_{eclin} \quad (30)$$

## 6.16 Reaction `Bcl2_BeclinRelease`

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

### Reaction equation



### Reactant

Table 51: Properties of each reactant.

Id	Name	SBO
Bcl2_Beclin		

### Modifier

Table 52: Properties of each modifier.

Id	Name	SBO
Bcl2_Beclin		

### Products

Table 53: Properties of each product.

Id	Name	SBO
Bcl2		
Beclin		

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{16} = k_{\text{relBcl2Beclin}} \cdot \text{Bcl2\_Beclin} \quad (32)$$

## 6.17 Reaction `Bcl2_Beclin_I_Binding`

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

### Reaction equation



## Reactants

Table 54: Properties of each reactant.

Id	Name	SBO
Bcl2		
Beclin_I		

## Modifiers

Table 55: Properties of each modifier.

Id	Name	SBO
Bcl2		
Beclin_I		

## Product

Table 56: Properties of each product.

Id	Name	SBO
Bcl2_Beclin_I		

## Kinetic Law

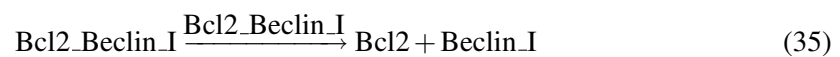
**Derived unit** contains undeclared units

$$v_{17} = k_{\text{binBcl2Beclin}} \cdot \text{Bcl2} \cdot \text{Beclin\_I} \quad (34)$$

### 6.18 Reaction Bcl2\_Beclin\_I Release

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

#### Reaction equation



## Reactant

Table 57: Properties of each reactant.

Id	Name	SBO
Bcl2_Beclin_I		

## Modifier

Table 58: Properties of each modifier.

Id	Name	SBO
Bcl2_Beclin_I		

## Products

Table 59: Properties of each product.

Id	Name	SBO
Bcl2		
Beclin_I		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{18} = k_{\text{relBcl2Beclin}} \cdot \text{Bcl2\_Beclin\_I} \quad (36)$$

## 6.19 Reaction BeclinInactivation

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

### Reaction equation



## Reactant

Table 60: Properties of each reactant.

Id	Name	SBO
Beclin		

## Modifier

Table 61: Properties of each modifier.

Id	Name	SBO
Beclin		

## Product

Table 62: Properties of each product.

Id	Name	SBO
Beclin_I		

## Kinetic Law

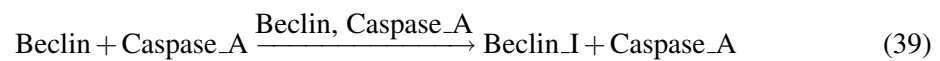
**Derived unit** contains undeclared units

$$v_{19} = \text{kinactBec} \cdot \text{Beclin} \quad (38)$$

### 6.20 Reaction `BeclinInactivationByCaspase`

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

#### Reaction equation



## Reactants

Table 63: Properties of each reactant.

Id	Name	SBO
Beclin		
Caspase_A		

## Modifiers

Table 64: Properties of each modifier.

Id	Name	SBO
Beclin		
Caspase_A		

## Products

Table 65: Properties of each product.

Id	Name	SBO
Beclin_I		
Caspase_A		

## Kinetic Law

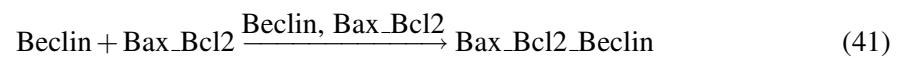
**Derived unit** contains undeclared units

$$v_{20} = \text{kinactBecCasp} \cdot \text{Beclin} \cdot \text{Caspase\_A} \quad (40)$$

## 6.21 Reaction `BeclinBindingToBax_Bcl2`

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

### Reaction equation



## Reactants

Table 66: Properties of each reactant.

Id	Name	SBO
Beclin		
Bax_Bcl2		

## Modifiers

Table 67: Properties of each modifier.

Id	Name	SBO
Beclin		
Bax_Bcl2		

## Product

Table 68: Properties of each product.

Id	Name	SBO
Bax_Bcl2_Beclin		

## Kinetic Law

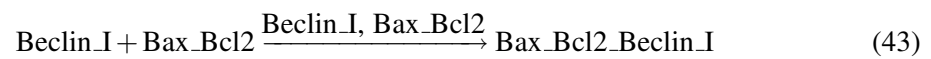
**Derived unit** contains undeclared units

$$v_{21} = k_{\text{binBecToBaxBcl2}} \cdot \text{Beclin} \cdot \text{Bax\_Bcl2} \quad (42)$$

## 6.22 Reaction `BeclinIBindingToBax_Bcl2`

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

## Reaction equation



## Reactants

Table 69: Properties of each reactant.

Id	Name	SBO
Beclin_I		
Bax_Bcl2		

## Modifiers

Table 70: Properties of each modifier.

Id	Name	SBO
Beclin_I		

Id	Name	SBO
Bax_Bcl2		

## Product

Table 71: Properties of each product.

Id	Name	SBO
Bax_Bcl2_Beclin_I		

## Kinetic Law

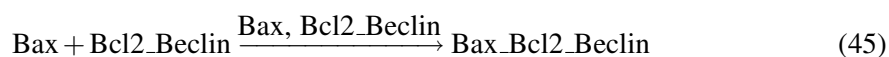
**Derived unit** contains undeclared units

$$v_{22} = k_{\text{binBecToBaxBcl2}} \cdot \text{Beclin\_I} \cdot \text{Bax\_Bcl2} \quad (44)$$

## 6.23 Reaction [BaxBindingToBcl2\\_Beclin](#)

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

## Reaction equation



## Reactants

Table 72: Properties of each reactant.

Id	Name	SBO
Bax		
Bcl2_Beclin		

## Modifiers

Table 73: Properties of each modifier.

Id	Name	SBO
Bax		
Bcl2_Beclin		



## Product

Table 74: Properties of each product.

Id	Name	SBO
Bax_Bcl2_Beclin		

## Kinetic Law

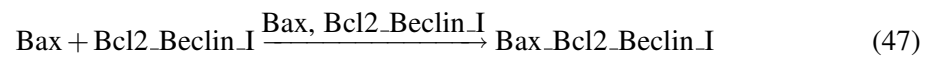
**Derived unit** contains undeclared units

$$v_{23} = k_{\text{binBaxToBcl2Bec}} \cdot \text{Bax} \cdot \text{Bcl2\_Beclin} \quad (46)$$

### 6.24 Reaction `BaxBindingToBcl2_BeclinI`

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

## Reaction equation



## Reactants

Table 75: Properties of each reactant.

Id	Name	SBO
Bax		
Bcl2_Beclin_I		

## Modifiers

Table 76: Properties of each modifier.

Id	Name	SBO
Bax		
Bcl2_Beclin_I		

## Product

Table 77: Properties of each product.

Id	Name	SBO
Bax_Bcl2_Beclin_I		

### Kinetic Law

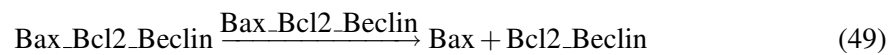
**Derived unit** contains undeclared units

$$v_{24} = k_{\text{binBaxToBcl2Bec}} \cdot \text{Bax} \cdot \text{Bcl2\_Beclin\_I} \quad (48)$$

### 6.25 Reaction BaxDissociation\_Bax\_Bcl2\_Beclin

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

### Reaction equation



### Reactant

Table 78: Properties of each reactant.

Id	Name	SBO
Bax_Bcl2_Beclin		

### Modifier

Table 79: Properties of each modifier.

Id	Name	SBO
Bax_Bcl2_Beclin		

### Products

Table 80: Properties of each product.

Id	Name	SBO
Bax		
Bcl2_Beclin		

## Kinetic Law

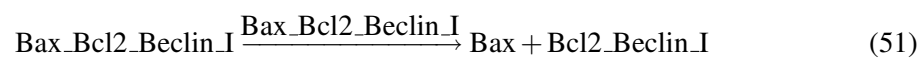
**Derived unit** contains undeclared units

$$v_{25} = k_{rel} Bax_{Bcl2Bec} \cdot Bax_{Bcl2Beclin\_I} \quad (50)$$

## 6.26 Reaction `BaxDissociation_Bax_Bcl2_Beclin_I`

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

### Reaction equation



### Reactant

Table 81: Properties of each reactant.

Id	Name	SBO
Bax_Bcl2_Beclin_I		

### Modifier

Table 82: Properties of each modifier.

Id	Name	SBO
Bax_Bcl2_Beclin_I		

### Products

Table 83: Properties of each product.

Id	Name	SBO
Bax		
Bcl2_Beclin_I		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{26} = k_{rel} Bax_{Bcl2Bec} \cdot Bax_{Bcl2Beclin\_I} \quad (52)$$

## 6.27 Reaction [BeclinDissociation\\_Bax\\_Bcl2\\_Beclin](#)

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

### Reaction equation



### Reactant

Table 84: Properties of each reactant.

Id	Name	SBO
Bax_Bcl2_Beclin		

### Modifier

Table 85: Properties of each modifier.

Id	Name	SBO
Bax_Bcl2_Beclin		

### Products

Table 86: Properties of each product.

Id	Name	SBO
Beclin		
Bax_Bcl2		

### Kinetic Law

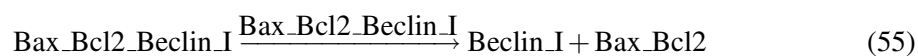
**Derived unit** contains undeclared units

$$v_{27} = \text{krelBecBaxBcl2} \cdot \text{Bax\_Bcl2\_Beclin} \quad (54)$$

## 6.28 Reaction [Beclin\\_I\\_Dissociation\\_Bax\\_Bcl2\\_Beclin](#)

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

### Reaction equation



Reactant

Table 87: Properties of each reactant.

Id	Name	SBO
Bax_Bcl2_Beclin_I		

Modifier

Table 88: Properties of each modifier.

Id	Name	SBO
Bax_Bcl2_Beclin_I		

Products

Table 89: Properties of each product.

Id	Name	SBO
Beclin_I		
Bax_Bcl2		

Kinetic Law

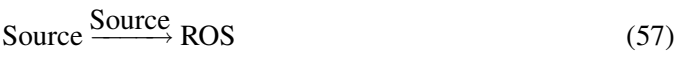
**Derived unit** contains undeclared units

$$v_{28} = krelBecBaxBcl2 \cdot Bax\_Bcl2\_Beclin\_I \tag{56}$$

6.29 Reaction ROS\_generation

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

Reaction equation



Reactant

Table 90: Properties of each reactant.

Id	Name	SBO
Source		

## Modifier

Table 91: Properties of each modifier.

Id	Name	SBO
Source		

## Product

Table 92: Properties of each product.

Id	Name	SBO
ROS		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{29} = k_{\text{genROS}} \cdot \text{Source} \quad (58)$$

## 6.30 Reaction ROS\_removal

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

### Reaction equation



## Reactant

Table 93: Properties of each reactant.

Id	Name	SBO
ROS		

## Modifier

Table 94: Properties of each modifier.

Id	Name	SBO
ROS		

## Product

Table 95: Properties of each product.

Id	Name	SBO
Sink		

## Kinetic Law

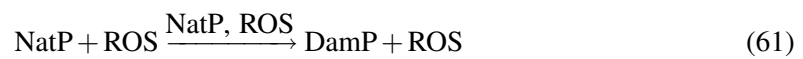
**Derived unit** contains undeclared units

$$v_{30} = \text{kremROS} \cdot \text{ROS} \quad (60)$$

### 6.31 Reaction *Protein\_Damage\_by\_ROS*

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

#### Reaction equation



## Reactants

Table 96: Properties of each reactant.

Id	Name	SBO
NatP		
ROS		

## Modifiers

Table 97: Properties of each modifier.

Id	Name	SBO
NatP		
ROS		

## Products

Table 98: Properties of each product.

Id	Name	SBO
DamP		
ROS		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{31} = \frac{k_{\text{damNatP}} \cdot \text{NatP} \cdot \text{ROS}}{10 + \text{ROS}} \quad (62)$$

### 6.32 Reaction Removal\_DamP\_by\_Autophagy

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

## Reaction equation



## Reactants

Table 99: Properties of each reactant.

Id	Name	SBO
DamP		
Lys_A		

## Modifiers



Table 100: Properties of each modifier.

Id	Name	SBO
	DamP	
	Lys_A	

## Product

Table 101: Properties of each product.

Id	Name	SBO
	Lys_A	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{32} = kdegDamP \cdot DamP \cdot Lys\_A \quad (64)$$

## 6.33 Reaction `Production_of_AGEproducts`

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

## Reaction equation



## Reactant

Table 102: Properties of each reactant.

Id	Name	SBO
	Source	

## Modifier

Table 103: Properties of each modifier.

Id	Name	SBO
	Source	

## Product

Table 104: Properties of each product.

Id	Name	SBO
AGEprod		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{33} = k_{\text{prodAGE}} \cdot \text{Source} \quad (66)$$

### 6.34 Reaction RAGE\_activation

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

## Reaction equation



## Reactant

Table 105: Properties of each reactant.

Id	Name	SBO
AGEprod		

## Modifier

Table 106: Properties of each modifier.

Id	Name	SBO
AGEprod		

## Products

Table 107: Properties of each product.

Id	Name	SBO
AGEprod		

Id	Name	SBO
RAGE		

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{34} = k_{act}RAGE \cdot AGE_{prod} \quad (68)$$

### 6.35 Reaction ROS\_production\_by\_RAGE

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

#### Reaction equation



#### Reactant

Table 108: Properties of each reactant.

Id	Name	SBO
RAGE		

#### Modifier

Table 109: Properties of each modifier.

Id	Name	SBO
RAGE		

#### Products

Table 110: Properties of each product.

Id	Name	SBO
RAGE		
ROS		

## Kinetic Law

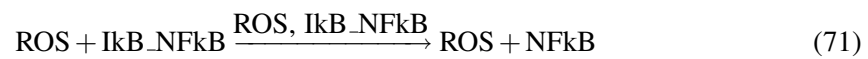
**Derived unit** contains undeclared units

$$v_{35} = k_{\text{genROSbyRAGE}} \cdot \text{RAGE} \quad (70)$$

## 6.36 Reaction IkB\_degradation\_via\_ROS

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

### Reaction equation



### Reactants

Table 111: Properties of each reactant.

Id	Name	SBO
ROS		
IkB_NFkB		

### Modifiers

Table 112: Properties of each modifier.

Id	Name	SBO
ROS		
IkB_NFkB		

### Products

Table 113: Properties of each product.

Id	Name	SBO
ROS		
NFkB		

## Kinetic Law

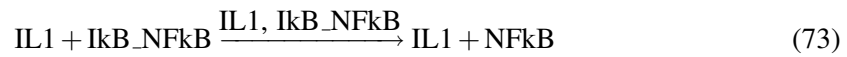
**Derived unit** contains undeclared units

$$v_{36} = k_{degIkB} \cdot ROS \cdot IkB\_NFkB \quad (72)$$

### 6.37 Reaction `IkB_degradation_via_IL1`

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

#### Reaction equation



#### Reactants

Table 114: Properties of each reactant.

Id	Name	SBO
IL1		
IkB_NFkB		

#### Modifiers

Table 115: Properties of each modifier.

Id	Name	SBO
IL1		
IkB_NFkB		

#### Products

Table 116: Properties of each product.

Id	Name	SBO
IL1		
NFkB		

#### Kinetic Law

**Derived unit** contains undeclared units

$$v_{37} = k_{degIkB} \cdot IL1 \cdot IkB\_NFkB \quad (74)$$

### 6.38 Reaction NFkB\_inactivation

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

#### Reaction equation



#### Reactants

Table 117: Properties of each reactant.

Id	Name	SBO
	NFkB	
	IkB	

#### Modifiers

Table 118: Properties of each modifier.

Id	Name	SBO
	NFkB	
	IkB	

#### Product

Table 119: Properties of each product.

Id	Name	SBO
	IkB_NFkB	

#### Kinetic Law

**Derived unit** contains undeclared units

$$v_{38} = \text{kinactNFkB} \cdot \text{NFkB} \cdot \text{IkB} \quad (76)$$

### 6.39 Reaction RAGE\_inactivation

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

Reaction equation



Reactant

Table 120: Properties of each reactant.

Id	Name	SBO
RAGE		

Modifier

Table 121: Properties of each modifier.

Id	Name	SBO
RAGE		

Product

Table 122: Properties of each product.

Id	Name	SBO
Sink		

Kinetic Law

**Derived unit** contains undeclared units

$$v_{39} = \text{kinactRAGE} \cdot \text{RAGE}$$

(78)

6.40 Reaction `RAGE_upregulation_byNFkB`

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

Reaction equation



Reactant

Table 123: Properties of each reactant.

Id	Name	SBO
NFkB_P		

## Modifier

Table 124: Properties of each modifier.

Id	Name	SBO
NFkB_P		

## Products

Table 125: Properties of each product.

Id	Name	SBO
NFkB_P		
RAGE		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{40} = k_{\text{synRAGE}} \cdot \text{NFkB\_P} \quad (80)$$

### 6.41 Reaction IL1\_production

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

#### Reaction equation



## Reactant

Table 126: Properties of each reactant.

Id	Name	SBO
NFkB_P		



## Modifier

Table 127: Properties of each modifier.

Id	Name	SBO
NFkB_P		

## Products

Table 128: Properties of each product.

Id	Name	SBO
NFkB_P		
IL1		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{41} = k_{\text{synIL1}} \cdot \text{NFkB\_P} \quad (82)$$

### 6.42 Reaction [IL1\\_degradation](#)

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

#### Reaction equation



## Reactant

Table 129: Properties of each reactant.

Id	Name	SBO
IL1		

## Modifier

Table 130: Properties of each modifier.

Id	Name	SBO
IL1		

## Product

Table 131: Properties of each product.

Id	Name	SBO
Sink		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{42} = kdegIL1 \cdot IL1 \quad (84)$$

## 6.43 Reaction Ikb\_production

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

## Reaction equation



## Reactant

Table 132: Properties of each reactant.

Id	Name	SBO
NFkB_P		

## Modifier

Table 133: Properties of each modifier.

Id	Name	SBO
NFkB_P		

## Products

Table 134: Properties of each product.

Id	Name	SBO
	NFkB_P	
	IkB	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{43} = k_{\text{synIkB}} \cdot \text{NFkB\_P} \quad (86)$$

## 6.44 Reaction `MMP13_production`

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

### Reaction equation



## Reactant

Table 135: Properties of each reactant.

Id	Name	SBO
	IL1	

## Modifier

Table 136: Properties of each modifier.

Id	Name	SBO
	IL1	

## Products

Table 137: Properties of each product.

Id	Name	SBO
IL1		
proMMP13		

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{44} = k_{\text{synMMP13}} \cdot \text{IL1} \quad (88)$$

### 6.45 Reaction `MMP13_removal`

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

### Reaction equation



### Reactant

Table 138: Properties of each reactant.

Id	Name	SBO
MMP13		

### Modifier

Table 139: Properties of each modifier.

Id	Name	SBO
MMP13		

### Product

Table 140: Properties of each product.

Id	Name	SBO
Sink		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{45} = kdegMMP13 \cdot MMP13 \quad (90)$$

## 6.46 Reaction `MMP2_production`

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

### Reaction equation



### Reactant

Table 141: Properties of each reactant.

Id	Name	SBO
IL1		

### Modifier

Table 142: Properties of each modifier.

Id	Name	SBO
IL1		

### Products

Table 143: Properties of each product.

Id	Name	SBO
IL1		
proMMP2		

## Kinetic Law

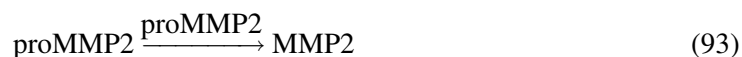
**Derived unit** contains undeclared units

$$v_{46} = ksynMMP2 \cdot IL1 \quad (92)$$

### 6.47 Reaction MMP\_activation

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

#### Reaction equation



#### Reactant

Table 144: Properties of each reactant.

Id	Name	SBO
proMMP2		

#### Modifier

Table 145: Properties of each modifier.

Id	Name	SBO
proMMP2		

#### Product

Table 146: Properties of each product.

Id	Name	SBO
MMP2		

#### Kinetic Law

**Derived unit** contains undeclared units

$$v_{47} = k_{\text{actMMP2}} \cdot \text{proMMP2} \quad (94)$$

### 6.48 Reaction MMP2\_degradation

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

#### Reaction equation



## Reactant

Table 147: Properties of each reactant.

Id	Name	SBO
MMP2		

## Modifier

Table 148: Properties of each modifier.

Id	Name	SBO
MMP2		

## Product

Table 149: Properties of each product.

Id	Name	SBO
Sink		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{48} = kdegMMP2 \cdot MMP2 \quad (96)$$

## 6.49 Reaction ADAMTS5\_production

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

### Reaction equation



## Reactant

Table 150: Properties of each reactant.

Id	Name	SBO
IL1		

## Modifier

Table 151: Properties of each modifier.

Id	Name	SBO
IL1		

## Products

Table 152: Properties of each product.

Id	Name	SBO
IL1		
ADAMTS5		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{49} = k_{\text{synADAMTS5}} \cdot \text{IL1} \quad (98)$$

### 6.50 Reaction ADAMTS5\_removal

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

#### Reaction equation



## Reactant

Table 153: Properties of each reactant.

Id	Name	SBO
ADAMTS5		

## Modifier



Table 154: Properties of each modifier.

Id	Name	SBO
ADAMTS5		

## Product

Table 155: Properties of each product.

Id	Name	SBO
Sink		

## Kinetic Law

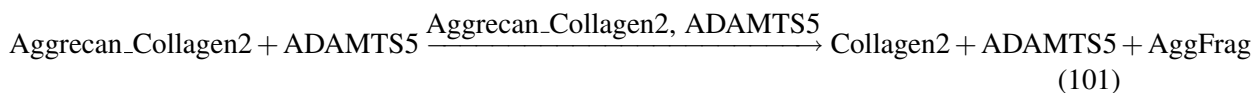
**Derived unit** contains undeclared units

$$v_{50} = kdegADAMTS5 \cdot ADAMTS5 \quad (100)$$

## 6.51 Reaction Aggrecan\_degradation

This is an irreversible reaction of two reactants forming three products influenced by two modifiers.

### Reaction equation



## Reactants

Table 156: Properties of each reactant.

Id	Name	SBO
Aggrecan_Collagen2		
ADAMTS5		

## Modifiers

Table 157: Properties of each modifier.

Id	Name	SBO
	AggreCan_Collagen2	
	ADAMTS5	

## Products

Table 158: Properties of each product.

Id	Name	SBO
	Collagen2	
	ADAMTS5	
	AggFrag	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{51} = kdegAggreCan \cdot AggreCan\_Collagen2 \cdot ADAMTS5 \quad (102)$$

## 6.52 Reaction [Collagen\\_degradation](#)

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

### Reaction equation



## Reactants

Table 159: Properties of each reactant.

Id	Name	SBO
	Collagen2	
	MMP13	

## Modifiers

Table 160: Properties of each modifier.

Id	Name	SBO
Collagen2		
MMP13		

## Products

Table 161: Properties of each product.

Id	Name	SBO
MMP13		
ColFrag		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{52} = kdegCollagen \cdot Collagen2 \cdot MMP13 \quad (104)$$

### 6.53 Reaction ROS\_production\_by\_DamP

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

#### Reaction equation



## Reactant

Table 162: Properties of each reactant.

Id	Name	SBO
DamP		

## Modifier

Table 163: Properties of each modifier.

Id	Name	SBO
DamP		

## Products

Table 164: Properties of each product.

Id	Name	SBO
	DamP	
	ROS	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{53} = k_{\text{genROSbyDamP}} \cdot \text{DamP} \quad (106)$$

## 6.54 Reaction `Protein_synthesis`

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

### Reaction equation



## Reactant

Table 165: Properties of each reactant.

Id	Name	SBO
	Source	

## Modifier

Table 166: Properties of each modifier.

Id	Name	SBO
	Source	

## Product

Table 167: Properties of each product.

Id	Name	SBO
NatP		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{54} = k_{\text{synNatP}} \cdot \text{Source} \quad (108)$$

## 6.55 Reaction SOD\_synthesis

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

## Reaction equation



## Reactant

Table 168: Properties of each reactant.

Id	Name	SBO
NFkB_P		

## Modifier

Table 169: Properties of each modifier.

Id	Name	SBO
NFkB_P		

## Products

Table 170: Properties of each product.

Id	Name	SBO
NFkB_P		
SOD		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{55} = k_{\text{synSOD}} \cdot \text{NFkB\_P} \quad (110)$$

## 6.56 Reaction SOD\_degradation

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

## Reaction equation



## Reactant

Table 171: Properties of each reactant.

Id	Name	SBO
SOD		

## Modifier

Table 172: Properties of each modifier.

Id	Name	SBO
SOD		

## Product

Table 173: Properties of each product.

Id	Name	SBO
Sink		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{56} = k_{\text{degSOD}} \cdot \text{SOD} \quad (112)$$

### 6.57 Reaction ROS\_removal\_by\_SOD

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

#### Reaction equation



#### Reactants

Table 174: Properties of each reactant.

Id	Name	SBO
ROS		
SOD		

#### Modifiers

Table 175: Properties of each modifier.

Id	Name	SBO
SOD		
ROS		

#### Product

Table 176: Properties of each product.

Id	Name	SBO
SOD		

#### Kinetic Law

**Derived unit** contains undeclared units

$$v_{57} = \text{kremROSbySOD} \cdot \text{SOD} \cdot \text{ROS} \quad (114)$$

### 6.58 Reaction p38\_phosphorylation

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

### Reaction equation



### Reactants

Table 177: Properties of each reactant.

Id	Name	SBO
p38		
IL1		

### Modifiers

Table 178: Properties of each modifier.

Id	Name	SBO
p38		
IL1		

### Products

Table 179: Properties of each product.

Id	Name	SBO
p38_P		
IL1		

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{58} = \text{kphosp38} \cdot \text{p38} \cdot \text{IL1} \quad (116)$$

## 6.59 Reaction p38\_phosphorylation\_via\_ROS

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

### Reaction equation





Reactants

Table 180: Properties of each reactant.

Id	Name	SBO
p38		
ROS		

Modifiers

Table 181: Properties of each modifier.

Id	Name	SBO
p38		
ROS		

Products

Table 182: Properties of each product.

Id	Name	SBO
p38_P		
ROS		

Kinetic Law

**Derived unit** contains undeclared units

$$v_{59} = kphosp38ROS \cdot p38 \cdot ROS \tag{118}$$

6.60 Reaction p38\_dephosphorylation

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

Reaction equation



Reactant

Table 183: Properties of each reactant.

Id	Name	SBO
p38_P		

## Modifier

Table 184: Properties of each modifier.

Id	Name	SBO
p38_P		

## Product

Table 185: Properties of each product.

Id	Name	SBO
p38		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{60} = k_{\text{dephosp38}} \cdot \text{p38\_P} \quad (120)$$

## 6.61 Reaction NFkB\_activation

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

## Reaction equation



## Reactants

Table 186: Properties of each reactant.

Id	Name	SBO
NFkB		
p38_P		

## Modifiers

Table 187: Properties of each modifier.

Id	Name	SBO
NFkB		
p38_P		

## Products

Table 188: Properties of each product.

Id	Name	SBO
NFkB_P		
p38_P		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{61} = k_{\text{phosNFkB}} \cdot \text{NFkB} \cdot \text{p38\_P} \quad (122)$$

### 6.62 Reaction NFkB\_dephosphorylation

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

#### Reaction equation



## Reactant

Table 189: Properties of each reactant.

Id	Name	SBO
NFkB_P		

## Modifier

Table 190: Properties of each modifier.

Id	Name	SBO
NFkB_P		

## Product

Table 191: Properties of each product.

Id	Name	SBO
NFkB		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{62} = k_{\text{dephosNFkB}} \cdot \text{NFkB\_P} \quad (124)$$

## 6.63 Reaction ROS\_production\_by\_p38\_P

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

## Reaction equation



## Reactant

Table 192: Properties of each reactant.

Id	Name	SBO
p38_P		

## Modifier

Table 193: Properties of each modifier.

Id	Name	SBO
p38_P		

## Products

Table 194: Properties of each product.

Id	Name	SBO
p38_P		
ROS		

## Kinetic Law

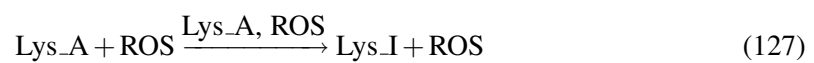
**Derived unit** contains undeclared units

$$v_{63} = k_{\text{genROSbyp38}} \cdot \text{p38\_P} \quad (126)$$

## 6.64 Reaction `Lysosome_damage_by_ROS`

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

## Reaction equation



## Reactants

Table 195: Properties of each reactant.

Id	Name	SBO
Lys_A		
ROS		

## Modifiers

Table 196: Properties of each modifier.

Id	Name	SBO
Lys_A		
ROS		

## Products

Table 197: Properties of each product.

Id	Name	SBO
Lys_I		
ROS		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{64} = \frac{k_{\text{damLys}} \cdot \text{Lys\_A} \cdot \text{ROS}}{10 + \text{ROS}} \quad (128)$$

## 6.65 Reaction *IntegrinActivationByMechanicalStress*

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

### Reaction equation



## Reactant

Table 198: Properties of each reactant.

Id	Name	SBO
Source		

## Modifier

Table 199: Properties of each modifier.

Id	Name	SBO
Source		

## Products

Table 200: Properties of each product.

Id	Name	SBO
Integrin		

Id	Name	SBO
IntegrinCount		

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{65} = kactIntegrin \cdot Source \quad (130)$$

### 6.66 Reaction *IntegrinInactivation*

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

### Reaction equation



### Reactant

Table 201: Properties of each reactant.

Id	Name	SBO
Integrin		

### Modifier

Table 202: Properties of each modifier.

Id	Name	SBO
Integrin		

### Product

Table 203: Properties of each product.

Id	Name	SBO
Sink		

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{66} = \text{kinactIntegrin} \cdot \text{Integrin} \quad (132)$$

### 6.67 Reaction Alk5Synthesis

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

#### Reaction equation



#### Reactant

Table 204: Properties of each reactant.

Id	Name	SBO
Source		

#### Modifier

Table 205: Properties of each modifier.

Id	Name	SBO
Source		

#### Product

Table 206: Properties of each product.

Id	Name	SBO
Alk5		

#### Kinetic Law

**Derived unit** contains undeclared units

$$v_{67} = \text{ksynAlk5} \cdot \text{Source} \quad (134)$$

### 6.68 Reaction TgfbActivationByIntegrin

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.



### Reaction equation



### Reactants

Table 207: Properties of each reactant.

Id	Name	SBO
Tgfb_I		
Integrin		

### Modifiers

Table 208: Properties of each modifier.

Id	Name	SBO
Tgfb_I		
Integrin		

### Products

Table 209: Properties of each product.

Id	Name	SBO
Tgfb_A		
Integrin		

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{68} = k_{act} \text{TgfbIntegrin} \cdot \text{Tgfb\_I} \cdot \text{Integrin} \quad (136)$$

## 6.69 Reaction TgfbActivationByMMP2

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

### Reaction equation



Reactants

Table 210: Properties of each reactant.

Id	Name	SBO
Tgfb_I		
MMP2		

Modifiers

Table 211: Properties of each modifier.

Id	Name	SBO
Tgfb_I		
MMP2		

Products

Table 212: Properties of each product.

Id	Name	SBO
Tgfb_A		
MMP2		

Kinetic Law

**Derived unit** contains undeclared units

$$v_{69} = k_{actTgfbMMP2} \cdot Tgfb\_I \cdot MMP2 \tag{138}$$

6.70 Reaction TgfbInactivation

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

Reaction equation



Reactant

Table 213: Properties of each reactant.

Id	Name	SBO
Tgfb_A		

## Modifier

Table 214: Properties of each modifier.

Id	Name	SBO
Tgfb_A		

## Product

Table 215: Properties of each product.

Id	Name	SBO
Tgfb_I		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{70} = \text{kinactTgfb} \cdot \text{Tgfb\_A} \quad (140)$$

## 6.71 Reaction Alk5Dimerisation

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

### Reaction equation



## Reactant

Table 216: Properties of each reactant.

Id	Name	SBO
Alk5		

## Modifier

Table 217: Properties of each modifier.

Id	Name	SBO
Alk5		

## Product

Table 218: Properties of each product.

Id	Name	SBO
Alk5_dimer		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{71} = \text{k dimer Alk5} \cdot \text{Alk5} \cdot (\text{Alk5} - 1) \cdot 0.5 \quad (142)$$

## 6.72 Reaction *Alk5Dedimerisation*

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

### Reaction equation



## Reactant

Table 219: Properties of each reactant.

Id	Name	SBO
Alk5_dimer		

## Modifier

Table 220: Properties of each modifier.

Id	Name	SBO
Alk5_dimer		

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

## Product

Table 221: Properties of each product.

Id	Name	SBO
Alk5		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{72} = k_{\text{dedimerAlk5}} \cdot \text{Alk5\_dimer} \quad (144)$$

## 6.73 Reaction Alk1Alk5Binding

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

## Reaction equation



## Reactants

Table 222: Properties of each reactant.

Id	Name	SBO
Alk1		
Alk5		

## Modifiers

Table 223: Properties of each modifier.

Id	Name	SBO
Alk1		
Alk5		

## Product

Table 224: Properties of each product.

Id	Name	SBO
Alk1_Alk5		

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{73} = k_{\text{binAlk1Alk5}} \cdot \text{Alk1} \cdot \text{Alk5} \quad (146)$$

### 6.74 Reaction Alk1Alk5Release

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

### Reaction equation



### Reactant

Table 225: Properties of each reactant.

Id	Name	SBO
Alk1_Alk5		

### Modifier

Table 226: Properties of each modifier.

Id	Name	SBO
Alk1_Alk5		

### Products

Table 227: Properties of each product.

Id	Name	SBO
Alk1		
Alk5		

## Kinetic Law

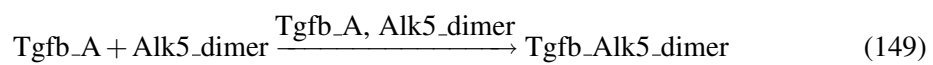
**Derived unit** contains undeclared units

$$v_{74} = k_{relAlk1Alk5} \cdot Alk1\_Alk5 \quad (148)$$

## 6.75 Reaction TgfbReceptorBindingAlk5

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

### Reaction equation



### Reactants

Table 228: Properties of each reactant.

Id	Name	SBO
Tgfb_A		
Alk5_dimer		

### Modifiers

Table 229: Properties of each modifier.

Id	Name	SBO
Tgfb_A		
Alk5_dimer		

### Product

Table 230: Properties of each product.

Id	Name	SBO
Tgfb_Alk5_dimer		

## Kinetic Law

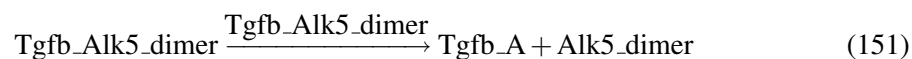
**Derived unit** contains undeclared units

$$v_{75} = k_{binTgfbAlk5} \cdot Tgfb\_A \cdot Alk5\_dimer \quad (150)$$

## 6.76 Reaction `TgfbReceptorRelease`

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

### Reaction equation



### Reactant

Table 231: Properties of each reactant.

Id	Name	SBO
Tgfb_Alk5_dimer		

### Modifier

Table 232: Properties of each modifier.

Id	Name	SBO
Tgfb_Alk5_dimer		

### Products

Table 233: Properties of each product.

Id	Name	SBO
Tgfb_A		
Alk5_dimer		

### Kinetic Law

**Derived unit** contains undeclared units

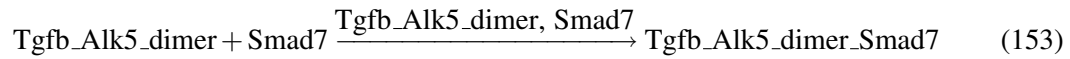
$$v_{76} = k_{\text{relTgfbAlk5}} \cdot \text{Tgfb\_Alk5\_dimer} \quad (152)$$

## 6.77 Reaction `Tgfb_Alk5_BindingSmad7`

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



### Reaction equation



### Reactants

Table 234: Properties of each reactant.

Id	Name	SBO
Tgfb_Alk5_dimer		
Smad7		

### Modifiers

Table 235: Properties of each modifier.

Id	Name	SBO
Tgfb_Alk5_dimer		
Smad7		

### Product

Table 236: Properties of each product.

Id	Name	SBO
Tgfb_Alk5_dimer_Smad7		

### Kinetic Law

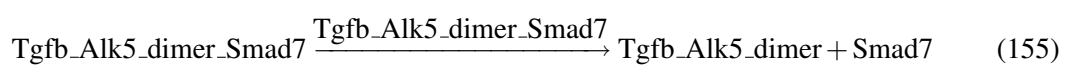
**Derived unit** contains undeclared units

$$v_{77} = k_{\text{binSmad7Alk5}} \cdot \text{Tgfb\_Alk5\_dimer} \cdot \text{Smad7} \quad (154)$$

## 6.78 Reaction Tgfb\_Alk5\_Smad7Release

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

### Reaction equation



Reactant

Table 237: Properties of each reactant.

Id	Name	SBO
Tgfb_Alk5_dimer_Smad7		

Modifier

Table 238: Properties of each modifier.

Id	Name	SBO
Tgfb_Alk5_dimer_Smad7		

Products

Table 239: Properties of each product.

Id	Name	SBO
Tgfb_Alk5_dimer Smad7		

Kinetic Law

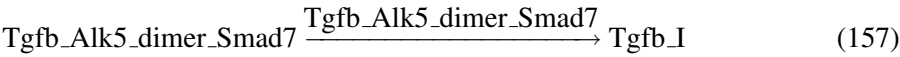
**Derived unit** contains undeclared units

$$v_{78} = krelSmad7Alk5 \cdot Tgfb\_Alk5\_dimer\_Smad7 \tag{156}$$

6.79 Reaction Alk5\_Smad7Degradation

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

Reaction equation



Reactant

Table 240: Properties of each reactant.

Id	Name	SBO
Tgfb_Alk5_dimer_Smad7		

## Modifier

Table 241: Properties of each modifier.

Id	Name	SBO
Tgfb_Alk5_dimer_Smad7		

## Product

Table 242: Properties of each product.

Id	Name	SBO
Tgfb_I		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{79} = kdegSmad7Alk5 \cdot Tgfb\_Alk5\_dimer\_Smad7 \quad (158)$$

## 6.80 Reaction TgfbReceptorBindingAlk1

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

### Reaction equation



## Reactants

Table 243: Properties of each reactant.

Id	Name	SBO
Tgfb_A		
Alk1_Alk5		

## Modifiers

Table 244: Properties of each modifier.

Id	Name	SBO
Tgfb_A		
Alk1_Alk5		

## Product

Table 245: Properties of each product.

Id	Name	SBO
Tgfb_Alk1_Alk5		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{80} = k_{\text{binTgfbAlk1}} \cdot \text{Tgfb\_A} \cdot \text{Alk1\_Alk5} \quad (160)$$

### 6.81 Reaction TgfbAlk1Release

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

#### Reaction equation



## Reactant

Table 246: Properties of each reactant.

Id	Name	SBO
Tgfb_Alk1_Alk5		

## Modifier

Table 247: Properties of each modifier.

Id	Name	SBO
Tgfb_Alk1_Alk5		

## Products

Table 248: Properties of each product.

Id	Name	SBO
Tgfb_A Alk1_Alk5		

## Kinetic Law

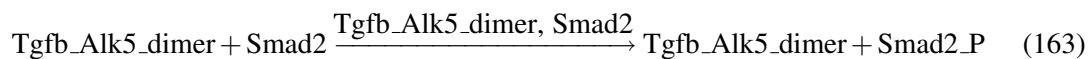
**Derived unit** contains undeclared units

$$v_{81} = krelTgfbAlk1 \cdot Tgfb\_Alk1\_Alk5 \quad (162)$$

## 6.82 Reaction Smad2Phosphorylation

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

### Reaction equation



## Reactants

Table 249: Properties of each reactant.

Id	Name	SBO
Tgfb_Alk5_dimer Smad2		

## Modifiers

Table 250: Properties of each modifier.

Id	Name	SBO
	Tgfb_Alk5_dimer	
	Smad2	

## Products

Table 251: Properties of each product.

Id	Name	SBO
	Tgfb_Alk5_dimer	
	Smad2_P	

## Kinetic Law

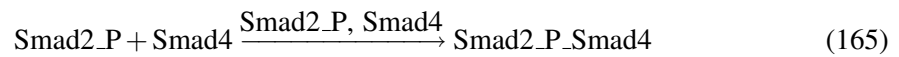
**Derived unit** contains undeclared units

$$v_{82} = k_{\text{phosSmad2}} \cdot \text{Tgfb\_Alk5\_dimer} \cdot \text{Smad2} \quad (164)$$

## 6.83 Reaction [Smad2Smad4Binding](#)

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

### Reaction equation



## Reactants

Table 252: Properties of each reactant.

Id	Name	SBO
	Smad2_P	
	Smad4	

## Modifiers

Table 253: Properties of each modifier.

Id	Name	SBO
Smad2_P		
Smad4		

## Product

Table 254: Properties of each product.

Id	Name	SBO
Smad2_P_Smad4		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{83} = k_{binSmad2Smad4} \cdot Smad2\_P \cdot Smad4 \quad (166)$$

## 6.84 Reaction Smad2PSmad4Release

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

### Reaction equation



## Reactant

Table 255: Properties of each reactant.

Id	Name	SBO
Smad2_P_Smad4		

## Modifier

Table 256: Properties of each modifier.

Id	Name	SBO
Smad2_P_Smad4		

## Products

Table 257: Properties of each product.

Id	Name	SBO
Smad2_P		
Smad4		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{84} = k_{rel} \text{Smad2Smad4} \cdot \text{Smad2\_P\_Smad4} \quad (168)$$

### 6.85 Reaction [Smad2DephosphorylationNuc](#)

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

## Reaction equation



## Reactant

Table 258: Properties of each reactant.

Id	Name	SBO
Smad2_P		

## Modifier

Table 259: Properties of each modifier.

Id	Name	SBO
Smad2_P		

## Product



Table 260: Properties of each product.

Id	Name	SBO
Smad2		

### Kinetic Law

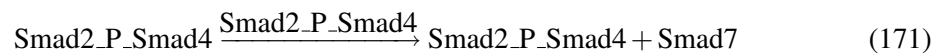
**Derived unit** contains undeclared units

$$v_{85} = k_{\text{dephosSmad2}} \cdot \text{Smad2\_P} \quad (170)$$

### 6.86 Reaction Smad7Synthesis

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

### Reaction equation



### Reactant

Table 261: Properties of each reactant.

Id	Name	SBO
Smad2_P_Smad4		

### Modifier

Table 262: Properties of each modifier.

Id	Name	SBO
Smad2_P_Smad4		

### Products

Table 263: Properties of each product.

Id	Name	SBO
Smad2_P_Smad4		
Smad7		

## Kinetic Law

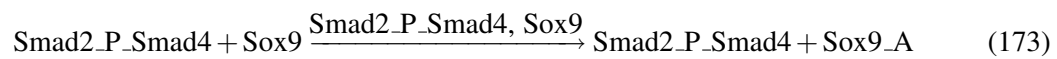
**Derived unit** contains undeclared units

$$v_{86} = k_{\text{synSmad7}} \cdot \text{Smad2\_P\_Smad4} \quad (172)$$

## 6.87 Reaction Sox9Activation

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

### Reaction equation



### Reactants

Table 264: Properties of each reactant.

Id	Name	SBO
Smad2_P_Smad4		
Sox9		

### Modifiers

Table 265: Properties of each modifier.

Id	Name	SBO
Smad2_P_Smad4		
Sox9		

### Products

Table 266: Properties of each product.

Id	Name	SBO
Smad2_P_Smad4		
Sox9_A		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{87} = k_{actSox9} \cdot Smad2\_P\_Smad4 \cdot Sox9 \quad (174)$$

### 6.88 Reaction Sox9Inactivation

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

#### Reaction equation



#### Reactant

Table 267: Properties of each reactant.

Id	Name	SBO
Sox9_A		

#### Modifier

Table 268: Properties of each modifier.

Id	Name	SBO
Sox9_A		

#### Product

Table 269: Properties of each product.

Id	Name	SBO
Sox9		

#### Kinetic Law

**Derived unit** contains undeclared units

$$v_{88} = k_{inactSox9} \cdot Sox9\_A \quad (176)$$

### 6.89 Reaction Sox9BasalTranscription

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

Reaction equation



Reactant

Table 270: Properties of each reactant.

Id	Name	SBO
Source		

Modifier

Table 271: Properties of each modifier.

Id	Name	SBO
Source		

Product

Table 272: Properties of each product.

Id	Name	SBO
Sox9mRNA		

Kinetic Law

**Derived unit** contains undeclared units

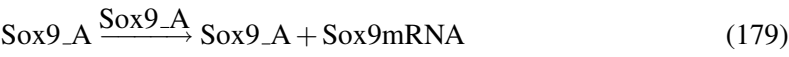
$v_{89} = k_{\text{synSox9mRNA}} \cdot \text{Source}$

(178)

6.90 Reaction Sox9EnhancedTranscription

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

Reaction equation



Reactant

Table 273: Properties of each reactant.

Id	Name	SBO
Sox9_A		

## Modifier

Table 274: Properties of each modifier.

Id	Name	SBO
Sox9_A		

## Products

Table 275: Properties of each product.

Id	Name	SBO
Sox9_A		
Sox9mRNA		

## Kinetic Law

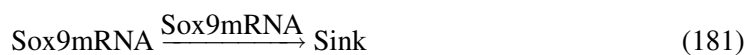
**Derived unit** contains undeclared units

$$v_{90} = k_{\text{synSox9mRNA}} \cdot \text{Sox9\_A} \quad (180)$$

### 6.91 Reaction Sox9mRNA\_Degradation

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

## Reaction equation



## Reactant

Table 276: Properties of each reactant.

Id	Name	SBO
Sox9mRNA		

## Modifier

Table 277: Properties of each modifier.

Id	Name	SBO
Sox9mRNA		

## Product

Table 278: Properties of each product.

Id	Name	SBO
Sink		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{91} = kdegSox9mRNA \cdot Sox9mRNA \quad (182)$$

## 6.92 Reaction Sox9Translation

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

### Reaction equation



## Reactant

Table 279: Properties of each reactant.

Id	Name	SBO
Sox9mRNA		

## Modifier

Table 280: Properties of each modifier.

Id	Name	SBO
Sox9mRNA		

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

## Products

Table 281: Properties of each product.

Id	Name	SBO
Sox9mRNA		
Sox9		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{92} = k_{\text{synSox9}} \cdot \text{Sox9mRNA} \quad (184)$$

## 6.93 Reaction Sox9Degradation

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

## Reaction equation



## Reactant

Table 282: Properties of each reactant.

Id	Name	SBO
Sox9		

## Modifier

Table 283: Properties of each modifier.

Id	Name	SBO
Sox9		

## Product

Table 284: Properties of each product.

Id	Name	SBO
Sink		

### Kinetic Law

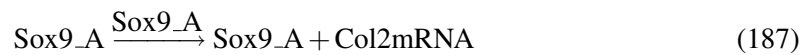
**Derived unit** contains undeclared units

$$v_{93} = kdegSox9 \cdot Sox9 \quad (186)$$

## 6.94 Reaction Collagen2EnhancedTranscriptionBySox9

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

### Reaction equation



### Reactant

Table 285: Properties of each reactant.

Id	Name	SBO
Sox9_A		

### Modifier

Table 286: Properties of each modifier.

Id	Name	SBO
Sox9_A		

### Products

Table 287: Properties of each product.

Id	Name	SBO
Sox9_A		
Col2mRNA		



## Kinetic Law

**Derived unit** contains undeclared units

$$v_{94} = k_{\text{synCol2mRNA}} \cdot \text{Sox9\_A} \quad (188)$$

## 6.95 Reaction Collagen2TranscriptionBySmad2Smad4

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

### Reaction equation



### Reactant

Table 288: Properties of each reactant.

Id	Name	SBO
Smad2_P_Smad4		

### Modifier

Table 289: Properties of each modifier.

Id	Name	SBO
Smad2_P_Smad4		

### Products

Table 290: Properties of each product.

Id	Name	SBO
Smad2_P_Smad4		
Col2mRNA		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{95} = k_{\text{synCol2mRNA}} \cdot \text{Smad2\_P\_Smad4} \quad (190)$$

### 6.96 Reaction Col2mRNA\_Degradation

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

#### Reaction equation



#### Reactant

Table 291: Properties of each reactant.

Id	Name	SBO
Col2mRNA		

#### Modifier

Table 292: Properties of each modifier.

Id	Name	SBO
Col2mRNA		

#### Product

Table 293: Properties of each product.

Id	Name	SBO
Sink		

#### Kinetic Law

**Derived unit** contains undeclared units

$$v_{96} = k_{\text{degCol2mRNA}} \cdot \text{Col2mRNA} \quad (192)$$

### 6.97 Reaction Collagen2Translation

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

#### Reaction equation



Reactant

Table 294: Properties of each reactant.

Id	Name	SBO
Col2mRNA		

Modifier

Table 295: Properties of each modifier.

Id	Name	SBO
Col2mRNA		

Products

Table 296: Properties of each product.

Id	Name	SBO
Col2mRNA		
Collagen2		

Kinetic Law

**Derived unit** contains undeclared units

$$v_{97} = k_{\text{synCol2}} \cdot \text{Col2mRNA} \tag{194}$$

6.98 Reaction AggrecanEnhancedTranscription

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

Reaction equation



Reactant

Table 297: Properties of each reactant.

Id	Name	SBO
Sox9_A		

## Modifier

Table 298: Properties of each modifier.

Id	Name	SBO
Sox9_A		

## Products

Table 299: Properties of each product.

Id	Name	SBO
Sox9_A		
AcanmRNA		

## Kinetic Law

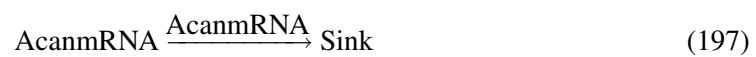
**Derived unit** contains undeclared units

$$v_{98} = k_{\text{synAcanmRNA}} \cdot \text{Sox9\_A} \quad (196)$$

## 6.99 Reaction AcanmRNA\_Degradation

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

## Reaction equation



## Reactant

Table 300: Properties of each reactant.

Id	Name	SBO
AcanmRNA		

## Modifier

Table 301: Properties of each modifier.

Id	Name	SBO
AcanmRNA		

## Product

Table 302: Properties of each product.

Id	Name	SBO
Sink		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{99} = kdegAcanmRNA \cdot AcanmRNA \quad (198)$$

## 6.100 Reaction AggreCanTranslation

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

### Reaction equation



## Reactant

Table 303: Properties of each reactant.

Id	Name	SBO
AcanmRNA		

## Modifier

Table 304: Properties of each modifier.

Id	Name	SBO
AcanmRNA		

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

## Products

Table 305: Properties of each product.

Id	Name	SBO
	AcanmRNA	
	Aggrecan	

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{100} = k_{\text{synAggrecan}} \cdot \text{AcanmRNA} \quad (200)$$

### 6.101 Reaction AggrecanCollagen2Binding

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

## Reaction equation



## Reactants

Table 306: Properties of each reactant.

Id	Name	SBO
	Aggrecan	
	Collagen2	

## Modifiers

Table 307: Properties of each modifier.

Id	Name	SBO
	Aggrecan	
	Collagen2	

## Product

Table 308: Properties of each product.

Id	Name	SBO
	AggreCan_Collagen2	

## Kinetic Law

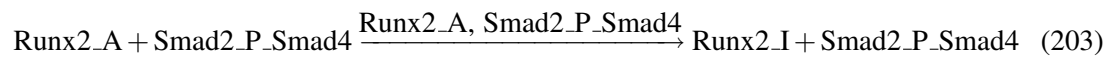
**Derived unit** contains undeclared units

$$v_{101} = k_{\text{binAggreCanCollagen2}} \cdot \text{AggreCan} \cdot \text{Collagen2} \quad (202)$$

### 6.102 Reaction [Runx2\\_InhibitionBySmad2](#)

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

## Reaction equation



## Reactants

Table 309: Properties of each reactant.

Id	Name	SBO
	Runx2_A	
	Smad2_P_Smad4	

## Modifiers

Table 310: Properties of each modifier.

Id	Name	SBO
	Runx2_A	
	Smad2_P_Smad4	

## Products

Table 311: Properties of each product.

Id	Name	SBO
Runx2_I		
Smad2_P_Smad4		

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{102} = \text{kinactRunx2} \cdot \text{Runx2\_A} \cdot \text{Smad2\_P\_Smad4} \quad (204)$$

### 6.103 Reaction Alk5Degradation

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

### Reaction equation



### Reactant

Table 312: Properties of each reactant.

Id	Name	SBO
Alk5		

### Modifier

Table 313: Properties of each modifier.

Id	Name	SBO
Alk5		

### Product

Table 314: Properties of each product.

Id	Name	SBO
Sink		



## Kinetic Law

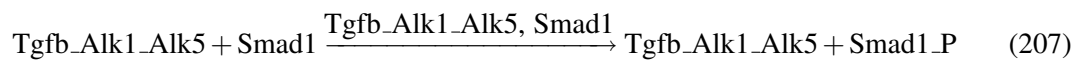
**Derived unit** contains undeclared units

$$v_{103} = kdegAlk5 \cdot Alk5 \quad (206)$$

### 6.104 Reaction `Smad1Activation`

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

#### Reaction equation



#### Reactants

Table 315: Properties of each reactant.

Id	Name	SBO
Tgfb_Alk1_Alk5		
Smad1		

#### Modifiers

Table 316: Properties of each modifier.

Id	Name	SBO
Tgfb_Alk1_Alk5		
Smad1		

#### Products

Table 317: Properties of each product.

Id	Name	SBO
Tgfb_Alk1_Alk5		
Smad1_P		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{104} = k_{\text{phos}} \text{Smad1} \cdot \text{Tgfb\_Alk1\_Alk5} \cdot \text{Smad1} \quad (208)$$

## 6.105 Reaction Smad1Dephosphorylation

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

### Reaction equation



### Reactant

Table 318: Properties of each reactant.

Id	Name	SBO
Smad1_P		

### Modifier

Table 319: Properties of each modifier.

Id	Name	SBO
Smad1_P		

### Product

Table 320: Properties of each product.

Id	Name	SBO
Smad1		

## Kinetic Law

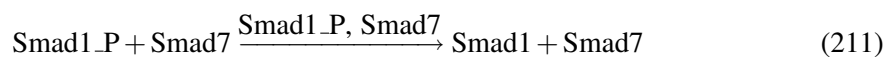
**Derived unit** contains undeclared units

$$v_{105} = k_{\text{dephos}} \text{Smad1} \cdot \text{Smad1\_P} \quad (210)$$

### 6.106 Reaction `Smad1DephosphorylationViaSmad7`

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

#### Reaction equation



#### Reactants

Table 321: Properties of each reactant.

Id	Name	SBO
	Smad1_P	
	Smad7	

#### Modifiers

Table 322: Properties of each modifier.

Id	Name	SBO
	Smad1_P	
	Smad7	

#### Products

Table 323: Properties of each product.

Id	Name	SBO
	Smad1	
	Smad7	

#### Kinetic Law

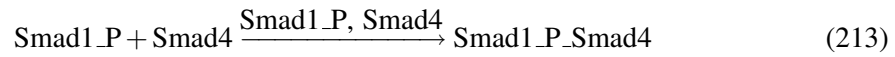
**Derived unit** contains undeclared units

$$v_{106} = k_{\text{dephosSmad1Smad7}} \cdot \text{Smad1\_P} \cdot \text{Smad7} \quad (212)$$

### 6.107 Reaction `Smad1Smad4Binding`

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

### Reaction equation



### Reactants

Table 324: Properties of each reactant.

Id	Name	SBO
	Smad1_P	
	Smad4	

### Modifiers

Table 325: Properties of each modifier.

Id	Name	SBO
	Smad1_P	
	Smad4	

### Product

Table 326: Properties of each product.

Id	Name	SBO
	Smad1_P_Smad4	

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{107} = k_{\text{binSmad1Smad4}} \cdot \text{Smad1\_P} \cdot \text{Smad4} \quad (214)$$

### 6.108 Reaction `Smad1Smad4Release`

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

### Reaction equation



**Reactant**

Table 327: Properties of each reactant.

Id	Name	SBO
Smad1_P_Smad4		

## Modifier

Table 328: Properties of each modifier.

Id	Name	SBO
Smad1_P_Smad4		

## Products

Table 329: Properties of each product.

Id	Name	SBO
Smad1_P		
Smad4		

## Kinetic Law

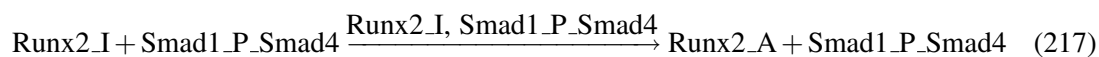
**Derived unit** contains undeclared units

$$v_{108} = krelSmad1Smad4 \cdot Smad1\_P\_Smad4 \quad (216)$$

### 6.109 Reaction `Runx2ActivationBySmad1`

This is an irreversible reaction of two reactants forming two products influenced by two modifiers.

#### Reaction equation



## Reactants

Table 330: Properties of each reactant.

Id	Name	SBO
Runx2_I		
Smad1_P_Smad4		

## Modifiers

Table 331: Properties of each modifier.

Id	Name	SBO
Runx2_I		
Smad1_P_Smad4		

## Products

Table 332: Properties of each product.

Id	Name	SBO
Runx2_A		
Smad1_P_Smad4		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{109} = k_{actRunx2} \cdot Runx2\_I \cdot Smad1\_P\_Smad4 \quad (218)$$

### 6.110 Reaction [MMP13InductionByRunx2](#)

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

#### Reaction equation



## Reactant

Table 333: Properties of each reactant.

Id	Name	SBO
Runx2_A		

## Modifier

Table 334: Properties of each modifier.

Id	Name	SBO
Runx2_A		

## Products

Table 335: Properties of each product.

Id	Name	SBO
proMMP13		
Runx2_A		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{110} = k_{\text{synMMP13Runx2}} \cdot \text{Runx2\_A} \quad (220)$$

### 6.111 Reaction Alk1Synthesis

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

## Reaction equation



## Reactant

Table 336: Properties of each reactant.

Id	Name	SBO
Source		

## Modifier

Table 337: Properties of each modifier.

Id	Name	SBO
Source		



## Product

Table 338: Properties of each product.

Id	Name	SBO
Alk1		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{111} = k_{\text{synAlk1}} \cdot \text{Source} \quad (222)$$

### 6.112 Reaction Alk1Degradation

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

## Reaction equation



## Reactant

Table 339: Properties of each reactant.

Id	Name	SBO
Alk1		

## Modifier

Table 340: Properties of each modifier.

Id	Name	SBO
Alk1		

## Product

Table 341: Properties of each product.

Id	Name	SBO
Sink		

Id	Name	SBO
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### Kinetic Law

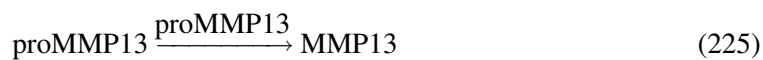
**Derived unit** contains undeclared units

$$v_{112} = kdegAlk1 \cdot Alk1 \quad (224)$$

### 6.113 Reaction MMP13Activation

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

### Reaction equation



### Reactant

Table 342: Properties of each reactant.

Id	Name	SBO
proMMP13		

### Modifier

Table 343: Properties of each modifier.

Id	Name	SBO
proMMP13		

### Product

Table 344: Properties of each product.

Id	Name	SBO
MMP13		

### Kinetic Law

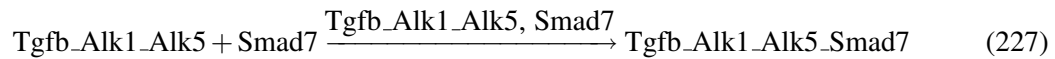
**Derived unit** contains undeclared units

$$v_{113} = k_{actMMP13} \cdot \text{proMMP13} \quad (226)$$

#### 6.114 Reaction [Tgfb\\_Alk1\\_Alk5\\_BindingSmad7](#)

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

##### Reaction equation



##### Reactants

Table 345: Properties of each reactant.

Id	Name	SBO
Tgfb_Alk1_Alk5		
Smad7		

##### Modifiers

Table 346: Properties of each modifier.

Id	Name	SBO
Tgfb_Alk1_Alk5		
Smad7		

##### Product

Table 347: Properties of each product.

Id	Name	SBO
Tgfb_Alk1_Alk5_Smad7		

##### Kinetic Law

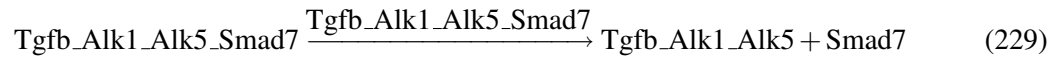
**Derived unit** contains undeclared units

$$v_{114} = k_{binSmad7Alk1} \cdot \text{Tgfb\_Alk1\_Alk5} \cdot \text{Smad7} \quad (228)$$

#### 6.115 Reaction [Tgfb\\_Alk1\\_Alk5\\_Smad7Release](#)

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

### Reaction equation



### Reactant

Table 348: Properties of each reactant.

Id	Name	SBO
Tgfb_Alk1_Alk5_Smad7		

### Modifier

Table 349: Properties of each modifier.

Id	Name	SBO
Tgfb_Alk1_Alk5_Smad7		

### Products

Table 350: Properties of each product.

Id	Name	SBO
Tgfb_Alk1_Alk5_Smad7		

### Kinetic Law

**Derived unit** contains undeclared units

$$v_{115} = \text{krelSmad7Alk1} \cdot \text{Tgfb\_Alk1\_Alk5\_Smad7} \quad (230)$$

### 6.116 Reaction Alk1\_Smad7Degradation

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

### Reaction equation



### Reactant

Table 351: Properties of each reactant.

Id	Name	SBO
Tgfb_Alk1_Alk5_Smad7		

## Modifier

Table 352: Properties of each modifier.

Id	Name	SBO
Tgfb_Alk1_Alk5_Smad7		

## Product

Table 353: Properties of each product.

Id	Name	SBO
Tgfb_I		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{116} = kdegSmad7Alk1 \cdot Tgfb\_Alk1\_Alk5\_Smad7 \quad (232)$$

### 6.117 Reaction [Smad7Degradation](#)

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

## Reaction equation



## Reactant

Table 354: Properties of each reactant.

Id	Name	SBO
Smad7		

## Modifier

Table 355: Properties of each modifier.

Id	Name	SBO
Smad7		

## Product

Table 356: Properties of each product.

Id	Name	SBO
Sink		

## Kinetic Law

**Derived unit** contains undeclared units

$$v_{117} = kdegSmad7 \cdot Smad7 \quad (234)$$

## 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 `AcanmRNA`

**Initial amount** 0 item

This species takes part in six reactions (as a reactant in `AcanmRNA_Degradation`, `AggrecanTranslation` and as a product in `AggrecanEnhancedTranscription`, `AggrecanTranslation` and as a modifier in `AcanmRNA_Degradation`, `AggrecanTranslation`).

$$\frac{d}{dt}AcanmRNA = v_{98} + v_{100} - v_{99} - v_{100} \quad (235)$$

## 7.2 Species ADAMTS5

**Initial amount** 0 item

This species takes part in six reactions (as a reactant in [ADAMTS5\\_removal](#), [Aggrecan\\_degradation](#) and as a product in [ADAMTS5\\_production](#), [Aggrecan\\_degradation](#) and as a modifier in [ADAMTS5\\_removal](#), [Aggrecan\\_degradation](#)).

$$\frac{d}{dt}\text{ADAMTS5} = v_{49} + v_{51} - v_{50} - v_{51} \quad (236)$$

## 7.3 Species AGEprod

**Initial amount** 0 item

This species takes part in four reactions (as a reactant in [RAGE\\_activation](#) and as a product in [Production\\_of\\_AGEproducts](#), [RAGE\\_activation](#) and as a modifier in [RAGE\\_activation](#)).

$$\frac{d}{dt}\text{AGEprod} = v_{33} + v_{34} - v_{34} \quad (237)$$

## 7.4 Species Alk1

**Initial amount** 500 item

This species takes part in six reactions (as a reactant in [Alk1Alk5Binding](#), [Alk1Degradation](#) and as a product in [Alk1Alk5Release](#), [Alk1Synthesis](#) and as a modifier in [Alk1Alk5Binding](#), [Alk1Degradation](#)).

$$\frac{d}{dt}\text{Alk1} = v_{74} + v_{111} - v_{73} - v_{112} \quad (238)$$

## 7.5 Species Alk1\_Alk5

**Initial amount** 0 item

This species takes part in six reactions (as a reactant in [Alk1Alk5Release](#), [TgfbReceptorBindingAlk1](#) and as a product in [Alk1Alk5Binding](#), [TgfbAlk1Release](#) and as a modifier in [Alk1Alk5Release](#), [TgfbReceptorBindingAlk1](#)).

$$\frac{d}{dt}\text{Alk1\_Alk5} = v_{73} + v_{81} - v_{74} - v_{80} \quad (239)$$

## 7.6 Species Alk5

**Initial amount** 500 item

This species takes part in nine reactions (as a reactant in [Alk5Dimerisation](#), [Alk1Alk5Binding](#), [Alk5Degradation](#) and as a product in [Alk5Synthesis](#), [Alk5Dedimerisation](#), [Alk1Alk5Release](#) and as a modifier in [Alk5Dimerisation](#), [Alk1Alk5Binding](#), [Alk5Degradation](#)).

$$\frac{d}{dt}\text{Alk5} = v_{67} + 2 v_{72} + v_{74} - 2 v_{71} - v_{73} - v_{103} \quad (240)$$

## 7.7 Species Alk5\_dimer

**SBO:0000607** dimer

**Initial amount** 0 item

This species takes part in six reactions (as a reactant in [Alk5Dedimerisation](#), [TgfbReceptorBindingAlk5](#) and as a product in [Alk5Dimerisation](#), [TgfbReceptorRelease](#) and as a modifier in [Alk5Dedimerisation](#), [TgfbReceptorBindingAlk5](#)).

$$\frac{d}{dt}\text{Alk5\_dimer} = v_{71} + v_{76} - v_{72} - v_{75} \quad (241)$$

## 7.8 Species Bax

**Initial amount** 0 item

This species takes part in twelve reactions (as a reactant in [CaspaseActivation](#), [Bax\\_Bcl2Binding](#), [BaxBindingToBcl2\\_Beclin](#), [BaxBindingToBcl2\\_BeclinI](#) and as a product in [CaspaseActivation](#), [Bax\\_Bcl2Release](#), [BaxDissociation\\_Bax\\_Bcl2\\_Beclin](#), [BaxDissociation\\_Bax\\_Bcl2\\_Beclin-I](#) and as a modifier in [CaspaseActivation](#), [Bax\\_Bcl2Binding](#), [BaxBindingToBcl2\\_Beclin](#), [BaxBindingToBcl2\\_BeclinI](#)).

$$\frac{d}{dt}\text{Bax} = v_1 + v_{14} + v_{25} + v_{26} - v_1 - v_{13} - v_{23} - v_{24} \quad (242)$$

## 7.9 Species Bax\_Bcl2

**Initial amount** 90 item

This species takes part in nine reactions (as a reactant in [Bax\\_Bcl2Release](#), [BeclinBindingToBax-Bcl2](#), [BeclinIBindingToBax\\_Bcl2](#) and as a product in [Bax\\_Bcl2Binding](#), [BeclinDissociation-Bax\\_Bcl2\\_Beclin](#), [Beclin\\_I\\_Dissociation\\_Bax\\_Bcl2\\_Beclin](#) and as a modifier in [Bax-Bcl2Release](#), [BeclinBindingToBax\\_Bcl2](#), [BeclinIBindingToBax\\_Bcl2](#)).

$$\frac{d}{dt}\text{Bax\_Bcl2} = v_{13} + v_{27} + v_{28} - v_{14} - v_{21} - v_{22} \quad (243)$$

## 7.10 Species Bax\_Bcl2\_Beclin

**Initial amount** 10 item

This species takes part in six reactions (as a reactant in [BaxDissociation\\_Bax\\_Bcl2\\_Beclin](#), [BeclinDissociation\\_Bax\\_Bcl2\\_Beclin](#) and as a product in [BeclinBindingToBax\\_Bcl2](#), [BaxBindingToBcl2\\_Beclin](#) and as a modifier in [BaxDissociation\\_Bax\\_Bcl2\\_Beclin](#), [BeclinDissociation-Bax\\_Bcl2\\_Beclin](#)).

$$\frac{d}{dt}\text{Bax\_Bcl2\_Beclin} = v_{21} + v_{23} - v_{25} - v_{27} \quad (244)$$



### 7.11 Species [Bax\\_Bcl2\\_Beclin\\_I](#)

**Initial amount** 0 item

This species takes part in six reactions (as a reactant in [BaxDissociation\\_Bax\\_Bcl2\\_Beclin\\_I](#), [Beclin\\_I\\_Dissociation\\_Bax\\_Bcl2\\_Beclin](#) and as a product in [BeclinIBindingToBax\\_Bcl2](#), [BaxBindingToBcl2\\_BeclinI](#) and as a modifier in [BaxDissociation\\_Bax\\_Bcl2\\_Beclin\\_I](#), [Beclin\\_I\\_Dissociation\\_Bax\\_Bcl2\\_Beclin](#)).

$$\frac{d}{dt} \text{Bax\_Bcl2\_Beclin\_I} = v_{22} + v_{24} - v_{26} - v_{28} \quad (245)$$

### 7.12 Species [Bcl2](#)

**Initial amount** 30 item

This species takes part in 19 reactions (as a reactant in [InhibitCaspase3](#), [Bcl2Degradation](#), [Bcl2DegradationStressInduced](#), [Bcl2DegradationCaspaseInduced](#), [Bax\\_Bcl2Binding](#), [Bcl2\\_BeclinBinding](#), [Bcl2\\_Beclin\\_I\\_Binding](#) and as a product in [InhibitCaspase3](#), [Bcl2Synthesis](#), [Bax\\_Bcl2Release](#), [Bcl2\\_BeclinRelease](#), [Bcl2\\_Beclin\\_I\\_Release](#) and as a modifier in [InhibitCaspase3](#), [Bcl2Degradation](#), [Bcl2DegradationStressInduced](#), [Bcl2DegradationCaspaseInduced](#), [Bax\\_Bcl2Binding](#), [Bcl2\\_BeclinBinding](#), [Bcl2\\_Beclin\\_I\\_Binding](#)).

$$\frac{d}{dt} \text{Bcl2} = v_6 + v_9 + v_{14} + v_{16} + v_{18} - v_6 - v_{10} - v_{11} - v_{12} - v_{13} - v_{15} - v_{17} \quad (246)$$

### 7.13 Species [Bcl2\\_Beclin](#)

**Initial amount** 25 item

This species takes part in nine reactions (as a reactant in [InhibitCaspase2](#), [Bcl2\\_BeclinRelease](#), [BaxBindingToBcl2\\_Beclin](#) and as a product in [InhibitCaspase2](#), [Bcl2\\_BeclinBinding](#), [BaxDissociation\\_Bax\\_Bcl2\\_Beclin](#) and as a modifier in [InhibitCaspase2](#), [Bcl2\\_BeclinRelease](#), [BaxBindingToBcl2\\_Beclin](#)).

$$\frac{d}{dt} \text{Bcl2\_Beclin} = v_5 + v_{15} + v_{25} - v_5 - v_{16} - v_{23} \quad (247)$$

### 7.14 Species [Bcl2\\_Beclin\\_I](#)

**Initial amount** 0 item

This species takes part in six reactions (as a reactant in [Bcl2\\_Beclin\\_I\\_Release](#), [BaxBindingToBcl2\\_BeclinI](#) and as a product in [Bcl2\\_Beclin\\_I\\_Binding](#), [BaxDissociation\\_Bax\\_Bcl2\\_Beclin\\_I](#) and as a modifier in [Bcl2\\_Beclin\\_I\\_Release](#), [BaxBindingToBcl2\\_BeclinI](#)).

$$\frac{d}{dt} \text{Bcl2\_Beclin\_I} = v_{17} + v_{26} - v_{18} - v_{24} \quad (248)$$

## 7.15 Species *Beclin*

**Initial amount** 75 item

This species takes part in 13 reactions (as a reactant in [ActivateLysosome](#), [Bcl2\\_BeclinBinding](#), [BeclinInactivation](#), [BeclinInactivationByCaspase](#), [BeclinBindingToBax\\_Bcl2](#) and as a product in [ActivateLysosome](#), [Bcl2\\_BeclinRelease](#), [BeclinDissociation\\_Bax\\_Bcl2-Beclin](#) and as a modifier in [ActivateLysosome](#), [Bcl2\\_BeclinBinding](#), [BeclinInactivation](#), [BeclinInactivationByCaspase](#), [BeclinBindingToBax\\_Bcl2](#)).

$$\frac{d}{dt}\text{Beclin} = v_7 + v_{16} + v_{27} - v_7 - v_{15} - v_{19} - v_{20} - v_{21} \quad (249)$$

## 7.16 Species *Beclin\_I*

**Initial amount** 0 item

This species takes part in eleven reactions (as a reactant in [CaspaseActivationByBeclin\\_I](#), [Bcl2\\_Beclin\\_I\\_Binding](#), [BeclinIBindingToBax\\_Bcl2](#) and as a product in [CaspaseActivationByBeclin-I](#), [Bcl2\\_Beclin\\_I\\_Release](#), [BeclinInactivation](#), [BeclinInactivationByCaspase](#), [Beclin-I\\_Dissociation\\_Bax\\_Bcl2\\_Beclin](#) and as a modifier in [CaspaseActivationByBeclin\\_I](#), [Bcl2\\_Beclin\\_I\\_Binding](#), [BeclinIBindingToBax\\_Bcl2](#)).

$$\frac{d}{dt}\text{Beclin.I} = v_2 + v_{18} + v_{19} + v_{20} + v_{28} - v_2 - v_{17} - v_{22} \quad (250)$$

## 7.17 Species *Caspase\_A*

**Initial amount** 0 item

This species takes part in 15 reactions (as a reactant in [CaspaseInactivation1](#), [InhibitCaspase2](#), [InhibitCaspase3](#), [Bcl2DegradationCaspaseInduced](#), [BeclinInactivationByCaspase](#) and as a product in [CaspaseActivation](#), [CaspaseActivationByBeclin\\_I](#), [CaspaseActivationBy-p38](#), [Bcl2DegradationCaspaseInduced](#), [BeclinInactivationByCaspase](#) and as a modifier in [CaspaseInactivation1](#), [InhibitCaspase2](#), [InhibitCaspase3](#), [Bcl2DegradationCaspaseInduced](#), [BeclinInactivationByCaspase](#)).

$$\frac{d}{dt}\text{Caspase.A} = v_1 + v_2 + v_3 + v_{12} + v_{20} - v_4 - v_5 - v_6 - v_{12} - v_{20} \quad (251)$$

## 7.18 Species *Caspase\_I*

**Initial amount** 100 item

This species takes part in nine reactions (as a reactant in [CaspaseActivation](#), [CaspaseActivationByBeclin-I](#), [CaspaseActivationBy\\_p38](#) and as a product in [CaspaseInactivation1](#), [InhibitCaspase2](#), [InhibitCaspase3](#) and as a modifier in [CaspaseActivation](#), [CaspaseActivationByBeclin-I](#), [CaspaseActivationBy\\_p38](#)).

$$\frac{d}{dt}\text{Caspase.I} = v_4 + v_5 + v_6 - v_1 - v_2 - v_3 \quad (252)$$

### 7.19 Species Col2mRNA

**Initial amount** 0 item

This species takes part in seven reactions (as a reactant in [Col2mRNA\\_Degradation](#), [Collagen2Translation](#) and as a product in [Collagen2EnhancedTranscriptionBySox9](#), [Collagen2TranscriptionBySmad2Smad4](#), [Collagen2Translation](#) and as a modifier in [Col2mRNA\\_Degradation](#), [Collagen2Translation](#)).

$$\frac{d}{dt}\text{Col2mRNA} = v_{94} + v_{95} + v_{97} - v_{96} - v_{97} \quad (253)$$

### 7.20 Species DamP

**Initial amount** 0 item

This species takes part in six reactions (as a reactant in [Removal\\_DamP\\_by\\_Autophagy](#), [ROS\\_production\\_by\\_DamP](#) and as a product in [Protein\\_Damage\\_by\\_ROS](#), [ROS\\_production\\_by\\_DamP](#) and as a modifier in [Removal\\_DamP\\_by\\_Autophagy](#), [ROS\\_production\\_by\\_DamP](#)).

$$\frac{d}{dt}\text{DamP} = v_{31} + v_{53} - v_{32} - v_{53} \quad (254)$$

### 7.21 Species IkB

**Initial amount** 0 item

This species takes part in three reactions (as a reactant in [NFkB\\_inactivation](#) and as a product in [IkB\\_production](#) and as a modifier in [NFkB\\_inactivation](#)).

$$\frac{d}{dt}\text{IkB} = v_{43} - v_{38} \quad (255)$$

### 7.22 Species IkB\_NFkB

**Initial amount** 100 item

This species takes part in five reactions (as a reactant in [IkB\\_degradation\\_via\\_ROS](#), [IkB\\_degradation\\_via\\_IL1](#) and as a product in [NFkB\\_inactivation](#) and as a modifier in [IkB\\_degradation\\_via\\_ROS](#), [IkB\\_degradation\\_via\\_IL1](#)).

$$\frac{d}{dt}\text{IkB\_NFkB} = v_{38} - v_{36} - v_{37} \quad (256)$$

### 7.23 Species IL1

**Initial amount** 0 item

This species takes part in 18 reactions (as a reactant in [IkB\\_degradation\\_via\\_IL1](#), [IL1\\_degradation](#), [MMP13\\_production](#), [MMP2\\_production](#), [ADAMTS5\\_production](#), [p38\\_phosphorylation](#) and as a product in [IkB\\_degradation\\_via\\_IL1](#), [IL1\\_production](#), [MMP13\\_production](#), [MMP2\\_production](#), [ADAMTS5\\_production](#), [p38\\_phosphorylation](#) and as a modifier in [IkB\\_degradation\\_via\\_IL1](#), [IL1\\_degradation](#), [MMP13\\_production](#), [MMP2\\_production](#), [ADAMTS5\\_production](#), [p38\\_phosphorylation](#)).

$$\frac{d}{dt}IL1 = v_{37} + v_{41} + v_{44} + v_{46} + v_{49} + v_{58} - v_{37} - v_{42} - v_{44} - v_{46} - v_{49} - v_{58} \quad (257)$$

### 7.24 Species Lys\_A

**Initial amount** 40 item

This species takes part in eight reactions (as a reactant in [InhibitLysosome](#), [Removal\\_DamP\\_by\\_Autophagy](#), [Lysosome\\_damage\\_by\\_ROS](#) and as a product in [ActivateLysosome](#), [Removal\\_DamP\\_by\\_Autophagy](#) and as a modifier in [InhibitLysosome](#), [Removal\\_DamP\\_by\\_Autophagy](#), [Lysosome\\_damage\\_by\\_ROS](#)).

$$\frac{d}{dt}Lys\_A = v_7 + v_{32} - v_8 - v_{32} - v_{64} \quad (258)$$

### 7.25 Species Lys\_I

**Initial amount** 360 item

This species takes part in four reactions (as a reactant in [ActivateLysosome](#) and as a product in [InhibitLysosome](#), [Lysosome\\_damage\\_by\\_ROS](#) and as a modifier in [ActivateLysosome](#)).

$$\frac{d}{dt}Lys\_I = v_8 + v_{64} - v_7 \quad (259)$$

### 7.26 Species MMP13

**Initial amount** 0 item

This species takes part in six reactions (as a reactant in [MMP13\\_removal](#), [Collagen\\_degradation](#) and as a product in [Collagen\\_degradation](#), [MMP13Activation](#) and as a modifier in [MMP13\\_removal](#), [Collagen\\_degradation](#)).

$$\frac{d}{dt}MMP13 = v_{52} + v_{113} - v_{45} - v_{52} \quad (260)$$

### 7.27 Species MMP2

**Initial amount** 0 item

This species takes part in six reactions (as a reactant in [MMP2\\_degradation](#), [TgfbActivationByMMP2](#) and as a product in [MMP\\_activation](#), [TgfbActivationByMMP2](#) and as a modifier in [MMP2\\_degradation](#), [TgfbActivationByMMP2](#)).

$$\frac{d}{dt}\text{MMP2} = v_{47} + v_{69} - v_{48} - v_{69} \quad (261)$$

### 7.28 Species NatP

**Initial amount** 1500 item

This species takes part in three reactions (as a reactant in [Protein\\_Damage\\_by\\_ROS](#) and as a product in [Protein\\_synthesis](#) and as a modifier in [Protein\\_Damage\\_by\\_ROS](#)), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{d}{dt}\text{NatP} = 0 \quad (262)$$

### 7.29 Species NFkB

**Initial amount** 0 item

This species takes part in seven reactions (as a reactant in [NFkB\\_inactivation](#), [NFkB\\_activation](#) and as a product in [IkB\\_degradation\\_via\\_ROS](#), [IkB\\_degradation\\_via\\_IL1](#), [NFkB\\_dephosphorylation](#) and as a modifier in [NFkB\\_inactivation](#), [NFkB\\_activation](#)).

$$\frac{d}{dt}\text{NFkB} = v_{36} + v_{37} + v_{62} - v_{38} - v_{61} \quad (263)$$

### 7.30 Species NFkB\_P

**Initial amount** 0 item

This species takes part in 15 reactions (as a reactant in [RAGE\\_upregulation\\_byNFkB](#), [IL1\\_production](#), [IkB\\_production](#), [SOD\\_synthesis](#), [NFkB\\_dephosphorylation](#) and as a product in [RAGE\\_upregulation\\_byNFkB](#), [IL1\\_production](#), [IkB\\_production](#), [SOD\\_synthesis](#), [NFkB\\_activation](#) and as a modifier in [RAGE\\_upregulation\\_byNFkB](#), [IL1\\_production](#), [IkB\\_production](#), [SOD\\_synthesis](#), [NFkB\\_dephosphorylation](#)).

$$\frac{d}{dt}\text{NFkB.P} = v_{40} + v_{41} + v_{43} + v_{55} + v_{61} - v_{40} - v_{41} - v_{43} - v_{55} - v_{62} \quad (264)$$

### 7.31 Species p38

**Initial amount** 100 item

This species takes part in five reactions (as a reactant in [p38\\_phosphorylation](#), [p38\\_phosphorylation\\_via\\_ROS](#) and as a product in [p38\\_dephosphorylation](#) and as a modifier in [p38\\_phosphorylation](#), [p38\\_phosphorylation\\_via\\_ROS](#)).

$$\frac{d}{dt}p38 = v_{60} - v_{58} - v_{59} \quad (265)$$

### 7.32 Species p38\_P

**Initial amount** 0 item

This species takes part in 13 reactions (as a reactant in [CaspaseActivationBy\\_p38](#), [p38\\_dephosphorylation](#), [NFkB\\_activation](#), [ROS\\_production\\_by\\_p38\\_P](#) and as a product in [CaspaseActivationBy\\_p38](#), [p38\\_phosphorylation](#), [p38\\_phosphorylation\\_via\\_ROS](#), [NFkB\\_activation](#), [ROS\\_production\\_by\\_p38\\_P](#) and as a modifier in [CaspaseActivationBy\\_p38](#), [p38\\_dephosphorylation](#), [NFkB\\_activation](#), [ROS\\_production\\_by\\_p38\\_P](#)).

$$\frac{d}{dt}p38\_P = v_3 + v_{58} + v_{59} + v_{61} + v_{63} - v_3 - v_{60} - v_{61} - v_{63} \quad (266)$$

### 7.33 Species proMMP13

**Initial amount** 0 item

This species takes part in four reactions (as a reactant in [MMP13Activation](#) and as a product in [MMP13\\_production](#), [MMP13InductionByRunx2](#) and as a modifier in [MMP13Activation](#)).

$$\frac{d}{dt}proMMP13 = v_{44} + v_{110} - v_{113} \quad (267)$$

### 7.34 Species proMMP2

**Initial amount** 0 item

This species takes part in three reactions (as a reactant in [MMP\\_activation](#) and as a product in [MMP2\\_production](#) and as a modifier in [MMP\\_activation](#)).

$$\frac{d}{dt}proMMP2 = v_{46} - v_{47} \quad (268)$$

### 7.35 Species RAGE

**Initial amount** 0 item

This species takes part in seven reactions (as a reactant in [ROS\\_production\\_by\\_RAGE](#), [RAGE\\_inactivation](#) and as a product in [RAGE\\_activation](#), [ROS\\_production\\_by\\_RAGE](#), [RAGE-upregulation\\_byNFkB](#) and as a modifier in [ROS\\_production\\_by\\_RAGE](#), [RAGE\\_inactivation](#)).

$$\frac{d}{dt}RAGE = v_{34} + v_{35} + v_{40} - v_{35} - v_{39} \quad (269)$$

### 7.36 Species ROS

**Initial amount** 2 item

This species takes part in 23 reactions (as a reactant in [Bcl2DegradationStressInduced](#), [ROS\\_removal](#), [Protein\\_Damage\\_by\\_ROS](#), [Ikb\\_degradation\\_via\\_ROS](#), [ROS\\_removal\\_by\\_SOD](#), [p38\\_phosphorylation\\_via\\_ROS](#), [Lysosome\\_damage\\_by\\_ROS](#) and as a product in [Bcl2DegradationStressInduced](#), [ROS\\_generation](#), [Protein\\_Damage\\_by\\_ROS](#), [ROS\\_production\\_by\\_RAGE](#), [Ikb\\_degradation\\_via\\_ROS](#), [ROS\\_production\\_by\\_DamP](#), [p38\\_phosphorylation\\_via\\_ROS](#), [ROS\\_production\\_by\\_p38\\_P](#), [Lysosome\\_damage\\_by\\_ROS](#) and as a modifier in [Bcl2DegradationStressInduced](#), [ROS\\_removal](#), [Protein\\_Damage\\_by\\_ROS](#), [Ikb\\_degradation\\_via\\_ROS](#), [ROS\\_removal\\_by\\_SOD](#), [p38\\_phosphorylation\\_via\\_ROS](#), [Lysosome\\_damage\\_by\\_ROS](#)).

$$\begin{aligned} \frac{d}{dt}ROS = & v_{11} + v_{29} + v_{31} + v_{35} + v_{36} + v_{53} + v_{59} + v_{63} \\ & + v_{64} - v_{11} - v_{30} - v_{31} - v_{36} - v_{57} - v_{59} - v_{64} \end{aligned} \quad (270)$$

### 7.37 Species Runx2\_A

**Initial amount** 0 item

This species takes part in six reactions (as a reactant in [Runx2\\_InhibitionBySmad2](#), [MMP13InductionByRunx2](#) and as a product in [Runx2ActivationBySmad1](#), [MMP13InductionByRunx2](#) and as a modifier in [Runx2\\_InhibitionBySmad2](#), [MMP13InductionByRunx2](#)).

$$\frac{d}{dt}Runx2\_A = v_{109} + v_{110} - v_{102} - v_{110} \quad (271)$$

### 7.38 Species Runx2\_I

**Initial amount** 100 item

This species takes part in three reactions (as a reactant in [Runx2ActivationBySmad1](#) and as a product in [Runx2\\_InhibitionBySmad2](#) and as a modifier in [Runx2ActivationBySmad1](#)).

$$\frac{d}{dt}Runx2\_I = v_{102} - v_{109} \quad (272)$$

### 7.39 Species Smad1

**Initial amount** 600 item

This species takes part in four reactions (as a reactant in [Smad1Activation](#) and as a product in [Smad1Dephosphorylation](#), [Smad1DephosphorylationViaSmad7](#) and as a modifier in [Smad1Activation](#)).

$$\frac{d}{dt}\text{Smad1} = v_{105} + v_{106} - v_{104} \quad (273)$$

### 7.40 Species Smad1\_P

**Initial amount** 0 item

This species takes part in eight reactions (as a reactant in [Smad1Dephosphorylation](#), [Smad1DephosphorylationViaSmad7](#), [Smad1Smad4Binding](#) and as a product in [Smad1Activation](#), [Smad1Smad4Release](#) and as a modifier in [Smad1Dephosphorylation](#), [Smad1DephosphorylationViaSmad7](#), [Smad1Smad4Binding](#)).

$$\frac{d}{dt}\text{Smad1\_P} = v_{104} + v_{108} - v_{105} - v_{106} - v_{107} \quad (274)$$

### 7.41 Species Smad1\_P\_Smad4

**Initial amount** 0 item

This species takes part in six reactions (as a reactant in [Smad1Smad4Release](#), [Runx2ActivationBySmad1](#) and as a product in [Smad1Smad4Binding](#), [Runx2ActivationBySmad1](#) and as a modifier in [Smad1Smad4Release](#), [Runx2ActivationBySmad1](#)).

$$\frac{d}{dt}\text{Smad1\_P\_Smad4} = v_{107} + v_{109} - v_{108} - v_{109} \quad (275)$$

### 7.42 Species Smad2

**Initial amount** 600 item

This species takes part in three reactions (as a reactant in [Smad2Phosphorylation](#) and as a product in [Smad2DephosphorylationNuc](#) and as a modifier in [Smad2Phosphorylation](#)).

$$\frac{d}{dt}\text{Smad2} = v_{85} - v_{82} \quad (276)$$

### 7.43 Species Smad2\_P

**Initial amount** 0 item

This species takes part in six reactions (as a reactant in [Smad2Smad4Binding](#), [Smad2DephosphorylationNuc](#) and as a product in [Smad2Phosphorylation](#), [Smad2PSmad4Release](#) and as a modifier in [Smad2Smad4Binding](#), [Smad2DephosphorylationNuc](#)).

$$\frac{d}{dt}\text{Smad2\_P} = v_{82} + v_{84} - v_{83} - v_{85} \quad (277)$$



#### 7.44 Species Smad2\_P\_Smad4

**Initial amount** 0 item

This species takes part in 15 reactions (as a reactant in [Smad2PSmad4Release](#), [Smad7Synthesis](#), [Sox9Activation](#), [Collagen2TranscriptionBySmad2Smad4](#), [Runx2\\_InhibitionBySmad2](#) and as a product in [Smad2Smad4Binding](#), [Smad7Synthesis](#), [Sox9Activation](#), [Collagen2TranscriptionBySmad2Smad4](#), [Runx2\\_InhibitionBySmad2](#) and as a modifier in [Smad2PSmad4Release](#), [Smad7Synthesis](#), [Sox9Activation](#), [Collagen2TranscriptionBySmad2Smad4](#), [Runx2\\_InhibitionBySmad2](#)).

$$\frac{d}{dt}\text{Smad2\_P\_Smad4} = v_{83} + v_{86} + v_{87} + v_{95} + v_{102} - v_{84} - v_{86} - v_{87} - v_{95} - v_{102} \quad (278)$$

#### 7.45 Species Smad4

**Initial amount** 600 item

This species takes part in six reactions (as a reactant in [Smad2Smad4Binding](#), [Smad1Smad4Binding](#) and as a product in [Smad2PSmad4Release](#), [Smad1Smad4Release](#) and as a modifier in [Smad2Smad4Binding](#), [Smad1Smad4Binding](#)).

$$\frac{d}{dt}\text{Smad4} = v_{84} + v_{108} - v_{83} - v_{107} \quad (279)$$

#### 7.46 Species Smad7

**Initial amount** 0 item

This species takes part in twelve reactions (as a reactant in [Tgfb\\_Alk5\\_BindingSmad7](#), [Smad1DephosphorylationViaSmad7](#), [Tgfb\\_Alk1\\_Alk5\\_BindingSmad7](#), [Smad7Degradation](#) and as a product in [Tgfb\\_Alk5\\_Smad7Release](#), [Smad7Synthesis](#), [Smad1DephosphorylationViaSmad7](#), [Tgfb\\_Alk1\\_Alk5\\_Smad7Release](#) and as a modifier in [Tgfb\\_Alk5\\_BindingSmad7](#), [Smad1DephosphorylationViaSmad7](#), [Tgfb\\_Alk1\\_Alk5\\_BindingSmad7](#), [Smad7Degradation](#)).

$$\frac{d}{dt}\text{Smad7} = v_{78} + v_{86} + v_{106} + v_{115} - v_{77} - v_{106} - v_{114} - v_{117} \quad (280)$$

#### 7.47 Species SOD

**Initial amount** 2 item

This species takes part in six reactions (as a reactant in [SOD\\_degradation](#), [ROS\\_removal\\_by\\_SOD](#) and as a product in [SOD\\_synthesis](#), [ROS\\_removal\\_by\\_SOD](#) and as a modifier in [SOD\\_degradation](#), [ROS\\_removal\\_by\\_SOD](#)).

$$\frac{d}{dt}\text{SOD} = v_{55} + v_{57} - v_{56} - v_{57} \quad (281)$$

## 7.48 Species Sox9

**Initial amount** 100 item

This species takes part in six reactions (as a reactant in [Sox9Activation](#), [Sox9Degradation](#) and as a product in [Sox9Inactivation](#), [Sox9Translation](#) and as a modifier in [Sox9Activation](#), [Sox9Degradation](#)).

$$\frac{d}{dt}\text{Sox9} = v_{88} + v_{92} - v_{87} - v_{93} \quad (282)$$

## 7.49 Species Sox9\_A

**Initial amount** 0 item

This species takes part in twelve reactions (as a reactant in [Sox9Inactivation](#), [Sox9EnhancedTranscription](#), [Collagen2EnhancedTranscriptionBySox9](#), [AggrecanEnhancedTranscription](#) and as a product in [Sox9Activation](#), [Sox9EnhancedTranscription](#), [Collagen2EnhancedTranscriptionBySox9](#), [AggrecanEnhancedTranscription](#) and as a modifier in [Sox9Inactivation](#), [Sox9EnhancedTranscription](#), [Collagen2EnhancedTranscriptionBySox9](#), [AggrecanEnhancedTranscription](#)).

$$\frac{d}{dt}\text{Sox9\_A} = v_{87} + v_{90} + v_{94} + v_{98} - v_{88} - v_{90} - v_{94} - v_{98} \quad (283)$$

## 7.50 Species Sox9mRNA

**Initial amount** 10 item

This species takes part in seven reactions (as a reactant in [Sox9mRNA\\_Degradation](#), [Sox9Translation](#) and as a product in [Sox9BasalTranscription](#), [Sox9EnhancedTranscription](#), [Sox9Translation](#) and as a modifier in [Sox9mRNA\\_Degradation](#), [Sox9Translation](#)).

$$\frac{d}{dt}\text{Sox9mRNA} = v_{89} + v_{90} + v_{92} - v_{91} - v_{92} \quad (284)$$

## 7.51 Species Tgfb\_A

**Initial amount** 0 item

This species takes part in ten reactions (as a reactant in [TgfbInactivation](#), [TgfbReceptorBindingAlk5](#), [TgfbReceptorBindingAlk1](#) and as a product in [TgfbActivationByIntegrin](#), [TgfbActivationByMMP2](#), [TgfbReceptorRelease](#), [TgfbAlk1Release](#) and as a modifier in [TgfbInactivation](#), [TgfbReceptorBindingAlk1](#), [TgfbReceptorBindingAlk5](#)).

$$\frac{d}{dt}\text{Tgfb\_A} = v_{68} + v_{69} + v_{76} + v_{81} - v_{70} - v_{75} - v_{80} \quad (285)$$

### 7.52 Species `Tgfb_Alk1_Alk5`

**Initial amount** 0 item

This species takes part in nine reactions (as a reactant in `TgfbAlk1Release`, `Smad1Activation`, `Tgfb_Alk1_Alk5_BindingSmad7` and as a product in `TgfbReceptorBindingAlk1`, `Smad1Activation`, `Tgfb_Alk1_Alk5_Smad7Release` and as a modifier in `TgfbAlk1Release`, `Smad1Activation`, `Tgfb_Alk1_Alk5_BindingSmad7`).

$$\frac{d}{dt}\text{Tgfb\_Alk1\_Alk5} = v_{80} + v_{104} + v_{115} - v_{81} - v_{104} - v_{114} \quad (286)$$

### 7.53 Species `Tgfb_Alk1_Alk5_Smad7`

**Initial amount** 0 item

This species takes part in five reactions (as a reactant in `Tgfb_Alk1_Alk5_Smad7Release`, `Alk1_Smad7Degradation` and as a product in `Tgfb_Alk1_Alk5_BindingSmad7` and as a modifier in `Tgfb_Alk1_Alk5_Smad7Release`, `Alk1_Smad7Degradation`).

$$\frac{d}{dt}\text{Tgfb\_Alk1\_Alk5\_Smad7} = v_{114} - v_{115} - v_{116} \quad (287)$$

### 7.54 Species `Tgfb_Alk5_dimer`

**Initial amount** 0 item

This species takes part in nine reactions (as a reactant in `TgfbReceptorRelease`, `Tgfb_Alk5_BindingSmad7`, `Smad2Phosphorylation` and as a product in `TgfbReceptorBindingAlk5`, `Tgfb_Alk5_Smad7Release`, `Smad2Phosphorylation` and as a modifier in `TgfbReceptorRelease`, `Tgfb_Alk5_BindingSmad7`, `Smad2Phosphorylation`).

$$\frac{d}{dt}\text{Tgfb\_Alk5\_dimer} = v_{75} + v_{78} + v_{82} - v_{76} - v_{77} - v_{82} \quad (288)$$

### 7.55 Species `Tgfb_Alk5_dimer_Smad7`

**Initial amount** 0 item

This species takes part in five reactions (as a reactant in `Tgfb_Alk5_Smad7Release`, `Alk5_Smad7Degradation` and as a product in `Tgfb_Alk5_BindingSmad7` and as a modifier in `Tgfb_Alk5_Smad7Release`, `Alk5_Smad7Degradation`).

$$\frac{d}{dt}\text{Tgfb\_Alk5\_dimer\_Smad7} = v_{77} - v_{78} - v_{79} \quad (289)$$

### 7.56 Species AggFrag

**Initial amount** 0 item

This species takes part in one reaction (as a product in [Aggrecan.degradation](#)).

$$\frac{d}{dt}\text{AggFrag} = v_{51} \quad (290)$$

### 7.57 Species Aggrecan

**Initial amount** 0 item

This species takes part in three reactions (as a reactant in [AggrecanCollagen2Binding](#) and as a product in [AggrecanTranslation](#) and as a modifier in [AggrecanCollagen2Binding](#)).

$$\frac{d}{dt}\text{Aggrecan} = v_{100} - v_{101} \quad (291)$$

### 7.58 Species Aggrecan\_Collagen2

**Initial amount** 1000 item

This species takes part in three reactions (as a reactant in [Aggrecan.degradation](#) and as a product in [AggrecanCollagen2Binding](#) and as a modifier in [Aggrecan.degradation](#)).

$$\frac{d}{dt}\text{Aggrecan\_Collagen2} = v_{101} - v_{51} \quad (292)$$

### 7.59 Species ColFrag

**Initial amount** 0 item

This species takes part in one reaction (as a product in [Collagen.degradation](#)).

$$\frac{d}{dt}\text{ColFrag} = v_{52} \quad (293)$$

### 7.60 Species Collagen2

**Initial amount** 0 item

This species takes part in six reactions (as a reactant in [Collagen.degradation](#), [AggrecanCollagen2Binding](#) and as a product in [Aggrecan.degradation](#), [Collagen2Translation](#) and as a modifier in [Collagen.degradation](#), [AggrecanCollagen2Binding](#)).

$$\frac{d}{dt}\text{Collagen2} = v_{51} + v_{97} - v_{52} - v_{101} \quad (294)$$

### 7.61 Species Integrin

**Initial amount** 0 item

This species takes part in six reactions (as a reactant in [IntegrinInactivation](#), [TgfbActivationByIntegrin](#) and as a product in [IntegrinActivationByMechanicalStress](#), [TgfbActivationByIntegrin](#) and as a modifier in [IntegrinInactivation](#), [TgfbActivationByIntegrin](#)).

$$\frac{d}{dt}\text{Integrin} = v_{65} + v_{68} - v_{66} - v_{68} \quad (295)$$

### 7.62 Species Tgfb\_I

**Initial amount** 200 item

This species takes part in seven reactions (as a reactant in [TgfbActivationByIntegrin](#), [TgfbActivationByMMP2](#) and as a product in [TgfbInactivation](#), [Alk5\\_Smad7Degradation](#), [Alk1\\_Smad7Degradation](#) and as a modifier in [TgfbActivationByIntegrin](#), [TgfbActivationByMMP2](#)).

$$\frac{d}{dt}\text{Tgfb\_I} = v_{70} + v_{79} + v_{116} - v_{68} - v_{69} \quad (296)$$

### 7.63 Species Sink

**SBO:0000291** empty set

**Initial amount** 0 item

This species takes part in 18 reactions (as a product in [Bcl2Degradation](#), [Bcl2DegradationStressInduced](#), [Bcl2DegradationCaspaseInduced](#), [ROS\\_removal](#), [RAGE\\_inactivation](#), [IL1\\_degradation](#), [MMP13\\_removal](#), [MMP2\\_degradation](#), [ADAMTS5\\_removal](#), [SOD\\_degradation](#), [IntegrinInactivation](#), [Sox9mRNA\\_Degradation](#), [Sox9Degradation](#), [Col2mRNA\\_Degradation](#), [AcanmRNA\\_Degradation](#), [Alk5Degradation](#), [Alk1Degradation](#), [Smad7Degradation](#)), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{d}{dt}\text{Sink} = 0 \quad (297)$$

### 7.64 Species Source

**SBO:0000291** empty set

**Initial amount** 1 item

This species takes part in 16 reactions (as a reactant in [Bcl2Synthesis](#), [ROS\\_generation](#), [Production\\_of\\_AGEproducts](#), [Protein\\_synthesis](#), [IntegrinActivationByMechanicalStress](#), [Alk5Synthesis](#), [Sox9BasalTranscription](#), [Alk1Synthesis](#) and as a modifier in [Bcl2Synthesis](#), [ROS\\_generation](#), [Production\\_of\\_AGEproducts](#), [Protein\\_synthesis](#), [IntegrinActivationByMechanicalS](#)

[Alk5Synthesis](#), [Sox9BasalTranscription](#), [Alk1Synthesis](#)), which do not influence its rate of change because this constant species is on the boundary of the reaction system:

$$\frac{d}{dt}\text{Source} = 0 \quad (298)$$

## 7.65 Species [IntegrinCount](#)

**Initial amount** 0 item

This species takes part in one reaction (as a product in [IntegrinActivationByMechanicalStress](#)).

$$\frac{d}{dt}\text{IntegrinCount} = v_{65} \quad (299)$$

## A Glossary of Systems Biology Ontology Terms

**SBO:0000291 empty set:** Entity defined by the absence of any actual object. An empty set is often used to represent the source of a creation process or the result of a degradation process.

**SBO:0000607 dimer:** A macromolecular complex composed of two monomeric units, which may or may not be identical. Monomers are usually non-covalently bound

SBML<sup>2</sup>TeX was developed by Andreas Dräger<sup>a</sup>, Hannes Planatscher<sup>a</sup>, Dieudonné M Wouamba<sup>a</sup>, Adrian Schröder<sup>a</sup>, Michael Hucka<sup>b</sup>, Lukas Endler<sup>c</sup>, Martin Golebiewski<sup>d</sup> and Andreas Zell<sup>a</sup>. Please see <http://www.ra.cs.uni-tuebingen.de/software/SBML2LaTeX> for more information.

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