

SBML Model Report

Model name: “Stortelder1997 - Thrombin Generation Amidolytic Activity”



May 5, 2016

1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by Michael Schubert¹ at August 26th 2011 at 4:35 p. m. and last time modified at October ninth 2014 at 5:03 p. m. Table 1 provides an overview of the quantities of all components of this model.

Table 1: Number of components in this model, which are described in the following sections.

Element	Quantity	Element	Quantity
compartment types	0	compartments	1
species types	0	species	12
events	0	constraints	0
reactions	8	function definitions	1
global parameters	14	unit definitions	2
rules	1	initial assignments	0

Model Notes

Stortelder1997 - Thrombin Generation Amidolytic Activity

Mathematical modelling of a part of the blood coagulation mechanism.

This model is described in the article: [Mathematical modelling in blood coagulation : simulation and parameter estimation](#). Stortelder W.J.H., Hemker P.W., Hemker, H.C.CWI. Modelling, Analysis and Simulation, No. R 9720, p.1-11.

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Abstract:

This paper describes the mathematical modelling of a part of the blood coagulation mechanism. The model includes the activation of factor X by a purified enzyme from Russel's Viper Venom (RVV), factor V and prothrombin, and also comprises the inactivation of the products formed. In this study we assume that in principle the mechanism of the process is known. However, the exact structure of the mechanism is unknown, and the process still can be described by different mathematical models. These models are put to test by measuring their capacity to explain the course of thrombin generation as observed in plasma after recalcification in presence of RVV. The mechanism studied is mathematically modelled as a system of differential-algebraic equations (DAEs). Each candidate model contains some freedom, which is expressed in the model equations by the presence of unknown parameters. For example, reaction constants or initial concentrations are unknown. The goal of parameter estimation is to determine these unknown parameters in such a way that the theoretical (i.e., computed) results fit the experimental data within measurement accuracy and to judge which modifications of the chemical reaction scheme allow the best fit. We present results on model discrimination and estimation of reaction constants, which are hard to obtain in another way.

This model is hosted on [BioModels Database](#) and identified by: [BIOMD0000000358](#) .

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 three are predefined by SBML and not mentioned in the model.

2.1 Unit `time`

Name `time`

Definition 60 s

2.2 Unit `substance`

Name `substance`

Definition nmol

2.3 Unit `volume`

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

Definition 1

2.4 Unit area

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

Definition m^2

2.5 Unit length

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

Definition m

3 Compartment

This model contains one compartment.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
compartment_1	compartment_1		3	1	litre	<input checked="" type="checkbox"/>	

3.1 Compartment `compartment_1`

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

Name `compartment_1`

4 Species

This model contains twelve species. Section 9 provides further details and the derived rates of change of each species.

Table 3: Properties of each species.

Id	Name	Compartment	Derived Unit	Constant	Boundary Condition
X	X	compartment_1	$\text{nmol} \cdot \text{l}^{-1}$	\square	\square
Xa	Xa	compartment_1	$\text{nmol} \cdot \text{l}^{-1}$	\square	\square
Xa_ATIII	Xa_ATIII	compartment_1	$\text{nmol} \cdot \text{l}^{-1}$	\square	\square
PL	PL	compartment_1	$\text{nmol} \cdot \text{l}^{-1}$	\square	\square
PT	PT	compartment_1	$\text{nmol} \cdot \text{l}^{-1}$	\square	\square
Va	Va	compartment_1	$\text{nmol} \cdot \text{l}^{-1}$	\square	\square
IIa	IIa	compartment_1	$\text{nmol} \cdot \text{l}^{-1}$	\square	\square
V	V	compartment_1	$\text{nmol} \cdot \text{l}^{-1}$	\square	\square
II	II	compartment_1	$\text{nmol} \cdot \text{l}^{-1}$	\square	\square
IIa_alpha2M	IIa_alpha2M	compartment_1	$\text{nmol} \cdot \text{l}^{-1}$	\square	\square
IIa_ATIII	IIa_ATIII	compartment_1	$\text{nmol} \cdot \text{l}^{-1}$	\square	\square
RVV	RVV	compartment_1	$\text{nmol} \cdot \text{l}^{-1}$	\square	\square

5 Parameters

This model contains 14 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
kcat_X	kcat_X	0000025	239.100		<input checked="" type="checkbox"/>
km_X	km_X	0000371	23.650		<input checked="" type="checkbox"/>
ki_Xa	ki_Xa	0000035	4.531		<input checked="" type="checkbox"/>
k_PT	k_PT	0000037	122.900		<input checked="" type="checkbox"/>
k_PL	k_PL	0000038	801.400		<input checked="" type="checkbox"/>
kcat_V	kcat_V	0000025	7.844		<input checked="" type="checkbox"/>
km_V	km_V	0000371	149.700		<input checked="" type="checkbox"/>
kcat_II	kcat_II	0000025	43.870		<input checked="" type="checkbox"/>
km_II	km_II	0000371	62.250		<input checked="" type="checkbox"/>
kcat_2	kcat_2	0000025	12.400		<input checked="" type="checkbox"/>
km_2	km_2	0000371	0.061		<input checked="" type="checkbox"/>
ki- _IIaAlpha2M	ki_IIaAlpha2M	0000035	0.176		<input checked="" type="checkbox"/>
ki_IIaATIII	ki_IIaATIII	0000035	0.786		<input checked="" type="checkbox"/>
AmAct	AmAct		0.000		<input type="checkbox"/>

6 Function definition

This is an overview of one function definition.

6.1 Function definition `HenriMichaelisMenten_irreversible_kcat`

Name Henri-Michaelis-Menten (irreversible) kcat

Arguments kcat, enzyme, substrate, Km

Mathematical Expression

$$\frac{kcat \cdot enzyme \cdot substrate}{Km + substrate} \quad (1)$$

7 Rule

This is an overview of one rule.

7.1 Rule AmAct

Rule AmAct is an assignment rule for parameter AmAct :

$$\text{AmAct} = [\text{IIa}] + 0.556 \cdot [\text{IIa.alpha2M}] \quad (2)$$

8 Reactions

This model contains eight 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	R1	R1	$X \xrightarrow{RVV} Xa$	
2	R2	R2	$Xa \longrightarrow Xa_ATIII$	
3	R3	R3	$Va + Xa + PL \rightleftharpoons PT$	
4	R4	R4	$V \xrightarrow{IIa} Va$	
5	R5	R5	$II \xrightarrow{PT} IIa$	
6	R6	R6	$II \xrightarrow{Xa} IIa$	
7	R7	R7	$IIa \longrightarrow IIa_alpha2M$	
8	R8	R8	$IIa \longrightarrow IIa_ATIII$	

8.1 Reaction R1

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

Name R1

Reaction equation



Reactant

Table 6: Properties of each reactant.

Id	Name	SBO
X	X	0000010

Modifier

Table 7: Properties of each modifier.

Id	Name	SBO
RVV	RVV	0000461

Product

Table 8: Properties of each product.

Id	Name	SBO
X _a	X _a	0000011

Kinetic Law

SBO:0000028 enzymatic rate law for irreversible non-modulated non-interacting unireactant enzymes

Derived unit contains undeclared units

$$v_1 = \text{vol}(\text{compartment}_1) \cdot \text{HenriMichaelisMenten_irreversible_kcat}(\text{kcat}_X, [\text{RVV}], [X], \text{km}_X) \quad (4)$$

$$\text{HenriMichaelisMenten_irreversible_kcat}(\text{kcat}, \text{enzyme}, \text{substrate}, \text{Km}) = \frac{\text{kcat} \cdot \text{enzyme} \cdot \text{substrate}}{\text{Km} + \text{substrate}} \quad (5)$$

$$\text{HenriMichaelisMenten_irreversible_kcat}(\text{kcat}, \text{enzyme}, \text{substrate}, \text{Km}) = \frac{\text{kcat} \cdot \text{enzyme} \cdot \text{substrate}}{\text{Km} + \text{substrate}} \quad (6)$$

8.2 Reaction R2

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

Name R2

Reaction equation



Reactant

Table 9: Properties of each reactant.

Id	Name	SBO
Xa	Xa	0000010

Product

Table 10: Properties of each product.

Id	Name	SBO
Xa_ATIII	Xa_ATIII	0000011

Kinetic Law

SBO:0000049 mass action rate law for first order irreversible reactions, continuous scheme

Derived unit contains undeclared units

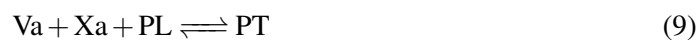
$$v_2 = \text{vol}(\text{compartment}_1) \cdot k_{i_Xa} \cdot [\text{Xa}] \quad (8)$$

8.3 Reaction R3

This is a reversible reaction of three reactants forming one product.

Name R3

Reaction equation



Reactants

Table 11: Properties of each reactant.

Id	Name	SBO
Va	Va	0000010
Xa	Xa	0000010
PL	PL	0000010

Product

Table 12: Properties of each product.

Id	Name	SBO
PT	PT	0000011

Kinetic Law

SBO:0000122 mass action rate law for third order forward, first order reverse, reversible reactions, three reactants, continuous scheme

Derived unit contains undeclared units

$$v_3 = \text{vol}(\text{compartment}_1) \cdot (k_{\text{PT}} \cdot [\text{Va}] \cdot [\text{Xa}] \cdot [\text{PL}] - k_{\text{PL}} \cdot [\text{PT}]) \quad (10)$$

8.4 Reaction R4

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

Name R4

Reaction equation



Reactant

Table 13: Properties of each reactant.

Id	Name	SBO
v	V	0000010

Modifier

Table 14: Properties of each modifier.

Id	Name	SBO
IIa	IIa	0000461

Product

Table 15: Properties of each product.

Id	Name	SBO
Va	Va	0000011

Kinetic Law

SBO:0000028 enzymatic rate law for irreversible non-modulated non-interacting unireactant enzymes

Derived unit contains undeclared units

$$v_4 = \text{vol}(\text{compartment}_1) \cdot \text{HenriMichaelisMenten_irreversible_kcat}(\text{kcat}_V, [\text{IIa}], [\text{V}], \text{km}_V) \quad (12)$$

$$\begin{aligned} & \text{HenriMichaelisMenten_irreversible_kcat}(\text{kcat}, \text{enzyme}, \text{substrate}, \text{Km}) \\ &= \frac{\text{kcat} \cdot \text{enzyme} \cdot \text{substrate}}{\text{Km} + \text{substrate}} \end{aligned} \quad (13)$$

$$\begin{aligned} & \text{HenriMichaelisMenten_irreversible_kcat}(\text{kcat}, \text{enzyme}, \text{substrate}, \text{Km}) \\ &= \frac{\text{kcat} \cdot \text{enzyme} \cdot \text{substrate}}{\text{Km} + \text{substrate}} \end{aligned} \quad (14)$$

8.5 Reaction R5

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

Name R5

Reaction equation



Reactant

Table 16: Properties of each reactant.

Id	Name	SBO
II	II	0000010

Modifier

Table 17: Properties of each modifier.

Id	Name	SBO
PT	PT	0000461

Product

Table 18: Properties of each product.

Id	Name	SBO
IIa	IIa	0000011

Kinetic Law

SBO:0000028 enzymatic rate law for irreversible non-modulated non-interacting unireactant enzymes

Derived unit contains undeclared units

$$v_5 = \text{vol}(\text{compartment}_1) \cdot \text{HenriMichaelisMenten_irreversible_kcat}(\text{kcat_II}, [\text{PT}], [\text{II}], \text{km_II}) \quad (16)$$

$$\begin{aligned} & \text{HenriMichaelisMenten_irreversible_kcat}(\text{kcat}, \text{enzyme}, \text{substrate}, \text{Km}) \\ &= \frac{\text{kcat} \cdot \text{enzyme} \cdot \text{substrate}}{\text{Km} + \text{substrate}} \end{aligned} \quad (17)$$

$$\begin{aligned} & \text{HenriMichaelisMenten_irreversible_kcat}(\text{kcat}, \text{enzyme}, \text{substrate}, \text{Km}) \\ &= \frac{\text{kcat} \cdot \text{enzyme} \cdot \text{substrate}}{\text{Km} + \text{substrate}} \end{aligned} \quad (18)$$

8.6 Reaction R6

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

Name R6

Reaction equation



Reactant

Table 19: Properties of each reactant.

Id	Name	SBO
II	II	0000010

Modifier

Table 20: Properties of each modifier.

Id	Name	SBO
Xa	Xa	0000461

Product

Table 21: Properties of each product.

Id	Name	SBO
IIa	IIa	0000011

Kinetic Law

SBO:0000028 enzymatic rate law for irreversible non-modulated non-interacting unireactant enzymes

Derived unit contains undeclared units

$$v_6 = \text{vol}(\text{compartment}_1) \cdot \text{HenriMichaelisMenten_irreversible_kcat}(\text{kcat}_2, [\text{Xa}], [\text{II}], \text{km}_2) \quad (20)$$

$$\begin{aligned} & \text{HenriMichaelisMenten_irreversible_kcat}(\text{kcat}, \text{enzyme}, \text{substrate}, \text{Km}) \\ &= \frac{\text{kcat} \cdot \text{enzyme} \cdot \text{substrate}}{\text{Km} + \text{substrate}} \end{aligned} \quad (21)$$

$$\begin{aligned} & \text{HenriMichaelisMenten_irreversible_kcat}(\text{kcat}, \text{enzyme}, \text{substrate}, \text{Km}) \\ &= \frac{\text{kcat} \cdot \text{enzyme} \cdot \text{substrate}}{\text{Km} + \text{substrate}} \end{aligned} \quad (22)$$

8.7 Reaction R7

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

Name R7

Reaction equation



Reactant

Table 22: Properties of each reactant.

Id	Name	SBO
IIa	IIa	0000010

Product

Table 23: Properties of each product.

Id	Name	SBO
IIa_alpha2M	IIa_alpha2M	0000011

Kinetic Law

SBO:0000049 mass action rate law for first order irreversible reactions, continuous scheme

Derived unit contains undeclared units

$$v_7 = \text{vol}(\text{compartment}_1) \cdot k_{i_IIaAlpha2M} \cdot [\text{IIa}] \quad (24)$$

8.8 Reaction R8

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

Name R8

Reaction equation



Reactant

Table 24: Properties of each reactant.

Id	Name	SBO
IIa	IIa	0000010

Product

Table 25: Properties of each product.

Id	Name	SBO
IIa_ATIII	IIa_ATIII	0000011

Kinetic Law

SBO:0000049 mass action rate law for first order irreversible reactions, continuous scheme

Derived unit contains undeclared units

$$v_8 = \text{vol}(\text{compartment}_1) \cdot k_{i_IIaATIII} \cdot [\text{IIa}] \quad (26)$$

9 Derived Rate Equations

When interpreted as an ordinary differential equation framework, this model implies the following set of equations for the rates of change of each species.

Identifiers for kinetic laws highlighted in gray cannot be verified to evaluate to units of SBML substance per time. As a result, some SBML interpreters may not be able to verify the consistency of the units on quantities in the model. Please check if

- parameters without an unit definition are involved or
- volume correction is necessary because the `hasOnlySubstanceUnits` flag may be set to `false` and `spacialDimensions` > 0 for certain species.

9.1 Species X

Name X

Initial concentration 81.24998 nmol · l⁻¹

This species takes part in one reaction (as a reactant in R1).

$$\frac{d}{dt}X = -v_1 \quad (27)$$

9.2 Species Xa

Name Xa

Initial concentration 0 nmol · l⁻¹

This species takes part in four reactions (as a reactant in R2, R3 and as a product in R1 and as a modifier in R6).

$$\frac{d}{dt}Xa = v_1 - v_2 - v_3 \quad (28)$$

9.3 Species Xa_ATIII

Name Xa_ATIII

Initial concentration 0 nmol · l⁻¹

This species takes part in one reaction (as a product in R2).

$$\frac{d}{dt}Xa_ATIII = v_2 \quad (29)$$

9.4 Species PL

Name PL

Initial concentration 9.999997 nmol · l⁻¹

This species takes part in one reaction (as a reactant in R3).

$$\frac{d}{dt}PL = -v_3 \quad (30)$$

9.5 Species PT

Name PT

Initial concentration 0 nmol · l⁻¹

This species takes part in two reactions (as a product in R3 and as a modifier in R5).

$$\frac{d}{dt}PT = v_3 \quad (31)$$

9.6 Species Va

Name Va

Initial concentration 0 nmol · l⁻¹

This species takes part in two reactions (as a reactant in R3 and as a product in R4).

$$\frac{d}{dt}Va = v_4 - v_3 \quad (32)$$

9.7 Species IIa

Name IIa

Initial concentration 0 nmol · l⁻¹

This species takes part in five reactions (as a reactant in R7, R8 and as a product in R5, R6 and as a modifier in R4).

$$\frac{d}{dt}IIa = v_5 + v_6 - v_7 - v_8 \quad (33)$$

9.8 Species V

Name V

Initial concentration 6.711998 nmol · l⁻¹

This species takes part in one reaction (as a reactant in R4).

$$\frac{d}{dt}V = -v_4 \quad (34)$$

9.9 Species II

Name II

Initial concentration 509.2998 nmol · l⁻¹

This species takes part in two reactions (as a reactant in R5, R6).

$$\frac{d}{dt}II = -v_5 - v_6 \quad (35)$$

9.10 Species IIa_alpha2M

Name IIa_alpha2M

Initial concentration 0 nmol · l⁻¹

This species takes part in one reaction (as a product in R7).

$$\frac{d}{dt}IIa_alpha2M = v_7 \quad (36)$$

9.11 Species `IIa_ATIII`

Name `IIa_ATIII`

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

This species takes part in one reaction (as a product in [R8](#)).

$$\frac{d}{dt} \text{IIa_ATIII} = v_8 \quad (37)$$

9.12 Species `RVV`

Name `RVV`

Initial concentration $0.3349999 \text{ nmol} \cdot \text{l}^{-1}$

This species takes part in one reaction (as a modifier in [R1](#)).

$$\frac{d}{dt} \text{RVV} = 0 \quad (38)$$

A Glossary of Systems Biology Ontology Terms

SBO:0000010 reactant: Substance consumed by a chemical reaction. Reactants react with each other to form the products of a chemical reaction. In a chemical equation the Reactants are the elements or compounds on the left hand side of the reaction equation. A reactant can be consumed and produced by the same reaction, its global quantity remaining unchanged

SBO:0000011 product: Substance that is produced in a reaction. In a chemical equation the Products are the elements or compounds on the right hand side of the reaction equation. A product can be produced and consumed by the same reaction, its global quantity remaining unchanged

SBO:0000025 catalytic rate constant: Numerical parameter that quantifies the velocity of an enzymatic reaction

SBO:0000028 enzymatic rate law for irreversible non-modulated non-interacting unireactant enzymes: Kinetics of enzymes that react only with one substance, their substrate. The enzymes do not catalyse the reactions in both directions.

SBO:0000035 forward unimolecular rate constant, continuous case: Numerical parameter that quantifies the forward velocity of a chemical reaction involving only one reactant. This parameter encompasses all the contributions to the velocity except the quantity of the reactant. It is to be used in a reaction modelled using a continuous framework

SBO:0000037 forward trimolecular rate constant, continuous case: Numerical parameter that quantifies the forward velocity of a chemical reaction involving three reactants. This parameter encompasses all the contributions to the velocity except the quantity of the reactants. It is to be used in a reaction modelled using a continuous framework

SBO:0000038 reverse unimolecular rate constant, continuous case: Numerical parameter that quantifies the reverse velocity of a chemical reaction involving only one product. This parameter encompasses all the contributions to the velocity except the quantity of the product. It is to be used in a reaction modelled using a continuous framework

SBO:0000049 mass action rate law for first order irreversible reactions, continuous scheme: Reaction scheme where the products are created from the reactants and the change of a product quantity is proportional to the product of reactant activities. The reaction scheme does not include any reverse process that creates the reactants from the products. The change of a product quantity is proportional to the quantity of one reactant. It is to be used in a reaction modelled using a continuous framework.

SBO:0000122 mass action rate law for third order forward, first order reverse, reversible reactions, three reactants, continuous scheme: Reaction scheme where the products are created from the reactants and the change of a product quantity is proportional to the product of reactant activities. The reaction scheme does include a reverse process that creates the reactants from the products. The rate of the forward process is proportional to the product of three reactant quantities. The rate of the reverse process is proportional to the quantity of one product. It is to be used in a reaction modelled using a continuous framework.

SBO:0000371 Michaelis constant in quasi-steady state situation: Michaelis constant derived using a steady-state assumption for enzyme-substrate and enzyme-product intermediates. For example see Briggs-Haldane equation (SBO:0000031)

SBO:0000461 essential activator: A substance that is absolutely required for occurrence and stimulation of a reaction

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

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