# **SBML Model Report**

# Model name: "Schmitz2014 - RNA triplex formation"



March 3, 2017

# 1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by Felix Winter<sup>1</sup> at October 23<sup>rd</sup> 2013 at 8:46 p. m. and last time modified at July 28<sup>th</sup> 2014 at 1:23 p. m. Table 1 shows an overview of the quantities of all components of this model.

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

| Element           | Quantity | Element              | Quantity |
|-------------------|----------|----------------------|----------|
| compartment types | 0        | compartments         | 1        |
| species types     | 0        | species              | 10       |
| events            | 0        | constraints          | 0        |
| reactions         | 17       | function definitions | 4        |
| global parameters | 0        | unit definitions     | 1        |
| rules             | 0        | initial assignments  | 0        |

#### **Model Notes**

Schmitz2014 - RNA triplex formationThe model is parameterized using theparameters for gene CCDC3 from Supplementary Table S1. The twomiRNAs which form the triplex together with CCDC3 are miR-551b andmiR-138.

This model is described in the article:Cooperative gene regulation by microRNA pairs and their identification using a computational workflow.Schmitz U, Lai X, Winter F, Wolkenhauer O, Vera J, Gupta SK.Nucleic Acids Res. 2014 Jul; 42(12): 7539-7552

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#### Abstract:

MicroRNAs (miRNAs) are an integral part of gene regulation at the post-transcriptional level. Recently, it has been shown that pairs of miRNAs can repress the translation of a target mRNA in a cooperative manner, which leads to an enhanced effectiveness and specificity in target repression. However, it remains unclear which miRNA pairs can synergize and which genes are target of cooperative miRNA regulation. In this paper, we present a computational workflow for the prediction and analysis of cooperating miRNAs and their mutual target genes, which we refer to as RNA triplexes. The workflow integrates methods of miRNA target prediction; triplex structure analysis; molecular dynamics simulations and mathematical modeling for a reliable prediction of functional RNA triplexes and target repression efficiency. In a case study we analyzed the human genome and identified several thousand targets of cooperative gene regulation. Our results suggest that miRNA cooperativity is a frequent mechanism for an enhanced target repression by pairs of miRNAs facilitating distinctive and fine-tuned target gene expression patterns. Human RNA triplexes predicted and characterized in this study are organized in a web resource at www.sbi.uni-rostock.de/triplexrna/.

This model is hosted on BioModels Database and identified by: BIOMD0000000530.

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

Name substance

**Definition** mmol

#### 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** m<sup>2</sup>

# 2.4 Unit length

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

**Definition** m

# 2.5 Unit time

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

**Definition** s

# 3 Compartment

This model contains one compartment.

Table 2: Properties of all compartments.

| Id            | Name        | SBO | Spatial Dimensions | Size | Unit  | Constant | Outside |
|---------------|-------------|-----|--------------------|------|-------|----------|---------|
| compartment_1 | compartment |     | 3                  | 1    | litre |          |         |

# **3.1 Compartment** compartment\_1

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

Name compartment

# 4 Species

This model contains ten species. 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<br>Condi-<br>tion |
|-----------------------------|------------|---------------------------|-------------------------------------|----------|----------------------------|
| species_1                   | mRNA       | compartment_1             | $\operatorname{mmol} \cdot 1^{-1}$  |          |                            |
| species_2                   | miRNA_1    | ${	t compartment}_{	t 1}$ | $\mathrm{mmol}\cdot\mathrm{l}^{-1}$ |          |                            |
| species_3                   | miRNA_2    | ${\tt compartment\_1}$    | $\text{mmol} \cdot 1^{-1}$          |          |                            |
| ${	t species}_{	extsf{-}}4$ | duplex_1   | ${\tt compartment\_1}$    | $\text{mmol} \cdot 1^{-1}$          |          | $\Box$                     |
| species_5                   | duplex_2   | ${\tt compartment\_1}$    | $\text{mmol} \cdot 1^{-1}$          |          | $\Box$                     |
| species_6                   | triplex    | ${\tt compartment\_1}$    | $\text{mmol} \cdot 1^{-1}$          |          | $\Box$                     |
| species_7                   | TF_mRNA    | ${\tt compartment\_1}$    | $\text{mmol} \cdot 1^{-1}$          |          | $\Box$                     |
| species_8                   | TF_miRNA_1 | ${\tt compartment\_1}$    | $\text{mmol} \cdot 1^{-1}$          |          |                            |
| species_9                   | TF_miRNA_2 | ${\tt compartment\_1}$    | $\operatorname{mmol} \cdot 1^{-1}$  |          | $\Box$                     |
| ${\tt species\_10}$         | protein    | ${\tt compartment\_1}$    | $\text{mmol} \cdot l^{-1}$          |          |                            |

# 5 Function definitions

This is an overview of four function definitions.

#### **5.1 Function definition** function\_1

Name mRNA synthesis\_1

**Arguments** k\_syn\_mRNA, [species\_7]

**Mathematical Expression** 

$$k_syn_mRNA \cdot [species_7]$$
 (1)

#### **5.2 Function definition** function\_3

Name miRNA\_2 synthesis\_1

**Arguments** k\_syn\_miRNA\_2, [species\_9]

**Mathematical Expression** 

$$k_syn_miRNA_2 \cdot [species_9]$$
 (2)

#### **5.3 Function definition** function\_4

Name protein synthesis\_1

**Arguments** k\_syn\_prot, [species\_1]

**Mathematical Expression** 

$$k\_syn\_prot \cdot [species\_1]$$
 (3)

# **5.4 Function definition** function\_2

Name miRNA\_1 synthesis\_1

**Arguments** k\_syn\_miRNA\_1, [species\_8]

**Mathematical Expression** 

$$k_{syn_miRNA_1} \cdot [species_8]$$
 (4)

# **6 Reactions**

This model contains 17 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 4: Overview of all reactions

| No | Id                   | Name                  | Reaction Equation SBO   |
|----|----------------------|-----------------------|---|
| 1  | reaction_1           | duplex 1 association  | species_1 + species_2 $\xrightarrow{\text{species}\_1, \text{ species}\_2}$ species_4 |
| 2  | reaction_2           | duplex 2 association  | species_1 + species_3 $\xrightarrow{\text{species}\_1, \text{ species}\_3}$ species_5 |
| 3  | $reaction_3$         | triplex association   | species_1 + species_2 +   |
|    |                      |                       | species_3 species_1, species_2, species_3 species_6                                   |
| 4  | ${\tt reaction\_4}$  | mRNA synthesis        | $\emptyset \xrightarrow{\text{species}\_7, \text{ species}\_7} \text{species}\_1$     |
| 5  | reaction_5           | miRNA_1 synthesis     | $\emptyset \xrightarrow{\text{species\_8, species\_8}} \text{species\_2}$             |
| 6  | reaction_6           | miRNA_2 synthesis     | $\emptyset \xrightarrow{\text{species\_9, species\_9}} \text{species\_3}$             |
| 7  | reaction_7           | mRNA degradation      | $species_1 \xrightarrow{species_1} \emptyset$   |
| 8  | reaction_8           | miRNA_1 degradation   | species_2 $\xrightarrow{\text{species}\_2} \emptyset$                                 |
| 9  | ${\tt reaction\_9}$  | miRNA_2 degradation   | species_3 $\xrightarrow{\text{species}\_3} \emptyset$                                 |
| 10 | ${\tt reaction\_10}$ | duplex 1 dissociation | species_4 $\xrightarrow{\text{species}\_4}$ species_2 + species_1                     |
| 11 | ${\tt reaction\_11}$ | duplex 2 dissociation | species_5 $\xrightarrow{\text{species}\_5}$ species_3 + species_1                     |
| 12 | reaction_12          | triplex dissociation  | $species_6 \xrightarrow{species_6} species_2 + species_3 +$                           |
|    |                      |                       | species_1   |
| 13 | ${\tt reaction\_13}$ | duplex 1 degradation  | species_4 $\xrightarrow{\text{species}\_4} \emptyset$                                 |
| 14 | ${\tt reaction\_14}$ | duplex 2 degradation  | $species\_5 \xrightarrow{species\_5} \emptyset$                                       |

| Nº | Id          | Name                | Reaction Equation   | SBO |
|----|-------------|---------------------|---|-----|
| 15 | reaction_15 | triplex degradation | $species_6 \xrightarrow{species_6} \emptyset$                                     |     |
| 16 | reaction_16 | protein synthesis   | $\emptyset \xrightarrow{\text{species}\_1, \text{species}\_1} \text{species}\_10$ |     |
| 17 | reaction_17 | protein degradation | $species_10 \xrightarrow{species_10} \emptyset$                                   |     |

# **6.1 Reaction** reaction\_1

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

Name duplex 1 association

# **Reaction equation**

$$species_1 + species_2 \xrightarrow{species_1, species_2} species_4$$
 (5)

#### **Reactants**

Table 5: Properties of each reactant.

| Id                 | Name         | SBO |
|--------------------|--------------|-----|
| species_1          | mRNA         |     |
| ${\tt species\_2}$ | $miRNA_{-}1$ |     |

#### **Modifiers**

Table 6: Properties of each modifier.

| Id                  | Name | SBO |
|---------------------|------|-----|
| species_1 species_2 |      |     |

## **Product**

Table 7: Properties of each product.

| Id        | Name     | SBO |
|-----------|----------|-----|
| species_4 | duplex_1 |     |

#### **Kinetic Law**

$$v_1 = \text{vol}(\text{compartment}\_1) \cdot \text{k1} \cdot [\text{species}\_1] \cdot [\text{species}\_2]$$
 (6)

Table 8: Properties of each parameter.

| Id | Name | SBO | Value                  | Unit | Constant |
|----|------|-----|------------------------|------|----------|
| k1 | k1   | 4   | $4.5298 \cdot 10^{-2}$ | 4    |          |

# **6.2 Reaction** reaction\_2

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

Name duplex 2 association

# **Reaction equation**

species\_1 + species\_3 
$$\xrightarrow{\text{species}\_1, \text{ species}\_3}$$
 species\_5 (7)

#### **Reactants**

Table 9: Properties of each reactant.

| Id                  | Name | SBO |
|---------------------|------|-----|
| species_1 species_3 |      |     |

#### **Modifiers**

Table 10: Properties of each modifier.

| Id        | Name    | SBO |
|-----------|---------|-----|
| species_1 | mRNA    |     |
| species_3 | miRNA_2 |     |

#### **Product**

Table 11: Properties of each product.

| Id        | Name     | SBO |
|-----------|----------|-----|
| species_5 | duplex_2 |     |

#### **Kinetic Law**

$$v_2 = \text{vol} (\text{compartment}\_1) \cdot \text{k1} \cdot [\text{species}\_1] \cdot [\text{species}\_3]$$
 (8)

Table 12: Properties of each parameter.

| Id | Name | SBO | Value         | Unit | Constant       |
|----|------|-----|---------------|------|----------------|
| k1 | k1   | 1   | .30837 · 10-5 | 5    | $\overline{Z}$ |

#### **6.3 Reaction** reaction\_3

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

Name triplex association

# **Reaction equation**

$$species_1 + species_2 + species_3 \xrightarrow{species_1, species_2, species_3} species_6$$
 (9)

#### **Reactants**

Table 13: Properties of each reactant.

| Id        | Name         | SBO |
|-----------|--------------|-----|
| species_1 | mRNA         |     |
| species_2 | $miRNA_{-}1$ |     |
| species_3 | miRNA_2      |     |

#### **Modifiers**

Table 14: Properties of each modifier.

| Name         | SBO                        |
|--------------|----------------------------|
| mRNA         |                            |
| $miRNA_{-}1$ |                            |
| $miRNA_2$    |                            |
|              | MRNA<br>miRNA_1<br>miRNA_2 |

Table 15: Properties of each product.

| Id        | Name    | SBO |
|-----------|---------|-----|
| species_6 | triplex |     |

**Derived unit** contains undeclared units

$$v_3 = \text{vol}(\text{compartment\_1}) \cdot \text{k1} \cdot [\text{species\_1}] \cdot [\text{species\_2}] \cdot [\text{species\_3}]$$
 (10)

Table 16: Properties of each parameter.

| Id | Name | SBO Value Unit | Constant |
|----|------|----------------|----------|
| k1 | k1   | 1.000          |          |

#### **6.4 Reaction** reaction\_4

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

Name mRNA synthesis

# **Reaction equation**

$$\emptyset \xrightarrow{\text{species}\_7, \text{ species}\_7} \text{species}\_1$$
 (11)

#### **Modifiers**

Table 17: Properties of each modifier.

| Id                  | Name               | SBO |
|---------------------|--------------------|-----|
| species_7 species_7 | TF_mRNA<br>TF_mRNA |     |

Table 18: Properties of each product.

| Id        | Name | SBO |
|-----------|------|-----|
| species_1 | mRNA |     |

**Derived unit** contains undeclared units

$$v_4 = \text{vol} (\text{compartment\_1}) \cdot \text{function\_1} (\text{k\_syn\_mRNA}, [\text{species\_7}])$$
 (12)

$$function_1(k_syn_mRNA, [species_7]) = k_syn_mRNA \cdot [species_7]$$
 (13)

function\_1 (k\_syn\_mRNA, [species\_7]) = k\_syn\_mRNA 
$$\cdot$$
 [species\_7] (14)

Table 19: Properties of each parameter.

| Id         | Name       | SBO Value Unit | Constant |
|------------|------------|----------------|----------|
| k_syn_mRNA | k_syn_mRNA | 1.0            |          |

#### **6.5 Reaction** reaction\_5

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

Name miRNA\_1 synthesis

#### **Reaction equation**

$$\emptyset \xrightarrow{\text{species\_8, species\_8}} \text{species\_2}$$
 (15)

#### **Modifiers**

Table 20: Properties of each modifier.

| Id | Name                     | SBO |
|----|--------------------------|-----|
| -  | TF_miRNA_1<br>TF_miRNA_1 |     |

Table 21: Properties of each product.

|           |         | <u> </u> |
|-----------|---------|----------|
| Id        | Name    | SBO      |
| species_2 | miRNA_1 |          |

Derived unit contains undeclared units

$$v_5 = \text{vol} (\text{compartment\_1}) \cdot \text{function\_2} (\text{k\_syn\_miRNA\_1}, [\text{species\_8}])$$
 (16)

$$function_2(k_syn_miRNA_1, [species_8]) = k_syn_miRNA_1 \cdot [species_8]$$
 (17)

$$function_2(k_syn_miRNA_1, [species_8]) = k_syn_miRNA_1 \cdot [species_8]$$
 (18)

Table 22: Properties of each parameter.

| Id            | Name          | SBO | Value | Unit | Constant |
|---------------|---------------|-----|-------|------|----------|
| k_syn_miRNA_1 | k_syn_miRNA_1 |     | 1.0   |      |          |

#### **6.6 Reaction** reaction\_6

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

Name miRNA\_2 synthesis

#### **Reaction equation**

$$\emptyset \xrightarrow{\text{species\_9, species\_9}} \text{species\_3}$$
 (19)

#### **Modifiers**

Table 23: Properties of each modifier.

| Id                  | Name                  | SBO |
|---------------------|-----------------------|-----|
| species_9 species_9 | TF_miRNA_2 TF_miRNA_2 |     |

Table 24: Properties of each product.

| Id        | Name    | SBO |
|-----------|---------|-----|
| species_3 | miRNA_2 |     |

Derived unit contains undeclared units

$$v_6 = \text{vol} (\text{compartment\_1}) \cdot \text{function\_3} (\text{k\_syn\_miRNA\_2}, [\text{species\_9}])$$
 (20)

$$function_3(k_syn_miRNA_2, [species_9]) = k_syn_miRNA_2 \cdot [species_9]$$
 (21)

Table 25: Properties of each parameter.

| Id            | Name          | SBO | Value | Unit | Constant |
|---------------|---------------|-----|-------|------|----------|
| k_syn_miRNA_2 | k_syn_miRNA_2 |     | 1.0   |      |          |

# **6.7 Reaction** reaction\_7

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

Name mRNA degradation

#### **Reaction equation**

$$species_{-1} \xrightarrow{species_{-1}} \emptyset$$
 (23)

#### Reactant

Table 26: Properties of each reactant.

| Id        | Name | SBO |
|-----------|------|-----|
| species_1 | mRNA |     |

#### **Modifier**

Table 27: Properties of each modifier.

| Id        | Name | SBO |
|-----------|------|-----|
| species_1 | mRNA |     |

**Derived unit** contains undeclared units

$$v_7 = \text{vol}(\text{compartment}_1) \cdot \text{k1} \cdot [\text{species}_1]$$
 (24)

Table 28: Properties of each parameter.

| Id | Name | SBO Value Unit | Constant |
|----|------|----------------|----------|
| k1 | k1   | 1.0            |          |

#### **6.8 Reaction** reaction\_8

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

Name miRNA\_1 degradation

#### **Reaction equation**

$$species_2 \xrightarrow{species_2} \emptyset$$
 (25)

#### Reactant

Table 29: Properties of each reactant.

| Id        | Name    | SBO |
|-----------|---------|-----|
| species_2 | miRNA_1 |     |

# **Modifier**

Table 30: Properties of each modifier.

| Id        | Name    | SBO |
|-----------|---------|-----|
| species_2 | miRNA_1 |     |

#### **Kinetic Law**

$$v_8 = \text{vol}(\text{compartment\_1}) \cdot \text{k1} \cdot [\text{species\_2}]$$
 (26)

Table 31: Properties of each parameter.

| Id | Name | SBO Value Unit | Constant |
|----|------|----------------|----------|
| k1 | k1   | 1.0            |          |

# **6.9 Reaction** reaction\_9

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

Name miRNA\_2 degradation

# **Reaction equation**

species\_3 
$$\xrightarrow{\text{species}\_3} \emptyset$$
 (27)

#### Reactant

Table 32: Properties of each reactant.

| Id        | Name    | SBO |
|-----------|---------|-----|
| species_3 | miRNA_2 | _   |

#### **Modifier**

Table 33: Properties of each modifier.

| Id        | Name    | SBO |
|-----------|---------|-----|
| species_3 | miRNA_2 |     |

#### **Kinetic Law**

$$v_9 = \text{vol} (\text{compartment}_1) \cdot \text{k1} \cdot [\text{species}_3]$$
 (28)

Table 34: Properties of each parameter.

| Id | Name       | SBO Value Unit | Constant |
|----|------------|----------------|----------|
| k1 | <b>k</b> 1 | 1.0            | Ø        |

# 6.10 Reaction reaction\_10

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

Name duplex 1 dissociation

# **Reaction equation**

species\_4 
$$\xrightarrow{\text{species}\_4}$$
 species\_2 + species\_1 (29)

#### Reactant

Table 35: Properties of each reactant.

| Id        | Name     | SBO |
|-----------|----------|-----|
| species_4 | duplex_1 |     |

#### **Modifier**

Table 36: Properties of each modifier.

| Id        | Name     | SBO |
|-----------|----------|-----|
| species_4 | duplex_1 |     |

## **Products**

Table 37: Properties of each product.

| Name            | SBO     |
|-----------------|---------|
| niRNA_1<br>nRNA |         |
|                 | niRNA_1 |

#### **Kinetic Law**

$$v_{10} = \text{vol} \left( \text{compartment\_1} \right) \cdot \text{k1} \cdot \left[ \text{species\_4} \right]$$
 (30)

Table 38: Properties of each parameter.

| Id | Name | SBO Value Unit | Constant |
|----|------|----------------|----------|
| k1 | k1   | 0.250          |          |

# 6.11 Reaction reaction\_11

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

Name duplex 2 dissociation

# **Reaction equation**

$$species\_5 \xrightarrow{species\_5} species\_3 + species\_1$$
 (31)

#### Reactant

Table 39: Properties of each reactant.

| Id        | Name     | SBO |
|-----------|----------|-----|
| species_5 | duplex_2 |     |

#### **Modifier**

Table 40: Properties of each modifier.

| Id        | Name     | SBO |
|-----------|----------|-----|
| species_5 | duplex_2 |     |

#### **Products**

Table 41: Properties of each product.

| Id                  | Name | SBO |
|---------------------|------|-----|
| species_3 species_1 |      |     |

# **Kinetic Law**

$$v_{11} = \text{vol}(\text{compartment}\_1) \cdot \text{k1} \cdot [\text{species}\_5]$$
 (32)

Table 42: Properties of each parameter.

| Id | Name | SBO Value Unit | Constant |
|----|------|----------------|----------|
| k1 | k1   | 0.241          |          |

#### **6.12 Reaction** reaction\_12

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

Name triplex dissociation

# **Reaction equation**

species\_6 
$$\xrightarrow{\text{species}\_6}$$
 species\_2 + species\_3 + species\_1 (33)

#### Reactant

Table 43: Properties of each reactant.

| Id        | Name    | SBO |
|-----------|---------|-----|
| species_6 | triplex |     |

## **Modifier**

Table 44: Properties of each modifier.

| Id        | Name    | SBO |
|-----------|---------|-----|
| species_6 | triplex |     |

Table 45: Properties of each product.

| Name    | SBO                |
|---------|--------------------|
| miRNA_1 |                    |
| miRNA_2 |                    |
| mRNA    |                    |
|         | miRNA_1<br>miRNA_2 |

**Derived unit** contains undeclared units

$$v_{12} = \text{vol} (\text{compartment\_1}) \cdot \text{k1} \cdot [\text{species\_6}]$$
 (34)

Table 46: Properties of each parameter.

| Id | Name | SBO Value Unit | Constant |
|----|------|----------------|----------|
| k1 | k1   | 0.188          | Ø        |

# **6.13 Reaction** reaction\_13

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

Name duplex 1 degradation

#### **Reaction equation**

species\_4 
$$\xrightarrow{\text{species}\_4} \emptyset$$
 (35)

#### Reactant

Table 47: Properties of each reactant.

| Id        | Name     | SBO |
|-----------|----------|-----|
| species_4 | duplex_1 |     |

# **Modifier**

Table 48: Properties of each modifier.

| Id        | Name     | SBO |
|-----------|----------|-----|
| species_4 | duplex_1 |     |

#### **Kinetic Law**

$$v_{13} = \text{vol} (\text{compartment\_1}) \cdot \text{k1} \cdot [\text{species\_4}]$$
 (36)

Table 49: Properties of each parameter.

| Id | Name | SBO Value Unit | Constant |
|----|------|----------------|----------|
| k1 | k1   | 1.0            |          |

# 6.14 Reaction reaction\_14

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

Name duplex 2 degradation

# **Reaction equation**

species\_5 
$$\xrightarrow{\text{species}\_5} \emptyset$$
 (37)

#### Reactant

Table 50: Properties of each reactant.

| Id        | Name     | SBO |
|-----------|----------|-----|
| species_5 | duplex_2 |     |

#### **Modifier**

Table 51: Properties of each modifier.

| Id        | Name     | SBO |
|-----------|----------|-----|
| species_5 | duplex_2 |     |

#### **Kinetic Law**

$$v_{14} = \text{vol} (\text{compartment}_{-1}) \cdot \text{k1} \cdot [\text{species}_{-5}]$$
 (38)

Table 52: Properties of each parameter.

| Id | Name | SBO Value Unit | Constant |
|----|------|----------------|----------|
| k1 | k1   | 1.0            | Ø        |

#### **6.15 Reaction** reaction\_15

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

Name triplex degradation

# **Reaction equation**

$$species_6 \xrightarrow{species_6} \emptyset$$
 (39)

#### Reactant

Table 53: Properties of each reactant.

| Id        | Name    | SBO |
|-----------|---------|-----|
| species_6 | triplex |     |

#### **Modifier**

Table 54: Properties of each modifier.

| Id        | Name    | SBO |
|-----------|---------|-----|
| species_6 | triplex |     |

## **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{15} = \text{vol} (\text{compartment\_1}) \cdot \text{k1} \cdot [\text{species\_6}]$$
 (40)

Table 55: Properties of each parameter.

| Id | Name | SBO Value Unit | Constant       |
|----|------|----------------|----------------|
| k1 | k1   | 1.0            | $\overline{Z}$ |

# **6.16 Reaction** reaction\_16

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

Name protein synthesis

#### **Reaction equation**

$$\emptyset \xrightarrow{\text{species\_1, species\_1}} \text{species\_10}$$
 (41)

#### **Modifiers**

Table 56: Properties of each modifier.

| Id | Name         | SBO |
|----|--------------|-----|
|    | mRNA<br>mRNA |     |

#### **Product**

Table 57: Properties of each product.

| Id         | Name    | SBO |
|------------|---------|-----|
| species_10 | protein |     |

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{16} = \text{vol}(\text{compartment\_1}) \cdot \text{function\_4}(\text{k\_syn\_prot},[\text{species\_1}])$$
 (42)

$$function_4(k_syn_prot, [species_1]) = k_syn_prot \cdot [species_1]$$
 (43)

$$function\_4(k\_syn\_prot,[species\_1]) = k\_syn\_prot \cdot [species\_1]$$
 (44)

Table 58: Properties of each parameter.

| Id         | Name       | SBO Value Unit | Constant |
|------------|------------|----------------|----------|
| k_syn_prot | k_syn_prot | 1.0            |          |

#### **6.17 Reaction** reaction\_17

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

Name protein degradation

#### **Reaction equation**

$$species_{-}10 \xrightarrow{species_{-}10} \emptyset$$
 (45)

#### Reactant

Table 59: Properties of each reactant.

| Id         | Name    | SBO |
|------------|---------|-----|
| species_10 | protein |     |

#### **Modifier**

Table 60: Properties of each modifier.

| Id         | Name    | SBO |
|------------|---------|-----|
| species_10 | protein |     |

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{17} = \text{vol}(\text{compartment}_1) \cdot \text{k1} \cdot [\text{species}_10]$$
 (46)

Table 61: Properties of each parameter.

| Id | Name | SBO Value Unit | Constant |
|----|------|----------------|----------|
| k1 | k1   | 1.0            |          |

# 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 species\_1

#### Name mRNA

#### Initial concentration 1 mmol·l<sup>-1</sup>

This species takes part in 14 reactions (as a reactant in reaction\_1, reaction\_2, reaction\_3, reaction\_7 and as a product in reaction\_4, reaction\_10, reaction\_11, reaction\_12 and as a modifier in reaction\_1, reaction\_2, reaction\_3, reaction\_7, reaction\_16, reaction\_16).

$$\frac{d}{dt} \text{species}_{1} = |v_{4}| + |v_{10}| + |v_{11}| + |v_{12}| - |v_{1}| - |v_{2}| - |v_{3}| - |v_{7}|$$
(47)

## 7.2 Species species\_2

#### Name miRNA\_1

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

This species takes part in nine reactions (as a reactant in reaction\_1, reaction\_3, reaction\_8 and as a product in reaction\_5, reaction\_10, reaction\_12 and as a modifier in reaction\_1, reaction\_3, reaction\_8).

$$\frac{d}{dt} \text{species} \cdot 2 = |v_5| + |v_{10}| + |v_{12}| - |v_1| - |v_3| - |v_8| \tag{48}$$

# **7.3 Species** species\_3

## Name miRNA\_2

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

This species takes part in nine reactions (as a reactant in reaction\_2, reaction\_3, reaction\_9 and as a product in reaction\_6, reaction\_11, reaction\_12 and as a modifier in reaction\_2, reaction\_3, reaction\_9).

$$\frac{d}{dt} \text{species}_{3} = |v_{6}| + |v_{11}| + |v_{12}| - |v_{2}| - |v_{3}| - |v_{9}|$$
(49)

#### 7.4 Species species\_4

## Name duplex\_1

#### Initial concentration $0 \text{ mmol} \cdot 1^{-1}$

This species takes part in five reactions (as a reactant in reaction\_10, reaction\_13 and as a product in reaction\_1 and as a modifier in reaction\_10, reaction\_13).

$$\frac{d}{dt} \text{species}_{4} = |v_{1}| - |v_{10}| - |v_{13}| \tag{50}$$

# **7.5 Species** species\_5

Name duplex\_2

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

This species takes part in five reactions (as a reactant in reaction\_11, reaction\_14 and as a product in reaction\_2 and as a modifier in reaction\_11, reaction\_14).

$$\frac{d}{dt} \text{species}_{5} = |v_{2}| - |v_{11}| - |v_{14}| \tag{51}$$

# **7.6 Species** species\_6

Name triplex

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

This species takes part in five reactions (as a reactant in reaction\_12, reaction\_15 and as a product in reaction\_3 and as a modifier in reaction\_12, reaction\_15).

$$\frac{d}{dt} \text{species}_{.6} = |v_3| - |v_{12}| - |v_{15}| \tag{52}$$

# 7.7 Species species\_7

Name TF\_mRNA

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

This species takes part in two reactions (as a modifier in reaction\_4, reaction\_4).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species}_{-}7 = 0 \tag{53}$$

# **7.8 Species** species\_8

Name TF\_miRNA\_1

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

This species takes part in two reactions (as a modifier in reaction\_5, reaction\_5).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{species}_{-}8 = 0 \tag{54}$$

# **7.9 Species** species\_9

Name TF\_miRNA\_2

Initial concentration  $1 \text{ } \mathrm{mmol} \cdot l^{-1}$ 

This species takes part in two reactions (as a modifier in reaction\_6, reaction\_6).

$$\frac{d}{dt} \text{species}_{9} = 0 \tag{55}$$

# 7.10 Species species\_10

Name protein

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

This species takes part in three reactions (as a reactant in reaction\_17 and as a product in reaction\_16 and as a modifier in reaction\_17).

$$\frac{d}{dt} \text{species}_{-10} = |v_{16}| - |v_{17}| \tag{56}$$

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