

SBML Model Report

**Model name: “Markevich2004_MAPK-
_phosphoRandomMM”**



May 6, 2016

1 General Overview

This is a document in SBML Level 2 Version 1 format. This model was created by Nicolas Le Novre¹ at May 24th 2005 at 10:57 a. m. and last time modified at May 15th 2012 at 9:42 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 | 6 |
| events | 0 | constraints | 0 |
| reactions | 7 | function definitions | 0 |
| global parameters | 15 | unit definitions | 1 |
| rules | 0 | initial assignments | 0 |

Model Notes

The model corresponds to the schema 3 of Markevich et al 2004, as described in the figure 2 and the supplementary table S3, and modelled using Michaelis-Menten like kinetics. Phosphorylations follow distributive random kinetics, while dephosphorylations follow an ordered mechanism.

¹EMBL-EBI, lenov@ebi.ac.uk

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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 nanomole (default)

Definition nmol

2.2 Unit `volume`

Notes Litre is the predefined SBML unit for volume.

Definition l

2.3 Unit `area`

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

Definition m²

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 |
|------|------|-----|-----------------------|------|-------|-------------------------------------|---------|
| cell | cell | | 3 | 1 | litre | <input checked="" type="checkbox"/> | |

3.1 Compartment `cell`

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

Name `cell`

4 Species

This model contains six 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 Condition |
|------|--------|-------------|-----------------------------------|-------------------------------------|--------------------------|
| M | ERK | cell | $\text{nmol} \cdot \text{l}^{-1}$ | <input type="checkbox"/> | <input type="checkbox"/> |
| MpY | ERK-PY | cell | $\text{nmol} \cdot \text{l}^{-1}$ | <input type="checkbox"/> | <input type="checkbox"/> |
| MpT | ERK-PT | cell | $\text{nmol} \cdot \text{l}^{-1}$ | <input type="checkbox"/> | <input type="checkbox"/> |
| Mpp | ERK-PP | cell | $\text{nmol} \cdot \text{l}^{-1}$ | <input type="checkbox"/> | <input type="checkbox"/> |
| MEK | MEK | cell | $\text{nmol} \cdot \text{l}^{-1}$ | <input checked="" type="checkbox"/> | <input type="checkbox"/> |
| MKP3 | MKP3 | cell | $\text{nmol} \cdot \text{l}^{-1}$ | <input checked="" type="checkbox"/> | <input type="checkbox"/> |

5 Parameters

This model contains 15 global parameters.

Table 4: Properties of each parameter.

| Id | Name | SBO | Value | Unit | Constant |
|-------|-------|-----|---------|------|-------------------------------------|
| Km1 | Km1 | | 410.000 | | <input checked="" type="checkbox"/> |
| kcat1 | kcat1 | | 1.080 | | <input checked="" type="checkbox"/> |
| Km2 | Km2 | | 40.000 | | <input checked="" type="checkbox"/> |
| kcat2 | kcat2 | | 0.007 | | <input checked="" type="checkbox"/> |
| Km3 | Km3 | | 20.000 | | <input checked="" type="checkbox"/> |
| kcat3 | kcat3 | | 0.008 | | <input checked="" type="checkbox"/> |
| Km4 | Km4 | | 300.000 | | <input checked="" type="checkbox"/> |
| kcat4 | kcat4 | | 0.450 | | <input checked="" type="checkbox"/> |
| Km5 | Km5 | | 22.000 | | <input checked="" type="checkbox"/> |
| kcat5 | kcat5 | | 0.084 | | <input checked="" type="checkbox"/> |
| Km6 | Km6 | | 18.000 | | <input checked="" type="checkbox"/> |
| kcat6 | kcat6 | | 0.060 | | <input checked="" type="checkbox"/> |
| Km7 | Km7 | | 34.000 | | <input checked="" type="checkbox"/> |
| kcat7 | kcat7 | | 0.108 | | <input checked="" type="checkbox"/> |
| Km8 | Km8 | | 40.000 | | <input checked="" type="checkbox"/> |

6 Reactions

This model contains seven 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 | v1 | phosphorylation of ERK on Tyr | $M \xrightarrow{\text{MEK, MpT}} \text{MpY}$ | |
| 2 | v2 | phosphorylation of ERK-PY on Thr | $\text{MpY} \xrightarrow{\text{MEK, M, MpT}} \text{Mpp}$ | |
| 3 | v3 | phosphorylation of ERK on Thr | $M \xrightarrow{\text{MEK, MpY}} \text{MpT}$ | |
| 4 | v4 | phosphorylation of ERK-PT on Tyr | $\text{MpT} \xrightarrow{\text{MEK, M, MpY}} \text{Mpp}$ | |
| 5 | v5 | dephosphorylation of ERK-PP on Tyr | $\text{Mpp} \xrightarrow{\text{MKP3, MpY, M}} \text{MpT}$ | |
| 6 | v6 | dephosphorylation of ERK-PT | $\text{MpT} \xrightarrow{\text{MKP3, Mpp, MpY}} M$ | |
| 7 | v7 | dephosphorylation of ERK-PY | $\text{MpY} \xrightarrow{\text{MKP3, Mpp, MpT}} M$ | |

6.1 Reaction v1

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

Name phosphorylation of ERK on Tyr

Reaction equation



Reactant

Table 6: Properties of each reactant.

| Id | Name | SBO |
|----|------|-----|
| M | ERK | |

Modifiers

Table 7: Properties of each modifier.

| Id | Name | SBO |
|-----|--------|-----|
| MEK | MEK | |
| MpT | ERK-PT | |

Product

Table 8: Properties of each product.

| Id | Name | SBO |
|-----|--------|-----|
| MpY | ERK-PY | |

Kinetic Law

Derived unit contains undeclared units

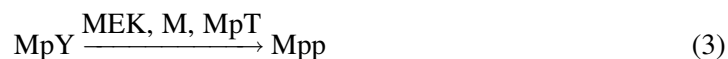
$$v_1 = \text{vol}(\text{cell}) \cdot \frac{\frac{k_{\text{cat}1} \cdot [\text{MEK}] \cdot [\text{M}]}{K_{\text{m}1}}}{1 + [\text{M}] \cdot \frac{K_{\text{m}1} + K_{\text{m}3}}{K_{\text{m}1} \cdot K_{\text{m}3}} + \frac{[\text{MpY}]}{K_{\text{m}2}} + \frac{[\text{MpT}]}{K_{\text{m}4}}} \quad (2)$$

6.2 Reaction v2

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

Name phosphorylation of ERK-PY on Thr

Reaction equation



Reactant

Table 9: Properties of each reactant.

| Id | Name | SBO |
|-----|--------|-----|
| MpY | ERK-PY | |

Modifiers

Table 10: Properties of each modifier.

| Id | Name | SBO |
|-----|--------|-----|
| MEK | MEK | |
| M | ERK | |
| MpT | ERK-PT | |

Product

Table 11: Properties of each product.

| Id | Name | SBO |
|-----|--------|-----|
| Mpp | ERK-PP | |

Kinetic Law

Derived unit contains undeclared units

$$v_2 = \text{vol}(\text{cell}) \cdot \frac{\frac{k_{\text{cat}2} \cdot [\text{MEK}] \cdot [\text{MpY}]}{K_{\text{m}2}}}{1 + [\text{M}] \cdot \frac{K_{\text{m}1} + K_{\text{m}3}}{K_{\text{m}1} \cdot K_{\text{m}3}} + \frac{[\text{MpY}]}{K_{\text{m}2}} + \frac{[\text{MpT}]}{K_{\text{m}4}}} \quad (4)$$

6.3 Reaction v3

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

Name phosphorylation of ERK on Thr

Reaction equation



Reactant

Table 12: Properties of each reactant.

| Id | Name | SBO |
|----|------|-----|
| M | ERK | |

Modifiers

Table 13: Properties of each modifier.

| Id | Name | SBO |
|-----|--------|-----|
| MEK | MEK | |
| MpY | ERK-PY | |

Product

Table 14: Properties of each product.

| Id | Name | SBO |
|-----|--------|-----|
| MpT | ERK-PT | |

Kinetic Law

Derived unit contains undeclared units

$$v_3 = \text{vol}(\text{cell}) \cdot \frac{\frac{k_{\text{cat}3} \cdot [\text{MEK}] \cdot [\text{M}]}{K_{\text{m}3}}}{1 + [\text{M}] \cdot \frac{K_{\text{m}1} + K_{\text{m}3}}{K_{\text{m}1} \cdot K_{\text{m}3}} + \frac{[\text{MpY}]}{K_{\text{m}2}} + \frac{[\text{MpT}]}{K_{\text{m}4}}} \quad (6)$$

6.4 Reaction v4

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

Name phosphorylation of ERK-PT on Tyr

Reaction equation



Reactant

Table 15: Properties of each reactant.

| Id | Name | SBO |
|-----|--------|-----|
| MpT | ERK-PT | |

Modifiers

Table 16: Properties of each modifier.

| Id | Name | SBO |
|-----|--------|-----|
| MEK | MEK | |
| M | ERK | |
| MpY | ERK-PY | |

Product

Table 17: Properties of each product.

| Id | Name | SBO |
|-----|--------|-----|
| Mpp | ERK-PP | |

Kinetic Law

Derived unit contains undeclared units

$$v_4 = \text{vol}(\text{cell}) \cdot \frac{\frac{k_{\text{cat}4} \cdot [\text{MEK}] \cdot [\text{MpT}]}{K_{\text{m}4}}}{1 + [\text{M}] \cdot \frac{K_{\text{m}1} + K_{\text{m}3}}{K_{\text{m}1} \cdot K_{\text{m}3}} + \frac{[\text{MpY}]}{K_{\text{m}2}} + \frac{[\text{MpT}]}{K_{\text{m}4}}} \quad (8)$$

6.5 Reaction v5

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

Name dephosphorylation of ERK-PP on Tyr

Reaction equation



Reactant

Table 18: Properties of each reactant.

| Id | Name | SBO |
|-----|--------|-----|
| Mpp | ERK-PP | |

Modifiers

Table 19: Properties of each modifier.

| Id | Name | SBO |
|------|--------|-----|
| MKP3 | MKP3 | |
| MpY | ERK-PY | |
| M | ERK | |

Product

Table 20: Properties of each product.

| Id | Name | SBO |
|-----|--------|-----|
| MpT | ERK-PT | |

Kinetic Law

Derived unit contains undeclared units

$$v_5 = \text{vol}(\text{cell}) \cdot \frac{\frac{k_{\text{cat}5} \cdot [\text{MKP3}] \cdot [\text{Mpp}]}{K_{\text{m}5}}}{1 + \frac{[\text{Mpp}]}{K_{\text{m}5}} + \frac{[\text{MpT}]}{K_{\text{m}6}} + \frac{[\text{MpY}]}{K_{\text{m}7}} + \frac{[\text{M}]}{K_{\text{m}8}}} \quad (10)$$

6.6 Reaction v6

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

Name dephosphorylation of ERK-PT

Reaction equation



Reactant

Table 21: Properties of each reactant.

| Id | Name | SBO |
|-----|--------|-----|
| MpT | ERK-PT | |

Modifiers

Table 22: Properties of each modifier.

| Id | Name | SBO |
|------|--------|-----|
| MKP3 | MKP3 | |
| Mpp | ERK-PP | |
| MpY | ERK-PY | |

Product

Table 23: Properties of each product.

| Id | Name | SBO |
|----|------|-----|
| M | ERK | |

Kinetic Law

Derived unit contains undeclared units

$$v_6 = \text{vol}(\text{cell}) \cdot \frac{\frac{\text{kat}6 \cdot [\text{MKP3}] \cdot [\text{MpT}]}{\text{Km}6}}{1 + \frac{[\text{Mpp}]}{\text{Km}5} + \frac{[\text{MpT}]}{\text{Km}6} + \frac{[\text{MpY}]}{\text{Km}7} + \frac{[\text{M}]}{\text{Km}8}} \quad (12)$$

6.7 Reaction v7

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

Name dephosphorylation of ERK-PY

Reaction equation



Reactant

Table 24: Properties of each reactant.

| Id | Name | SBO |
|-----|--------|-----|
| MpY | ERK-PY | |

Modifiers

Table 25: Properties of each modifier.

| Id | Name | SBO |
|------|--------|-----|
| MKP3 | MKP3 | |
| Mpp | ERK-PP | |
| MpT | ERK-PT | |

Product

Table 26: Properties of each product.

| Id | Name | SBO |
|----|------|-----|
| M | ERK | |

Kinetic Law

Derived unit contains undeclared units

$$v_7 = \text{vol}(\text{cell}) \cdot \frac{\frac{\text{kcat7} \cdot [\text{MKP3}] \cdot [\text{MpY}]}{\text{Km7}}}{1 + \frac{[\text{Mpp}]}{\text{Km5}} + \frac{[\text{MpT}]}{\text{Km6}} + \frac{[\text{MpY}]}{\text{Km7}} + \frac{[\text{M}]}{\text{Km8}}} \quad (14)$$

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 M

Name ERK

Initial concentration $800 \text{ nmol} \cdot \text{l}^{-1}$

This species takes part in seven reactions (as a reactant in [v1](#), [v3](#) and as a product in [v6](#), [v7](#) and as a modifier in [v2](#), [v4](#), [v5](#)).

$$\frac{d}{dt}M = v_6 + v_7 - v_1 - v_3 \quad (15)$$

7.2 Species MpY

Name ERK-PY

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

This species takes part in seven reactions (as a reactant in [v2](#), [v7](#) and as a product in [v1](#) and as a modifier in [v3](#), [v4](#), [v5](#), [v6](#)).

$$\frac{d}{dt}MpY = v_1 - v_2 - v_7 \quad (16)$$

7.3 Species MpT

Name ERK-PT

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

This species takes part in seven reactions (as a reactant in [v4](#), [v6](#) and as a product in [v3](#), [v5](#) and as a modifier in [v1](#), [v2](#), [v7](#)).

$$\frac{d}{dt}MpT = v_3 + v_5 - v_4 - v_6 \quad (17)$$

7.4 Species Mpp

Name ERK-PP

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

This species takes part in five reactions (as a reactant in [v5](#) and as a product in [v2](#), [v4](#) and as a modifier in [v6](#), [v7](#)).

$$\frac{d}{dt}Mpp = v_2 + v_4 - v_5 \quad (18)$$

7.5 Species MEK

Name MEK

Initial concentration $180 \text{ nmol} \cdot \text{l}^{-1}$

This species takes part in four reactions (as a modifier in [v1](#), [v2](#), [v3](#), [v4](#)).

$$\frac{d}{dt}\text{MEK} = 0 \quad (19)$$

7.6 Species MKP3

Name MKP3

Initial concentration $100 \text{ nmol} \cdot \text{l}^{-1}$

This species takes part in three reactions (as a modifier in [v5](#), [v6](#), [v7](#)).

$$\frac{d}{dt}\text{MKP3} = 0 \quad (20)$$

SBML2^ATeX was developed by Andreas Dräger^a, Hannes Planatscher^a, Dieudonné M Wouamba^a, Adrian Schröder^a, Michael Hucka^b, Lukas Endler^c, Martin Golebiewski^d and Andreas Zell^a. Please see <http://www.ra.cs.uni-tuebingen.de/software/SBML2LaTeX> for more information.

^aCenter for Bioinformatics Tübingen (ZBIT), Germany

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

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

^dEML Research gGmbH, Heidelberg, Germany