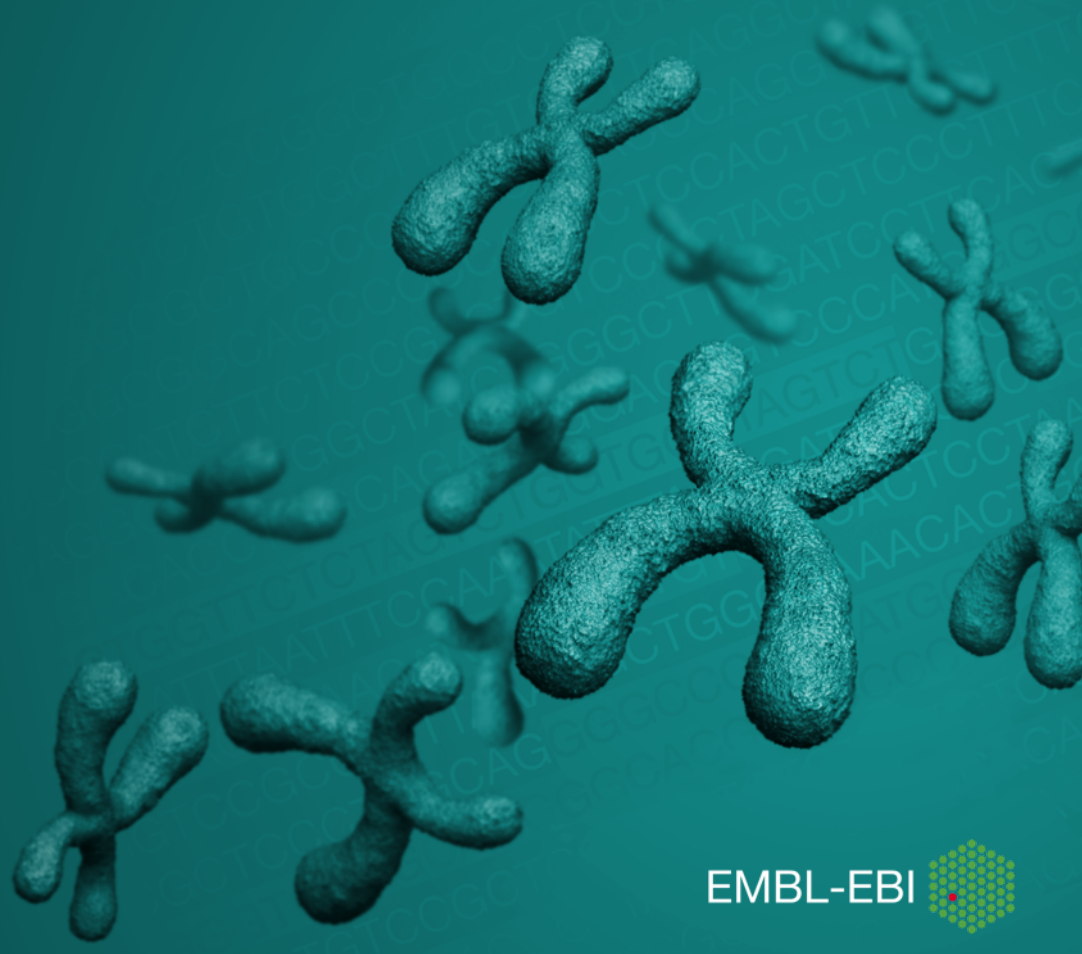
BioModels Database

Repository of mathematical models of biological processes



Nick Juty

ICSB Tutorial, 4th September 2013
Copenhagen, DK

EMBL-EBI

Outline

EMBL-EBI and its data resources

Introduction to BioModels Database

Demonstration of its usage

How can BioModels Database facilitate my research?

European Bioinformatics Institute

- Part of the European Molecular Biology Laboratory (EMBL)
- International, non-profit research institute
- Europe's hub for biological data services and research

Data resources at EMBL-EBI

Genes, genomes & variation

- European Nucleotide Archive (ENA)
- EBI Metagenomics
- Ensembl
- Ensembl Genomes
- European Genome–phenome Archive
- Non-redundant patent sequence databases

Expression

- ArrayExpress
- Expression Atlas
- MetaboLights
- PRIDE

Proteins

- UniProt: the Universal Protein Resource
- InterPro
- Pfam

Molecular & cellular structure

- Protein Data Bank in Europe
- Electron Microscopy Data Bank

Chemical biology

- ChEBI
- ChEMBL
- Patent compounds

Reactions, interactions & pathways

- IntAct
- Reactome

Cross-domain resources

- Europe PubMed Central
- Gene Ontology

Systems

- BioModels Database
- BioSamples Database
- Enzyme Portal

What is BioModels Database?

Portal to the modeling world, providing models and associated tools and resources

- Public repository of computational models of biological processes
  - models encoded in standard formats
  - semantically enriched with cross-references to external data resources (annotation)

- A large number of the hosted models are:
  - described in the scientific literature
  - manually curated

`http://www.ebi.ac.uk/biomodels/`

Types of models available

- Biochemical models
  - interactions between molecules in multiple cellular compartments
- Pharmacometrics models
  - tumor growth and treatment response
- Electrophysiology models
  - membrane voltage, current flow, concentration of various ions intra- and extracellularly, ...
- Disease models
  - neurodegenerative, diabetes, blood coagulation, infectious diseases (outbreak of zombie infection), ...
- Ecosystem models
  - interaction of living organisms in a given environment
- ...

Terms of use

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This is a human-readable summary of the **Legal Code (read the full text)**.

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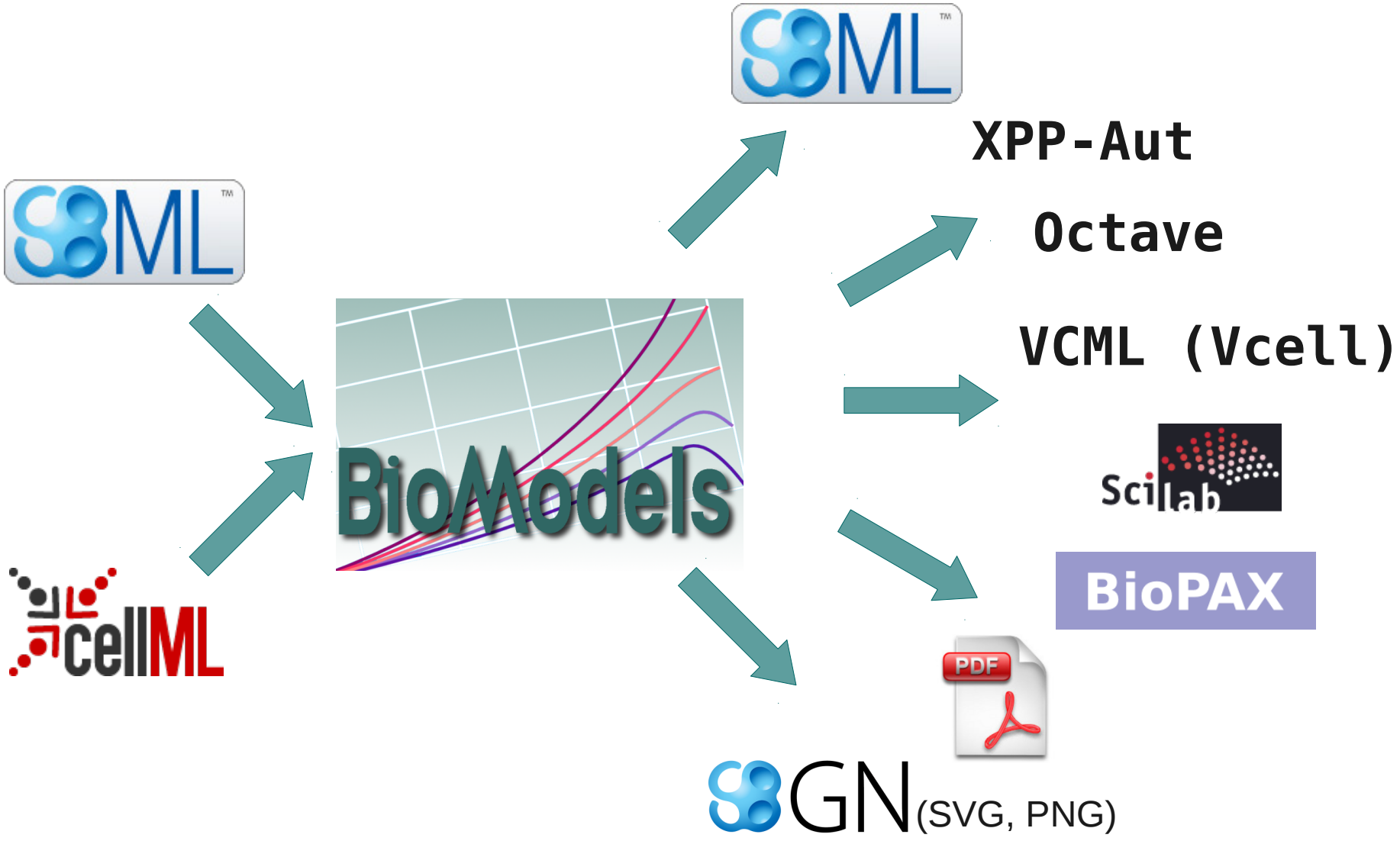
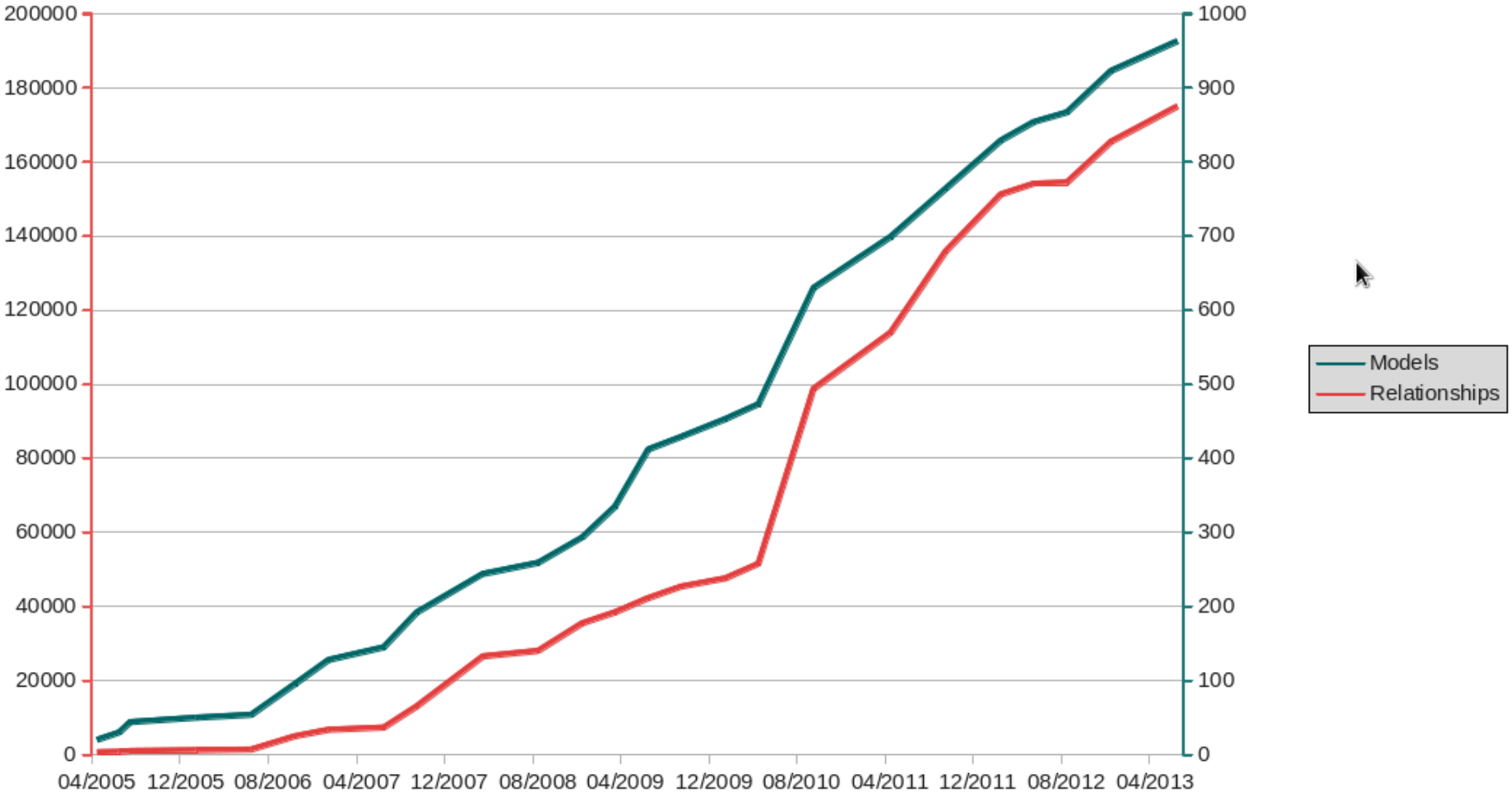
Supported formats

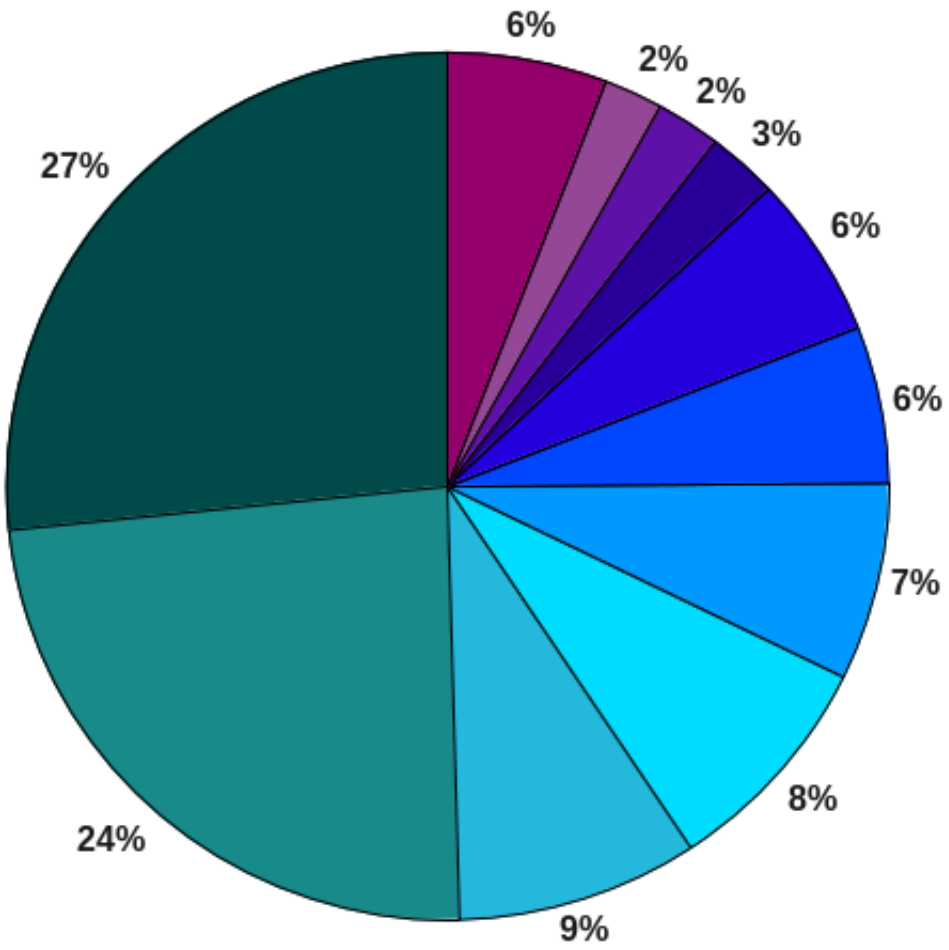


Content evolution



Based on the subset of models published in the literature

Models (curated): classification based on GO



Model provenance

- From authors prior to publication
  - supported (listed in instructions for authors) by more than 300 journals (including: Molecular Systems Biology, PLoS journals, BioMedCentral journals, RSC publication group ...)
- Submitted by curators
  - implemented from literature
  - imported from journal supplementary materials
  - exchanged with other repositories (DOQCS, CellML Model Repository, JWS Online, ...)
- Projects generating large numbers of quantitative models
  - Path2Models, ...
- Provided by other people curating models out of interest

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All models are provided under the terms of the Creative Commons CC0 Public Domain Dedication, cf. our terms of use. This means that the models are available freely for use, modification and distribution, to all users. More information about BioModels Database can be found in the frequently asked questions (FAQ).

Models published in the literature

- Browse curated models
- Browse curated models using GO
- Browse curated models using Taxonomy
- Browse non-curated models

Path2Models

Submit a model

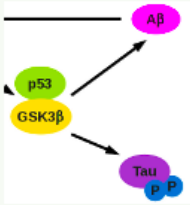
Links

- Main instance at EMBL-EBI, UK
- Mirror at Caltech, USA
- Project on SourceForge
- Web Services
- Download archived models

Model of the month

July, 2013

The interaction of p53 with GSK3β under stressed conditions has important role in Alzheimer's disease. Here, Proctor and Gray (2010) has demonstrated by a mathematical model that this interaction leads to an increased activity of GSK3β, hyper-phosphorylation of tau and increased production of amyloid β.



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News

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18 June 2013 **25th release**

We are pleased to announce the twenty-fifth release of BioModels Database! The resource now publicly provides 143013 models. Numerous new models have been made available, several have been updated and various new features have been unveiled.

13 May 2013 **Bioinformatician position available**

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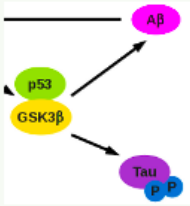

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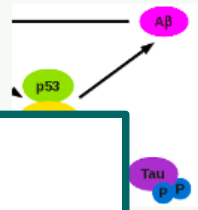

BioModels identifier:

Person:

SBML elements: match the **exact phrase**

Annotation (full text): UniProt Knowledgebase

Annotation (full text): Publication

Annotation (full text): Gene Ontology MAPK cascade

Annotation (identifier): PubChem-compound

Annotation (identifier): KEGG Reaction

Annotation (identifier): Enzyme Nomenclature

Compose by: and or

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Path2Models

Submit a model

BioModels ID	Name	Publication ID	Last Modified
BIOMD0000000003	Goldbeter1991 - Min Mit Oscil	1833774	2013-05-16T14:38:01+00:00
BIOMD0000000004	Goldbeter1991 - Min Mit Oscil, Expl Inact	1833774	2012-12-11T15:30:15+00:00
BIOMD0000000009	Huang1996 - Ultrasensitivity in MAPK cascade	8816754	2013-07-16T10:02:42+00:00
BIOMD0000000010	Kholodenko2000 - Ultrasensitivity and negative feedback bring oscillations in MAPK cascade	10712587	2013-07-16T10:04:39+00:00
BIOMD0000000011	Levchenko2000_MAPK_noScaffold	10823939	2013-06-03T13:36:09+00:00

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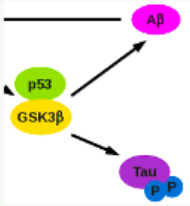

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Search results

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Model page

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BIOMD0000000010 - Kholodenko2000 - Ultrasensitivity and negative feedback bring oscillations in MAPK cascade

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Model | Overview | Math | Physical entities | Parameters | Curation

Reference Publication

Publication ID: 10712587

Kholodenko BN.
Negative feedback and ultrasensitivity can bring about oscillations in the mitogen-activated protein kinase cascades.
Eur. J. Biochem. 2000 Mar; 267(6): 1583-1588
Department of Pathology, Anatomy and Cell Biology, Thomas Jefferson University, Philadelphia, PA 19107, USA. Boris.Kholodenko@mail.tju.edu [more]

Model

Original Model: *BIOMD0000000010.xml.origin*

Submitter: Nicolas Le Novère

Submission ID: MODEL6615119181

Submission Date: 13 Sep 2005 12:39:02 UTC

Last Modification Date: 15 Jul 2013 12:31:02 UTC

Creation Date: 12 Feb 2005 00:18:12 UTC

Encoders: Herbert Sauro

	bqbiol:isVersionOf	Gene Ontology MAPK cascade
set #1	bqbiol:isHomologTo	Reactome REACT_634
	bqbiol:occursIn	Taxonomy Xenopus laevis

Model cross-references

BIOMD0000000010 - Kholodenko2000 - Ultrasensitivity and negative feedback bring oscillations in MAPK cascade

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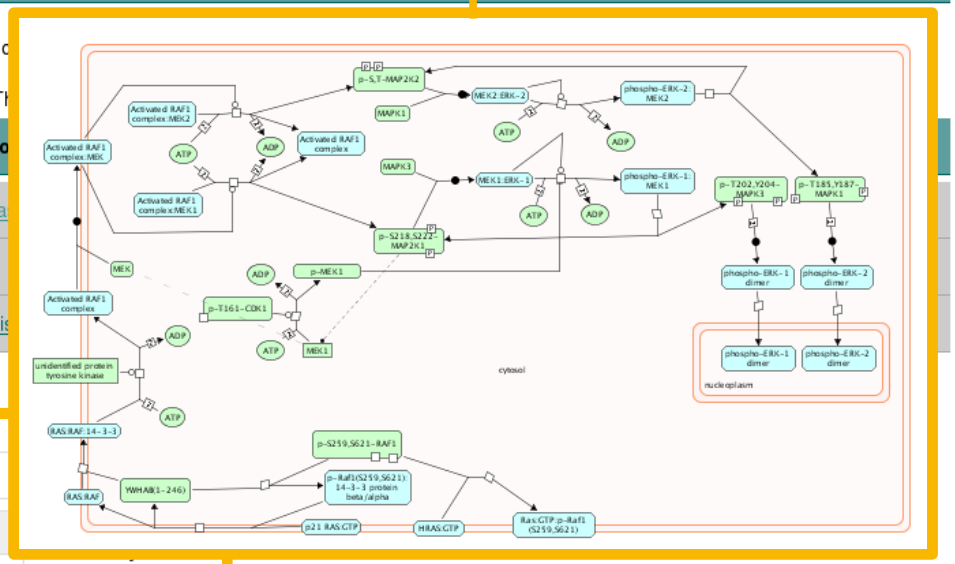


SPECIES **Xenopus laevis (African clawed frog)**

UniProtKB (16,000) | Branch (3) | Taxonomy help

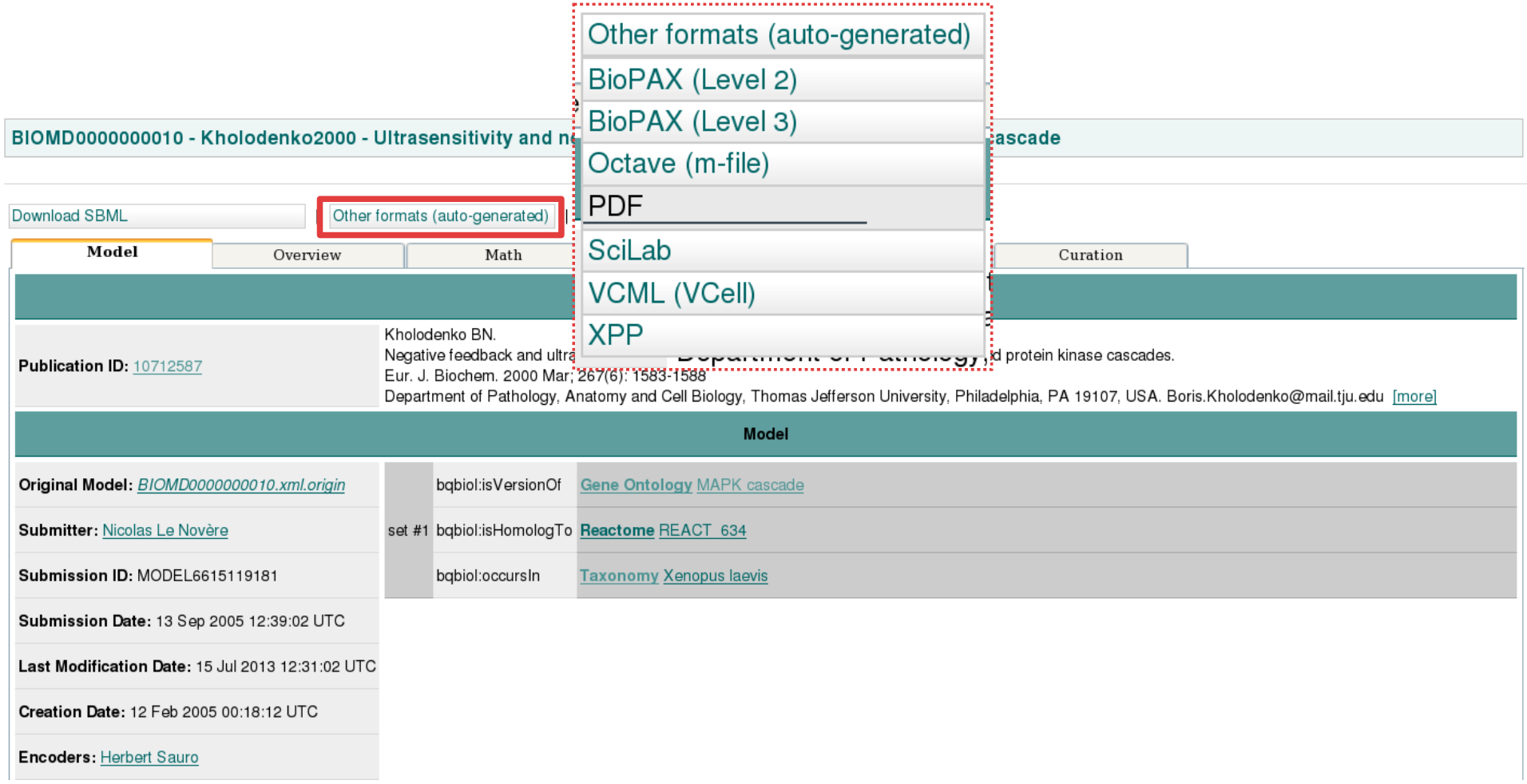
Mnemonic	XENLA
Taxon identifier	8355
Scientific name	Xenopus laevis

Taxonomy navigation

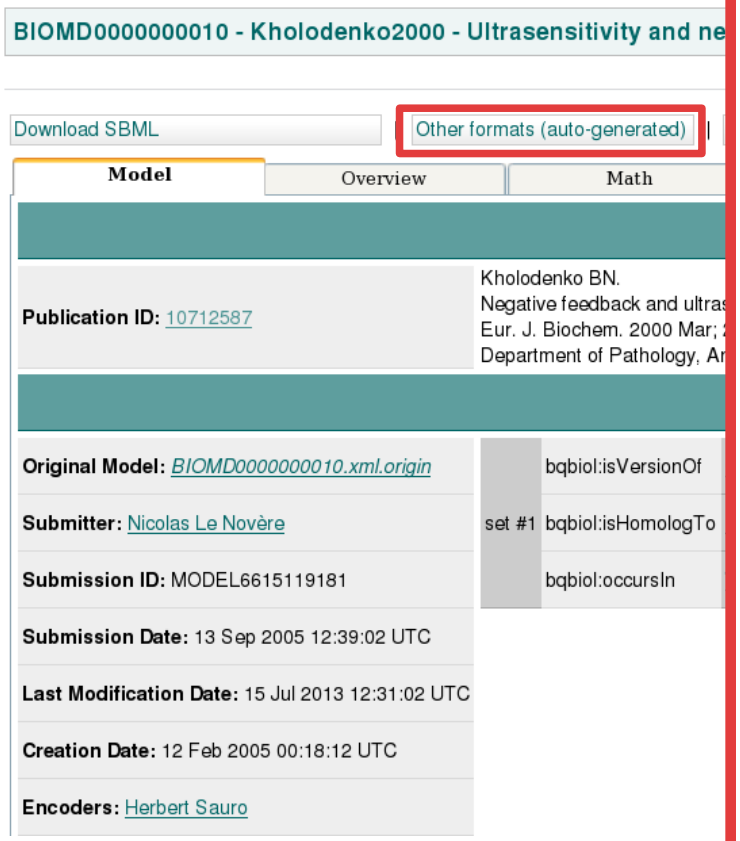
› Xenopus
› Xenopus laevis laevis
› Xenopus laevis poweri
› Xenopus laevis sudanensis

to copyright.

Model exports



Human readable summary (PDF)



SBML Model Report

Model name: "Kholodenko2000 - Ultrasensitivity and negative feedback bring oscillations in MAPK cascade"

SBML2LaTeX

July 15, 2013

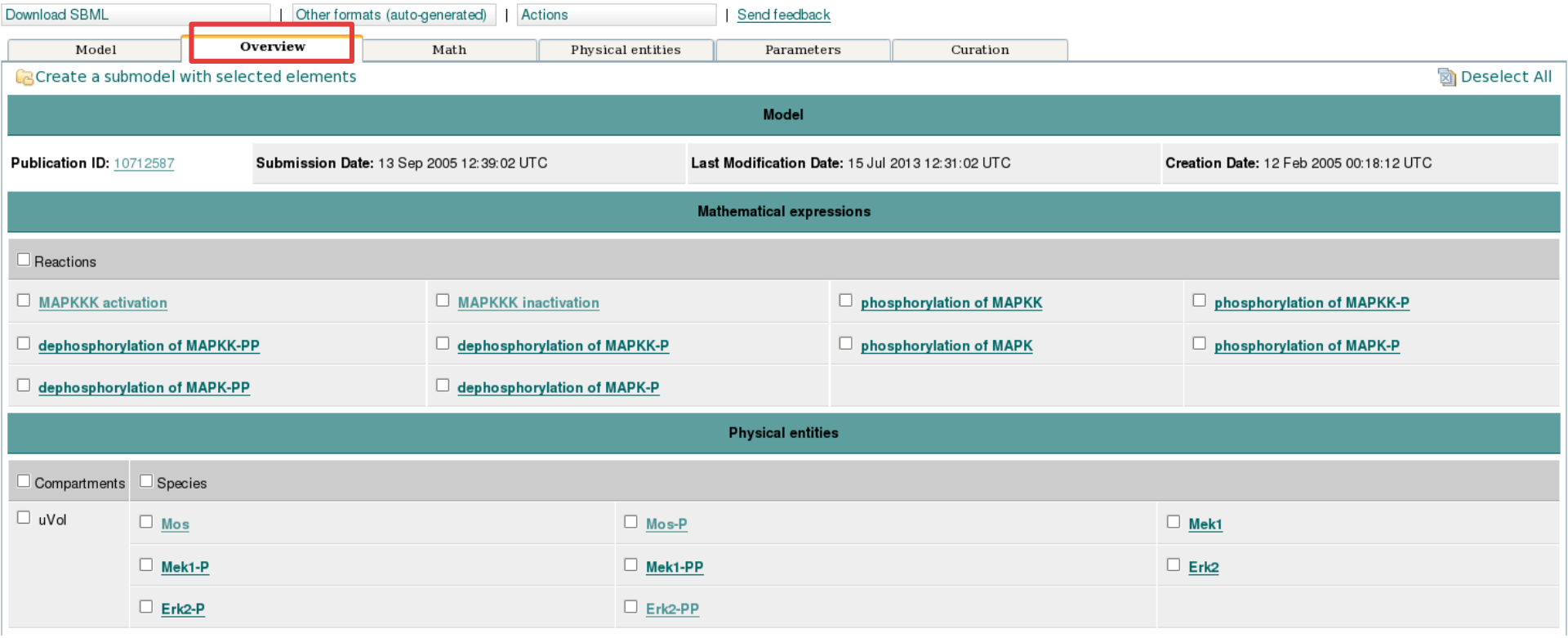
1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by Herbert Sauro[1] at February twelveth 2005 at 0:18 a. m. and last time modified at December eleventh 2012 at 4:17 p. m. Table 1 gives an overview of the quantities of all components of this model.

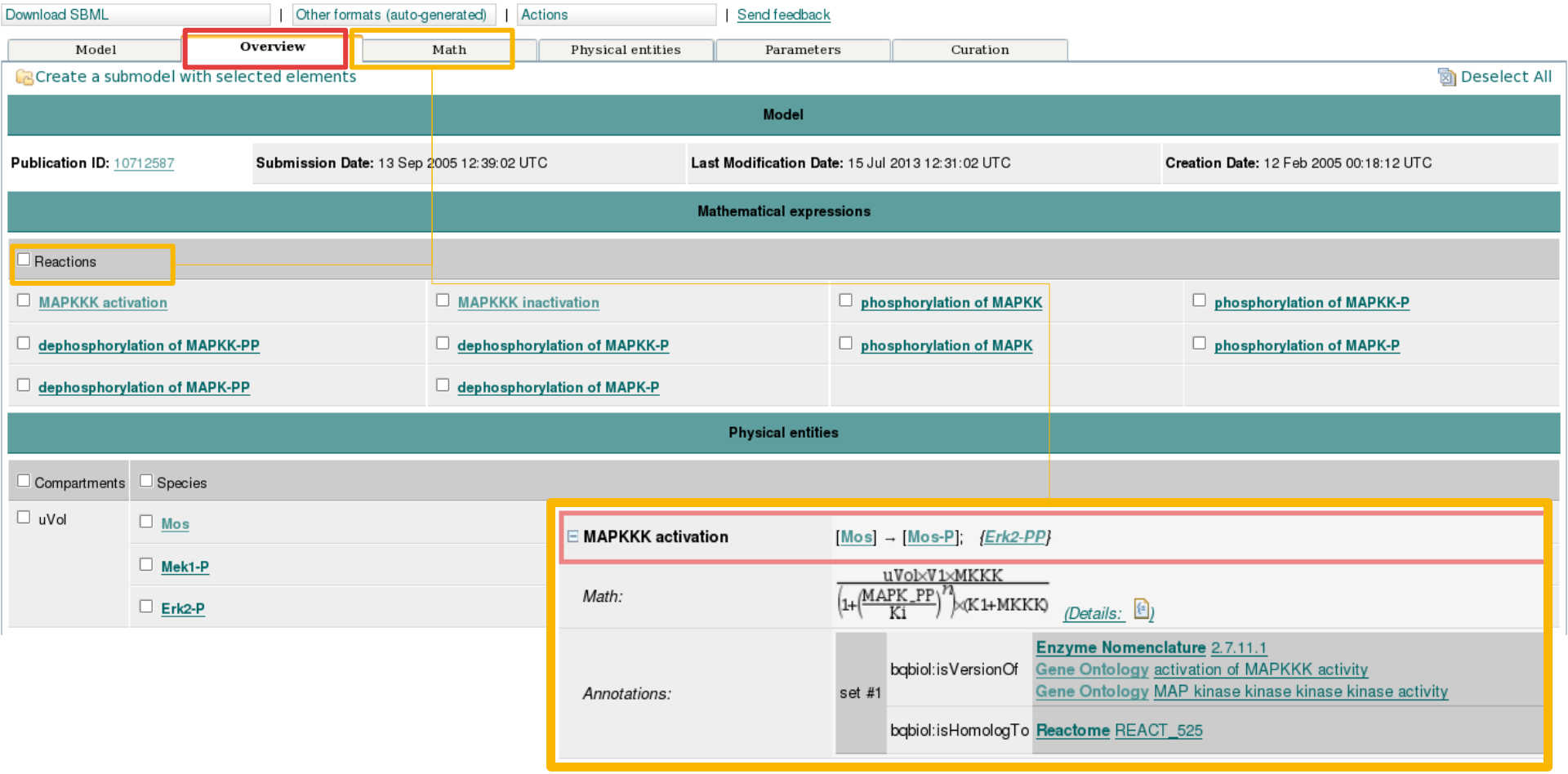
Table 1: Number of components in this model, which are described in the following sections.

Element	Quantity	Element	Quantity
compartment types	0	compartments	1
species types	0	species	8
events	0	constraints	0
reactions	10	function definitions	0
global parameters	0	unit definitions	1
rules	0	initial assignments	0

Model overview



Model maths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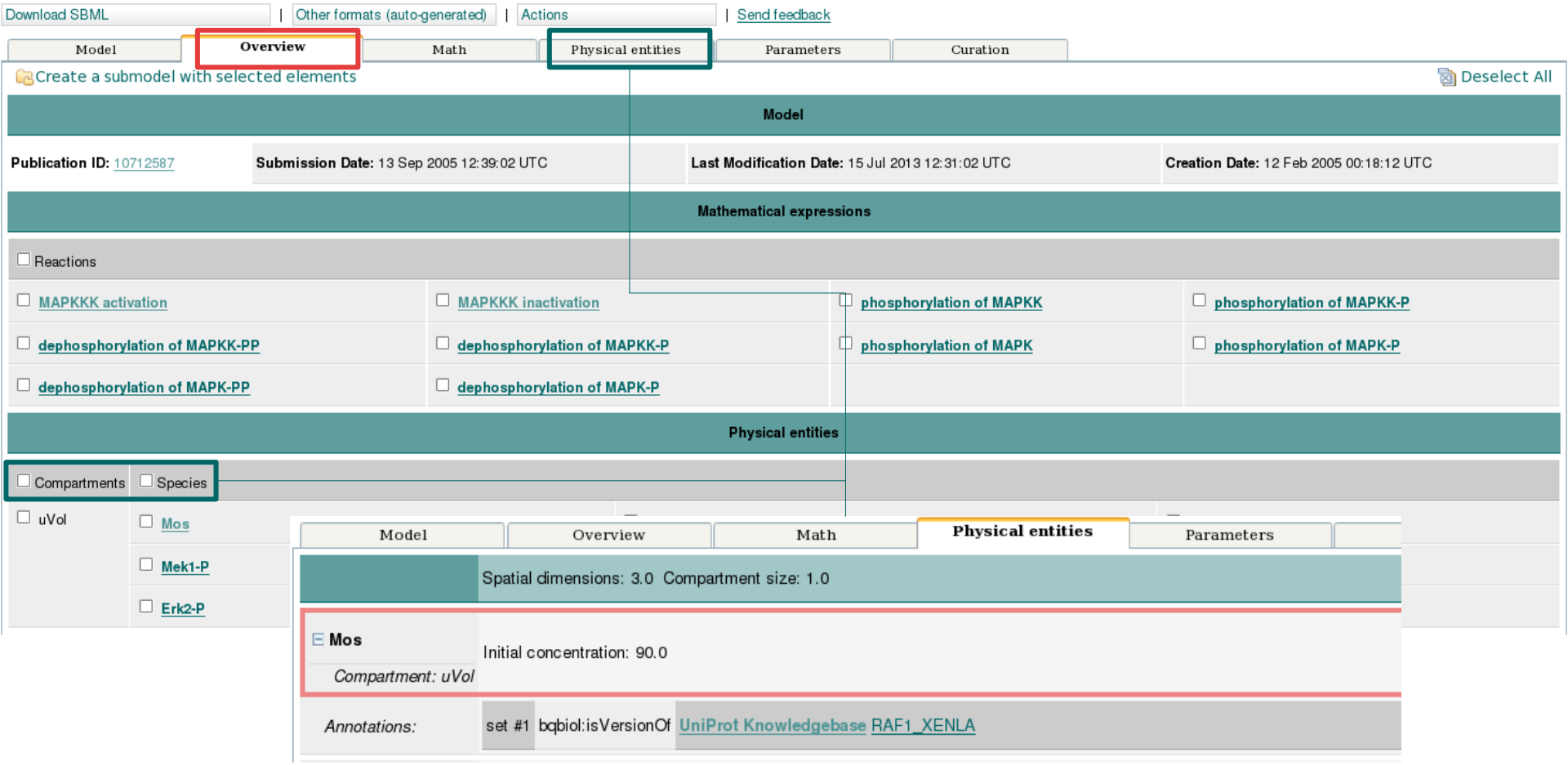
Model
Overview
Math
Physical entities
Parameters
Curation
Create a submodel with selected elements
Deselect All
Model
Publication ID: 10712587
Submission Date: 13 Sep 2005 12:39:02 UTC
Last Modification Date: 15 Jul 2013 12:31:02 UTC
Creation Date: 12 Feb 2005 00:18:12 UTC
Mathematical expressions
Reactions
MAPKKK activation
MAPKKK inactivation
phosphorylation of MAPKK
phosphorylation of MAPKK-P
dephosphorylation of MAPKK-PP
dephosphorylation of MAPKK-P
phosphorylation of MAPK
phosphorylation of MAPK-P
dephosphorylation of MAPK-PP
dephosphorylation of MAPK-P
Physical entities
Compartments
Species
uVol
Mos
Mek1-P
Erk2-P
MAPKKK activation
[Mos] → [Mos-P]; {Erk2-PP}
Math:
(Details:
Annotations:
set #1
bqbiol:isVersionOf
Enzyme Nomenclature 2.7.11.1
Gene Ontology activation of MAPKKK activity
Gene Ontology MAP kinase kinase kinase kinase activity
bqbiol:isHomologTo
Reactome REACT_525

Model variables



Curation

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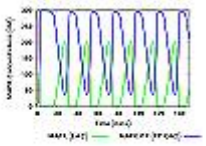
Model | Overview | Math | Physical entities | Parameters | **Curation**

Representative curation result(s)



Curator's comment: (*updated:* 15 Jul 2013 13:30:51 BST)

Figure 2A of the reference publication has been reproduced using Copasi 4.10 (Build 55). The oscillations of active MAPK (PP-Erk2) and inactive MAPK (Erk2) is shown here.

Curation

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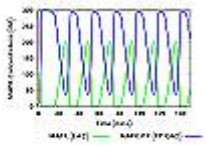

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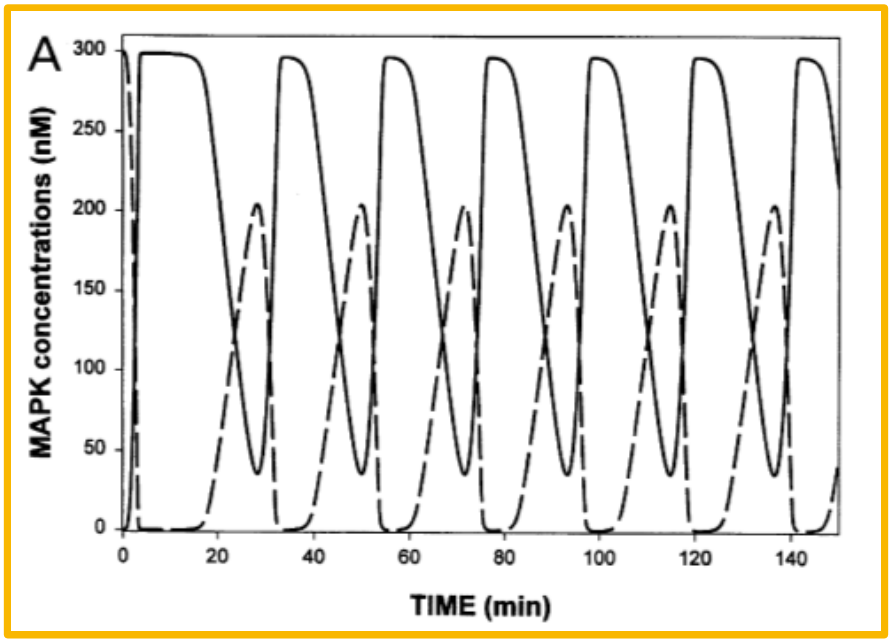

original article

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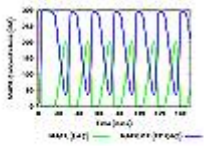

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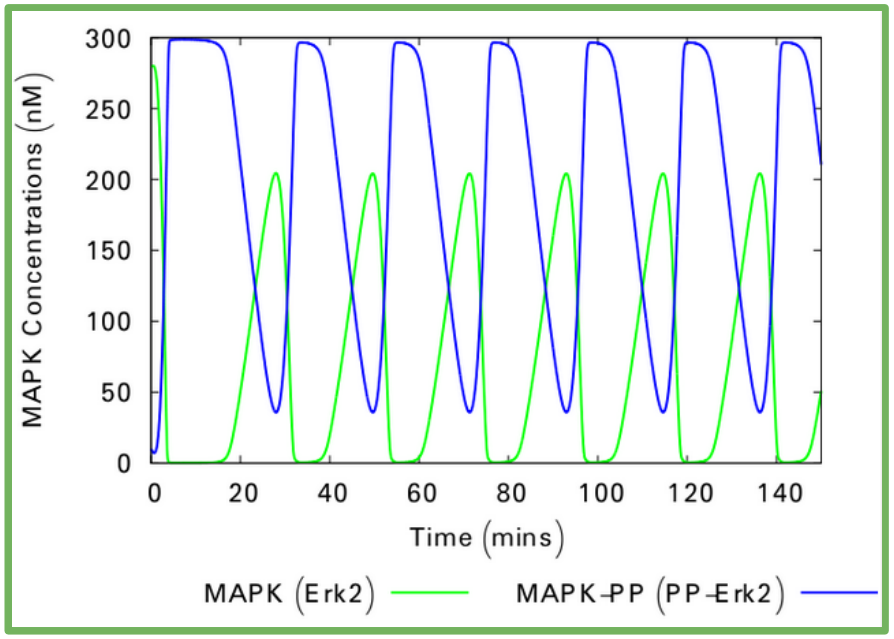
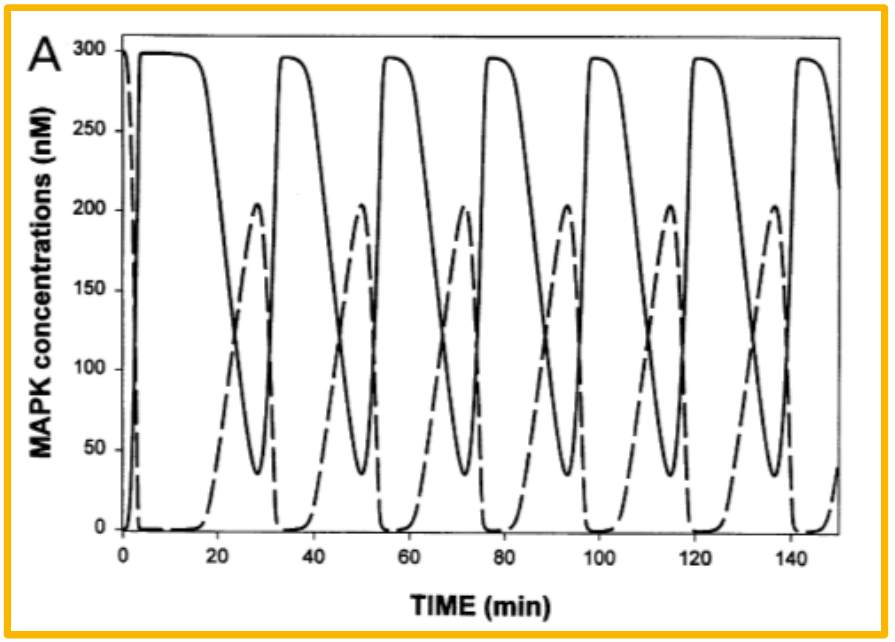
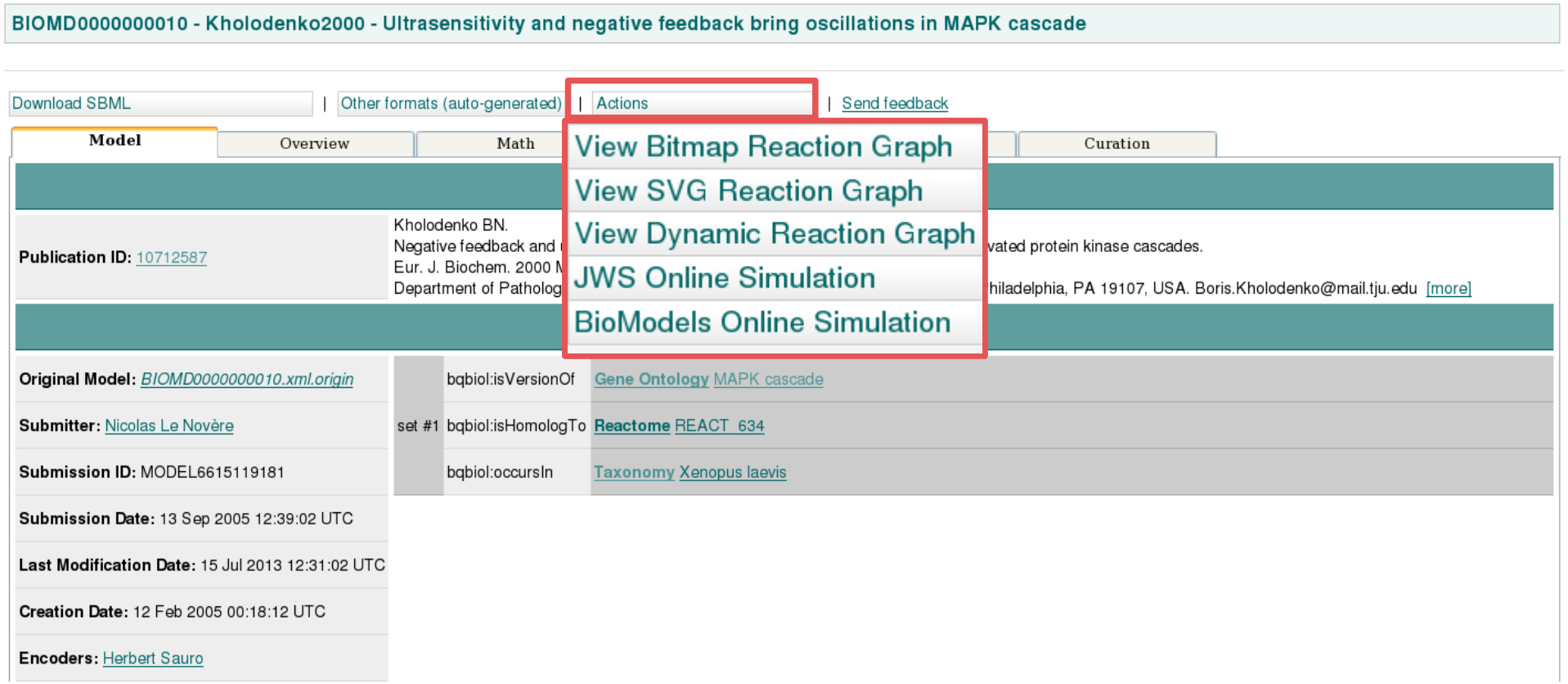


using COPASI



original article

Model simulation



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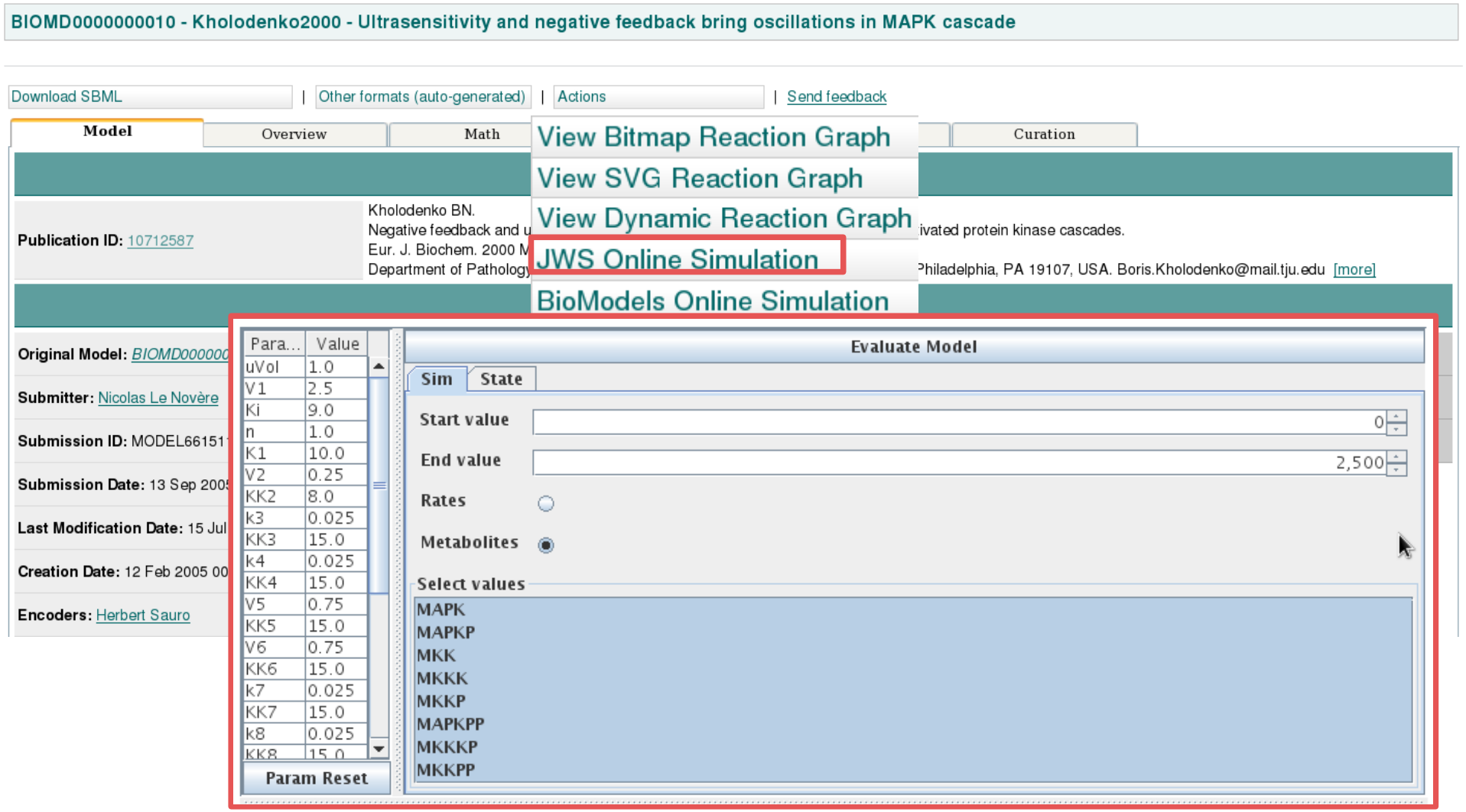

Graphical representation (SBGN)

BIOMD0000000010 - Kholodenko2000 - Ultrasensitivity and negative feedback bring oscillations in MAPK cascade

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Last Modification Date: 15 Jul 2013 12:31:02 UTC

Creation Date: 12 Feb 2005 00:18:12 UTC

Encoders: Herbert Sauro

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	bqbiol:isHomologTo	Reactome REACT	
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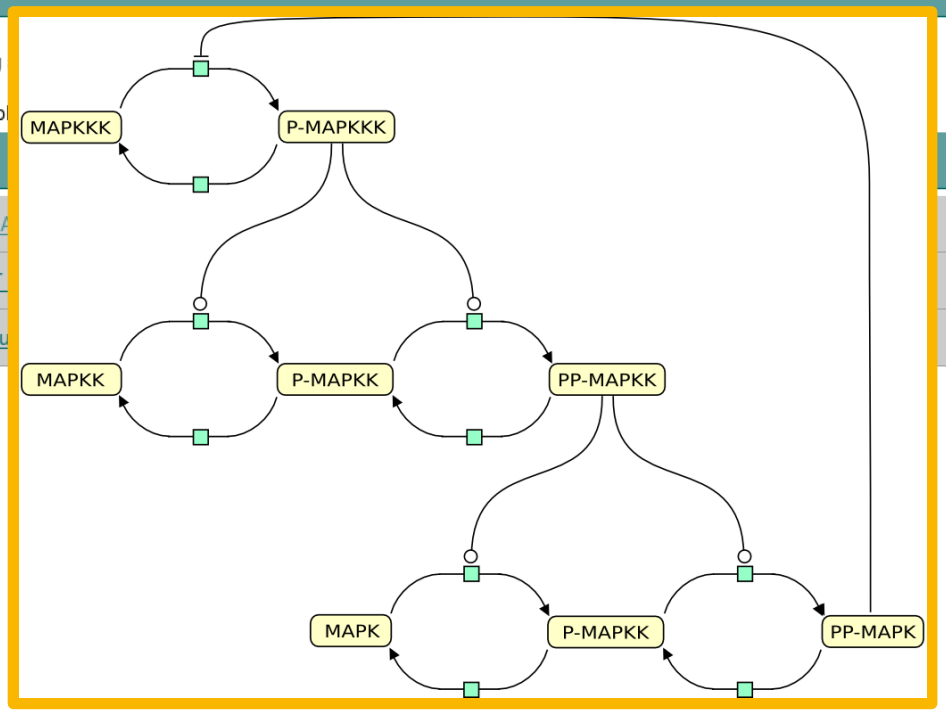
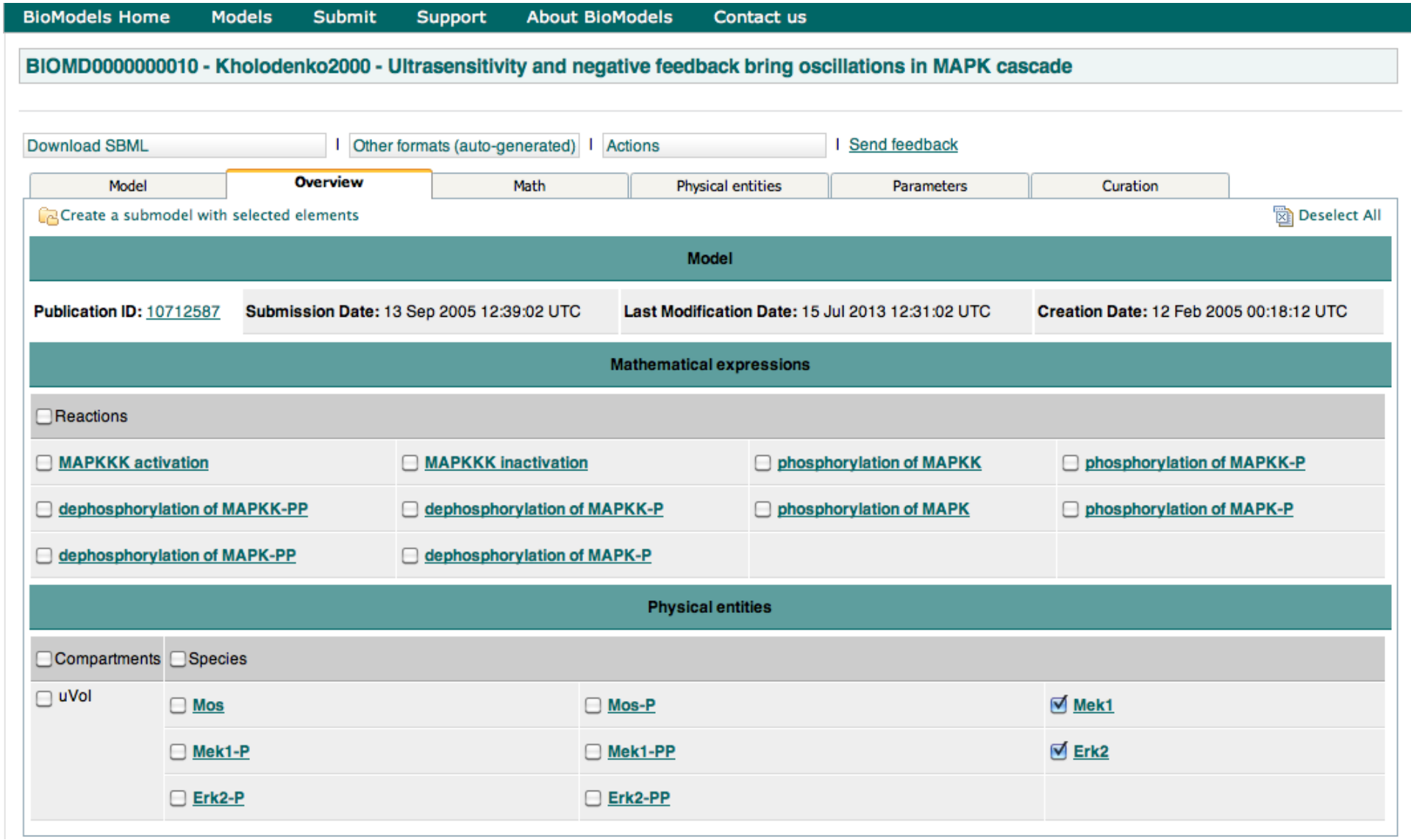


Sub-model creation



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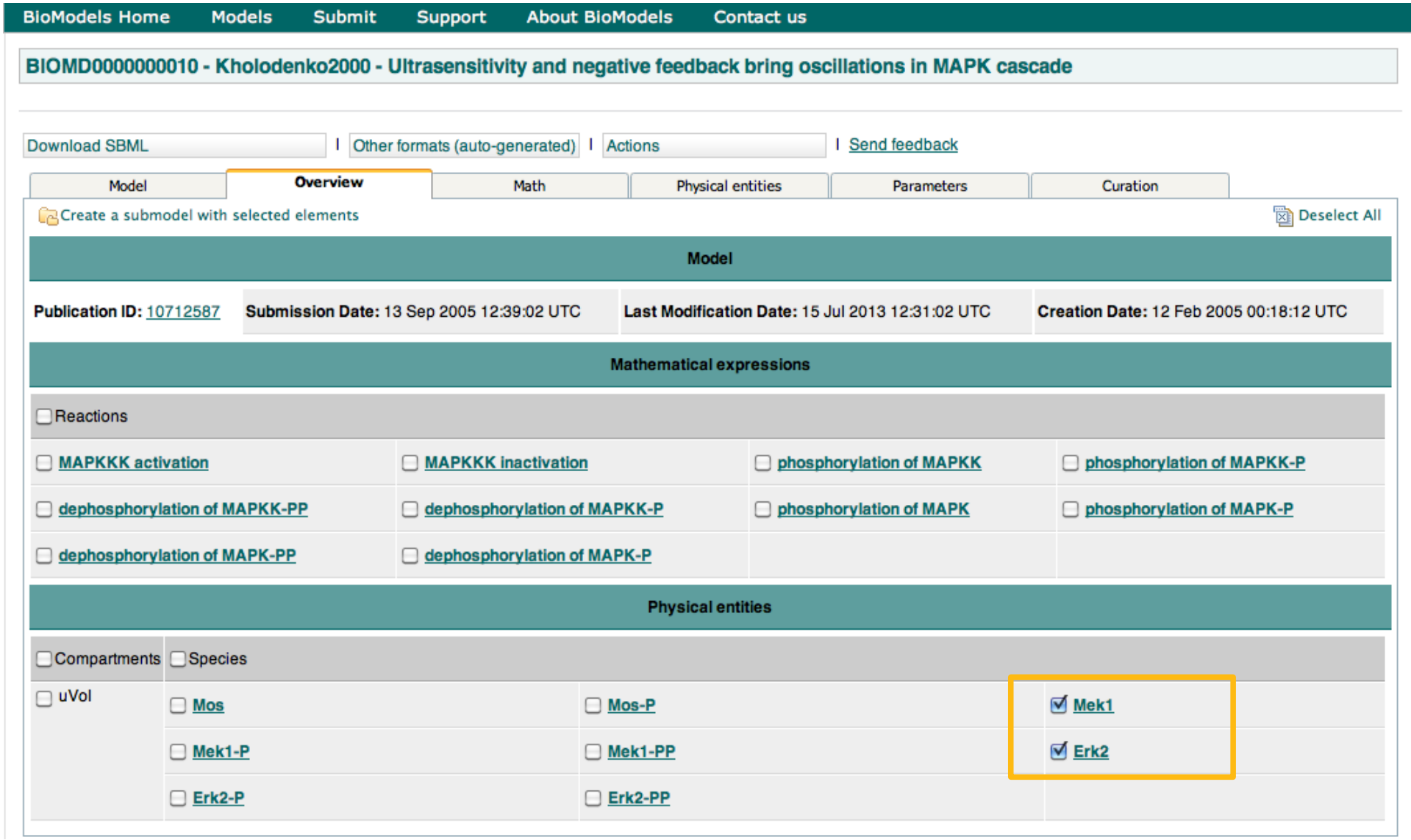
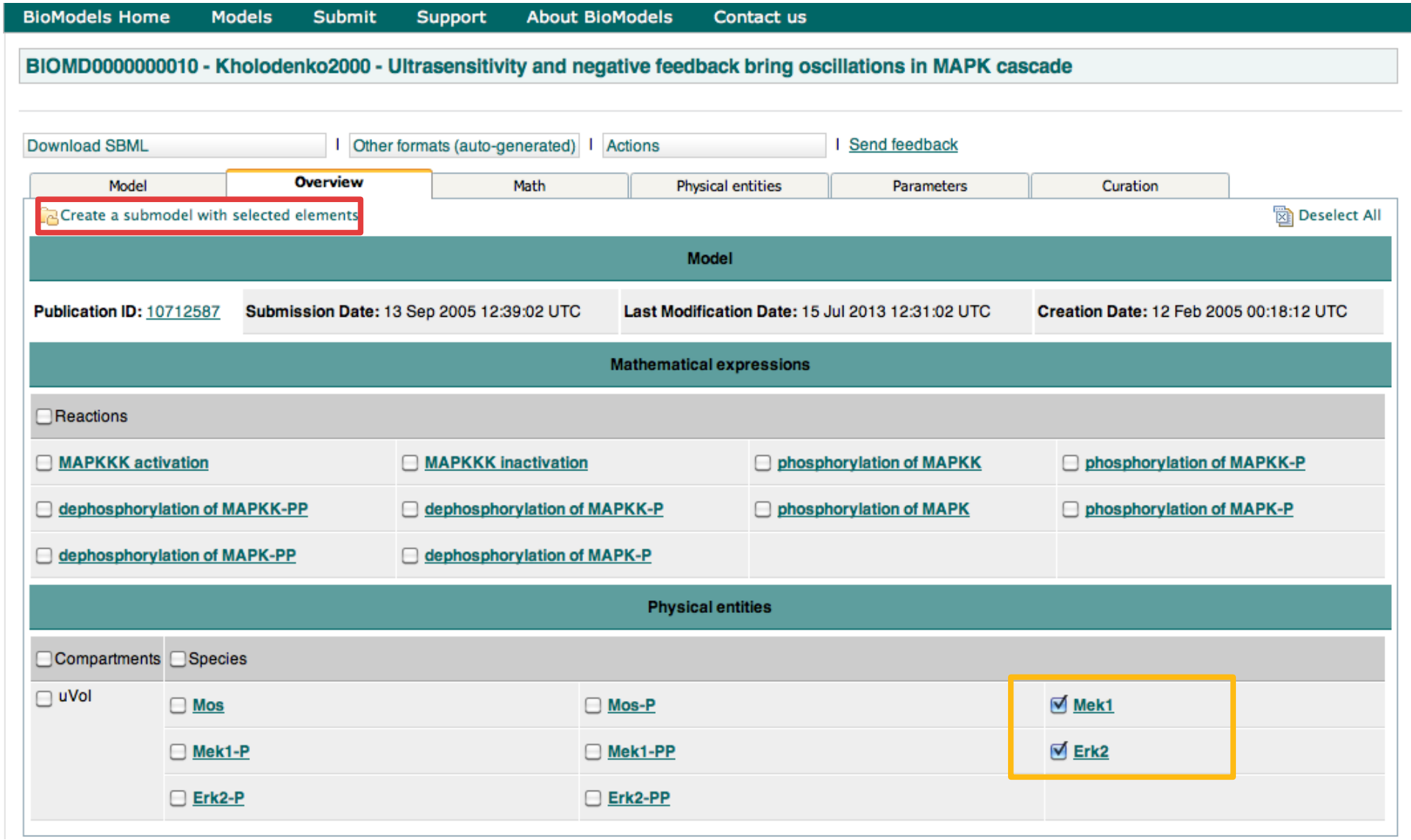


Sub-model creation



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Model | Overview | Math | Physical entities | Parameters | Curation | **Submodel1**

View the submodel in SBML

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Reactions (4)	
⊞ **phosphorylation of MAPKK**	[Mek1] → [Mek1-P]; *{Mos-P}*
⊞ **dephosphorylation of MAPKK-P**	[Mek1-P] → [Mek1];
⊞ **phosphorylation of MAPK**	[Erk2] → [Erk2-P]; *{Mek1-PP}*
⊞ **dephosphorylation of MAPK-P**	[Erk2-P] → [Erk2];

Compartments (1)	
uVol *Referred to as: uVol*	

Species (6)	
⊞ **Mos-P** *Compartment: uVol*	Initial concentration: 10.0
⊞ **Mek1** *Compartment: uVol*	Initial concentration: 280.0
⊞ **Mek1-P** *Compartment: uVol*	Initial concentration: 10.0
⊞ **Mek1-PP** *Compartment: uVol*	Initial concentration: 10.0
⊞ **Erk2** *Compartment: uVol*	Initial concentration: 280.0
⊞ **Erk2-P** *Compartment: uVol*	Initial concentration: 10.0

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Reactions (4)

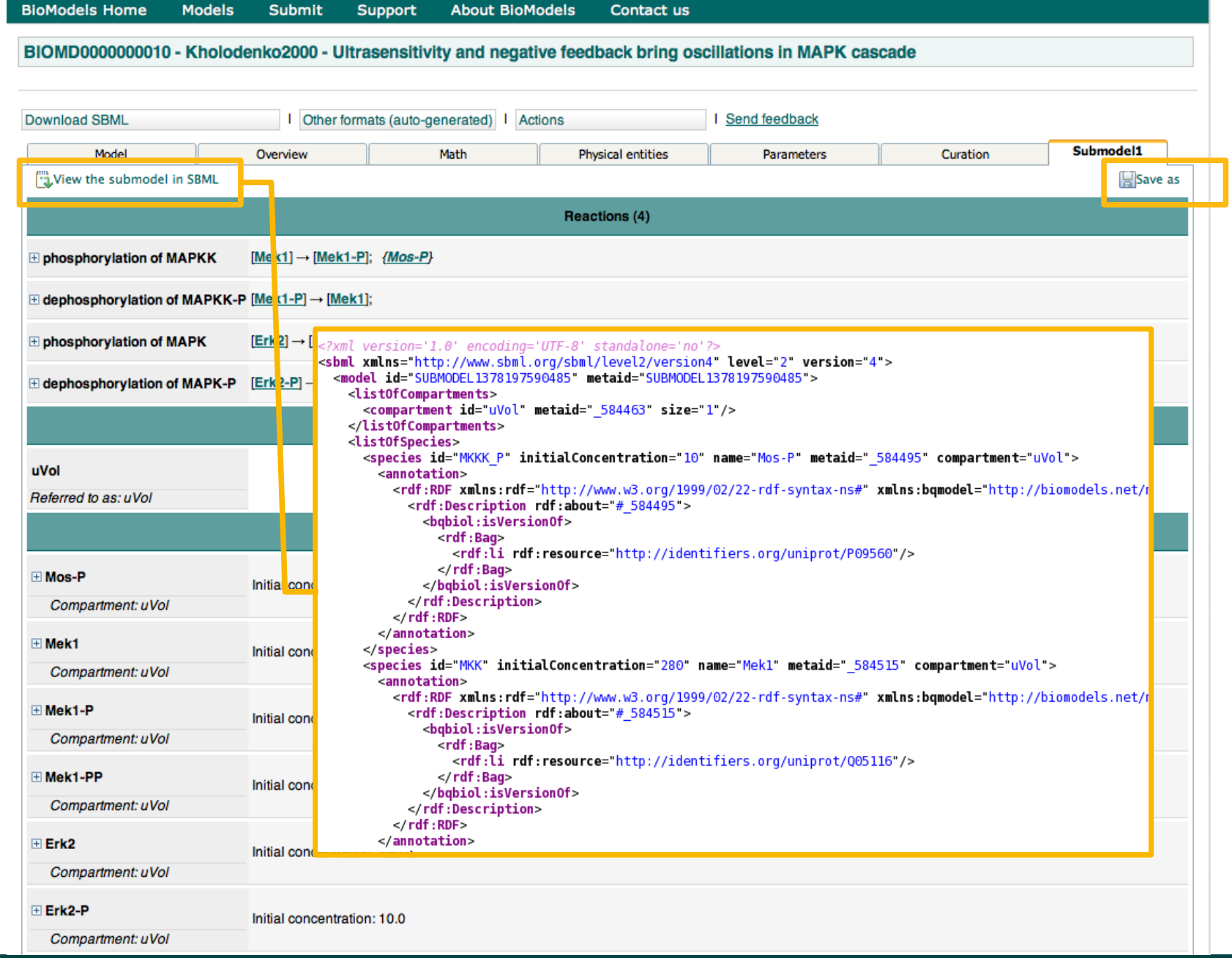
phosphorylation of MAPKK	[Mek1] → [Mek1-P]; *{Mos-P}*
dephosphorylation of MAPKK-P	[Mek1-P] → [Mek1];
phosphorylation of MAPK	[Erk2] → [Erk2-P]; *{Mek1-PP}*
dephosphorylation of MAPK-P	[Erk2-P] → [Erk2];

Compartments (1)

uVol *Referred to as: uVol*	

Species (6)

Mos-P *Compartment: uVol*	Initial concentration: 10.0
Mek1 *Compartment: uVol*	Initial concentration: 280.0
Mek1-P *Compartment: uVol*	Initial concentration: 10.0
Mek1-PP *Compartment: uVol*	Initial concentration: 10.0
Erk2 *Compartment: uVol*	Initial concentration: 280.0
Erk2-P *Compartment: uVol*	Initial concentration: 10.0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Reactions (4)
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uVol
Referred to as: uVol
Mos-P
Compartment: uVol
Mek1
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Mek1-P
Compartment: uVol
Mek1-PP
Compartment: uVol
Erk2
Compartment: uVol
Erk2-P
Initial concentration: 10.0
Compartment: uVol
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How can BioModels Database help me?

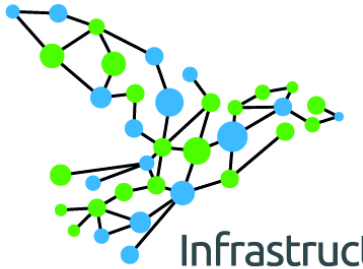
Portal to the modeling world, providing models and associated tools and resources

- provides a reference library of models
- provides building blocks to create new models
- facilitates decision making (experimentation/simulation cycle)
- benchmarking (SBMLsimulator, Virtual Cell, CellDesigner, ...)
- provides materials and tools to enable teaching:
  - model of the month

    `http://www.ebi.ac.uk/biomodels-main/modelmonth`
  - courses and tutorial

    `http://www.ebi.ac.uk/biomodels-main/courses`

Acknowledgments



Infrastructure for Systems Biology Europe

Innovative Medicines Initiative

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