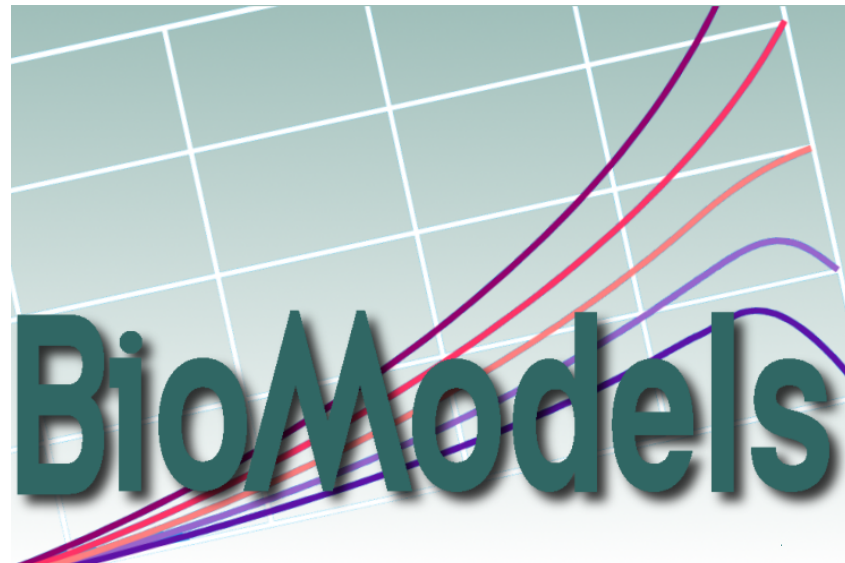


Using and contributing to BioModels

Ryan Gutenkunst

Molecular and Cellular Biology
University of Arizona

q-bio school - July 27, 2015



Reusing models

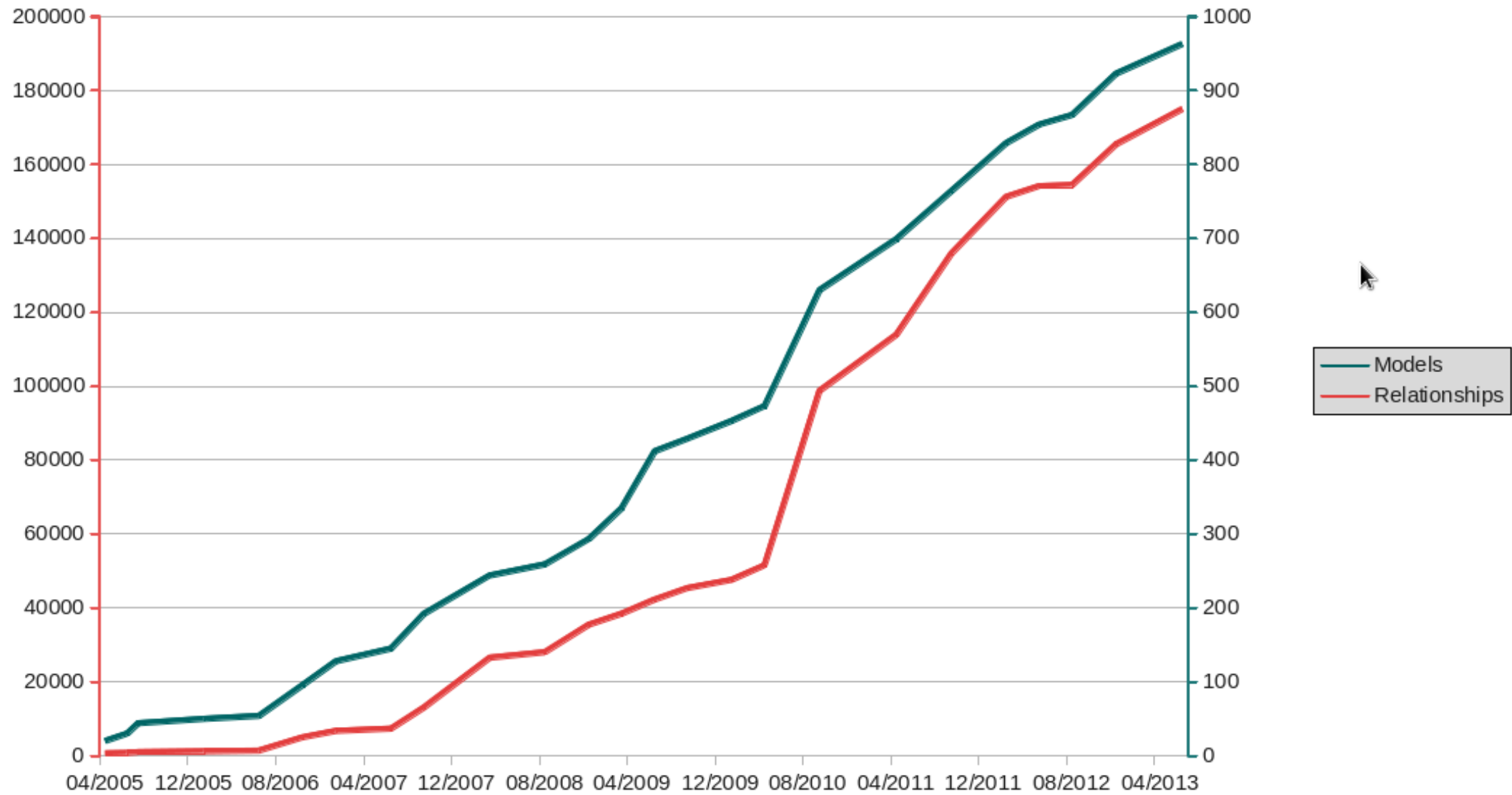
- **Availability**
- **Reliability**
- **Searchability**



Availability

- Models hosted at <http://biomodels.net>
- Stored in Systems Biology Markup Language (SBML)
 - Other formats coming soon
- Models can be added by authors prior to publication
- Internal or external curators can also submit models that they implemented from the literature
 - This means **you!**

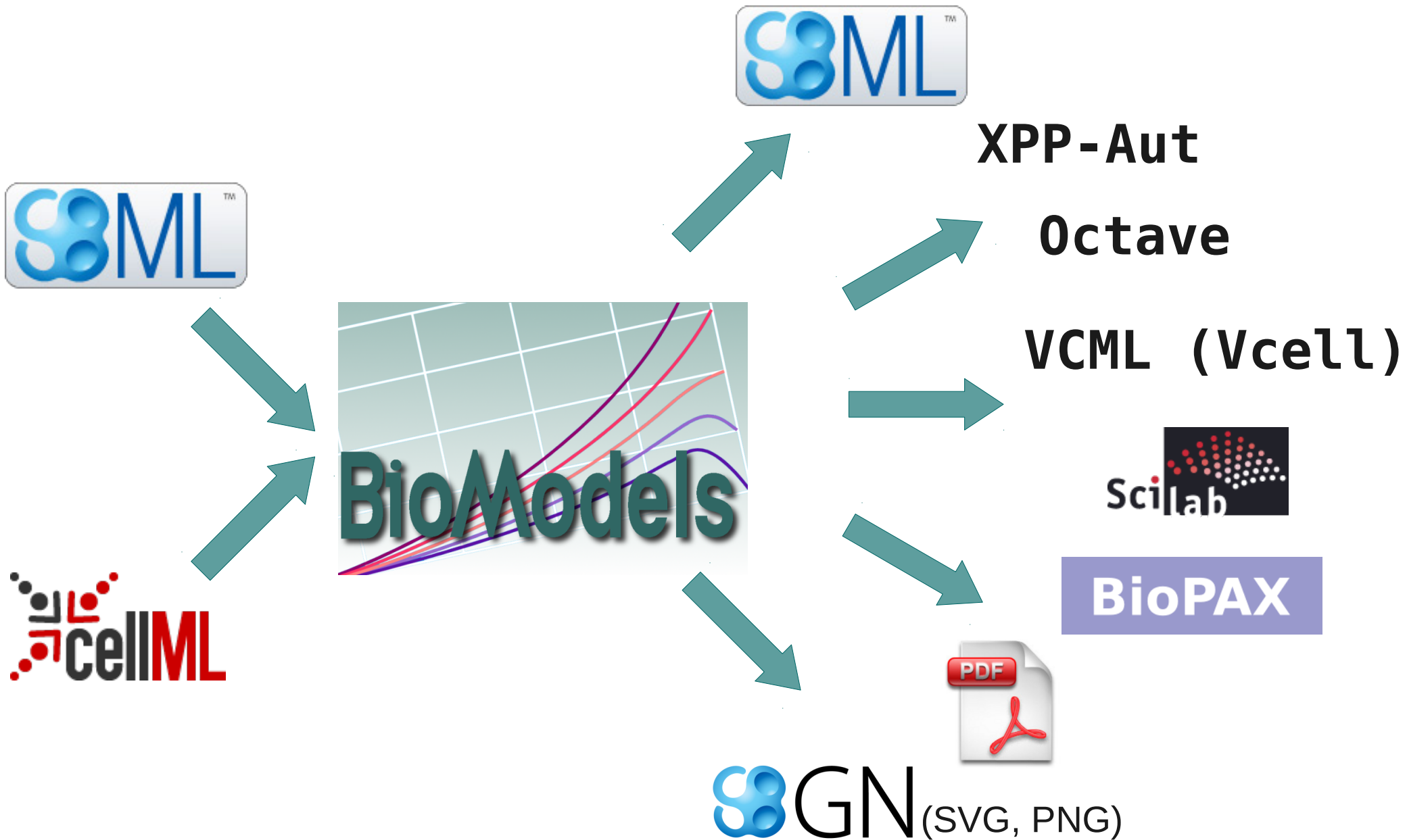
Availability



Systems Biology Markup Language

- Abstracts the biology from the mathematics, so same model can be ODE or stochastic simulation
- Entities in the model are **molecular species** that exist in **compartments**
- Species amounts change due to **reactions**
- Can also specify **events, assignment rules,** and **rate rules**
- **Parameters** can be local or global
- Representation is XML, so optimized for computer processing and extension

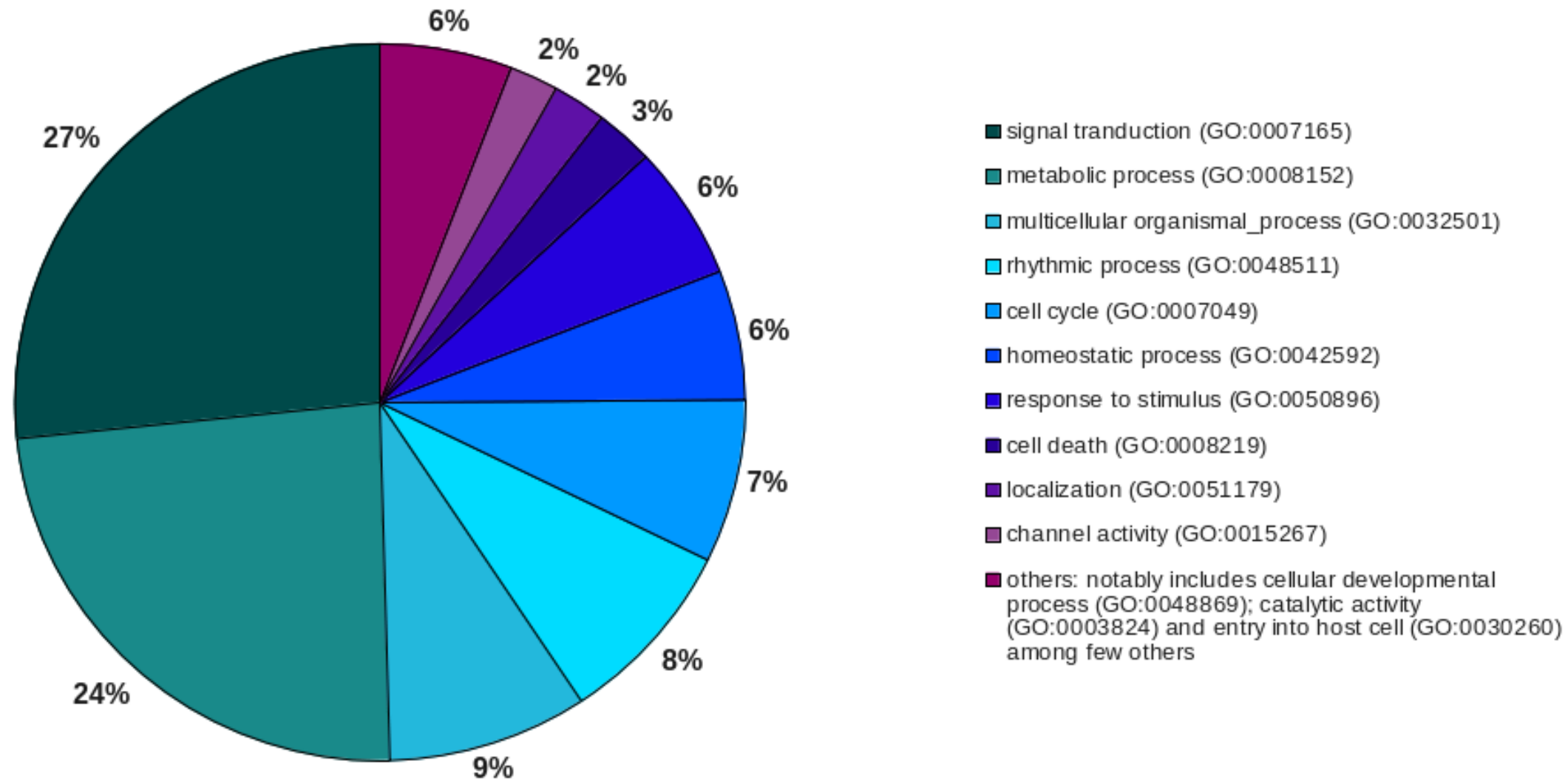
Model formats



Types of BioModels

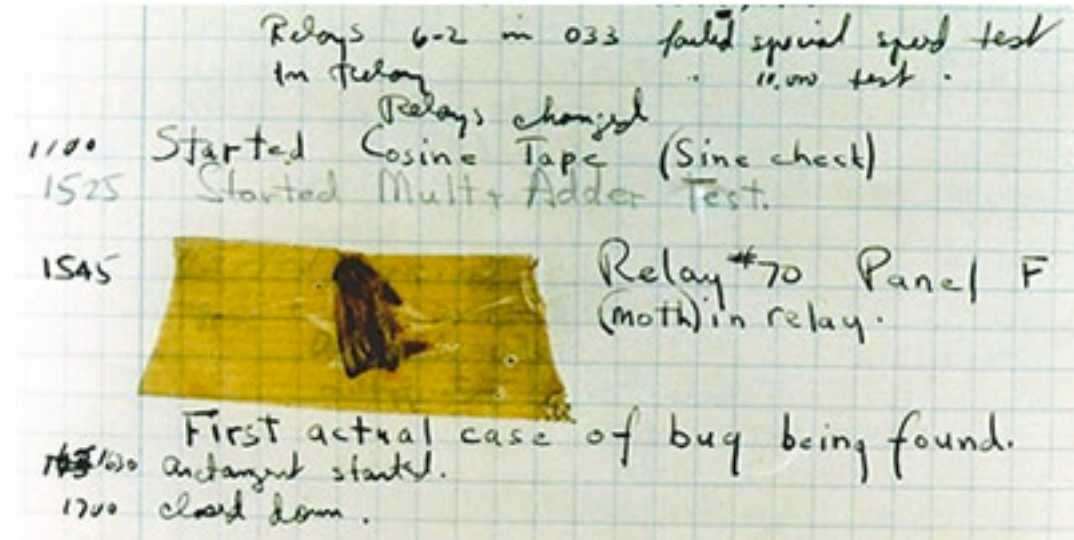
- Biochemical models
 - interactions between molecules in multiple cellular compartments
- Pharmacometrics models
 - tumor growth and treatment response
- Electrophysiology models
 - membrane voltage, current flow, concentration of various ions intra- and extracellularly, ...
- Disease models
 - neurodegenerative,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

Types of BioModels

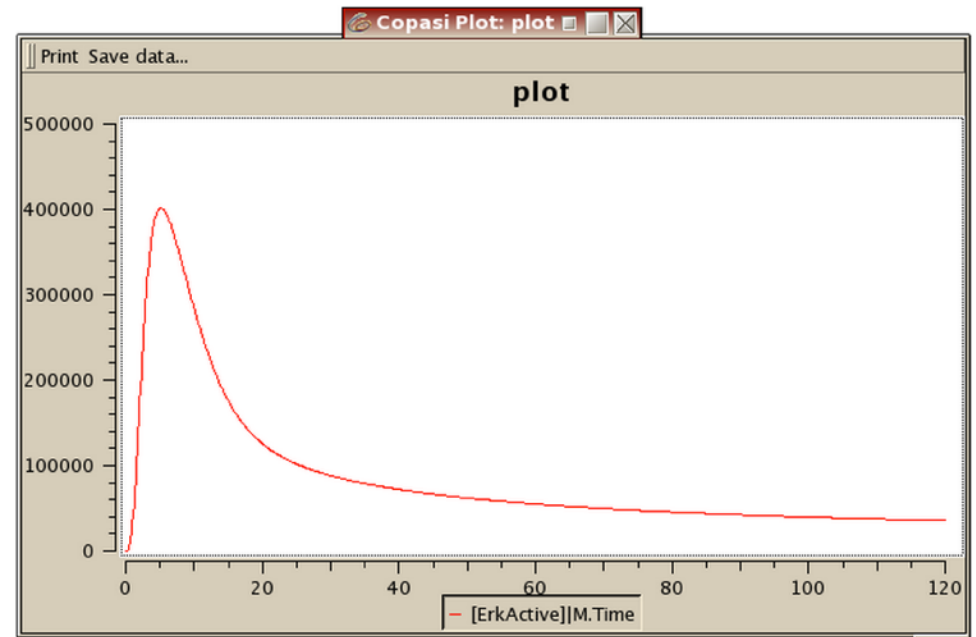


Reliability

- Nontrivial!
Equations in papers very often have typos or are incomplete.



- Curators ensure that the encoded model can reproduce at least one figure from the paper.



Searchability

- Models in BioModels are extensively annotated with links to other standard biological databases to unambiguously identify them
- Examples:
 - Biological processes: Gene Ontology (GO)
 - Proteins: UniProt
 - Small molecules: ChEBI
 - Pathways and reactions: KEGG, Reactome, etc.

Nomenclature is a problem

Kim et al. (2007) *Oncogene*

$$dX1/dt = -V1 + V2$$

$$V1 = k_1 * X1 * W$$

$$dX2/dt = V1 - V2$$

$$V2 = k_2 * X2$$

$$dX3/dt = V4 - V5 - V8 + V10$$

$$V3 = k_3 * X2 * X4$$

$$dX4/dt = -V3 - V4 + V5 + V6$$

$$V4 = k_4 * X4$$

$$dX5/dt = V3 - V6 - V32 + V33$$

$$V5 = k_5 * X3$$

$$dX6/dt = V3 - V6 + V7$$

$$V6 = k_{+6} * X5 * X6 - k_{-6} * X4$$

$$dX7/dt = -V7 - V17$$

$$V7 = k_{+7} * X7 * X12 - k_{-7} * X6$$

$$dX8/dt = V8 - V9$$

$$V8 = k_{+8} * X3 * X11 - k_{-8} * X8$$

$$dX9/dt = V9 - V10$$

$$V9 = k_9 * X8$$

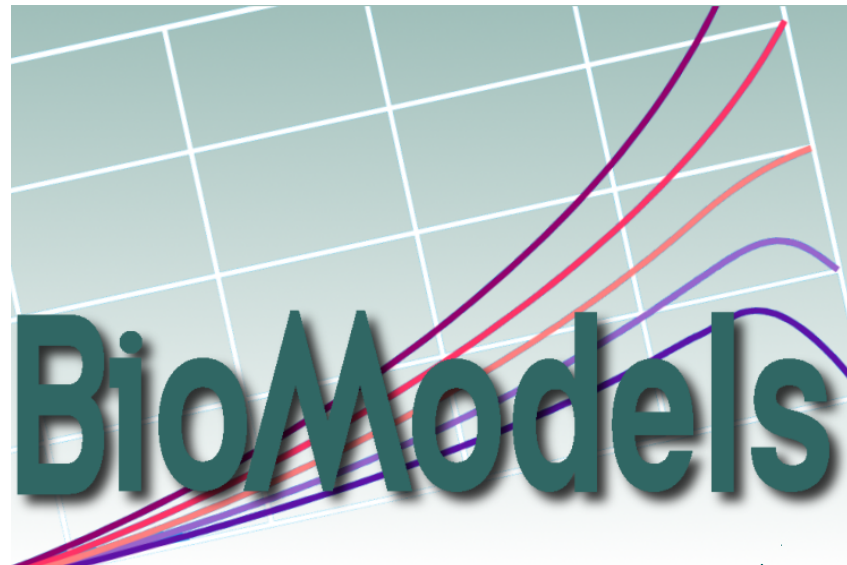
$$dX10/dt = V10 - V11$$

$$V10 = k_{10} * X9$$

Can you tell what XI is?

Uses of BioModels

- Benchmarking modeling and simulation tools
- Building blocks to generate more elaborate models
- Automated clustering and merging of models using annotations



Let's explore!

EMBL-EBI 



BioModels Database

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BIOMD0000000149 - Kim2007 - Crosstalk between Wnt and ERK pathways

[Download SBML](#) | [Other formats \(auto-generated\)](#) | [Actions](#) | [Send feedback](#)

Model

[Overview](#)

[Math](#)

[Physical entities](#)

[Parameters](#)

[Curation](#)

Reference Publication

Publication ID: [17237813](#)

Kim D, Rath O, Kolch W, Cho KH.
A hidden oncogenic positive feedback loop caused by crosstalk between Wnt and ERK pathways.
Oncogene 2007 Jul; 26(31): 4571-4579
College of Medicine, Seoul National University, Jongno-gu, Seoul, Korea. [\[more\]](#)

Model

Original Model: [BIOMD0000000149.origin](#)

set #1 bqmodel:isDerivedFrom [PubMed 14551908](#)
[DOI 10.1007/3-540-36481-1_11](#)

Submitter: [Harish Dharuri](#)

set #2 bqbiol:hasPart [Gene Ontology canonical Wnt signaling pathway](#)
[Gene Ontology MAPK cascade](#)

Submission ID: MODEL4159212701

set #3 bqbiol:hasVersion [Human Disease Ontology colorectal cancer](#)

Submission Date: 07 Sep 2007 07:16:04 UTC

bqbiol:hasTaxon [Taxonomy Homo sapiens](#)

Last Modification Date: 22 Oct 2014 12:15:45 UTC

set #4 bqbiol:hasPart [KEGG Pathway MAPK signaling pathway - Homo sapiens \(human\)](#)
[KEGG Pathway Wnt signaling pathway - Homo sapiens \(human\)](#)

Creation Date: 10 Jul 2007 13:55:45 UTC

set #5 bqbiol:occursIn [Brenda Tissue Ontology HEK-293 cell](#)