EMBL-EBI

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BioModels Database curation and annotation

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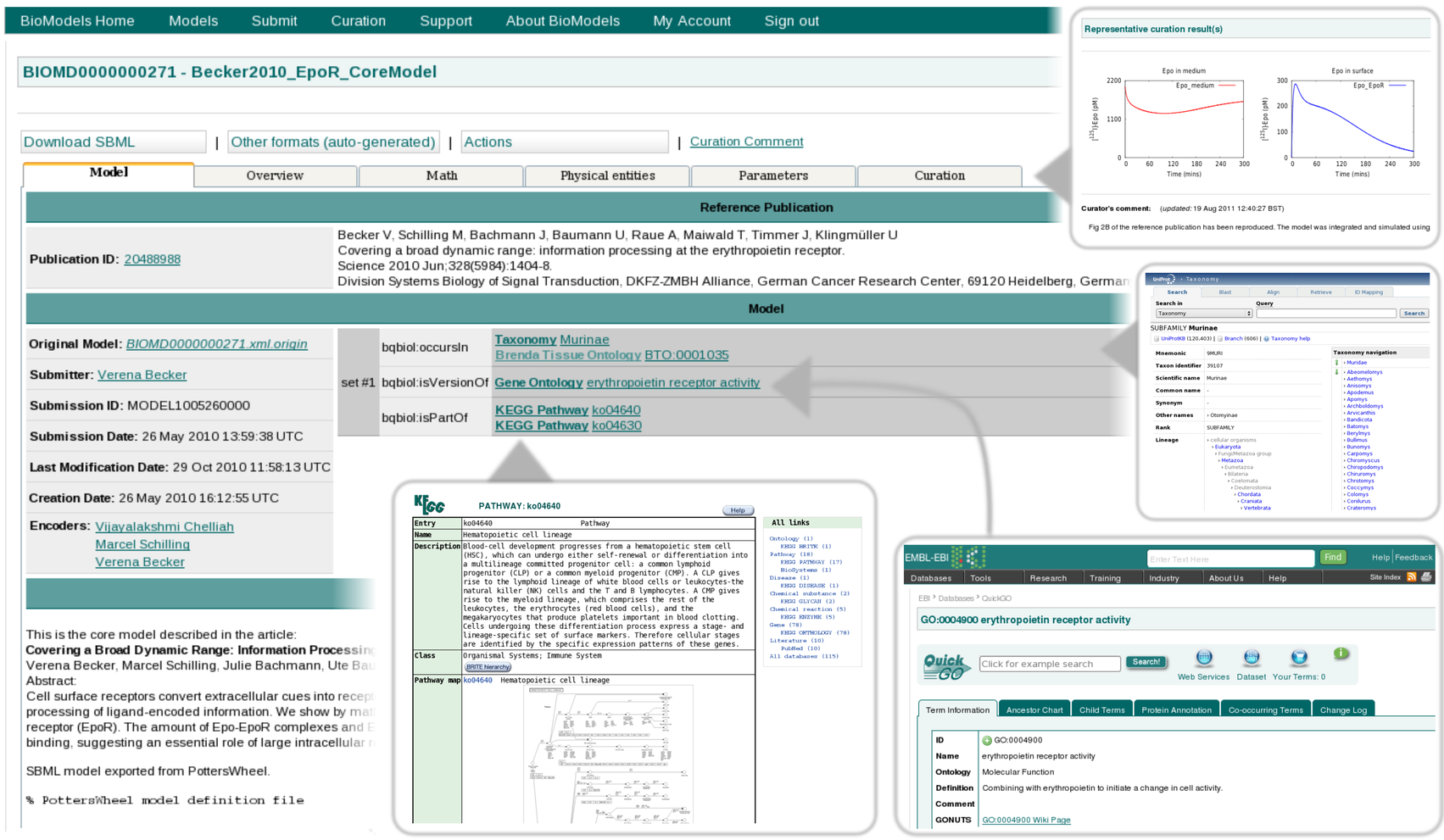
Introduction

The BioModels Database [1] is a freely accessible online resource (www.ebi.ac.uk/biomodels/) for storing, viewing, retrieving and analysing published, peer-reviewed quantitative models of biological processes.

It uses the Systems Biology Markup Language (SBML) [2] for model storage and internal representation, but allows submission and download of models in various other commonly used formats. Once submitted, the structure and dynamics of a model are checked thoroughly; in addition, the model elements are annotated with controlled vocabularies as well as linked to relevant data resources before publication in the BioModels Database. The models are distributed in two branches: the curated and the non-curated branch.

The MIRIAM guidelines [3] regarding the curation and annotation of quantitative kinetic models ascertain that proper metadata is added to a model. Annotations are based on information stored in the MIRIAM Registry (http://identifiers.org/registry), including ontologies such as the Systems Biology Ontology (SBO) [4].



Curation

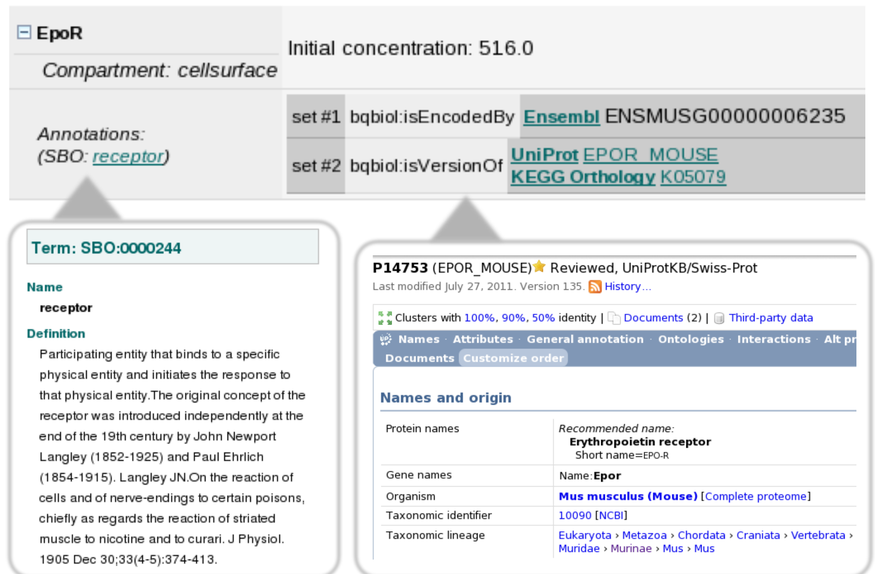
All models in the curated branch have to fulfill the MIRIAM requirements, such as being encoded in machine readable format and having been published in a peer-reviewed journal. Upon simulation, models need to reproduce the results of the referenced publication. If this is not the case, the curators contact the submitter, creators, and authors to find and correct potential errors. The simulation results and any deviations from the published version are recorded in the model's notes.

Non-kinetic models (e.g. for Flux Balance Analysis) or those in certain modeling frameworks (e.g. boolean logic or petri nets) are only considered for the non-curated branch up to now.

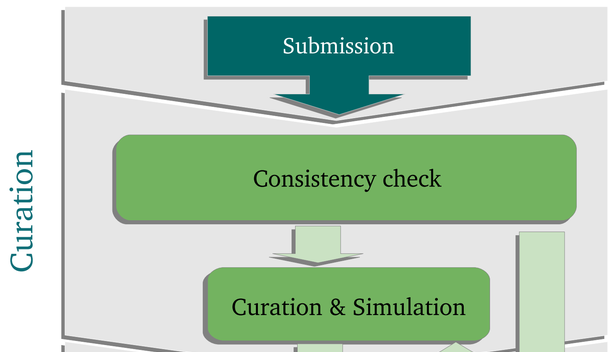
Annotation

For the model itself, as well as its containing entities, annotations and cross-references are added by means of MIRIAM URIs. They are encoded in the Resource Description Framework (RDF) and thus stored as a triplet consisting of a resource (e.g. UniProt), a resource identifier (e.g. P14753 - EpoR in the above model), and a BioModels.net qualifier that determines the relationship between the model entity and corresponding resource entry. Examples of such qualifiers are isVersionOf or hasPart.

SBO terms, used to describe the type of entity, roles in a reaction, rate laws, etc., are directly inserted in the corresponding sboTerm attribute (SBML L2V2 and above) of the annotated model element.

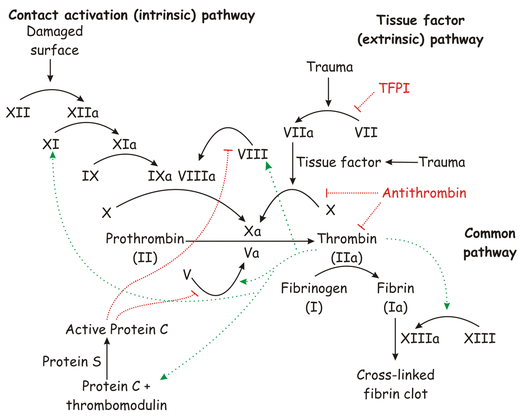


Processing pipeline



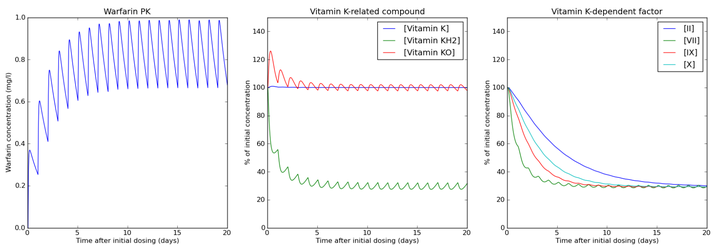
Curation projects focussing on particular biological topics

Blood Coagulation and factor deficiencies



Blood coagulation can be initiated by a so-called contact activator (e.g. trauma; this concerns the intrinsic coagulation pathway) or when tissue factor is exposed to the vasculature by non-endothelial cells (extrinsic pathway). Image: Wikipedia.

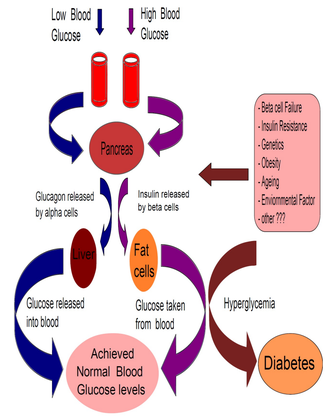
Example models BIOMD0000000338-340: Wajima T, Ibister G K, and Duffull S B. (2009). A Comprehensive Model for the Humoral Coagulation Network in Humans. Clinical Pharmacology and Therapeutics 86(3):290-298.



The authors use pharmacokinetic and -dynamic modelling of the effect of Warfarin (and other substances) on the plasma concentrations of Vitamin-K related compounds and factors. The model could be extended to any drug that acts on a coagulation factor. At all points of the virtual therapeutic administration, the outcome of clinical coagulation tests for extrinsic and intrinsic pathways are predicted.

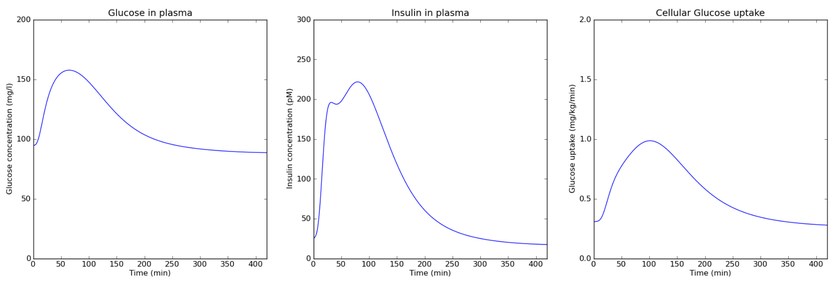
Diabetes and Glucose homeostasis

Glucose homeostasis is critically regulated by antagonistic action of insulin and glucagon. Disturbance in the relationship between blood glucose and insulin result in metabolic disorders such as Diabetes, characterized by chronic hyperglycemia. However, under hypoglycemic condition, in contrast to insulin, glucagon elevates and maintains the blood glucose level to normal (cf. schema on the right).



Example model BIOMD0000000356: Nyman E et al. (2011). A hierarchical whole body modeling approach elucidates the link between in vitro insulin signalling and in vivo glucose homeostasis. Journal of Biological Chemistry 286:26028-41

Using a hierarchical modelling approach, the authors have developed a whole body model of glucose homeostasis, which links the intracellular insulin-insulin receptor binding mechanism and glucose transport in adipocytes to macroscopic glucose dynamics.



References

[1] Le Novère N et al. (2010). BioModels Database: An enhanced, curated and annotated resource for published quantitative kinetic models. BMC Systems Biology 4:92
[2] Hucka M et al. (2003). The systems biology markup language (SBML): a medium for representation and exchange of biochemical network models. Bioinformatics 19:524-31
[3] Laibe C and Le Novère N (2007). MIRIAM Resources: tools to generate and resolve robust cross-references in Systems Biology. BMC Systems Biology 1:58
[4] Le Novère N et al. (2006). Adding semantics in kinetic models of biochemical pathways. Proc. of the 2nd Int. ESCEC Symp. 137-53

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