

Semantic annotation of kinetic models in Systems Biology

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With the rise of Systems Biology as one of the most active fields in life sciences, computational models of biological processes have become meeting points between theoreticians and experimentalists. The construction of large quantitative models will only be achieved if we solve the problems of integration (of models belonging to the same level), encapsulation (of models belonging to lower levels) and communication (between models and other types of quantitative data) [1]. If we want the interfaces to be generic enough to allow for anybody to leverage on existing research and toolkits, a fundamental requirement is the existence of community-developed standards of annotation and ontologies. A first step is to encode them using standard formats such as SBML [2]. However, syntactic correctness is not sufficient to ensure unambiguous interpretation of model structure and results. Moreover, the description of a model, whether its structure, or the mathematics, is different from describing its behaviour, as resulting from its instantiation in computer simulations.

We developed two ontologies in order to enrich the information provided with the models, but also to help integrations of models, and integration of models with other types of knowledge. The Systems Biology Ontology (SBO) [3] is a set of controlled vocabularies that add a semantic layer to the biochemical and mathematical descriptions of a model, and act as a glue between different levels and types of representation. The current branches classify the functional and physical types of components (e.g. "competitive inhibitor", but also "macromolecule"), quantitative parameters (e.g. "Michaelis constant"), modelling framework (e.g. "continuous framework"), mathematical expressions (e.g. "reversible mass action kinetics") and types of events (e.g. "binding"). Annotation with SBO terms is an official part of the SBML specification since Level 2 Version 2. However, SBO is not tied to SBML, and is part of the Open Biomedical Ontology. SBO is available under OBO, XML and OWL formats (<http://www.ebi.ac.uk/sbo/>).

While SBO annotation defines the semantic of a model structure, it does not permit to describe dynamical behaviours, either experimental -used to generate the model - or computational, resulting from a derived simulation. The Terminology for the Description of Dynamics (TEDDY) is a nascent effort to classify the behaviours of variables (e.g. "oscillation", "bistable behaviour"), the characteristics of those behaviours (e.g. "period", "bifurcation") and the functionalities of modules (e.g. "negative feedback", "integrator"). Note that the use of TEDDY vocabularies largely outreach Computational Systems Biology. While the relationships used by SBO are limited to subclassing, TEDDY possess a richer set of relationships, that is expected to grow. TEDDY is available under the OWL format (<http://http://www.ebi.ac.uk/compneur-srv/teddy/>)

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