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Beyond Structure: KiSAO and TEDDY – Two Ontologies Addressing Pragmatical and Dynamical Aspects of Computational Models in Systems Biology

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Introduction

Computational models are becoming more and more the central scientific paradigm for understanding the complexity of living systems. With the increasing number and size of these models there is a growing need for model reuse and exchange. Furthermore, detailed models are not manageable without computer support. There are efforts to formalise the mathematical structure of models (e.g. SBML) and to standardise the kinetic and biological meaning of model components (e.g. SBO, GO, UniProt). However, formalising only the structure of computational models is not sufficient to easily exchange and reuse models and to achieve full computer support for modelling. We also need to formalise the pragmatical and dynamical aspects of models. For this purpose we propose two ontologies: The Kinetic Simulation Algorithm Ontology (KiSAO) and the TErminology for the Description of DYnamics (TEDDY).

KiSAO

KiSAO classifies simulation algorithms applicable to biological models using different categories and a hierarchy of algorithm versions. Each term contains information about synonyms, a definition and a publication reference.

Classification

Simulation algorithms are classified wrt. the following dimensions:

- algorithm using deterministic/stochastic rules, e. g. *Euler forward* vs. *Smoluchowski equation based method*
- Spatial/non-spatial approaches, e. g. *Green's function reaction dynamics* vs. *Euler forward*
- discrete/continuous variables, e. g. *Cellular automata* vs. *Livermore solver*
- fixed/adaptive time-step approaches, e. g. *Cellular automata* vs. *Green's function reaction dynamics*

Algorithm Hierarchy

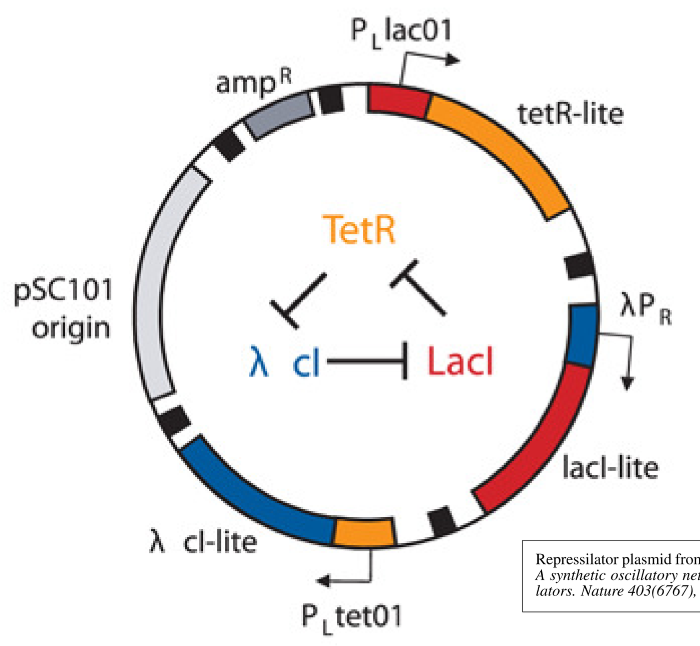
The algorithms are arranged in a subclass hierarchy, e.g.

algorithm using stochastic rules (`KiSAO:0000036`)
  ↖ `is-a`
Gillespie-like stochastic simulation method (`KiSAO:0000025`)
  ↖ `is-a`
sub-volume stochastic reaction-diffusion algorithm (`KiSAO:0000095`)

Example Model

For demonstration of KiSAO and TeDDY annotations, we use the well-known example of the "Repressilator" as published by Elowitz and Laiber (2000). The mathematical model describes a negative-feedback loop consisting of three repressor genes and their promoters. The model does not describe a natural system but in contrast is an artificial oscillating network. It is used to show how the ability of the system to oscillate depends on critical parameters. Furthermore, the influence of stochastic effects of the system behaviour is investigated. The model is build up of three different mRNA concentrations and the corresponding protein concentrations. The species are involved in transcription, translation and degradation processes.

The repressilator model can be found in BioModels Database (`BIOMD0000000012`). We use `COPASI` for the simulations shown on this poster.



Repressilator plasmid from *M.B. Elowitz and S. Leibler: A synthetic oscillatory network of transcriptional regulators. Nature 403(6767), Jan. 2000, pp. 335–338.*

TEDDY

The aim of TEDDY is to provide terms for describing and characterising dynamical behaviours, observable dynamical phenomena, and control elements of biological models and biological systems in Systems Biology and Synthetic Biology. TEDDY has the following main categories:

Temporal Behaviour

terms for the actual (temporal) dynamical behaviour of models, e.g. *Damped Oscillation*, *Stable Fixed Point*

Behaviour Characteristic

terms for characterising concrete behaviours (e.g. *Period*) and for discriminating between types of behaviours (e.g. *Stable* vs. *Unstable*)

Behaviour Diversification

terms for the ability of systems to exhibit different behaviours dependent on parameters (e.g. *Supercritical Hopf Bifurcation*) and with respect to perturbations (e.g. *Bi-Stability*)

Functional Motifs

terms for structural features of systems necessary for specific behaviours (e.g. *Negative Feedback*) and intended for specific functions (e.g. *Integrator*)

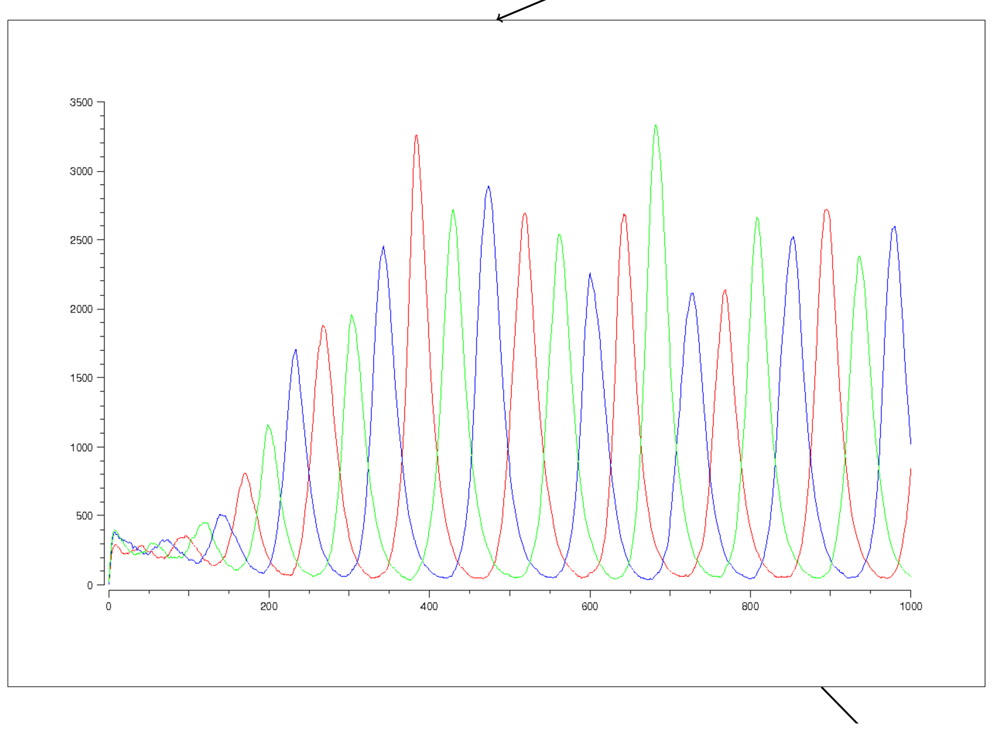
`KiSAO:0000027`
Gibson and Bruck's next reaction method
stochastic algorithm

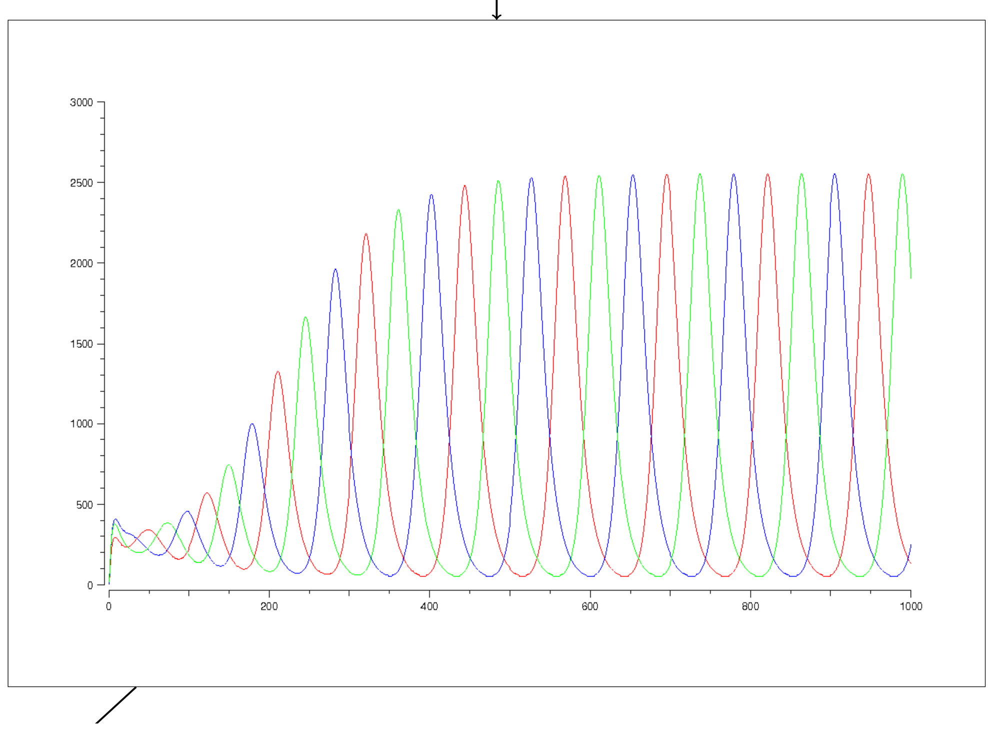
simulation using a stochastic approach

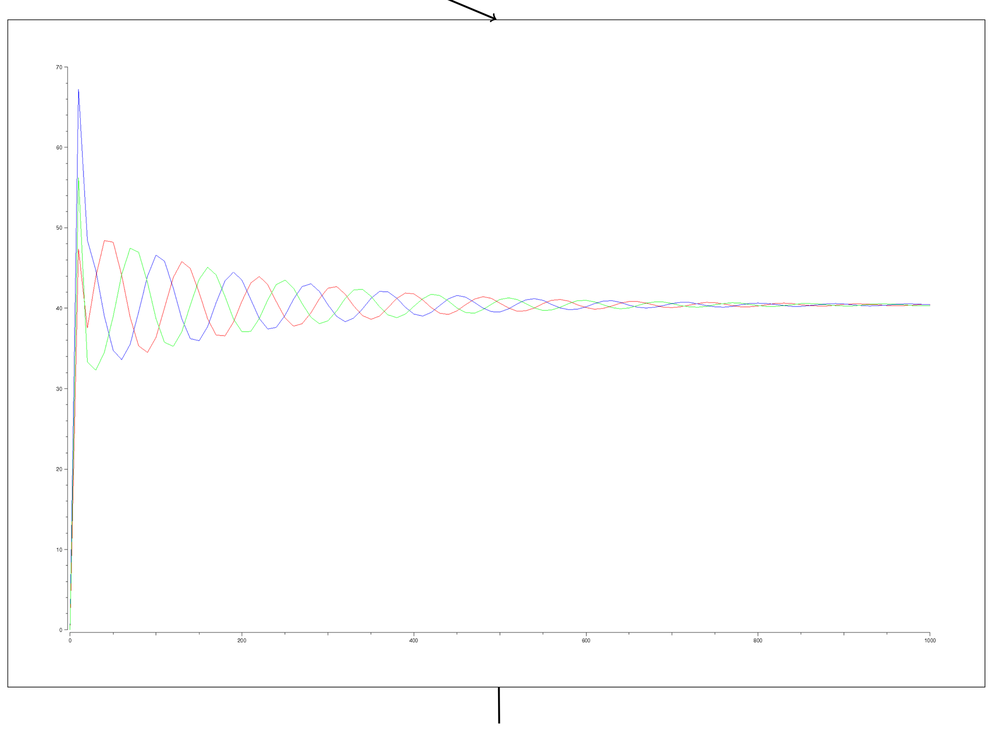
simulation using a deterministic approach

simulation using a deterministic approach different parameter set

`KiSAO:0000088`
Livermore solver for ordinary differential equations with automatic method switching
deterministic algorithm







`isA` `isA` `isA`

`TEDDY_0000114`
Stable Limit Cycle (Sustained Oscillation)

`TEDDY_0000063`
Damped Oscillation

`dependsOn` `hasSuperPart` `hasSubPart` `convergeTo`

`TEDDY_0000034`
Negative Feedback

`TEDDY_0000074`
Supercritical Hopf Bifurcation

`hasSuperPart` `hasSubPart`

`TEDDY_0000129`
Unstable Fixed Point

`TEDDY_0000126`
Stable Spiral Point

`http://www.ebi.ac.uk/compneur-srv/kisao`

`http://teddyontology.sourceforge.net/`