Barbaric Robustness Monitoring Revisited for STL* in Parasim

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Model

Model is represented in the format of Systems Biology Markup Language (SBML). It is a standard established for systems biology based on XML for the electronic storage and exchange of mathematical models of biochemical systems.

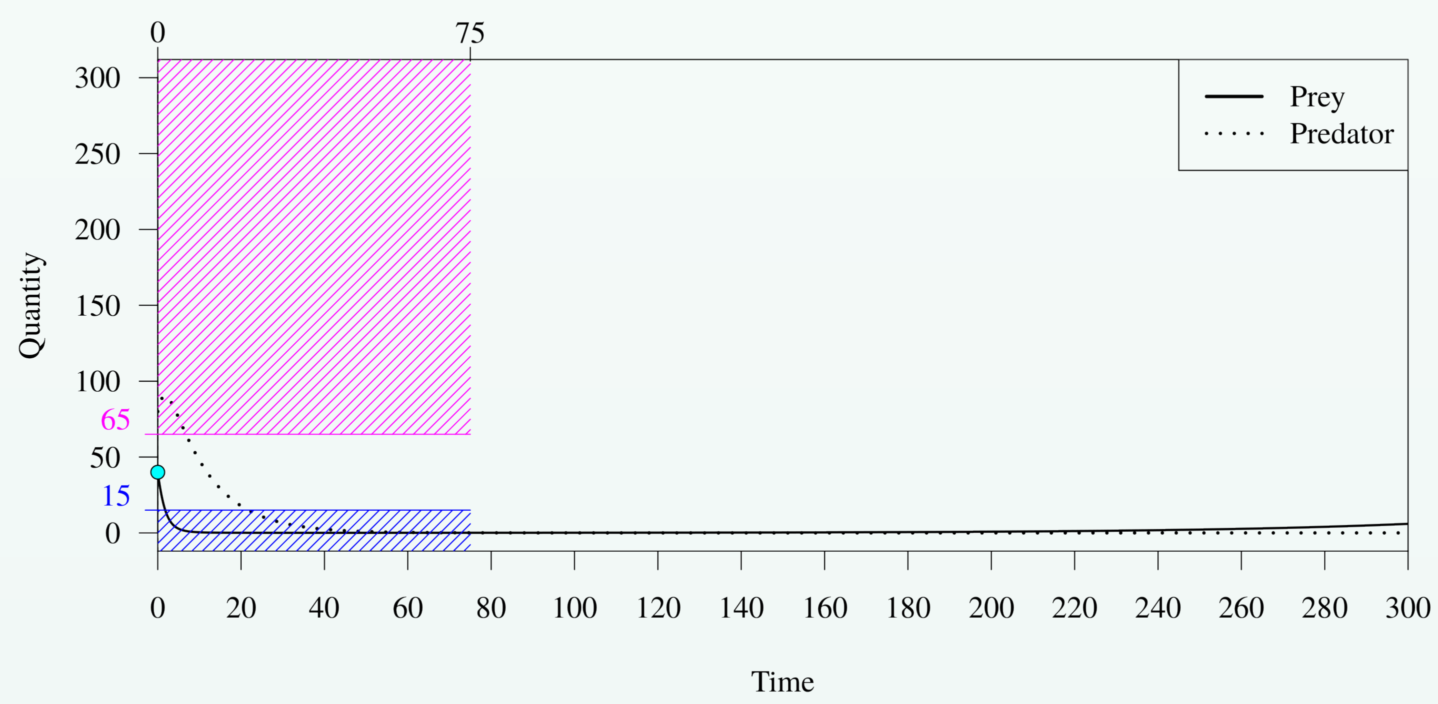
As an example, we use the *predator-prey* model, which attains oscillatory behaviour for a wide variety of parameters. We use a variant of the Lotka-Volterra model [1, 2] represented by the following ordinary differential equations:

$$\frac{dX}{dt} = \nu X - \alpha X Y \qquad \frac{dY}{dt} = \alpha X Y - 0.1 \times Y$$

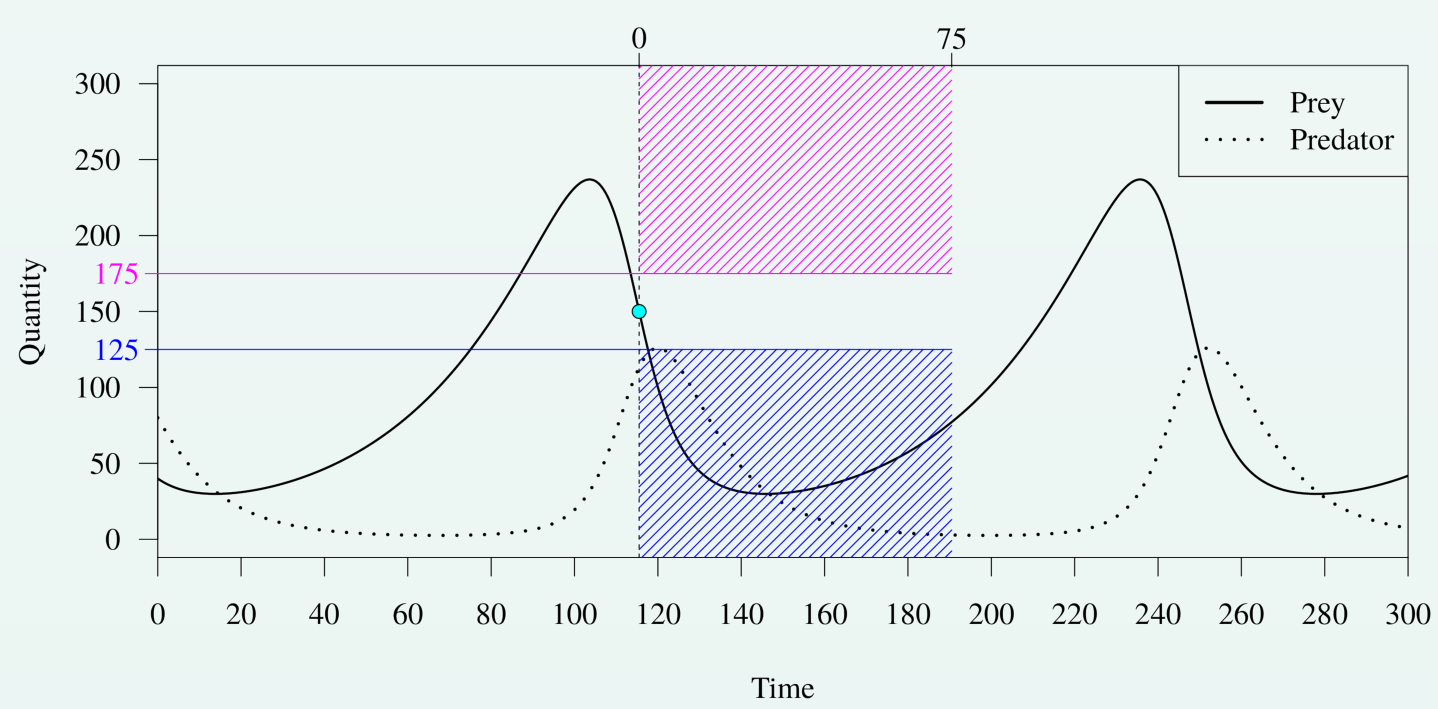
The model simulates a situation where a **prey** (species X) is hunted by a **predator** (species Y) with the simplifying assumption that predator birth rate and prey death rate are equal and proportional to the probability of prey and predator contact, and thus to the product of both species populations. There are two unknown parameters: *prey natality* (ν) and *predation rate* (α).

Parasim

Parasim is a Java-based open-source tool with a graphical user interface for computing robustness of an STL* formula in an ODE model with respect to a given set of parameters perturbation. Given an SBML model, a formula, and a perturbation set, Parasim samples the perturbation set into points and for each point simulates the model and computes robustness of the resulting signal with respect to STL* robustness measure [4]. In the neighbourhood of signals with low robustness, additional points are sampled. To reduce analysis execution time, formula optimising algorithms are implemented and incorporated into the robustness monitoring procedure.



A simulation of the model with parameter values $\nu = 3 \times 10^{-2}$ and $\alpha = 6.5 \times 10^{-3}$. The simulation does not exhibit the oscillatory behaviour, which clearly violates the property ψ. The cyan point depicts an example where the sub-formula representing an increase of prey population is violated. Areas satisfying sub-formulae for increase and decrease of prey population are highlighted in the appropriate colours.



A simulation of the model with parameter values $\nu = 3 \times 10^{-2}$ and $\alpha = 10^{-3}$. The simulation captures oscillatory behaviour, however, it does not satisfy the property ψ. The cyan point depicts an example where sub-formula representing increase of prey population is violated. Due to the oscillation period, the prey population does not reach a satisfying value in the time horizon of 75 time units. Areas corresponding to sub-formulae for increase and decrease of prey population are highlighted in the appropriate colours.

Property

Property is specified by a formula in STL* – Signal Temporal Logic extended with freeze operator [3]. STL allows to express properties of individual signals (discretised continuous trajectories) by means of numerical simulation. The expressiveness of STL* is enhanced by signal-value freeze operator storing values at a particular time point, which may be referred to in the later time point.

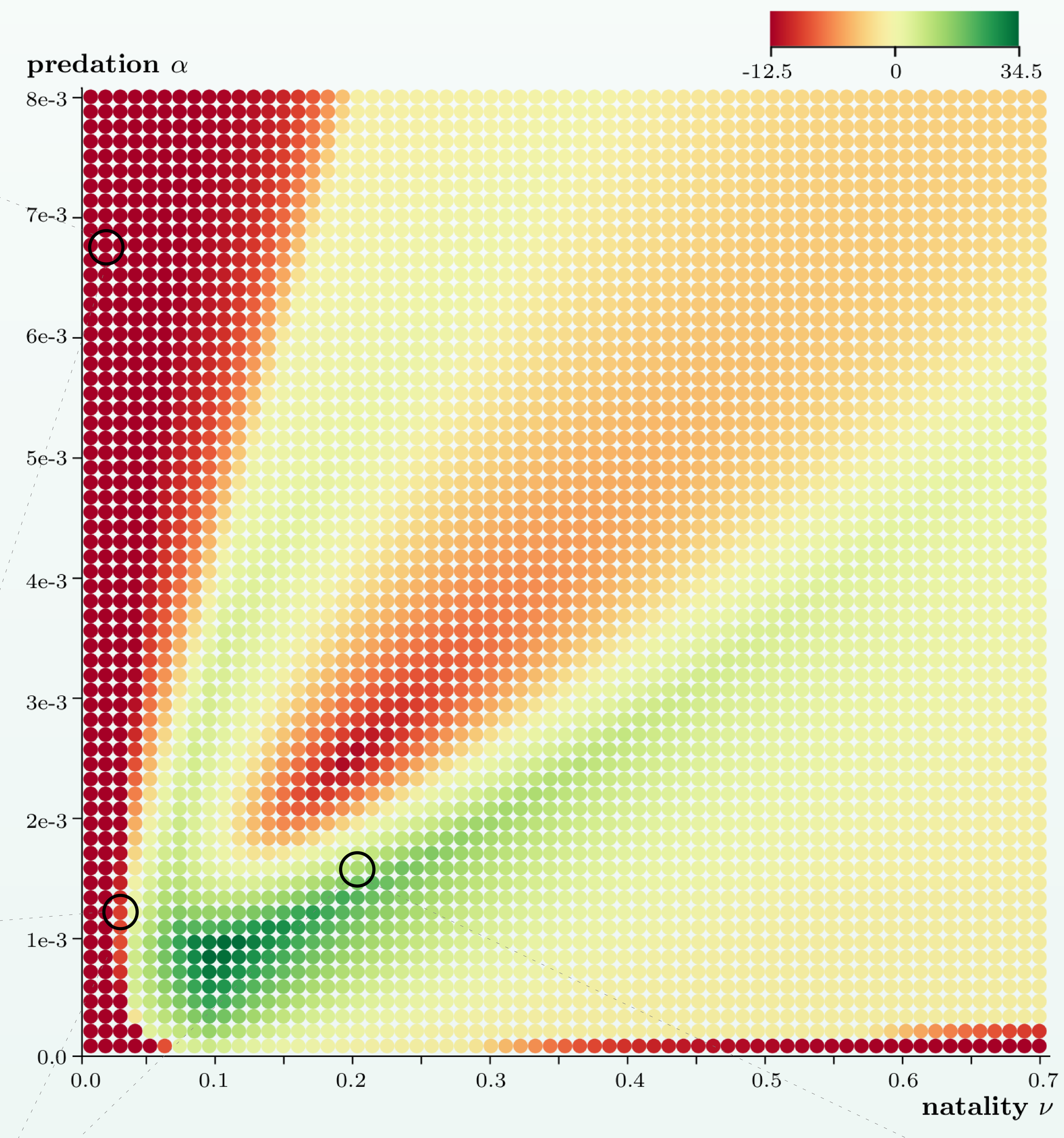
We consider the perturbation set $\nu \in [10^{-2}, 0.35]$ and $\alpha \in [10^{-3}, 2.5 \times 10^{-3}]$ for both parameters and a property specified in STL* given by the following formula:

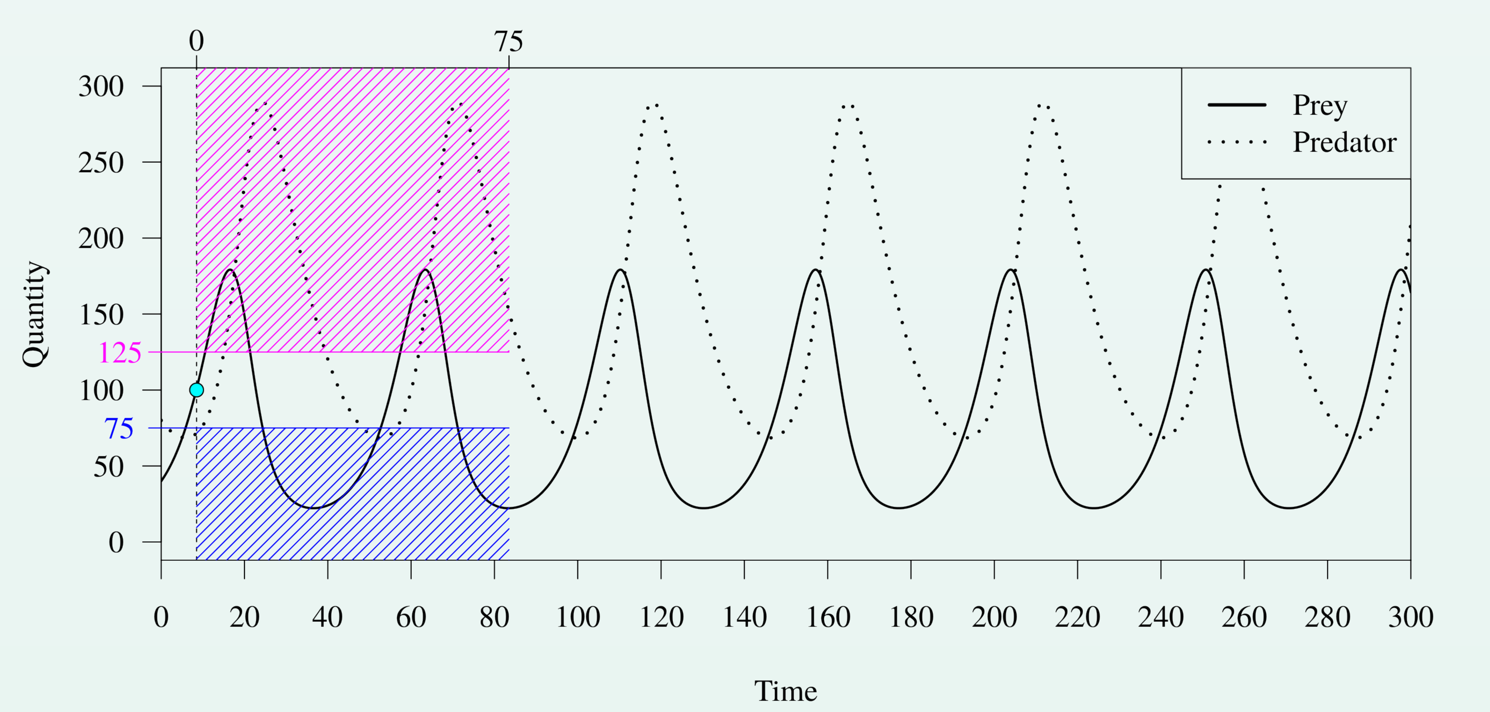
$$\psi = \mathbf{G}_{[0,300]}\left(\mathbf{F}_{[0,50]^*}\left(\mathbf{F}_{[0,75]}(X^* - X \geq 25) \wedge \mathbf{F}_{[0,75]}(X - X^* \geq 25)\right)\right)$$

The formula describes an oscillatory behaviour with particular restrictions on its amplitude and period. It requires that a time point T appears in the first 50 time units such that the population of prey must increase and decrease (in arbitrary order) by at least 25 individuals within the next 75 time units from T. Such fluctuation in prey population must appear again within at most 50 time units since the previous T, repeatedly in the horizon of 300 time units.

Robustness

Robustness of property ψ in the predator-prey model with respect to the given perturbation sets for *natality* ν and *predation* α parameters. Visualisation of the results is provided in terms of 2D projections showing the points in the perturbation space (green/red points show areas where the property is satisfied/violated, the corresponding positive/negative robustness degree is shown by the colour shade). The plot shows that amplitude of prey population oscillation is affected by both prey natality and predation rate.





A simulation of the model with parameter values $\nu = 0.2$ and $\alpha = 1.3 \times 10^{-3}$ capturing oscillatory behaviour satisfying the property ψ. The cyan point depicts an example where ψ holds. Areas satisfying sub-formulae for increase and decrease of prey population are highlighted in the appropriate colours. Note, there are plenty of points satisfying ψ in the range of 50 time units from the cyan point.

[1] Lotka A. J.: Elements of Physical Biology. Williams and Wilkins, Baltimore (1925)
[2] Volterra V.: Variations and Fluctuations of the Number of Individuals in Animal Species living together. Journal du Conseil 3, 3–51 (1928)
[3] Brim, L. et al.: STL*: Extending Signal Temporal Logic with Signal-Value Freezing Operator. Information and Computation, Academic Press (2014)
[4] Brim, L. et al.: Robustness Analysis for Value-Freezing Signal Temporal Logic. HSB, pp. 20–36 (2013)

This work has been supported by the Czech National Infrastructure grant LM2015055 and by the Czech Science Foundation grant GA15-11089S.

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