



System design of stochastic models using robustness of temporal properties



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ABSTRACT

Stochastic models such as Continuous-Time Markov Chains (CTMC) and Stochastic Hybrid Automata (SHA) are powerful formalisms to model and to reason about the dynamics of biological systems, due to their ability to capture the stochasticity inherent in biological processes. A classical question in formal modelling with clear relevance to biological modelling is the model checking problem, i.e. calculate the probability that a behaviour, expressed for instance in terms of a certain temporal logic formula, may occur in a given stochastic process. However, one may not only be interested in the notion of satisfiability, but also in the capacity of a system to maintain a particular emergent behaviour unaffected by the perturbations, caused e.g. from extrinsic noise, or by possible small changes in the model parameters. To address this issue, researchers from the verification community have recently proposed several notions of *robustness* for temporal logic providing suitable definitions of distance between a trajectory of a (deterministic) dynamical system and the boundaries of the set of trajectories satisfying the property of interest. The contributions of this paper are twofold. First, we extend the notion of robustness to stochastic systems, showing that this naturally leads to a distribution of robustness degrees. By discussing three examples, we show how to approximate the distribution of the robustness degree and the *average robustness*. Secondly, we show how to exploit this notion to address the *system design problem*, where the goal is to optimise some control parameters of a stochastic model in order to maximise robustness of the desired specifications.

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1. Introduction

Biological systems at the single cell level are inherently stochastic. Molecules inside cells perform random movements (*random walk*) and the reactions among them may occur when the probability of collision is high enough. The number of molecules of each species at each time point is therefore a random process: assuming instantaneous reactions, this process can be modelled as a Markovian (i.e. memoryless) discrete state, continuous time process. When the number of

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molecules of each species involved is large, so that many reactions happen in any small interval of time, stochastic effects can be neglected. However, if the concentration of the molecules (of at least some of the species) is low the stochasticity plays an important role and must be taken into account [1]. Stochastic models such as Continuous-Time Markov Chains (CTMC) [2] and Stochastic Hybrid Automata [3] are particularly powerful and suitable formalisms to model and to reason about biological systems defined as stochastic systems over time.

A classical question in formal modelling is to calculate the probability that a behavioural property, expressed in temporal logic, may occur in a given stochastic process, with specified parameters. *Probabilistic Model Checking* [4,5] (PMC) is a well-established verification technique that provides a quantitative answer to such a question. The algorithm used to calculate this probability [6] produces the exact solution, as it operates directly on the structure of the Markov chain. Despite the success and the importance of PMC, this technique suffers some computational limitations, either due to state space explosion or to the difficulty (impossibility) in checking analytically formulae in specific logics, like Metric Temporal Logic (MTL) [5,7]. Furthermore, PMC provides only a quantitative measure of the *satisfiability* (yes/no answer) of a temporal logic specification (i.e. the probability of the property being true).

However, especially when we deal with stochastic models, the notion of satisfiability may be not enough to determine the capacity of a system to maintain a particular emergent behaviour unaffected by the uncertainty of the perturbations due to its stochastic nature or by possible small changes in the model parameters. A similar issue also arises when considering the satisfiability of a property by deterministic dynamical systems which may be subject to extrinsic noise or uncertainty in the parameter. To address this question in the deterministic case, researchers from the verification community have proposed several notions of *temporal logic based robustness* [8–10], providing suitable definitions of distance between a trajectory of a system and the behavioural property of interest, expressed in terms of a temporal logic formula. These effectively endow the logic of interest with quantitative semantics, allowing us to capture not only whether a property is satisfied but also *how much* it is satisfied. A similar notion of robustness for stochastic models would clearly be desirable but, to our knowledge, has not been formalised yet.

The contributions of this paper are twofold. First, we provide a simulation-based method to define a notion of robust satisfiability in stochastic models. Simulation-based approaches, such as statistical model checking [11], can be used to estimate for a stochastic model the *robust satisfiability distribution* for a given temporal logic formula, with a guarantee of asymptotic correctness. This distribution is the key to understand how the behaviour specified by the logic temporal formula is affected by the stochasticity of the system. In particular, in this paper we consider two indicators of this distribution: the *average robustness* and the *conditional average robustness* of a formula being true or false. We discuss how to compute the robust satisfiability distribution and its indicators on two biological examples. Secondly, we show how to exploit the average robustness to address the *system design problem*, where the goal is to optimise (few) control parameters of a stochastic model in order to maximise these indicators. The proposed approach takes advantage of Gaussian Process Upper Confidence Bound (GP-UCB) algorithm introduced in [12].

The paper is structured as follows: in Section 2 we introduce the background material. In Section 3 we discuss the robustness of stochastic models using the quantitative semantics of the Signal Temporal Logic (STL). In Section 4 we present some experimental results for the robustness of STL formulae for three stochastic models that we have chosen as our case studies: the Schlögl system, a Repressor-like model of the circadian clock of *Ostreococcus Tauri*, and a Feed-Forward motif of a gene regulatory network. In Section 5 we show an application of the robust semantics to the system design problem. The related works and the final discussion are in Section 7.

2. Background

We now introduce some material needed in the rest of the paper. We start from a general definition of stochastic process, in order to fix the notation and introduce the space of trajectories of the system, which plays a central role in our approach. Then we instantiate this general framework in different ways, presenting Population Continuous Time Markov Chains, Stochastic Differential Equations and Stochastic Hybrid Systems, describing as these particular semantics may arise as models of biological systems. We then briefly introduce the Skorokhod metric, which endows the space of trajectories with a natural topology. At the end of the section, we introduce the Signal Temporal Logic, including its boolean and quantitative semantics.

2.1. Stochastic processes

Stochastic processes are useful mathematical constructs to describe the random evolution of a system in time. The following definition formalises the intuitive concept of random evolution.

Definition 1. Let (Ω, \mathcal{A}, P) be a probability space¹ and $E \subseteq \mathbb{R}^p$. A continuous time stochastic process with values in E is a collection of E -valued random variables $\mathbf{X}(t)$, indexed by $t \in [0, \infty)$ and defined on the same probability space (Ω, \mathcal{A}, P) .

¹ Here Ω is the sample space, \mathcal{A} is a sigma-algebra, and P a probability measure. See [13] for an introduction of measure and probability theory.

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