End-to-end Statistical Model Checking for Parameterization and Stability Analysis of ODE Models

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Note: Part [8] of the paper we present here has been accepted and presented to the QEST conference of Sept. '22, in Warsaw, Poland. The editors, Erika Ábrahám and Marco Paolieri, proposed us to submit an extension for the special issue of TOMACS '23, which we accepted. This presentation would be related to this extension, though we will reintroduce problematics and results from the QEST article.

Abstract

All scientific branches share the common concept of modeling. When a scientist studies a real-life system, the first step he or she goes through is to build a model that gathers all the existing knowledge of the target system. This model is then used as a proxy of the system it represents in order to analyze it, perform simulations or predictions. In several fields, such as Biology, Chemistry, Physics or Engineering, models do not represent a single system but are instead an abstraction for a *family* of systems that share common traits but might exhibit some internal variability. This internal variability can either be left out by considering that the model represents the "average" individual in the family, or taken into account inside of the model through the use of non-determinism, probabilities or parametricity.

When considering parametric models, scientists have to go through a phase of parameterization, which consists in confronting the model with experimental observations of the (family of) system(s) it represents in order to find the parameter values that best fit this (family of) system(s). In most cases, parameterization techniques are *deterministic* [14].

They lead to deterministic parameter values that best fit the experimental data, i.e. producing the best fit for the "average" individual. In this paper, we instead focus on a technique that allows to select parameter values that best fit *under variability*, i.e. that produce the best *probabilistic* fit for the *whole family*.

Parameterization, or *parameter synthesis* has been the topic of many works in the context of probabilistic systems [4-7, 9]. Symbolic techniques such as parametric model checking [1, 3] are often difficult to use in practice because they require automata-based models while real-life models are often expressed either with computer programs or with differential equation models. Statistical Model Checking (SMC) [10], on the other hand, is a simulation-based technique that allows to estimate, with formal guarantees, the probability that a given (probabilistic) model satisfies a given property. Because it is simulation-based, it can be applied to any stochastic model for which simulations can be performed. SMC has been successfully applied to perform parameterization of real-life models expressed using several formalisms such as parametric Markov chains [2], parametric Python programs [13], or even parametric Ordinary Differential Equation systems (ODEs) [11]. Unfortunately, the formal guarantees obtained through SMC are linked to the simulation space (i.e. the produced traces) and not to the original model itself. When the model consists in sets of ODEs, as in [11], numerical resolution methods are used in order to solve the ODEs and perform simulations, which means that the formal guarantees obtained through SMC cannot apply to the original ODE model.

Our main contribution is to bridge the gap between the original ODE model and the results of the parameterization procedure by *combining the statistical guarantees of SMC with the global approximation error of standard numerical resolution methods.* As in [11], we consider ODE models with structural parameters. We assume that these models represent families of real-life systems that need to match some data through simulation. We build on the logic proposed in [11] to express our properties of interest and also consider expected reward properties that might be of interest in practice. We use SMC to grade parameter values by

estimating the expectation of a given reward function for these values while taking internal variability into account. We then extend our result by applying this technique to initial values of the associated Cauchy problem, and prove we have the same kind of guarantees. Contrarily to what is done in [11], the accuracy of this estimation is guaranteed w.r.t. the original ODE model.

To illustrate our results, we perform the parameterization of a state-of-the-art model taken from the literature using our technique, as well as a study on initial condition, more precisely regarding the stability of some critical values. In this context, and because modelers are often interested by this information in practice, we propose a global evaluation of the value spaces that allows us to get a complete picture of the adequacy of the values w.r.t. the given data. This choice is done by interest only, since our results are generic and could be applied to any search technique, such as the local ones performed in [11].

Intuition. To give an intuition of our contribution, we provide an informal summary of the method we present in this paper, in the context of parameterization, though the method is the same in the context of stability analysis. Recall that, given a dataset and a parametric ODE system, the objective is to find a solution to a parametric ODE system (i.e. parameter values) that satisfies a property φ w.r.t. the dataset, which is, given a distance $\delta > 0$, "the solution stays in a tunnel of radius δ around the data"; we also want to acquire statistical guarantees on said result. The main issue is that we can only simulate our model by solving the ODE system using numerical resolution methods. Hence, we cannot directly verify whether exact solutions (x) of the system satisfy φ and instead have to rely on approximate solutions (y). We therefore proceed as follows: we start by discretizing the set of parameter values into a grid; Then, we evaluate each point of this grid using the procedure detailed below; Finally, we use the resulting scores to select the "best" parameter values w.r.t φ. The score of a given parameter value $\boldsymbol{\lambda}$ is computed as follows, and illustrated in figs. 1 and 2.

1. We set the parameter value to $\boldsymbol{\lambda}$. Through a careful study of the ODE system, we give a bound on the distance ε between exact (x) and approximate (y) solutions. We emphasize that this bound depends on (1) the chosen resolution technique and (2) the chosen integration step. We show that this distance is uniformly stable w.r.t. internal variability around $\boldsymbol{\lambda}$, but also that it can be uniformly bounded on the global set of solutions (i.e. independently of $\boldsymbol{\lambda}$).
2. We propose two new properties φ_1 and φ_2 that will be verified on the approximate solutions y, and depend on the above distance. This amounts to changing the size of the tunnel around the experimental dataset. We compute (estimations of) the respective probabilities p_1 and p_2 and prove that the probability p that x satisfies φ lies between p_1 and p_2.
3. We provide statistical guarantees of our estimation, i.e. a confidence interval for our estimation of p, and use this estimation as the score for parameter value $\boldsymbol{\lambda}$.

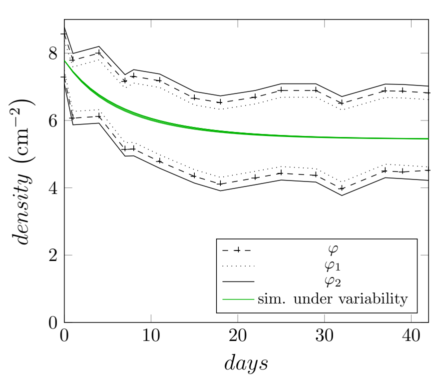

Fig. 1. Tunnels corresponding to the properties $\varphi, \varphi_1, \varphi_2$ and accepted simulations.

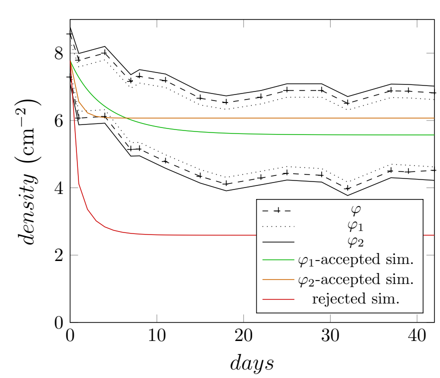

Fig. 2. φ-accepted, φ_2-accepted and rejected solutions.

The study on stability proved to be a bit more complex, as we couldn't use the usual mathematical definitions [12] which rely on an infinity of values to be satisfied. Instead, we built a bounded definition of stability, by requiring that the traces stay at an abitrary distance from the data for an arbitrary amount of time. This definition, though less precise than the mathematical one, allows us to conduct the same study as before, and experimentally exhibit a stable behavior in certain regions of the state space as we can see in figs. 3 and 4. In these figures, the color represents the expected distance between the equilibrium x_e and the trace induced by each discrete value of the space: the darker the point, the closer the trace. Note that fig. 4 depicts the distance to the *closest* equilibrium, and is the combination of the studies on the stability of both equilibria $x_{e,1}$ and $x_{e,2}$.

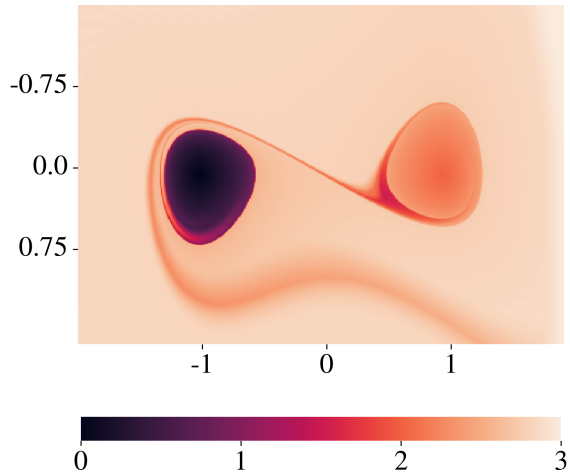

Fig. 3. Basin of attraction for $x_e = (-1, 0)$, the left equilibrium of the system.

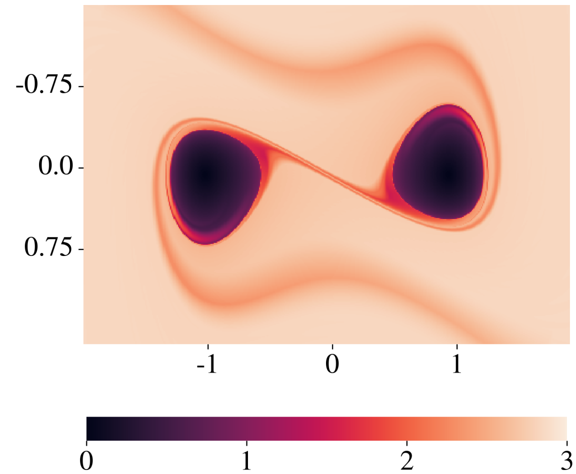

Fig. 4. Basins of attraction for $x_{e,1} = (-1, 0)$ and $x_{e,2} = (1, 0)$, the two equilibria of the system.

It is worth noting that the underlying theory is generic: the integration method as well as the statistical estimation method can be chosen arbitrarily as long as they provide the usual guarantees. In this paper, we use Runge-Kutta and Monte-Carlo for the sake of example. We also emphasize that the nature of the problem is also arbitrary: we chose two examples from the literature to have references regarding the coherence of the results, but this method may be applied to *any* ODE model, including systems for which the theoritical analysis proves too complicated, for instance in the case of systems of high order. Moreover, the genericity of the method makes it readily usable for hybrid systems.

References

1. Baier, C., de Alfaro, L., Forejt, V., Kwiatkowska, M.: Model checking probabilistic systems. In: Handbook of Model Checking, pp. 963–999. Springer (2018). https://doi.org/10.1007/978-3-319-10575-8_28
2. Bao, R., Attiogbe, C., Delahaye, B., Fournier, P., Lime, D.: Parametric statistical model checking of UAV flight plan. In: International Conference on Formal Techniques for Distributed Objects, Components, and Systems. pp. 57–74. Springer (2019). https://doi.org/10.1007/978-3-030-21759-4_4
3. Daws, C.: Symbolic and parametric model checking of discrete-time Markov chains. In: International Colloquium on Theoretical Aspects of Computing. pp. 280–294. Springer (2004). https://doi.org/10.1007/978-3-540-31862-0_21
4. Dehnert, C., Junges, S., Jansen, N., Corzilius, F., Volk, M., Bruintjes, H., Katoen, J.P., Ábrahám, E.: Prophesy: A probabilistic parameter synthesis tool. In: International Conference on Computer Aided Verification. pp. 214–231. Springer (2015). https://doi.org/10.1007/978-3-319-21690-4_13
5. Gainer, P., Hahn, E.M., Schewe, S.: Accelerated model checking of parametric Markov chains. In: International Symposium on Automated Technology for Verification and Analysis. pp. 300–316. Springer (2018). https://doi.org/10.1007/978-3-030-01090-4_18
6. Gyori, B.M., Liu, B., Paul, S., Ramanathan, R., Thiagarajan, P.: Approximate probabilistic verification of hybrid systems. In: International Workshop on Hybrid Systems Biology. pp. 96–116. Springer (2015). https://doi.org/10.1007/978-3-319-26916-0_6
7. Han, T., Katoen, J.P., Mereacre, A.: Approximate parameter synthesis for probabilistic time-bounded reachability. In: 2008 Real-Time Systems Symposium. pp. 173–182. IEEE (2008). https://doi.org/10.1109/RTSS.2008.19
8. Julien, D., Cantin, G., Delahaye, B.: End-to-End Statistical Model Checking for Parametric ODE Models. In: Ábrahám, E., Paolieri, M. (eds.) QEST: International Conference on Quantitative Evaluation of Systems. Lecture Notes in Computer Science, vol. 13479, pp. 85–06. Springer International Publishing, Warsaw, Poland (Sep 2022). https://doi.org/10.1007/978-3-031-16336-4_5, `https://hal.archives-ouvertes.fr/hal-03824899`, main reference for Central Limit Theorem used in Julien2022.
9. Katoen, J.P.: The probabilistic model checking landscape. In: Proceedings of the 31st Annual ACM/IEEE Symposium on Logic in Computer Science. pp. 31–45 (2016). https://doi.org/10.1145/2933575.2934574
10. Legay, A., Delahaye, B., Bensalem, S.: Statistical model checking: An overview. In: International Conference on Runtime Verification. pp. 122–135. Springer (2010). https://doi.org/10.1007/978-3-642-16612-9_11
11. Liu, B., Gyori, B.M., Thiagarajan, P.S.: Statistical model checking-based analysis of biological networks, pp. 63–92. Springer International Publishing (2019). https://doi.org/10.48550/arXiv.1812.01091
12. Lyapunov, A.M.: General problem of the stability of motion. Control Theory and Applications Series, Taylor & Francis (1992)
13. Ramondenc, S., Eveillard, D., Guidi, L., Lombard, F., Delahaye, B.: Probabilistic modeling to estimate jellyfish ecophysiological properties and size distributions. Scientific Reports **10**(1), 1–13 (2020). https://doi.org/10.1038/s41598-020-62357-5
14. Ramsay, J.O., Hooker, G., Campbell, D., Cao, J.: Parameter estimation for differential equations: A generalized smoothing approach. Journal of the Royal Statistical Society: Series B (Statistical Methodology) **69**(5), 741–796 (2007). https://doi.org/10.1111/j.1467-9868.2007.00610.x