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Guaranteed computation methods for compartmental in-series models under uncertainty

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ABSTRACT

The pattern of some real phenomenon can be described by compartmental in-series models. Nevertheless, most of these processes are characterized by their variability, which produces that the exact values of the model parameters are uncertain, although they can be bounded by intervals.

The aim of this paper is to compute tight solution envelopes that guarantee the inclusion of all possible behaviors of such processes. Current methods, such as monotonicity analysis, enable us to obtain guaranteed solution envelopes. However, if the model includes non-monotone compartments or parameters, the computation of solution envelopes may produce a significant overestimation.

Our proposal consists of performing a change of variables in which the output is unaltered, and the model obtained is monotone with respect to the uncertain parameters. The monotonicity of the new system allows us to compute the output bounds for the original system without overestimation. These model transformations have been developed for linear and non-linear systems. Furthermore, if the conditions are not completely satisfied, a novel method to compute tight solution envelopes is proposed. The methods exposed in this paper have been applied to compute tight solution envelopes for two different models: a linear system for glucose modeling and a non-linear system for an epidemiological model.

1. Introduction

Compartmental systems have been widely used to simulate processes from many different real situations emerging from biology, economics, engineering, medicine, human sciences and many other research fields. When studying a real process with a mathematical system, there is always some mismatch between the model and reality, caused because mathematical models are usually a simplified version of the actual processes. Furthermore, a common characteristic of any real phenomenon is variability, leading to parametric uncertainty. Therefore, the exact values for the initial conditions and model parameters are unknown, although they can be bounded by intervals. While there is a single possible behavior for a model with constant parameters, parametric uncertainty produces a set of different possible solutions. Hence, the computation of solution envelopes acquires importance.

Monte Carlo approaches have been used to implement these kinds of systems. They consist in performing a large number of different simulations by the variation of the parameter values [1]. These methods have been widely used to deal with uncertainty due to their easy computation. However, the computational cost of Monte Carlo approaches increases

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proportionally to the number of simulations executed and, moreover, they never guarantee that the bounds obtained include all the possible solutions, independently to the number of simulations [2]. This inclusion guarantee is needed for error-bounded parametric identification and constraint-satisfaction problems.

Trajectory-based approaches have been also applied to obtain solution envelopes [3–5]. Compared with Monte Carlo simulations, monotonicity analysis guarantees that the actual response is inside the envelopes. However, if the model analyzed includes any non-monotone state or parameter, the computation of solution envelopes may produce a significant overestimation. If the overestimation is high, it could not be useful from a practical point of view, for instance, in an insulin therapy for diabetes patients [6].

This work is an extension of the paper [7], which aims to compute tight solution envelopes for compartmental in-series models under parametric uncertainty. The solution envelopes computed must guarantee the inclusion of all possible solutions and minimize the overestimation. The proposal consists in performing a change of variables of the original model to obtain a monotone system with respect to its states and parameters, and keeping the output unaltered. As all the states and parameters of the new model are monotone, output bounds can be computed without overestimation. In [7], these model transformations were formulated in a lemma for bidirectional chains. In this work, we propose an additional lemma for unidirectional chains that requires fewer conditions. Furthermore, when the system does not completely satisfy the lemma conditions, we propose a new method to compute tight solution envelopes that consists in the application of an upper and a lower bounding model.

This work has been organized as follows: In Section 2, uncertain systems are introduced. In Section 3, compartmental in-series models are presented. In Section 4, several new methods are proposed for the analysis of the system monotonicity with respect to the parameters. In Section 5, a novel technique is proposed for near-monotone systems. In Section 6, the proposed methods are applied to compute the output bounds for linear and non-linear models. Finally, Section 7 outlines the conclusions of this study.

2. Uncertain systems

Continuous-time compartmental systems are described by an initial-value problem (IVP):

$$\begin{aligned} &\dot{x}(t,p) = f(t,x,p,u), \qquad x(t_0) = x_0, \\ &x \in \mathbb{R}^n,\ t \in \mathbb{R},\ p \in \mathbb{R}^{n_p},\ u \in \mathbb{R}^n \end{aligned} \tag{1}$$

where f is the vector function with components f_i, x is the state vector, p is the parameter vector, n_p is the number of parameters, and u is the input vector. The solution of (1) is denoted by $x(t; t_0, x_0, p, u)$.

As parametric uncertainty is considered, initial conditions and parameter values are unknown, but they can be bounded by intervals. Representing intervals in bold, interval vectors $\mathbf{p}$, $\mathbf{u}$ and $\mathbf{x_0}$ include all possible values for the parameters p, for the input vector u and for the initial conditions x_0 of the model, respectively. The set of possible solutions derived from parametric uncertainty is denoted by $\mathbf{x}(t; t_0, \mathbf{x_0}, \mathbf{p}, \mathbf{u})$:

$$\mathbf{x}(t; t_0, \mathbf{x_0}, \mathbf{p}, \mathbf{u}) = \{x(t; t_0, x_0, p, u) \mid x_0 \in \mathbf{x_0},\ p \in \mathbf{p}, u \in \mathbf{u}\}.$$

The computation of solution envelopes plays a key role in the simulation of systems under parametric uncertainty. Such a computation can be performed by one-step-ahead iteration based on previous approximations of a set of point-wise trajectories generated by the selection of particular values of the parameters $p \in \mathbf{p}$, the input vector $u \in \mathbf{u}$ and the initial conditions $x_0 \in \mathbf{x_0}$ by using heuristics such as a monotonicity analysis of the system [8].

Monotone systems have very robust dynamical characteristics, since they respond to perturbations in a predictable way. The interconnection of monotone systems may be studied in an analytical way [9], by considering a flow $\mathbf{x}(t) = \phi(\mathbf{x_0}, t)$. A system is monotone with respect to the states, or simply monotone, if $\mathbf{x_0} \preceq \mathbf{y_0} \Rightarrow \phi(\mathbf{x_0}, t) \preceq \phi(\mathbf{y_0}, t)$ for all $t \geq 0$, where $\preceq$ is a given order relation. Cooperative systems form a class of monotone dynamical systems [4] in which

$$\frac{\partial f_i}{\partial x_j} \geq 0, \quad \text{for all } i \neq j,\ t \geq 0.$$

An upper bounding model and a lower bounding model are computed to obtain solution envelopes for the original model. The cooperative states take their upper (lower) bound value in an upper (lower) bounding model, while the monotone but non-cooperative states, known as competitive states, take their lower (upper) bound value in an upper (lower) bounding model. Nevertheless, in both cases non-monotone states have to be computed as intervals that produce a significant overestimation in the computation of solution envelopes.

The monotonicity of the system with respect to the parameters of the model can be analyzed by considering the parameters as system states in an extended model [3], that is, by performing a monotonicity analysis of a new system with $n + n_p$ states given by:

$$\begin{aligned} &\dot{x}_1(t) = f_1(t, x_1(t), x_2(t), \ldots, x_n(t), p_1(t), p_2(t), \ldots, u_1(t)) \\ &\vdots \\ &\dot{x}_n(t) = f_n(t, x_1(t), x_2(t), \ldots, x_n(t), p_1(t), p_2(t), \ldots, u_n(t)) \\ &\dot{p}_i(t) = 0 \quad \forall i \in \{1, \ldots, n_p\}. \end{aligned} \tag{2}$$