ON THE COMPUTATION OF OUTPUT BOUNDS OF PARALLEL INPUTS PHARMACOKINETIC MODELS WITH PARAMETRIC UNCERTAINTY

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Compartmental models are essential for the study of biological processes and their behaviour along time. Furthermore, these models are used in many diverse areas such as economy, engineering, medicine or human sciences. One of the characteristics of biological processes is variability, leading to significant parametric uncertainty when deriving mathematical models. The aim of this work is to study how uncertainty in parameters affects solution bounds.

Parallel inputs model consist of two or more linear chains connected together in parallel to form the input to one-compartment model. Each chain is formed by a number of identical compartments (this number can vary for each chain). This type of models has mostly been used to model biological processes in which inputs show effects on output with different delays in time. Some of its applications include the analysis of the double peak phenomenon in pharmacokinetics, as well as subcutaneous insulin absorption models.

In this work, computation of tight solution bounds in initial value problems (IVPs) for ordinary differential equations (ODEs) has been addressed, particularly for those that have the form of a parallel inputs model. For this purpose, monotone parameters with respect to the model (cooperative or not) as well as critical points of those non-monotone parameters have been studied. Furthermore, we have combined analytical solutions of some compartments with ODEs of others, transforming our complex IVP in a simpler IVP with just one compartment. With this method the propagation errors decrease significantly, obtaining a considerable improvement in the achievement of the solution bounds, in comparison with the results given by VNODE, one of the most powerful tools developed to compute bounds on solutions in IVPs for ODEs with uncertainty.

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