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BACHELOR PUBLICATION

Application of Sensitivity- and Uncertainty-based techniques for the assessment of epidemiological models in real-life study cases

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"We sail within a vast sphere, ever drifting in uncertainty, driven from end to end. When we think to attach ourselves to any point and to fasten to it, it wavers and leaves us; and if we follow it, it eludes our grasp, slips past us, and vanishes forever."

Blaise Pascal

UNIVERSIDAD EAFIT

Abstract

Escuela de Ciencias
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by Daniel Rojas Díaz

Uncertainty analysis (UA) and sensitivity analysis (SA) are tools to assess and to quantify the uncertainty spread from the input factors (parameters and initial states) to the model output, taking into account the effect of the interactions among those factors. Throughout the following works, I treat UA as a graphical assessment of uncertainty propagation based on Monte Carlo simulation, which makes it possible to state a range for the model output in cases where it is considered relevant. On the other hand, I privilege the global approach for SA instead of the local one, since the first attempts to quantify the uncertainty contribution of the model factors in their entire distribution range while the second one is only informative for a single locus in the distribution. In this way, when applying global UA/SA on a model, it is possible to identify those factors that mostly determine the model behavior. Furthermore, I have noticed that the concepts and principles of UA/SA are associated with other main tasks in modeling, as factors estimation and confidence intervals achievement: Briefly, those non-identifiable factors in a model (factors whose value can not be estimated uniquely from some information about output data) should belong to the categories of non-sensible or sensitive but correlated from SA; and, the sub-space of the space of factors where the factors may jointly exist producing a model output that fits, in some extent, to a given output data, could be approximately estimated with UA-based approaches, constituting a new kind of confidence interval. Thus, in this compendium, I present five works related to the applications of UA/SA techniques as well as its relevance. The objective of those applications evolves from the most logically immediate to some derived and more complex ones, though still preserving the model pertinence as a central topic.

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Contents

To Melba

Both her outright advice and unconditional support have forged and will continue to shape the path I started walking, and where I put this work as the first step.

Chapter 1

An alternative model to explain the vectorial capacity using as example *Aedes aegypti* case in dengue transmission

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1.2 Abstract

Vectorial capacity (VC), as a concept that describes the potential of a vector to transmit a pathogen, has had historical problems related to lacks in dimensional significance and high error propagation from parameters that take part in the model to output. Hence, values estimated with those equations are not sufficiently reliable to consider in control strategies or vector population study. In this paper, we propose a new VC model consistent at dimensional level, i.e., the definition and the equation of VC have same and consistent units, with a parameter estimation method and mathematical structure that reduces the uncertainty in model output, using as a case of study an Aedes aegypti population of the municipality of Bello, Colombia. After a literature review, we selected one VC equation following biological, measurability and dimensional criteria, then we rendered a local and global sensitivity analysis,

identifying the mortality rate of mosquitoes as a target component of the equation. Thus, we studied the Weibull and Exponential distributions as probabilistic models that represent the expectation of mosquitoes infective life, intending to include the best distribution in a selected VC structure. The proposed mortality rate estimation method includes a new parameter that represents an increase or decrease in vector mortality, as it may apply. We noticed that its estimation reduces the uncertainty associated with the expectation of mosquitoes' infective life expression, which also reduces the output range and variance in almost a half.

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Chapter 2

A novel algorithm for confidence sub-contour box estimation: An alternative to traditional confidence intervals

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2.2 Abstract

The factor estimation process is a really challenging task for non-linear models. Even whether researchers manage to successfully estimate model factors, they still must estimate their confidence intervals, which could require a high computational cost to turn them into informative measures. Some methods in the literature attempt to estimate regions within the estimation search space where factors may jointly exist and fit the real data (confidence contours), however, its estimation process raises several issues as the number of factors increases. Hence, in this paper, we focus on the estimation of a subregion within the confidence contour that we called as Confidence Sub-contour Box (CSB). We proposed two main algorithms for CSB estimation, as well as its interpretation and validation. Given the way we estimated CSB, we expected and validated some useful properties of this new kind of confidence interval: a user-defined uncertainty level, asymmetrical intervals, sensitivity assessment related to the interval length for each factor, and the identification of true-influential factors.

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Chapter 3

Global Sensitivity and Uncertainty Analyses - Confidence Subcontour Box (GSUA-CSB) Toolbox

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3.2 Abstract

Global Sensitivity and Uncertainty Analyses - Confidence Subcontour Box (GSUA-CSB) Toolbox is a product developed by Universidad EAFIT for command-line mathematical model validation in both of Simulink or Symbolic Math Toolbox environment. At present, the toolbox allows performing the following functions: To apply and visualize several variance-based sensitivity (SA) and uncertainty (UA) analysis, to estimate model parameters (PE) and to estimate the confidence sub-contour box (CSB) of previously estimated parameters. This toolbox has its basis on the previous work of Carlos Mario Vélez: GSUA of dynamical systems using variance-based methods, published in this mathworks file exchange link.

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Chapter 4

Influence of pulse-type inputs on parameter estimation and chemical control assessment in a dengue deterministic model

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4.2 Abstract

Many deterministic mathematical models of dengue spread usually use theoretical or measured-in-lab parameters, without worrying about the uncertainties in factors, such as quality and confidence of data, or changes in control inputs. Other models consider environmental conditions and apply parameter estimations to obtain experimental parameters. This is more in accordance with real situations and may even introduce climate changes as periodical continuous-time inputs; however, they do not include the estimations of the effects of aperiodic changes in inputs, such as chemical control (fumigation) of vectors. This study estimates parameters (including chemical control parameters) and confidence contours (a type of confidence interval) under uncertainty conditions using Matlab tools and data from the municipality of Bello (Colombia) during 2010–2014. Our study shows that introducing aperiodic pulse-type inputs into the mathematical model allows us to (i) estimate feasible parameters into confidence biological intervals, (ii) highlight the importance of chemical control as a method to control disease propagation, and (iii) reproduce

the endemic behavior. We obtained a model with new and verifiable biological parameters, described a methodology and a novel Matlab toolbox for parameter and confidence interval estimation under uncertainties, and performed reliable simulations showing the behavior of dengue spread in different interesting scenarios.

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Chapter 5

Sensitivity, uncertainty and identifiability analyses to define a dengue transmission model with real data of an endemic municipality of Colombia

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5.2 Abstract

Dengue disease is a major problem of public health surveillance entities in tropical and subtropical regions which makes a significant impact not only epidemiological but social and economical. There are many factors involved in the dengue transmission process. We can evaluate the importance of these factors through the formulation of mathematical models. However, the majority of these models in the literature tend to be overparameterized, with considerable uncertainty levels and over complex formulations. We aim to evaluate the structure, complexity, trustworthiness, and suitability of three models, which simulate the transmission of dengue disease, through different strategies. To achieve this goal, we perform structural and practical identifiability, sensitivity and uncertainty analyses to these models. The

results showed that the most simple model was more appropriate and reliable than the other two to simulate the dengue transmission disease when the only available information to fit them is the cumulative number of reported dengue cases in an endemic municipality of Colombia.

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