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Hopfield networks for identification of delay differential equations with an application to dengue fever epidemics in Cuba ☆

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ABSTRACT

This work is aimed at proposing an algorithm, based upon Hopfield networks, for estimating the parameters of delay differential equations. This neural estimator has been successfully applied to models described by Ordinary Differential Equations, whereas its application to systems with delays is a novel contribution. As a case in point, we present a model of dengue fever for the Cuban case, which is defined by a delay differential system. This epidemiological model is built upon the scheme of an SIR (susceptible, infected, recovered) population system, where both delays and time-varying parameters have been included. The latter are thus estimated by the proposed neural algorithm. Additionally, we obtain an expression of the Basic Reproduction Number for our model. Experimental results show the ability of the estimator to deal with systems with delays, providing plausible parameter estimations, which lead to predictions that are coherent with actual epidemiological data. Besides, when the Basic Reproduction Number is computed from the estimated parameter values, results suggest an evolution of the epidemic that is consistent with the observed infection. Hence the estimation could help health authorities to both predict the future trend of the epidemic and assess the efficiency of control measures.

1. Introduction

System identification can be defined as the determination of the internal properties of a system from measurable outputs [1]. In models that contain parameters, fitting the values of the model parameters is referred to as parametric identification or parameter estimation [2]. In this contribution, we describe a method for parameter estimation, based on Hopfield neural networks. The proposed algorithm presents two advantages over conventional techniques: it allows for a time-variant estimation of the parameters, and it can be formulated to estimate parameters of systems formulated by delay differential equations (DDE).

The application of mathematics to epidemiological modelling is a task that has been performed for a long time [3,4]. Building models of infectious diseases, validating them and estimating their parameters, allows, on one hand, to predict their evolution, and on the other hand, to develop sanitary policies in order to fight the diseases. Dengue fever is an infectious disease which has reappeared in subtropical regions of the American and African continent in the last decades. Therefore, modelling and identification of the dengue fever system have become an interesting study to be performed [5]. It has also been investigated the phenomenon of dengue overwintering [6], by providing interesting hypotheses on mosquito life cycle. These efforts, which have helped to construct a valuable theoretical framework for dengue analysis, face however a fundamental shortcoming when it comes to comparing the model to actual statistical data of the infection: the inclusion in the model of mosquito populations. There is no current or foreseeable way to measure the number of mosquitos that live in an area, let alone determine how many of them are infected by the virus. Consequently, the first objective of the paper is posing a model of dengue fever that dispenses with the explicit inclusion of mosquito populations. Conventional models of dengue represent the complete process of human–mosquito–human virus transmission by defining separate populations of humans and mosquitoes. Thus, there is an explicit passage of mosquitoes to an infected state, which in turn leads to a passage of healthy humans to infected individuals. In contrast, the presented model [7] only includes human populations, whereas the effectiveness of disease transmission by mosquitoes is accounted for by means of a mathematical expression, which includes a parameter that somehow measures the whole cycle from an infected human to a susceptible individual being infected. Due to the incubation period of the virus within the mosquito, the new infections are due to mosquitos that became infected in the past, thus the included parameter must be related to past values of

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infected human populations. Consequently, the model equations comprise delayed states, resulting in a delay differential equation. The benefit in this setting is that all populations are, in principle, measurable, which is accomplished at the cost of an increased mathematical complexity of the model. In order to confront the proposed model with actual epidemic data, the numeric values of the parameters must be computed, which is the motivation for the definition of a method for parameter estimation in DDE. Although the mechanisms that lead to the construction of the model are general, the model is defined with the particularities of the epidemics in Havana (Cuba) in mind, namely the disease is not endemic, so only one strain of the virus must be considered within each season. The proposed model is described in Section 2.1.

A threshold condition to ascertain the future evolution of an epidemic is given by the Basic Reproduction Number [8,9]. Intuitively, it can be defined as the average number of infections due to a single infected individual, so that when this value is less than one, the infection will eventually vanish by itself in the long run. We obtain the expression of the Basic Reproduction Number for the proposed model of dengue, by adapting the usual computation procedure to a DDE. The obtained formula depends on the values of the parameters and, in particular, of the parameter that represents the infection "hiding" the mosquito vector, mentioned above. This is an additional motivation for the definition and analysis of a method for estimating the parameters of a DDE. The obtention of the Basic Reproduction Number is explained in Section 2.2.

Although parametric identification has been extensively studied from a variety of viewpoints, the estimation of time-varying parameters is considered to pose significant difficulties, thus most theoretical convergence results are based on the assumption that parameters are constant [10]. Consequently, estimation algorithms that deal with time-varying parameters are still scarce. In the previous work, we defined an estimation method inspired by the optimization capability of Hopfield neural networks [11], and the convergence of the estimation towards the correct parameter values was proved, under mild assumptions, even in the case of time-varying parameters [12,13]. This method was successfully applied to robotics models and, in the epidemiological context, to the identification of the AIDS/HIV epidemics in Cuba [14,15]. In this work, the estimator is applied to a system defined by a DDE, for which there are few off-the-shelf estimation techniques. Section 3 describes the system identification method by means of Hopfield neural networks, and the way the estimation problem is solved by an optimization method is presented.

The use of neural networks within biomedicine is far from new [16]. Even restricting the search to dengue, neural networks have been used to analyse clinical symptoms of dengue-infected individuals, aiming at predicting the risk [17], and to forecast the day of defervescence [18], which is a critical indicator of the eventual start of the most severe symptoms of Dengue Haemorrhagic Fever. In the more specific context of epidemiological modelling, the number of dengue cases has been predicted by means of an artificial neural network [19]. However, the prediction model was constructed as a black box from climatological data, neglecting the information provided by existing mathematical models. The methodology that is presented in this paper provides a novel and appealing approach to epidemiological modelling, by combining the usage of an estimator inspired by neural networks, with the conventional epidemic models.

The proposal that is presented in this paper is not restricted to the development of a theoretical model, but it also includes the comparison of the model to the available epidemiological data. Several experiments have been carried out in order to assess the validity of the proposal, by using a set of actual statistical data of the epidemic in Havana (Cuba). Firstly, the parameters of the model have been estimated, and the obtained results are discussed. Then, the estimated parameters are substituted into the model, which is numerically integrated, showing an acceptable adjustment to real population data. Finally, the Basic Reproduction Number is computed and the result is interpreted in terms of the evolution of the epidemic, according to the development of fumigation campaigns. Simulation results and their meanings are presented in Section 4, whereas Section 5 summarizes the main conclusions and suggests some direction of future research.

2. Modelling dengue fever in Cuba

2.1. Dengue model equations

Dengue fever is a viral infectious disease mainly transmitted by the *Aedes Aegypti* mosquito. When a mosquito feeds off an infected human, blood containing viruses enters into the digestive system of the mosquito. After a latency period, which is considered to be approximately 8 days long, the virus spreads to the saliva of the mosquito. Then, a subsequent bite to a susceptible human leads to a new infection, whereas mosquitoes are apparently unaffected by the virus. Dengue Fever presents four different strains of the virus. An infected individual acquires immunity along his/her whole life to that particular virus strain. The disease presents a potentially lethal complication called Dengue Haemorrhagic Fever, which is thought to be associated with the infection by different strains of the virus.

As usual in mathematical modelling of infectious diseases, dengue fever epidemics will be modelled by an SIR model, i.e., a compartmental model where the population is divided into individuals who are susceptible (S) to the disease, individuals who are infected (I) and individuals who have recovered (R) and are thus immune to the dengue fever. The SIR model does not account for the existence of different strains of the virus, which is a reasonable assumption in the specific case of dengue in Cuba, since only one strain of the virus should be considered for a single season: this approximation is valid because in Cuba dengue is not an endemic disease and the outbreaks have always remain limited, thus two different strains have never appeared together.[1] Besides, there is no need to consider the mortality caused by dengue fever, because it is mainly caused by Dengue Haemorrhagic Fever, which is an unusual complication in Cuba.

In order to describe dengue epidemics, several SIR models have been previously proposed with varying degree of sophistication [5,6], but the common feature is the definition of populations of susceptible and infected mosquitoes (S_M, I_M), in addition to the human populations (S_H, I_H, R_H). Then, the disease spread can be modelled by the growth of the infected mosquito population, which in turn results in further human infections. However, the expectation to measure even an approximate size of mosquito populations goes far beyond any current procedure. Hence, the sizes of mosquito populations obtained by model simulations cannot be compared to actual data; likewise, identification algorithms cannot be applied to epidemic data in order to estimate the parameters of the model. This is a fundamental shortcoming of usual dengue models, since there is no way to perform quantitative model validation and prediction, because of the lack of data. In the model presented in this work, infections are regarded as occurring directly from an infected human to a susceptible one, rather than explicitly formulating the involvement of vectors. Nevertheless, the whole infection cycle is only accurately represented if the "contagion" is considered to be produced by the "contact" with an individual that belonged to the infected population *in the past*. Therefore, the model comprises the values of the infected

[1] Except for once in a minor outbreak.