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A deterministic model for highly contagious diseases: The case of varicella

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HIGHLIGHTS

- We propose a compartmental model for the spread of Varicella.
- We use real data for the seasonal pattern of infections to fit the model.
- We develop a method to obtain the infectivity parameter from the data.
- We show that infectivity must grow with time in the transient regime.

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ABSTRACT

The classic nonlinear Kermack–McKendrick model based upon a system of differential equations has been widely applied to model the rise and fall of global pandemic and also seasonal epidemic by introducing a forced harmonic infectivity which would change throughout the year. These methods work well in their respective domains of applicability, and for certain diseases, but they fail when both seasonality and high infectivity are combined. In this paper we consider a Susceptible–Infected–Recovered, or SIR, model with two latent states to model the propagation and evolutionary history of varicella in humans. We show that infectivity can be calculated from real data and we find a nonstandard seasonal variation that cannot be fitted with a single harmonic. Moreover, we show that infectivity for the present strains of the virus has raised following a sigmoid function in a period of several centuries. This could allow the design of vaccination strategies and the study of the epidemiology of varicella and herpes zoster.

1. Introduction

In their pioneering work of 1927, Kermack and McKendrick proposed a mathematical model for the evolution of infectious diseases based upon a system of differential equations [1,2]. In the original model three populations where considered: Susceptibles, S, which are healthy but can be infected, Infected, I, which have been communicated the bacteria or virus by contact with another infected individual, and Recovered, R, i.e., those infected individuals who have cleared the disease. The recovered individuals may become susceptible again after a period of immunity, in such a case the model is known with the acronym SIRS. Other combinations: SI, SIS or SIR have been considered. In some cases a state of latency is

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also introduced. Latent individuals are already infected but they have not developed the symptoms of the disease and they are usually not infectious or their infectiveness is reduced.

A characteristic of many infectious diseases is that they show seasonal patterns. Some examples are: Influenza [3], Respiratory Syncytial Virus or RSV [4,5], Rotavirus disease [6] or varicella [7]. The factors of this seasonal behavior are still unknown in many cases [8] and it is believed that several concurrent agents may be acting. Seasonality of infections by RSV have been associated to meteorological factors [9] such as temperature or humidity but also to ultraviolet radiation [10]. Dushoff et al. proposed a dynamical resonance mechanism for the amplification of oscillations in influenza pandemic [11], later on Acedo et al. discussed the emergence of seasonal behavior in network models without external forcing [12]. Production of Vitamin D has also been studied as a possible immunity factor in the seasonal variations of influenza [13]. In any case, it is still unclear what of these factors are direct causes of seasonality instead of mere correlates.

Concerning models based upon coupled differential equations and for the purpose of capturing the seasonal behavior, it is usual to introduce a forcing term in the transmission [4,5]. This term takes the form:

$$b = b_0 + b_1 \cos\left(\frac{2\pi t}{T} + \phi\right), \tag{1}$$

where $T = 1$ year, t is the time passed since the beginning of the year, usually measured in weeks, and ϕ is an offset phase to be deduced by fitting the real data. This oscillatory forcing of the infectivity allows very reasonable fitting for the epidemiological data of RSV [4,5] but it do not work for other highly contagious diseases as we will see in this paper and, in particular, for varicella, where b must be deduced from the incidence of the disease if any reliable fitting is to be found.

varicella is a highly contagious disease caused by the varicella Zoster Virus (VZV) [7,14,15]. This virus is the responsible for both varicella and Herpes Zoster and it has a very high prevalence in populations all around the world. varicella affects mostly children and, in most cases, it is a benign infection. Occasionally may complicate but it has a low death rate. However, it is more severe in adults [14].

The experiment we are going to perform will start retrieving and preparing data of varicella cases, then a simple model will be built. Furthermore, we will develop a procedure to calculate the values of the weekly transmission rate b_t. Thus, on the one hand we will see that the growing of the transmission rates of any year can be written as the transmission rates in the year 1 (base case) by a sigmoid function. On the other hand, we will prove that the approximation of the transmission rates b_t by a cosine seasonal forcing term as $b_0 + b_1 \cos(\frac{2\pi t+\phi}{52})$ will lead to a good approximation at the beginning but deteriorating soon as the time goes on.

We will show that the transmission rate follows the same pattern over the years and that the scale increases following a sigmoid behavior. Also, we show that, sometimes, it is not possible to capture the seasonal behavior using seasonal forcing terms in the transmission term and other strategies should be used. We will illustrate this using data of varicella incidence.

The problem we are discussing is known in the literature as the inverse problem in epidemiology, i.e., to find the forcing term from epidemiological data [16]. In a recent work, Marinov et al. have proposed a generalized least square method to find optimum values for the infectivity and recovery rates. However, these values are assumed to be constant over the whole interval as they apply their method to a short outbreak of influenza instead of considering the long term evolution of a pandemic. A similar method was used by Leecaster et al. [17] to study the variations from one year to another of the incidence of respiratory syncytial virus (RSV) infections. The problem of the seasonal variations of RSV has motivated many studies in which a relation to social factors, such as school terms, or weather data is considered [4]. But none of these factors is clearly statistically significant in the oscillations of the incidence of the disease. For these reasons, Novotni and Weber proposed a stochastic optimization method to deduce the infectivity function, $\beta(t)$, from the incidence data. They find that the dynamics of RSV can be modeled as "noisy limit cycles". A similar idea was proposed by Keeling et al. [18] to achieve an explanation of the seasonality in measles and whooping cough as a consequence of a contact rate governed by school terms.

The case of the inverse problem for highly contagious diseases, such as varicella, is marked by a particular difficulty because every year a large proportion of the cohort of children is infected. As a consequence the transmission rate becomes very large and, apart from the seasonal variations, we must also study the increase of the transmission rate year after year in such a way that a stationary state is finally achieved. Starting from an initial state with no recovered individuals we deduce the transmission rate from a deterministic recursive method. The process is repeated for the following years until a stationary seasonal infection rate is obtained. The results could then be used in the simulation of vaccination strategies for which a systematic modeling is still lacking.

To achieve these objectives we propose a new compartmental model with two latent states of one week duration. By using this model to fit the incidence data of varicella we estimate a non-sinusoidal temporal forcing term. We show that the infectivity rate must rescale year after year keeping its seasonal variations to allow the survival of the varicella strains. Moreover, it is found that the global prefactor for the infectivity is a sigmoid function and that the evolution to the stationary state takes four centuries, at least. This is compatible with the known large history of the varicella-zoster virus (VZV) [19].

The paper is organized as follows. In Section 2 we describe the retrieval and preparation of the data for varicella. In Section 3, we describe the model building. In this section we also state a procedure to calculate the variable transmission rates b_t and study the patterns they follow. In Section 4, we show that a seasonal forcing term does not perform as well as the variable transmission rates. Finally, in Section 5, we present the conclusions.

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