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Letter to Editor

Recurrence conditions for childhood infections

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ABSTRACT

The classic endemic model is used by Kuske et al. (2007) to study recurrence of childhood infections, which is a well-known but not well understood phenomenon. The conditions for recurrence that they derive are shown to agree with conditions for persistence.

1. Introduction

Childhood infections in large populations tended to recur with a remarkable regularity before the time when large scale vaccination was administered. This fact has posed a large challenge to mathematical modellers over a long time. There is a strong need to understand the mechanism that causes this behavior. It has been known since the time of Hamer (1906) and Soper (1929) that one needs to account for both demographic changes in the population of human hosts and the influence of infection and recovery to study this phenomenon. The search for further insight has proceeded on two different paths, one deterministic and the other one stochastic. Deterministic modellers have noted that their models predict that the number of infected individuals approaches an endemic infection level through damped oscillations, and that the damping does not agree with observations. Therefore, they have argued that additional factors need to be introduced in order to produce undamped oscillations. Review papers are given by Hethcote and Levin (1989) and by Bauch (2008). In addition to models with periodic forcing, one has studied models with delays, models with nonlinear incidence, models with variable population size, models with age structure, models with varying distributions of latent and infectious periods, models with chaos, and models with quarantine.

A completely different path, namely the stochastic one, was opened by Bartlett (1956). He suggested that a fully stochastic model would account for the observed recurrence of childhood infections, without any additional factors. He supported this suggestion by numerical simulation of a model that accounted for infection and recovery, and also for inflow of uninfected individuals, corresponding to a demographic force. Fifty years later, Bartlett's remarkable intuition in this regard has been beautifully supported by the model analysis given by Kuske et al. (2007). Their model is similar to the one used by Bartlett, but not identical. One important result in their paper is given by two criteria for the occurrence of sustained oscillations.

These criteria can be given simpler forms by careful treatment of the parameter space. The main aim of the present note is to derive these simplified expressions. The rather long discussion by Kuske et al. of the parameter ranges where the two criteria for sustained oscillations are satisfied can be materially shortened by use of our simplified expressions. We give also a slight improvement of the analysis of the deterministic version of the model.

The recurrence in the model is caused by demographic stochasticity sustaining nearly periodic oscillations. This phenomenon is called coherence resonance, as described by Kuske et al. (2007).

2. The model

The model analyzed by Kuske et al. was termed "the classic endemic model" by Hethcote (2000). Its deterministic version was analyzed by Hethcote (1974), while its stochastic counterpart was used by Nåsell (1999, 2005), in studying infection persistence and extinction times and the associated so-called critical community size. The model takes the form of a bivariate Markov chain $\{(S(t),I(t))\}$, where $S(t)$ stands for the number of susceptible individuals, and $I(t)$ for the number of infected individuals at time t.

This stochastic process is based on the hypothesis that the four transitions listed in Table 1 take place with the rates listed. The model contains four parameters, namely the expected population size N, the death rate per individual μ, the contact rate β, and the recovery rate per infected individual γ.

It is important for the analysis to carry through a reparametrization based on dimensional analysis and scaling. The method is known to be very useful for deterministic models in physics. It is discussed by Lin and Segel (1974), while its application to population biology models is described by Nåsell (1985). In this latter reference it is argued that population sizes, even though they are free from physical dimension, have what can be called "quasi-dimension". The desirability of non-dimensionalization is stressed. This is achieved by scaling that introduces parameters and state variables in the deterministic version of the model that are free of both physical dimension and quasi-dimension. Any parameter that can be eliminated by the simple expedient of scaling either a state variable or the independent variable representing time is called "innocent", while all other parameters are called "essential". These ideas are discussed by Nåsell (2002).

Kuske et al. introduce a dimensionless version of the model they study, but they do not pursue the nondimensionalization of the parameter space in a consistent way.

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Table 1
Transition rates for the stochastic version of the classic endemic model.

Transition	Transition rate
$(S,I)\to(S+1,I)$	μN
$(S,I)\to(S-1,I)$	μS
$(S,I)\to(S-1,I+1)$	$\beta SI/N$
$(S,I)\to(S,I-1)$	$(\mu+\gamma)I$

We reparametrize as in Nåsell (1999, 2005) by defining R_0 and α as follows:

$$R_0=\frac{\beta}{\gamma+\mu},\quad \alpha=\frac{\gamma+\mu}{\mu}. \tag{1}$$

Both of these parameters are free of dimension, and therefore independent of units of measurement. The first of these two new parameters, R_0, is referred to as the basic reproduction ratio. It serves the important role of identifying the threshold of the deterministic version of the model at $R_0=1$. The second of the two parameters, α, is the ratio of average life length to average duration of infection. Therefore, α is large for common childhood infections. As an example, we note that α for measles in a developed country is about 3500, where the average life length is $1/\mu=70$ years, and an infection lasts on the average about one week. The definition of R_0 is also given by Kuske et al., but they do not define α. In what follows, we shall use R_0 and α, but not β or γ.

After the reparametrization we still have four parameters, namely N, R_0, α, and μ. Among these parameters, we note that μ is innocent, since it can be eliminated by rescaling of time. Its inverse $1/\mu$ serves as a natural time unit for the model. Its value clearly depends on the time unit chosen. We shall find that the conditions for recurrence are independent of μ, and therefore independent of the time unit. Furthermore, N is innocent for the deterministic model, but not for the stochastic one. The two new parameters, R_0 and α, are free of quasi-dimension, but N and μ are not. In the analysis of the stochastic version of the model, we use the facts that both N and α are large.

In the analysis of this model by Nåsell (1999, 2005), approximations of the quasi-stationary distribution and of the time to extinction are derived. It is noted that qualitatively different results are obtained in three separate parameter regions. The identification of these regions makes use of a reparametrization that is expressed with the aid of a parameter ρ, defined as follows:

$$\rho=\frac{\sqrt{(R_0-1)N}}{\alpha}. \tag{2}$$

The three parameter regions are defined using asymptotic concepts as $N\to\infty$. Thus, there are two regions defined by $R_0>1$ and $R_0<1$, respectively, as $N\to\infty$, and a third region, called the transition region, defined by requiring that $\rho=\mathrm{O}(1)$ as $N\to\infty$. We note from the definition of ρ that $R_0\to1$ as $N\to\infty$ in the transition region. We note also that $\rho\to\infty$ as $N\to\infty$ in the region where $R_0>1$. This parameter region leads to a normal distribution of the marginal distribution of infected individuals in quasi-stationarity and to a large time to extinction. This is therefore the parameter region of interest in the study undertaken by Kuske et al. (2007).

3. The deterministic version of the model

The deterministic version of the model leads to the following system of differential equations for the state variables S and I:

$$S'=\mu N-\frac{\alpha\mu R_0}{N}SI-\mu S, \tag{3}$$

$$I'=\frac{\alpha\mu R_0}{N}SI-\alpha\mu I. \tag{4}$$

Note that we use the essential parameters R_0 and α here, and not the original rates β and γ. The equations also contain the innocent parameters N and μ. Both of them can be eliminated by using the scalings introduced by Kuske et al. and given below.

The system of differential equations above has two critical points, namely $(N,0)$ and (S_{eq},I_{eq}), where the coordinates of the second of these points are defined as follows:

$$S_{eq}=\frac{N}{R_0}, \tag{5}$$

$$I_{eq}=\frac{(R_0-1)N}{\alpha R_0}. \tag{6}$$

The first of these critical points corresponds to absence of infection, while the second one corresponds to an endemic infection level provided $R_0>1$. Bifurcation occurs at $R_0=1$, where the deterministic model has a threshold. The solutions of the deterministic model approach the endemic infection level (S_{eq},I_{eq}) as $t\to\infty$ if $R_0>1$ and $I(0)/N>0$. For realistic parameter values, these solutions show damped oscillations.

We follow Kuske et al. and introduce the dimensionless state variables

$$u=\frac{S-S_{eq}}{S_{eq}}, \tag{7}$$

$$v=\frac{I-I_{eq}}{I_{eq}}. \tag{8}$$

Applying these scalings in (3) and (4) will lead to elimination of N, which is an innocent parameter for the deterministic version of the model.

Furthermore, we define

$$\omega=\sqrt{\alpha(R_0-1)-R_0^2/4} \tag{9}$$

and

$$\Omega=\mu\omega, \tag{10}$$

where Ω is the angular frequency of the damped oscillations with which the solutions of the deterministic model approach the endemic infection level. We note that Kuske et al. also use Ω to denote this angular frequency, but that the expression they use for Ω is an approximation, while our expression is exact. Clearly, Ω has the same dimension as μ, while ω is free of dimension. Note also that ω is large, since α is.

We use Ω to define a dimensionless time s by setting

$$s=\Omega t. \tag{11}$$

The deterministic model for the scaled state variables u and v as functions of the scaled time s leads to the following system of differential equations:

$$\dot u=-\frac{R_0}{\omega}u-\frac{R_0-1}{\omega}(v+uv), \tag{12}$$

$$\dot v=\frac{\alpha}{\omega}u+\frac{\alpha}{\omega}uv, \tag{13}$$

where derivatives with respect to s are denoted by a dot. Note that this system of equations contains only two parameters, namely the two essential parameters R_0 and α.

We shall in particular be interested in the linearization of this system of differential equations about $u=0$ and $v=0$. The linearized system can be written as follows:

$$\begin{pmatrix}\dot u\\ \dot v\end{pmatrix}=\mathbf{M}\begin{pmatrix}u\\ v\end{pmatrix}, \tag{14}$$