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A STOCHASTIC MODELING OF RECURRENT MEASLES EPIDEMICS

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ABSTRACT
A simple stochastic mathematical model is developed and investigated for the dynamics of measles epidemic. The model, which is a multi-dimensional diffusion process, includes susceptible individuals, latent (exposed), infected and removed individuals. Stochastic effects are assumed to arise in the process of infection of susceptible individuals. Using the best currently available parameter values, the intrinsic variability in response to a given initial infection is examined by solving the stochastic system numerically. The results of the simulation seem to agree with the historical pattern of measles in Nigeria.

***Keywords*:** Stochastic model, measles, epidemiology, Wiener process, Euler scheme.

INTRODUCTION

Infectious diseases pose a great challenge to both humans and animals world-wide. Control and prevention are therefore important tasks both from a humane and economic point of views. Efficient intervention hinges on complete understanding of disease transmission and persistence (Finkenstadt *et al*., 2002). Dynamic modeling of diseases has contributed greatly to this (Anderson & May, 1991). In this work we focus on measles, a childhood disease.

Measles is a viral respiratory infection that attacks the immune system and is so contagious that any person not immunized will suffer from the disease when exposed. Measles virus causes rash, cough, running nose, eye irritation and fever. It can lead to ear infection, pneumonia, seizures, brain damage and death (WHO, 2005). Children under five years are most at risk. Measles infects about 30 to 40 million children each year and causing a mortality of over 500,000, often from complications related to pneumonia, diarrhea and malnutrition (WHO/UNICEF, 2001). Survivors are left with life-long disabilities that include blindness, deafness or brain damage.

Available records revealed that in 2003 alone, 530, 000 deaths were recorded in the world as a result of measles (WER, 2005). Despite the availability of measles vaccine for more than 40 years, many regions of the world are still being plagued by the disease. In 1989, the World Health Assembly set specific goals for the reduction in measles morbidity and mortality (WHO, 1990), resulting in the WHO/UNICEF measles mortality reduction and regional elimination strategic plan (WHO, 2005). Majority of measles deaths occur in 14 countries where immunization coverage for children was reported to be less than 50 %.

In 2005, measles killed more than 500 children in Nigeria. Of the 23,575 cases recorded in 2005, more than 90% were in Northern Nigeria, where people are wary of vaccinations largely for religious reasons (WHO, 2005). Because measles is both an epidemic and endemic disease, it is difficult to accurately estimate its incidence on the global level, particularly in the absence of reliable surveillance systems. Although many counties reported the number of incident cases directly to WHO, the heterogeneity of these systems with differential underreporting does not permit an accurate assessment of the global measles incidence. In view of these difficulties, models have been used to estimate the burden of measles.

Stochastic (probabilistic) reformulation of the theoretical model for recurrent measles epidemics originally put forward by Soper (1929) emphasized two important features of the stochastic model. One was that in large communities the theoretical tendency of the successive epidemics to damp down could be offset by random variability, and thus gives some possibility of representing actual statistics of measles incidence. The second was the tendency in small communities for the infection to die out when the number of susceptibles had dropped below its threshold value (Bartlett, 1960). Stochastic event-driven model best captures the robust nature of the critical community size and the associated pattern of fade-outs in childhood diseases. However, persistence of real world system is an emergent phenomenon and arises from the interaction between dynamics and stochasticity. Such phenomenon cannot be built into a model *a prior* and can only be determined by repeated simulation (Keeling & Grenfell, 2002).

This paper reports the result of a study on the spread of measles infection within the Nigeria population as a function of time. We intend to answer the question "under what condition does a small amount of initial infection invade an almost entirely susceptible population? And how does stochasticity in the fate of susceptible and infected individuals translates into uncertainty in epidemic projections and how can the uncertainty be characterised?

DESCRIPTION OF THE MODEL

The mathematical modeling of many real-life phenomena by means of random noisy perturbation are not possible by ordinary differential equations (ODEs), and hence are often modeled by using stochastic differential equations (SDEs) in order for the model to be realistic. In this section we model the dynamics of measles epidemic using coupled autonomous Ito SDE of the form:

$$dX(t) = g_0(X(t))dt + g_1(X(t))dW(t), \qquad X(t_0) = X_0, \ \ t \in [t_0\, T], \quad \ldots(1)$$

where g_0 and g_1 are real-valued functions and $W(t)$ is one dimensional standard Wiener process and the solution $X(t)$ is Ito process. We consider an epidemic model of type SEIR where the process of disease spread is such that the population can be divided into four distinct classes. Let S (t) be the number of uninfected, susceptible individuals at time t. The distinction is made between those infected individuals which do not immediately participate in infection called latently infected individuals and denoted by E(t) and actively infected individuals which are involved in transmission of the disease and which are denoted by I (t). Finally, we let R(t) denotes the number of individuals who have been infected and then removed from the possibility of being infected again or of spreading infection. Removal is carried out either through isolation from the rest of the population or through immunization against infection or through recovery from the disease with full immunity against re-infection or through death caused by the disease. We assume that the probability of an individual to undergo the infection process is proportional to the time interval, (t, t + δt), if the interval, δt, is sufficiently small. The probabilities of two or more transition to take place are zero during the time interval (t, t + δt), so that at most one transition occurs during this period. We assume that individuals in the susceptible class have the same probability of contacting the infected individuals and therefore, have the same probability of transiting to the exposed class.

Similarly, the individuals in the exposed and infected class have the same probability of being converted to the infected and removed classes respectively.

Variables and parameters

t Time in years since initial infection
S Individuals who are not infected but at the risk of infection
E Latently infected individuals who are not participating in infection
I Actively infected individuals who are involved in spreading the disease
R Individuals who have been removed by recovery, death or quarantine
μ Birth rate and death rates
β(t) Infection rate at time t.
γ Removal rate of infected individuals
v Rate at which latent individuals move to infected class
θ Proportion vaccinated
N Total population size.

In the following, upper case letters will be used to signify random variables and random processes. Then in (t, t + δt), let the change in the susceptible individuals be δS. Then if δt is small enough there are, in a simplified approach, two possibilities that δS is −1, with probability $\mu S\delta t$, or $\delta S = (\mu(1-\theta)N - \beta(t)SI)\delta t$ with probability 1 − β S I δt. Here β(t) is representing the probability per unit time per infected individual of a successful infection of a susceptible individual at time t. Similarly, one can evaluate the random changes δE, δI and δR in the latently, actively infected individuals and removed individuals respectively. Although the numbers of individuals are whole numbers, one may make continuous approximations for the various components. In a stochastic model, this can be done by determining the first and second infinitesimal moments of the components to obtain diffusion. In this approximation the components satisfy the following stochastic differential equations which are similar to well known deterministic models but with additional noise terms:

$$\begin{cases} dS = (\mu(1-\theta)N - \beta(t)SI - \mu S)dt + G_1 dW - G_2 dW - G_3 dW \\ dE = (\beta(t)SI - (\mu+\nu)E)dt + G_2 dW - G_4 dW - G_5 dW \\ dI = (\nu E - (\mu+\gamma)I)dt + G_5 dW - G_6 dW - G_7 dW \\ dR = (\theta\mu N + \gamma I - \mu R)dt + G_7 dW + G_8 dW - G_9 dW. \end{cases} \quad \ldots \quad (4)$$

Where $G_1 = \sqrt{\mu(1-\theta)N}; G_2 = \sqrt{\beta(t)SI}; G_3 = \sqrt{\mu S}; G_4 = \sqrt{\mu E}; \ G_5 = \sqrt{\nu E}; G_6 = \sqrt{\mu I}; G_7 = \sqrt{\gamma I} \ \ G_8 = \sqrt{\theta\mu N}$ and $G_9 = \sqrt{\mu R}$.

Here W is a standard Wiener process (i.e. mean 0, variance t at time t). Stochastic effects arise by virtue of the nature of interaction between susceptible and infected individuals. The parameter γ can be interpreted as the reciprocal of the mean infectious period. We generally assumed the per capita birth and death rates are equal and we denote by μ . The transmission rate is the product of the rate of contact among individuals and the probability that a susceptible individual who is contacted by an infectious individual will become infected. But the contact is not constant throughout the year. To see that, consider the fact that in the absence of vaccination, the average age at which a person is infected with measles is about 5 years (Earn, 2004), hence most susceptible are children. Children are in closer contact when school is in session, so the transmission rate varies seasonally. A crude approximation of this seasonality is to assume that β varies sinusoidally,

$$\beta(t) = \beta_0(1 + \beta_1 \cos 2\pi t). \quad \ldots \quad (3)$$

Here, β_0 is the mean transmission rate, β_1 is the amplitude of the seasonal variation and the time t is assumed to be measured in years. We incorporate the chance mechanism in the solutions by simulation as follows. Let S_n, E_n, I_n, R_n approximate the corresponding continuous variables at time $t = n\delta t$ where $n = 0,1,2,\ldots$. Then, we put

$$\begin{cases} S_{n+1} = S_n + (\mu(1-\theta)N - \beta(t)S_nI_n - \mu S_n)dt + \sqrt{\mu(1-\theta)N}\,dW_n - \sqrt{\beta(t)S_nI_n}\,dW_n - \sqrt{\mu S_n}\,dW_n, \\ E_{n+1} = E_n + (\beta(t)S_nI_n - (\mu+\nu)E_n)dt + \sqrt{\beta(t)S_nI_n}\,dW_n - \sqrt{\mu E_n}\,dW_n - \sqrt{\nu E_n}\,dW_n, \\ I_{n+1} = I_n + (\nu E_n - (\mu+\gamma)I_n)dt + \sqrt{\nu E_n}\,dW_n - \sqrt{\mu I_n}\,dW_n - \sqrt{\gamma I_n}\,dW_n, \\ R_{n+1} = R_n + (\theta\mu N + \gamma I_n - \mu R_n)dt + \sqrt{\theta\mu N}\,dW_n + \sqrt{\gamma I_n}\,dW_n - \sqrt{\mu R_n}\,dW_n. \end{cases} \quad \ldots \quad (4)$$

Equations (4) together provide a scheme for approximating solutions of the basic SEIR SDEs model.

SIMULATIONS

Many phenomena of interest in biology can be modeled by the use of diffusion processes satisfying a stochastic differential equation. In most cases exact solutions for such models are not available and it is advantageous to proceed via computer simulations. For instance, our SEIR SDEs cannot be solved to obtain formulae for the functions $S(t), E(t), I(t)$ and $R(t)$. Yet the epidemic curves that we are trying to explain are essentially given by $I(t)$, so it is hard to proceed without it. We therefore solved the model numerically using MATLAB (The Math works Inc., 2005). The time period for solution was 1980 < t < 2007 where $t = 0$ implies January, 1980. The equations were solved with the assumption that fifty percent of the population had been vaccinated to establish 'low control' pattern of epidemics. We used a total population of 69,629,000 corresponding to Nigeria population in 1980 (US Census Bureau, 2004) and employed values for the parameters that are currently available. We took $I(0) = 162106 \times (5/365)$ (the number of reported cases as a proportion of the length of the year) and $S(0) = 0.65N$, then we obtain the epidemic curve plotted in figure 3. We incorporated births per unit time and natural mortality rate μ (per capita) and since the time scale for substantial changes in birth rates (decades) is generally much longer than a measles epidemic (after few months), we assumed that the population size is constant.

For measles, estimates that are independent of the case report data indicates that the mean infectious period γ is 52 year^{-1} and the basic reproductive number R_0 is 18 (McLean, 1994) for Africa. Following Tobias & Roberts (1998), we estimated disease transmission coefficient as $\beta = 2.005 \times 10^{-4}\ year^{-1}$ and $\beta_1 = 0.11$. The initial value of μ follows from the assumption that net birth rate is equal to μN. Since we assumed a constant population size over the lifetime of the epidemic, we estimated $\mu = 0.039$ from the information on population of Nigeria in 2002 (US Census Bureau, 2004) (the first year for which we have data on net birth rate and total population size). We pecked $\theta = 0.5$ corresponding to the information available to us on measles vaccination in Nigeria (WHO/UNICEF, 2001). These

parameter values produced a reasonable agreement between the occurrence of epidemics and the observed historical pattern (WHO/UNICEF, 2008). The only difference being that stochastic extinctions and re-emergence of epidemic can be clearly seen in the simulated model (Fig.1). This can be attributed to the fact that the time scale of the epidemics as structured in months gives room for clear manifestation of extinction and re-emergence scenarios.

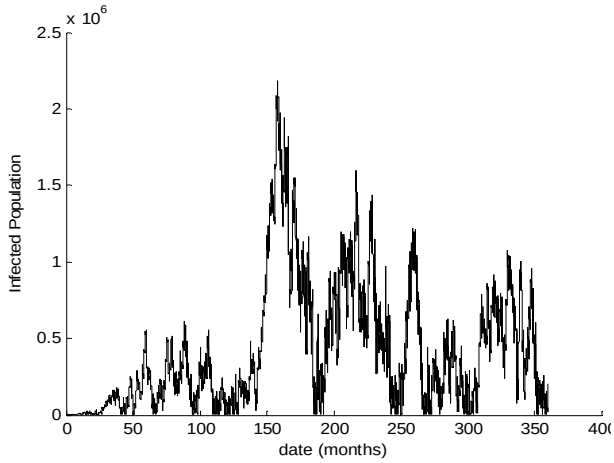

FIG. 1. MONTE CARLO SIMULATION OF MEASLES EPIDEMICS IN NIGERIA.

DISCUSSION

We simulated an SEIR stochastic differential equation model using the Euler scheme involving normal pseudo random numbers. The choice of using a discrete-time model to investigate measles dynamics is motivated by the fact that the distributions of latent and infectious periods are closer to a constant than to an exponential distribution and from the discrete nature of data available. Our objective is to estimate the time course of the dynamics of measles epidemic in Nigeria. In constructing the model we have assumed an unchanging population size and structure, with a constant birth and death rates. Figure 1 shows the Monte Carlo realization of the sample paths for the infected population. A 100,000 Monte Carlo realisation of the process were computed for the period of 360 months or 30 years. From the stochastic evolution of the epidemic, two patterns are noticeable: local extinctions and recurrence. However, there is the absence of clear pattern of measles oscillations. The results of model simulation point to the usefulness of stochastic modeling of the cases of measles generally and Nigeria in particular. We have seen that even in the face of low immunization coverage, the epidemic curve can be estimated in a meaningful way that can help public health workers. For instance, intensive immunization campaign within the population at risk to infection can avert the possibility of re-emergence of measles in 2009. However, there is a possibility of stochastic 'fade-outs" in 2010. We also observed that the dynamics of measles in Nigeria is generally characterized by underestimation in some years.

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