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Small amplitude, long period outbreaks in seasonally driven epidemics

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Abstract. It is now documented that childhood diseases such as measles, mumps, and chickenpox exhibit a wide range of recurrent behavior (periodic as well as chaotic) in large population centers in the first world. Mathematical models used in the past (such as the SEIR model with seasonal forcing) have been able to predict the onset of both periodic and chaotic sustained epidemics using parameters of childhood diseases. Although these models possess stable solutions which appear to have the correct frequency content, the corresponding outbreaks require extremely large populations to support the epidemic. This paper shows that by relaxing the assumption of uniformity in the supply of susceptibles, simple models predict stable long period oscillatory epidemics having small amplitude. Both coupled and single population models are considered.

Key words: Chaos – Nonlinear coupled oscillators – Epidemiology – Dynamics

1 Introduction

It is now well documented that childhood diseases which incur permanent immunity oscillate periodically, as well as exhibit chaotic behavior (Hethcote 1983; London and Yorke 1973; Yorke and London 1973; Schaeffer 1985; Yorke et al. 1979). Examples of such diseases are chickenpox, measles, and mumps. Another example of a disease which exhibits strong oscillations but does not fit exactly into the framework of the other childhood diseases is rubella, which exhibits outbreaks with periods as long as seven years. One common feature each of the abovementioned diseases has is that they have a maximum peak in their respective power spectrum of 1 year, which is reflected in the fact that peak-to-peak outbreaks have local maxima separated by one year. This annual behavior in childhood disease has been linked to the opening and closing of schools in the various cities (London and Yorke 1973; Fine and Clarkson 1980).

Given that the childhood diseases all have an annual seasonal component, spectral analysis reveals that their outbreaks can exhibit a widely varying range of longer interepidemic periods. In measles, periods on the order of 2–3 years have been observed. Mumps exhibits periods from 3–4 years, while rubella has been observed to have interepidemic outbreaks of 5–7 years. Chickenpox is the only disease which seems to exhibit a unique annual peak in its power spectrum corresponding to interepidemic outbreaks of 1 year (Olsen et al. 1990).

When the diseases are examined with respect to their incidence data as a time series, further analysis may be done to see what kind of recurrent behavior the populations produce. For example, measles in New York City in the pre-vaccine years has been observed as a biennial cycle, with two year interepidemic peaks separated by what appears to be noise (London and Yorke 1983). In Baltimore, where the population is much smaller than that of New York City, measles appears to have peak cases separated by either 2 or 3 years, where the large peak-to-peak years appear as a random sequence. So depending upon the population size and structure, measles can exhibit periodic or aperiodic behavior. Further analysis, using embedding techniques by Olsen et al. (1990) and Schaeffer and Kot (1985), reveals that measles can exhibit chaotic outbreaks based on a fundamental frequency. Their analysis suggests that the noise appearing between peaks in the outbreaks may be dominated by a deterministic process. Sugihara and May (1990) have further analyzed the data by computing decorrelation times for diseases such as measles and chickenpox by employing embedding techniques as well, and find that the data appear to be generated by a deterministic process. That is, the data have correlation times longer than that of randomly generated data. Other diseases, such as mumps, also have characteristics of chaotic behavior, whereas chickenpox appears to be periodic with additive noise (Olsen et al. 1990).

In summary, several important but common features can be distinguished for the childhood disease data:

1. There is always an annual component in the power spectrum. This means that there must be a seasonal driving force.

2. Most childhood diseases contain several periods.

3. These diseases (with the exception of rubella) induce lifelong immunity. There is no feedback mechanism from the recovered individuals to the susceptibles.

4. Subharmonic spectral peaks are observed in both large and small populations in the Western world. The behavior may be periodic with additive noise or chaotic with fundamental spectral peak.

Modelling periodic outbreaks in epidemics has been a central point of research in biomathematics. (For example, see Bailey 1975; Hethcote 1983, 1991; Hethcote et al. 1981; Anderson and May 1979, 1982; Dietz 1976.) From a modelling point of view, much of the observed phenomena can be qualitatively seen in very simple models. One model we have studied in great detail is called the SEIR model (Schwartz and Smith 1983; Schwartz 1985; Schwartz 1989). For many childhood diseases, the epidemiology is well known. Latent and infectious periods are known to very good accuracy. Other population dependent parameters, such as contact rates, birth rates, and death rates, are measured indirectly or are not known explicitly as functions of population size or time. However, given such a simple model SEIR model, many types of subharmonic and chaotic behavior may be observed for reasonable choices of parameters.

For models based upon the SEIR model, it has been proven that attracting subharmonic outbreaks of all periods may be found (Schwartz and Smith 1983). However, these subharmonics possess a very large peak outbreak in infectives and require a very large population to prevent all of the infective individuals from disappearing, causing the outbreak to disappear. This is unsatisfactory, since many of the characteristic subharmonics are observed in populations having sizes orders of magnitude smaller than those predicted by the models. The main question addressed in this paper is the following: Can small population centers support long period based outbreaks?

Since the most of the epidemiological parameters are well known, one method of modelling the epidemic is to examine the population structure. By assuming that populations can be grouped such that a large population center is connected with smaller population centers, models can be constructed which weakly couple several SEIR models together, each possessing different types of subharmonics. One main result of this paper is the following. Assume there are two population centers, one supporting a small annual cycle and the other supporting a large subharmonic cycle. Then weakly coupling the populations yields recurrent outbreaks which are small amplitude subharmonic outbreaks. By using the coupled population model as a paradigm, an immediate corollary follows which shows that a single population model can produce small amplitude/long period based behavior. This results from allowing the rate of input of susceptibles to be nonuniform in time, which is a more realistic assumption than having a constant input stream of susceptibles.

The layout of the rest of the paper is as follows. Section 2 describes and quickly reviews the basic properties of the SEIR epidemic model. The kinds of subharmonic behavior which can be sustained by the model will be given, and a perturbation analysis of the size of peaks will show how large a population is needed to sustain the epidemic. Section 3 describes the coupling of the SEIR models, and Sect. 4 illustrates numerically that small amplitude long period subharmonic behavior exists due to the weak coupling of the population centers. Section 5 will describe a simple modification to the single population model which demonstrates how small amplitude/long period based outbreaks can be achieved. Section 6 will discuss the qualitative aspects of the data for a few select cases, and compare them with the model. Section 7 summarizes the results, and reviews future work which needs to be done.

2 The SEIR model

2a Model derivation

We follow the assumptions and notation of Schwartz and Smith (1983). The reader should consult that paper for further details. Suppose the population is divided into four groups, each a function of time, t: **Susceptibles $S(t)$, Exposed $E(t)$, Infectives $I(t)$, Recovered $R(t)$**. For a disease which incurs permanent immunity, a unique path through each stage of the disease may be described. At birth, after an infant sheds its natural immunity, that individual becomes susceptible to the disease. Once that individual becomes susceptible, there is a probability of coming in contact with a member of the infective class. Since childhood diseases are easily transmitted, we suppose one contact is sufficient for the virus to spread, and the individual becomes exposed. After a period of latency, the exposed individual becomes infectious, and is now a member of the infective class. The infective member in turn enters the recovered class after a mean infectious period has lapsed, and remains in the recovered section until death.

The SEIR model describing the rate of change of each of the classes can now be written down:

$$\begin{aligned} S' &= \mu(1 - S) - \beta(t)IS \\ E' &= \beta(t)IS - (\mu + \alpha)E \\ I' &= \alpha E - (\mu + \gamma)I \\ R' &= \gamma I - \mu R \end{aligned} \tag{2.1}$$

In Eq. (2.1) we have made the assumptions that the population is uniformly mixing and of constant size. In particular, we assume the population is normalized to unity. The birth and death rates, μ, are equal, and $1/\alpha$ $(1/\gamma)$ is mean latent (infectious) period. The birth and death rates are also assumed to be constants, which will be relaxed later. The contact rate, β, is defined as the average number of effective contacts with other individuals per infective per unit time. By effective contact we mean contact between a susceptible and an infective in which the disease is transmitted. Seasonality is incorporated by allowing β to fluctuate periodically as a function of time; i.e., we assume $\beta(t) = \beta_0(1 + \delta \cos 2\pi t)$, where $0 \leqslant \delta < 1$. This is the mechanism which simulates the annual behavior of the outbreaks which appear so regularly in the data (London and Yorke 1973; Yorke and London 1973; Fine and Clarkson 1980), as well as in the spectral analysis.

2b A transformed model

In order to show how large the populations must be to support and epidemic modelled by Eq. (2.1), we need to transform the model and introduce a small parameter. When $\delta = 0$, Eq. (2.1) has two steady states given by (1, 0, 0, 0,) and $(S_c, E_c, I_c, R_c) = (1/Q, \quad (\mu + \gamma)I_c/\alpha, \quad \mu(Q-1)/\beta_0, \quad 1 - S_c - E_c - I_c)$. (See Schwartz, 1985 for details.) The reproductive rate of infection, Q, is a measure of the number of new cases generated by introducing one infective in a pool of susceptibles in one infectious period. The epidemic is sustained only if $Q > 1$. If $Q < 1$, the epidemic dies out and the number of infectives asymptotes to zero.

We indroduce a small parameter called the force of infection, ε, by setting $\varepsilon = \mu(Q - 1) > 0$. Following the transformations used in Schwartz and Smith (1983), Eq. (2.1) now becomes the following system:

$$\begin{aligned} \bar{x}' &= -\nu\bar{y} + \varepsilon f_1(\bar{x}, \bar{y}, \bar{z}, t, \varepsilon, \delta) \\ \bar{y}' &= \nu\bar{x}(1 + \bar{y}) + \frac{\nu\Delta_3\bar{x}\bar{z}}{\Delta_2 + \Delta_3} + \nu^2\delta \cos 2\pi z\left(1 + \bar{y} + \frac{\Delta_3\bar{z}}{\Delta_2 + \Delta_3}\right) \\ &\quad + f_2(\bar{x}, \bar{y}, \bar{z}, t, \varepsilon, \delta) \\ \varepsilon\bar{z}' &= -(\Delta_2 + \Delta_3)\bar{z} + \varepsilon f_3(\bar{x}, \bar{y}, \bar{z}, t, \varepsilon, \delta), \end{aligned} \tag{2.2}$$

where the f_i are periodic in t with period 1, and $f_i(0, 0, 0, t, 0, 0) = 0$, $i = 1, 2, 3$. Notice that when $\delta = 0$, the endemic steady state is at the origin.

2c Multiple recurrent epidemics and subharmonic behavior

When δ is small, it is known that both small amplitude and large amplitude subharmonic solutions may exist. The small amplitude solutions bifurcate from the steady endemic state when the forcing δ is turned on. These are small amplitude solutions of period 1 which bifurcate to period 2 when δ is increased. If δ is increased far enough, a period doubling cascade to chaos is observed. Since all the periods of the harmonics in this cascade are of the form 2^n, stable periods such 3 or 5 will not be observed in the pre-chaotic regime. Therefore, subharmonics such as periods 3 or greater must be found elsewhere.

Large amplitude oscillations occur as bifurcations from periodic orbits of a conservative system in the plane. When $\delta = \varepsilon = 0$ in Eq. (2.2), we have the following conservative system:

$$\begin{aligned} \bar{x}' &= -v\bar{y} \\ \bar{y}' &= v\bar{x}(1+\bar{y}) \\ \bar{z} &= 0. \end{aligned} \tag{2.3}$$

The origin is a center surrounded by periodic orbits with periods ranging between $2\pi/v$ and ∞. Equation (2.3) admits the first integral,

$$C = y - \log(1+y) + x^2/2, \tag{2.4}$$

where C is a constant. Notice that $y = -1$ is an invariant set of the conservative system, and therefore, as the periods of the orbits get larger, the orbits tend to spread out near this set. Now suppose $(x_n(t), y_n(t), 0)$ is a solution of Eq. (2.3) that is periodic with period n. Then it can be shown, for ε and δ sufficiently small, that there exists a periodic solution of period n to the original problem, Eq. (2.1), which is ε close to the period n solution of the conservative system. (See Schwartz and Smith (1983) for a proof.) These subharmonics can also be shown to appear as saddle-node pairs; i.e., just past the point of bifurcation, there exist two period n solutions, one asymptotically stable and the other a saddle.

Simulations for measles parameters have been carried out in Schwartz (1985) for the SEIR model to illustrate the relative sizes of the orbits. Since $2\pi/v\varepsilon$ (2, 3) for measles, large amplitude outbreaks are observed for periods 3, 4, 5 . . . . The size of these subharmonics, which are $O(1)$, are well above the period 1 branch of orbits, which are $O(\varepsilon)$. A more complete picture of these branches is seen by computing only the attractors of Eq. (2.1), which has been done in Schwartz (1989). It is seen that for the period 3 oscillation, a population size on the order of 10^6 is needed to sustain the epidemic, while for period 4 a population on the order of 10^8 is required. Compare this to the size of the population required to sustain the period 1 branch, which is on the order of 10^4. Therefore, population sizes which are required to sustain outbreaks having periods 3 and greater need to be several orders of magnitudes greater than that to sustain a simple period 1 cycle.

To see how such large amplitude outbreaks occur in the model, consider Eq. (2.3) having first integral given by Eq. (2.4). As the constant C approaches infinity, the periodic orbit becomes more triangular and is characterized by two different time scales. The periodic orbit appears as a slow evolution near $y = -1 + O(\exp(-C))$, where x ranges from $-(2C)^{1/2}$ to $(2C)^{1/2}$ during a time interval of $O(C^{1/2})$. This is followed by a large pulse in y which is on the order of $O(C)$, where x goes from $(2C)^{1/2}$ to $-(2C)^{1/2}$, and during an $O(C^{-1/2})$ time interval. The maximum value of y occurs at $x = 0$ and is given by $y = C + O(\ln(C))$ (Erneux and Schwartz 1990). The important point here is that when the oscillation is near the slow manifold $y = -1$, the population needed to sustain the epidemic needs to be of order $\exp(C)$.

The asymptotic analysis of Eq. (2.3) reveals the mechanism by which an ideal epidemic is generated. Just after a large peak in the infective population occurs, both susceptibles and infectives are reduced to low levels. If the number of infectives is very small, y is close to -1, and the infectives remain close to a steady level while the susceptible population builds up at a slow rate. It will take a long time before a sufficient supply of susceptibles is generated before a large infective peak occurs. The conservative model and analysis above shows that this buildup time is equal to $O(C^{1/2})$, which for large C, can be considerable. Just after the buildup of susceptibles, enough contacts are made in the population so the new susceptibles become infected, and the large peak again occurs, but on a much shorter time scale, $O(C^{-1/2})$.

In terms of the original epidemic variables, for a given period n orbit $(\bar{x}_n(t), \bar{y}_n(t), 0)$, the bifurcated period n orbit is given by

$$\begin{aligned} S(t) &= S_c\left(1 + \frac{\varepsilon}{v}\bar{x}_n(t) + O(\varepsilon^2)\right) \\ E(t) &= E_c(1 + \bar{y}_n(t) + O(\varepsilon)) \\ I(t) &= I_c(1 + \bar{y}_n(t) + O(\varepsilon)). \end{aligned} \tag{2.5}$$

Since the minimum value of y for large period n solutions is on the order of $-1 + O(\exp(-C))$, the infective, as well as the exposed classes are both $O(\exp(-C))$, where C is large for long period solutions.

Since these large outbreaks appear as perturbations to solution of the conservative system, and they appear as saddle-node pairs from a particular bifurcation point, we say that these large amplitude subharmonics appear as *primary saddle-node bifurcations* (Schwartz 1988). They are primary because they are the first period n bifurcations appearing as perturbations from a known periodic orbit of a conservative system. Furthermore, since these subharmonics require large populations of order e^C, we say the outbreak is a *population limited outbreak*, since the outbreaks which can be described are limited by the population considered. We now summarize the results of this section with a theorem which characterizes the long period outbreaks of the SEIR model.

Theorem. *Suppose* ε *and* δ *satisfy the hypotheses above and in Schwartz and Smith* (1983). *Then for* ε *and* δ *sufficiently small*:
1. *The* SEIR *model has subharmonic outbreaks of period n, where* $n > 2\pi/v$.
2. *The subharmonic outbreaks appear as primary saddle-node bifurcations.*
3. *The subharmonic outbreaks are population limited.*

An excellent example of the theorem is the case of the SEIR model using measles parameters. Here, primary saddle-node bifurcations having periods 3, 4, 5 . . . are population limited outbreaks. Although these outbreaks have the correct frequency content, they do not model small populations having the same period 3 information. The troughs of the outbreaks are quite steep, which means large populations would be needed to model the outbreaks without the epidemics dying out. In addition, the peaks are quite large.

The SEIR model in its current form can model outbreaks corresponding to long periods, but they are population limited outbreaks, and will not be sustained by populations which support only small amplitude period 1 outbreaks. We now consider one way to modify the problem allowing different populations supporting different types of behavior to interact.

3 Interacting populations – A model

Current models such as the SEIR model described above make the assumption that the populations are constant in size and uniformly mixing. Moreover, much of the city data contains the core city and its suburbs. This is true for both the New York City data and the Baltimore data. Based on this observation, the population may be considered to be composed of two groups: One population which is central and dominant, coupled to the other smaller populations.

We suppose, for simplicity in this paper, that there exist two populations which are coupled together. We define X_{ij} to be the exposure rate between group i and group j. Specifically, X_{ij} has the form

$$X_{ij}(t) = \beta_{ij}(t) I_i(t) S_j(t), \tag{3.1}$$

where the coupling contact rate is given by

$$\beta_{ij}(t) = \beta^0_{ij}(t)(1 + \beta^1_{ij} \cos 2\pi t), \tag{3.2}$$

and the subscripts refer to the particular subgroup of the population.

Implicit in the assumption that subgroups come in contact with one another is that the susceptibles are not required to be stationary. That is, susceptibles of one group may move to come in contact with infectious individuals from another group. This assumption implies that the rates of change of the susceptible groups include losses due to self infection and secondary group infection. That is, there is a small probability that some fraction of the susceptible population comes in contact with infectives from another group. For the 2 group model, the rates of change are given by the following sets of equations:

$$\begin{aligned}
S_1' &= \mu_1 - X_{11}(t) - X_{21}(t) - \mu_1 S_1 \\
E_1' &= X_{11}(t) + X_{21}(t) - (\mu_1 + 1/\gamma) E_1 \\
I_1' &= E_1/\gamma - (\mu_1 + 1/\alpha) I_1 \\
S_2' &= \mu_2 - X_{22}(t) - X_{12}(t) - \mu_2 S_2 \\
E_2' &= X_{22}(t) + X_{12}(t) - (\mu_2 + 1/\gamma) E_2 \\
I_2' &= E_2/\gamma - (\mu_2 + 1/\alpha) I_2 .
\end{aligned} \tag{3.3}$$

The equations modelling the recovered populations are obvious, and they are omitted. The birth and death rates, μ_i, $i = 1, 2$, for each subgroup are assumed to be equal. The latent and infectious periods are defined as in the original SEIR model.

4 Generation of small amplitude/long period based subharmonics

As discussed above, individual small populations modelled by the SEIR model can only sustain period 1 oscillations. The question addressed in this section is, Can small centers support long period behavior? The mechanism which we use to answer this question is the hypothesis that the small population centers are coupled weakly to a large population center which is capable of sustaining population limited outbreaks. We consider first the following uncoupled oscillator initialization for the model governed by Eq. (3.3).

Table 1

μ_1	0.02 (year)$^{-1}$
μ_2	0.02 (year)$^{-1}$
α	1/0.0279 (year)$^{-1}$
γ	1/0.01 (year)$^{-1}$
β_{ii}^0	1202 (year)$^{-1}$
β_{ii}^1	0.098 (year)$^{-1}$

The two groups are split into large and small amplitude oscillations of the following types. Group 1 is the small population, and group 2 is the large population. Since the sizes of the population are solely based upon the sizes of the simulated epidemics, group 1 will support a period 1 epidemic, and group 2 will support a period 3 epidemic. The parameters used in the simulations are listed in Table 1. The first part of the simulation considers the groups uncoupled. Figures 1a and 1b show the results for the small and large populations. The logarithm (base 10) of the infective classes are shown for each population, illustrating that the large population needs to be two orders of magnitude greater than the small population if the period 3 outbreak is to be sustained.

Given the initialized uncoupled oscillations, we now couple them weakly, and the coupling is assumed to be symmetric. The coupling strengths are given by $\beta_{ij}^0 = 1.0$. Relative to the self contact rate, β_i^0, the cross contact rate, or coupling strength, is 1 part in 1200. Figure 2a shows the large population in a period 3 based chaotic oscillation. The time series here is sampled at period 1 (or annual) intervals. The corresponding small amplitude oscillation is shown in Fig. 2b, and it is also chaotic. However, although it is primarily period 3 based, there are also peaks which are separated by 4 years, rather than 3 years. So coupling these two

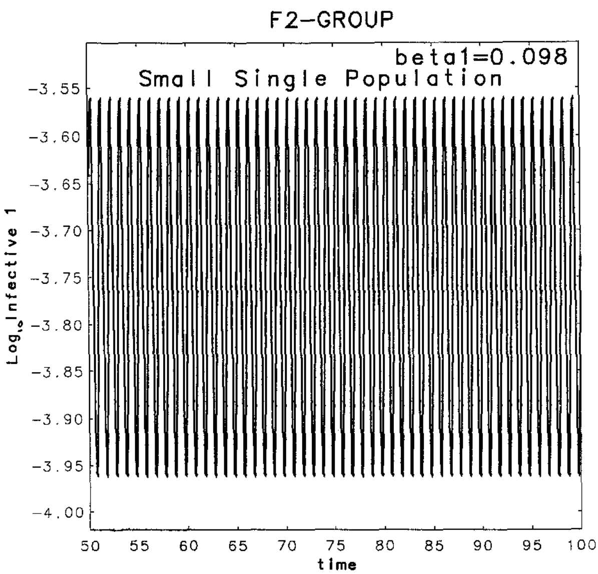

Fig. 1a. Small amplitude period 1 oscillation in the uncoupled system

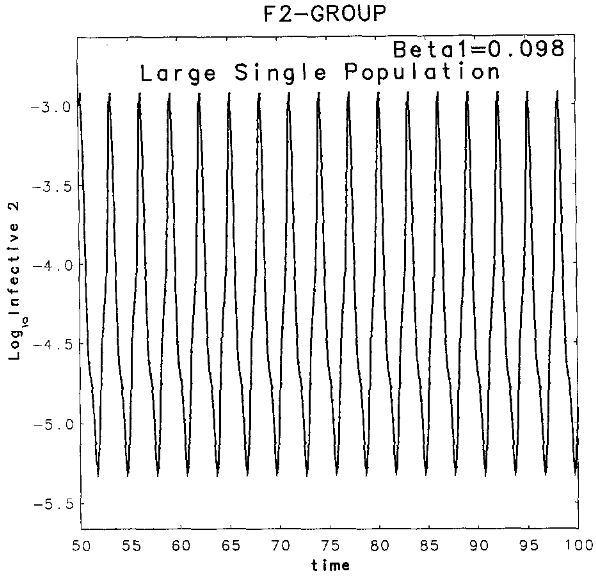

Fig. 1b. Large amplitude period 3 oscillation in the uncoupled system

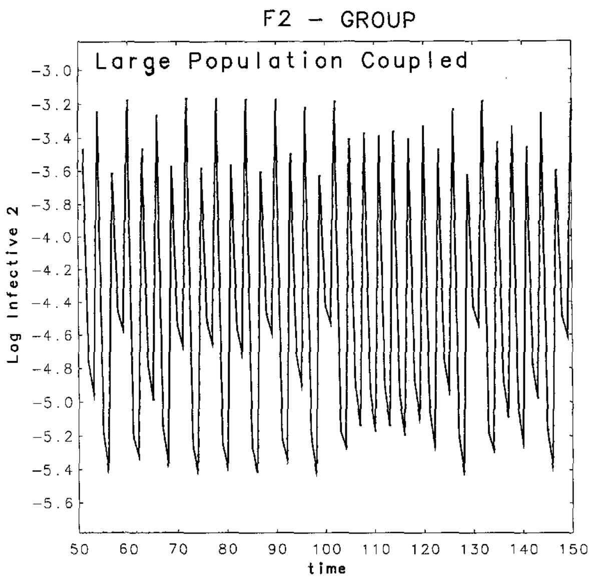

Fig. 2a. Chaotic large amplitude period 3 based time series of infectives in the coupled system. Points plotted anually

distinct forms of oscillations demonstrates numerically the existence of long period outbreaks. Furthermore, it is possible to simulate outbreaks which are not population limited in the small population component, and which have a mixture of several subharmonic frequencies. In this simulation, both period 3 and period 4 outbreaks occur.

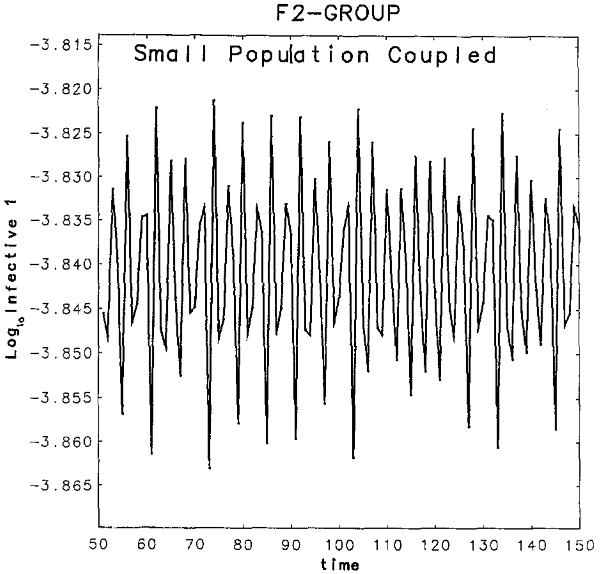

Fig. 2b. Chaotic small amplitude period 3 based time series in the coupled system. Points plotted annually

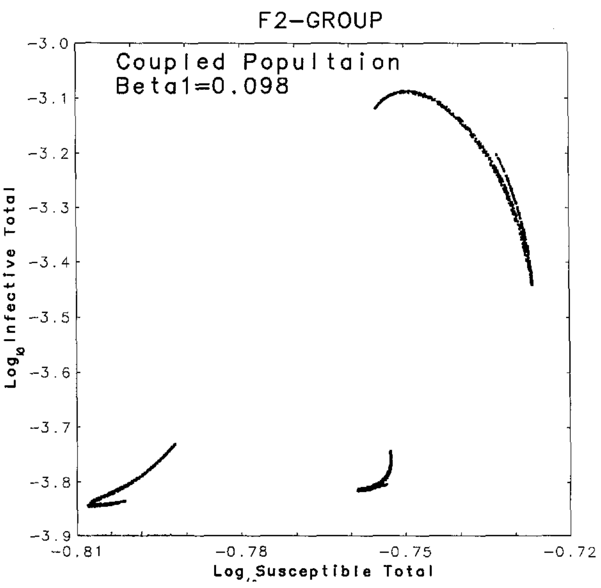

Fig. 3a. Projection of the chaotic attractor of the infective total vs. the susceptible total in the coupled system

It should be stated that when the population is taken together as a whole, the large amplitude outbreaks will dominate because the local maxima in the infectives is, in general, larger than those generated by the period 1 oscillations, as predicted by the theory in Sect. 2. To see the overall effect of the chaotic period 3 component, we plot a projection of the total number of infectives versus

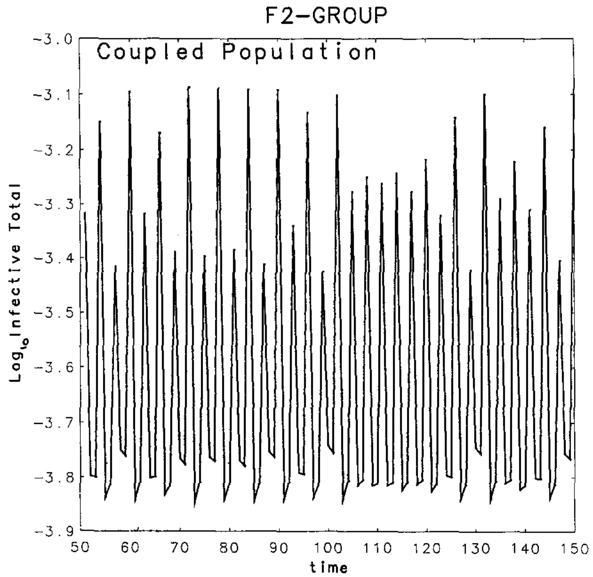

Fig. 3b. Chaotic time series of the period 3 based total infective population in the coupled system

the total number of susceptibles in Fig. 3a. There are three distinct pieces of the resulting projection, corresponding to the dominating peaks of the large amplitude oscillation. The period 3 interpeak interval is also evident in a time series plot of the total infective population, shown in Fig. 3b. Notice that there are two distinct kinds of period 3 based behavior. There is a period 6 type of behavior, which implies the dynamics is near a period 6 unstable orbit. There is also a section of the time series which is period 3 type, implying the dynamics is near a period 3 unstable orbit. The intermittent intervals of different kinds of period 3 based behavior are due to the characteristic that chaotic attractors contain an infinite number of periodic orbits, all of which are unstable (Guckenheimer and Holmes 1983).

5 Coupled populations as a paradigm to generate small amplitude/long period based behavior in single small populations

In modelling long period behavior coupled populations, one can examine the cause of the small amplitude long period behavior in the small population directly. In any epidemic model, the driving force of a given epidemic is the rate at which susceptibles are supplied to the population. For the SEIR model, it is the birth rate which supplies a constant stream of susceptibles into the population. In other models which do not incorporate permanent immunity, it is a combination of the birth rate and the feedback rate of susceptibles from the recovered population. Without such a stream, the epidemic would not be able to sustain itself.

5a Effective birth rates in small populations

From the analysis of an ideal outbreak given in Sect. 2, one observes that for long period outbreaks, there are two distinct time scales, both governing the rate

Table 2

Period	Birth Rate
1	0.101
2	0.0254
3	0.011
4	0.006
5	0.004

of growth and depletion of susceptibles. If the period of the outbreak is very long, then susceptibles grow very slowly for a long period of time before they are reduced in a short interval. Since the rate of change of susceptibles is governed by the birth rate, we hypothesize that the birth rate, on average, needs to be reduced in order to generate longer period harmonics. Indeed, the theorem in Schwartz and Smith (1983), shows that there is a relationship between the birth rate and the other epidemiological parameters for the existence of primary saddle-node bifurcations of period n. Specifically, we require that the birth rate be bounded by the following inequality:

$$\frac{4}{(Q-1)n^2}\left(\frac{1}{\alpha}+\frac{1}{\gamma}\right) < \mu + O(\varepsilon^2). \tag{5.1}$$

If the parameters for measles are plugged into the above inequality, then the birth rate μ can be computed for which one expects a period n PSNB to occur. The numerical results are given in Table 2. Table 2 shows that if μ is decreased, then higher order subharmonics are excited. This also explains why in the work of Aron (1990), when vaccination schemes are put into effect, long period, large amplitude behavior occurs. When vaccination schedules reduce the rate at which susceptibles are produced, the long period subharmonics are excited.

In the 2 group population, one can ask what is the driving force of the small amplitude/long period based behavior by computing the effective birth rate as a function of time. Since the loss of susceptibles due to contact with infectives from the large population is small, we consider that loss as a time dependent perturbation of the birth rate, μ. Therefore, we define an effective birth rate, μ_e, by

$$\mu_e(t) = \mu_1 - X_{21}(t), \tag{5.2}$$

where X_{21} is defined in Sect. 3.

For the period 3 based coupled oscillations performed in Sect. 4, we compute the effective birth rate as a function of time for the small population. The results are plotted in Fig. 4. There are two distinct time scales of the effective birth rate for the time series shown. For 2 years, μ_e is approximately constant, oscillating near the constant value of μ, which in this case is 0.02/year. During the third year, however, there is a rapid decrease followed by an increase in the birth rate. When the decrease in the birth rate occurs, the rate of introduction of susceptibles slows, hence slowing the growth rate of infectives. Then the birth rate increases, increasing the susceptible growth rate, with a resulting larger infective peak than previously. It is interesting to note that the overall change in the effective birth rate is approximately one per cent. However, even in the presence of such a small change, a completely qualitative change occurs in the solution. Namely, a period 1 solution is now interspersed with period 3 peaks in the infectives.

We close this section by making the following claim:

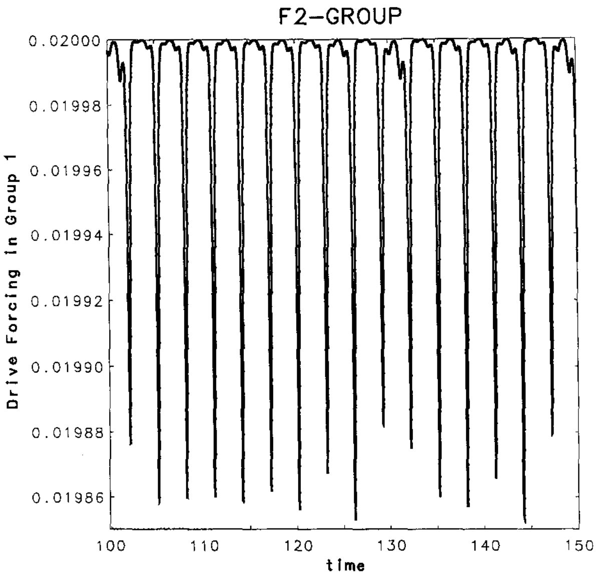

Fig. 4. The effective input rate of susceptibles as a function of time for the period 3 based chaotic attractor in the coupled system. The driving force is for the small population subgroup. The parameters were those used in Figs. 2 and 3

Conjecture 5.1 *Suppose that a small population supporting a period* 1 *cycle is weakly coupled to a large population supporting a period n cycle, where the period n outbreak is population limited. Then, for sufficiently small coupling coefficients, the small population supports a period n based outbreak, which is not population limited. Moreover, the effective birth rate exhibits small amplitude fluctuations which are period n based.*

We now discuss how this conjecture may be used to produce small amplitude oscillations having any period, and are stable.

5b Small amplitude/long-periodic oscillations in single populations

Conjecture 5.1 makes a distinct connection between small oscillations in the birth rate, and resulting peaks of the same period in the infective populations. To test further this hypothesis, we consider a single population modelled by the SEIR model. We make the assumption that the birth rate is not constant, but is allowed to depend on time. Furthermore, we assume that the birth rate is constant for a time interval of $n-1$. This is followed by a decrease to a local minimum followed by an increase to its original value in one period. Specifically, we suppose that there exist a μ_0, constant, and that for $t \in [0, n)$

$$\begin{aligned} \mu(t) &= \mu_0; \quad t \in [0, n-1) \\ \mu(t) &= \mu_0 - 2\Delta\mu_0[t-(p-1)]; \quad t \in [n-1, n-1/2) \qquad (5.3) \\ \mu(t) &= \mu_0 + 2\Delta\mu_0[t-n]; \quad t \in [n-1/2, n), \end{aligned}$$

where Δ is a positive constant less than unity.

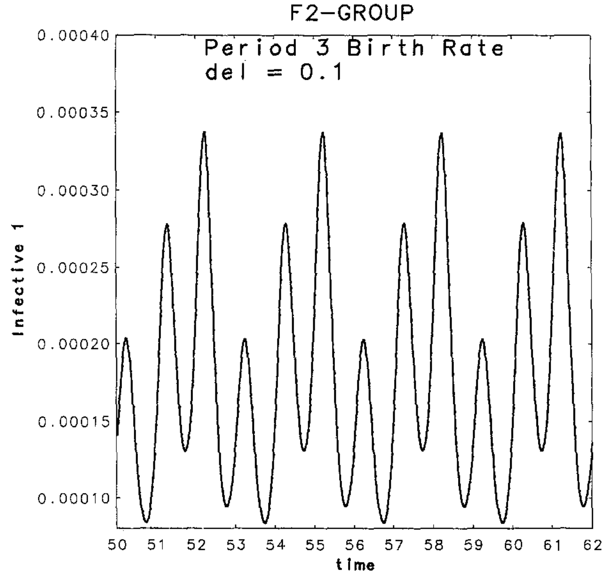

Fig. 5a. A period 3 based attractor time series for the SEIR model using a periodic birth rate of the form in Fig. 6. Here $\Delta = 0.1$. Notice the small amplitude, and the population needed to sustain the outbreak is $O(10^4)$

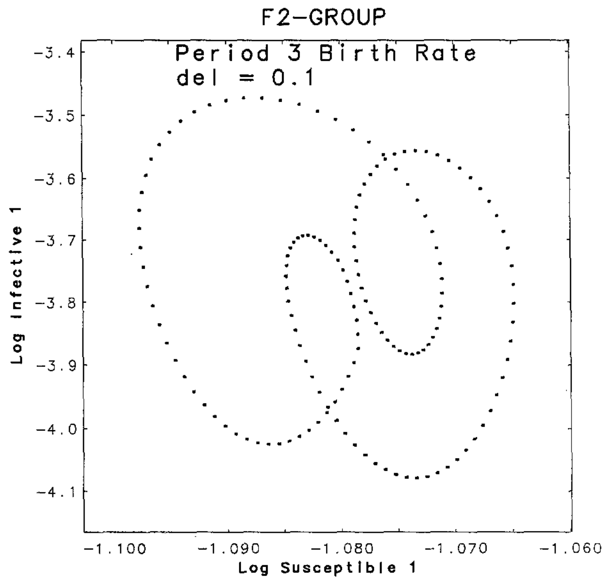

Fig. 5b. Same as in Fig. 2a, but the periodic attractor is plotted as a projection as I vs. S

We now consider the SEIR model with the addition of the time dependent periodic birth rate with period $n = 3$. The logarithm of the infective population is shown in Fig. 5a, clearly showing an outbreak which is periodic with period 3, and which is not population limited. As can be seen, there is a maximum peak in the infective class which occurs every three years. The projection of the period

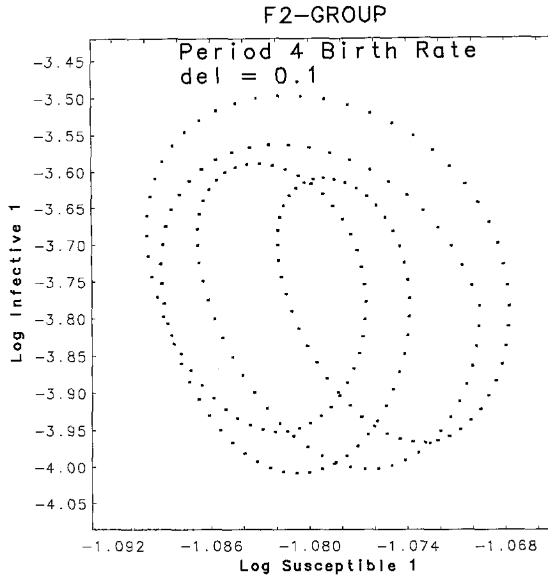

Fig. 6. A period 4 attractor. Here the birth rate is periodic with period 4, and $\Delta = 0.1$. Notice that the orbit is small amplitude and the population needed to sustain the outbreak is $O(10^4)$. The attractor is plotted as a projection of I vs. S

3 attractor is illustrated in Fig. 5b, clearly showing only one maximum value of infective.

We now repeat the calculation with a period 4 birth rate. Again, as Fig. 6 shows, the resulting infective class is periodic with period 4, with only one maximum every four years. Thus the mechanism of using fluctuations in the birth rate to slow the growth of susceptibles appears to be a viable one in which small amplitude outbreaks can have long period behavior. We make the following claim which summarizes the main points of this section:

Conjecture 5.2 *Suppose the* SEIR *model has birth rate periodic as defined by Eq.* (5.3), *having period n. Then for sufficiently small Δ, the* SEIR *model with periodic birth rate sustains small amplitude outbreaks which are periodic with period n, and which are not population limited. Furthermore, if the birth rate troughs appear randomly or chaotically, the resulting dynamics will also appear as such, respectively.*

The analysis of such a conjecture will appear elsewhere. We close this section by noting that although rubella exhibits childhood like dynamics, and sustains outbreaks as long as 7 years, no successful attempt to model this behavior has been made as far as we know. The difference in rubella is that due to assumed antibody shedding, there is a small probability that the recovered individuals re-enter the susceptible group after a period of time. So for rubella, at least, there may be an interplay between a decrease in the rate of introduction of susceptibles and an increase of the rate. If the re-introduction rate is much smaller than the decrease in the birth rate, then the SEIR model with time dependent birth rate can be applied, and we show that for period 7 introduction rates, Conjecture 5.2 implies the existence of a period 7 outbreaks. Just such a computation shows the result of a period 7 which is not population limited in Fig. 7. Although the SI projection appears to be complicated, it is periodic with period 7.

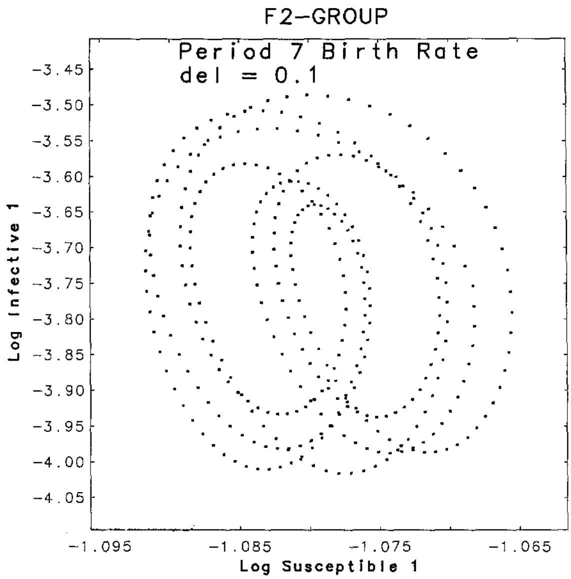

Fig. 7. A period 7 attractor. Here the birth rate is periodic with period 7, and $\Delta = 0.2$. The periodic attractor is plotted as a projection of I vs. S

6 A qualitative comparison with data

Although the SEIR model still cannot fully predict the kind of outbreak one observes in detail, some qualitative features can be observed. In Olsen et al. (1990), a careful description of the kinds of period-based behavior was computed for various cities in both the US and Europe. It is clear that chickenpox is the most regular cycle in that it has only one spectral peak at 1 year. In some cases, it is reported that chickenpox has a positive Lyapunov exponent, a possible indication of period 1 based chaotic behavior. Other diseases, such as measles and mumps, show spectral peaks at the 2, 3, and 4 year cycles, and exhibit chaos as well. For both large and small populations, the chaotic behavior fluctuates with periods 2 through 4 years.

The population sizes for measles vary from 1,000,000 in Copenhagen and Baltimore (Olsen et al.) to 8,000,000 in the New York Metropolitan area (London and Yorke 1983; Yorke and London 1983). However, similar behavior can be observed in annual data for even smaller populations. Examples of oscillations occurring in mumps data for Connecticut and Wisconsin are shown in Figs. 8 and 9, respectively. There are several period 3 based cycles in each set of data shown during the prevaccine years, and the infective population is on the order of 10^4. Therefore, subharmonic behavior can also be seen in small populations.

One other interesting observation can be seen in the Wisconsin data. After vaccination is started, the peaks in the number of cases become smaller, as is expected. However, the period between the largest peaks gets longer. That is, period 3 interpeak outbreaks shift to period 4 outbreaks, before the case number becomes negligible. The frequency shift is in qualitative agreement with the

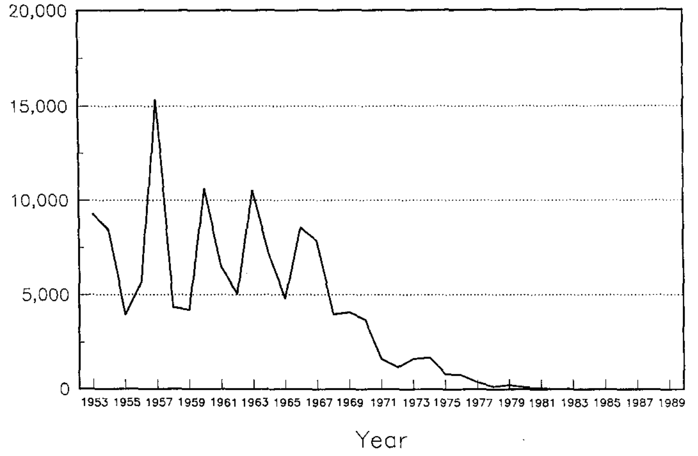

Fig. 8. Mumps Data for the state of Connecticut, reported cases 1953–1989. Annual cases are plotted for the years 1953–1989. Notice the prominent period 3 based peaks in the pre-vaccine years

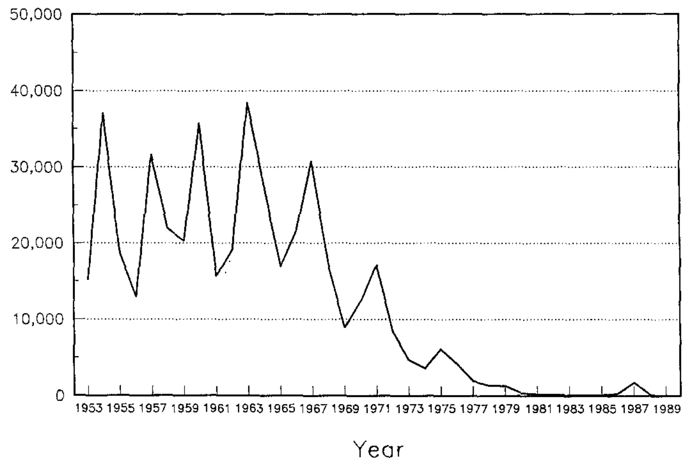

Fig. 9. Mumps Data for the state of Wisconsin, reported cases 1953–1989. Annual cases are plotted for the years 1953–1989. Notice the prominent period 3 based peaks in the pre-vaccine years

phenomenon predicted by Eq. (5.1) and Table 2, where a reduction in the rate at which susceptibles are introduced excites longer subharmonics.

7 Summary

We have explored two modelling techniques to generate small amplitude/long period based behavior in seasonally driven epidemics. In the first case, coupled populations were considered in which each population size is determined by the kind of outbreak it generates. When a large population is weakly coupled to a small population, the small population supports long period outbreaks which are not population limited. However, due to the large amplitude peaks of the large population, the dynamics of the total population is dominated by the large amplitude population limited subharmonic outbreak.

By using the coupled population model as a paradigm, a mechanism was discovered which generates small amplitude subharmonic behavior in small populations. By relaxing the assumption that the population has a constant input of susceptibles, it can be shown that a single population can sustain long period-based outbreaks which are not population limited. The sizes of these outbreaks are the same order of magnitude as a small amplitude period 1 outbreak.

By adjusting the period of fluctuations in the input of susceptibles, one can create any type of time series outbreak which is of small amplitude. Periodic outbreaks are only demonstrated in this paper for the single population model, but chaotic, as well as stochastic outbreaks can be predicted as well. Thus we have a very simple mechanism to generate the correct amplitude and frequency content of an outbreak.

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