1 Introduction

Infectious diseases affect millions of people every year. In fact, more than 17 million deaths worldwide each year are attributed to infectious diseases [6]. An *endemic* disease is a disease which persists over time in a given population or geographic region [4]. For example, prior to the development of the measles vaccine in the 1960's and eradication of measles from the United States in 2000, measles was endemic, exhibiting biennial cycles with alternating years of high and low incidence [1, 2, 5] (Figure 1).

Here we examine the work of [5] and study the dynamics of a seasonally-forced SEIR epidemic model for measles. We establish the model in generality, then make key simplifications to reduce the dimension. The reduced model provides motivation to predict the behavior of the original model. In particular, we observe the existence of periodic solutions for infinitely many choices of period [5].

2 Model

2.1 Basic SEIR Model

In the SEIR model [3], a population is divided into four categories (*compartments*): susceptible, infectious, exposed, and recovered (Table 1). An individual may only belong to one compartment at a given time. Letting S, E, I, R denote the fraction of the population in the susceptible, exposed, infectious, and recovered categories, respectively, movement between compartments is governed by the following system of ordinary differential equations:

$$\begin{aligned} \frac{dS}{dt} &= \mu - \mu S - \beta IS \\ \frac{dE}{dt} &= \beta IS - (\mu + \alpha)E \\ \frac{dI}{dt} &= \alpha E - (\mu + \gamma)I \\ \frac{dR}{dt} &= \gamma I - \mu R, \end{aligned}$$

where μ, β, α , and γ are described in Table 2. The contact rate, β , is defined as the average number of effective contacts per infectious individual per unit time. An *effective contact* is a contact between an infectious individual and a susceptible where the disease is successfully transmitted. This model assumes a fixed population size; that is,

$$S(t) + E(t) + I(t) + R(t) = 1.$$

Notice that from the S, E, and I compartments we have the description of the R compartment. Thus, we treat the model as a three-dimensional system without loss of information.

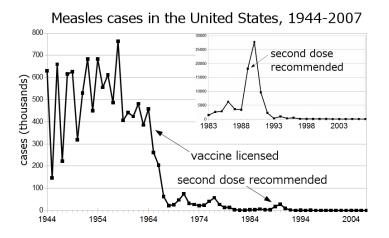


Figure 1: Number of measles cases in the United States per year. Figure originally published in [2]. Prior to the licensing of a measles vaccine in 1963, measles outbreaks occurred in biennial cycles, alternating years of high and low incidence.

2.2 Steady States of Basic SEIR Model

There are two steady states in the SEIR model: the trivial steady state at (S, E, I) = (1, 0, 0) where there is no disease present; and the *endemic steady state* at $(S, E, I) = (S_0, E_0, I_0)$ where

$$S_0 = \frac{(\mu + \alpha)(\mu + \gamma)}{\beta \alpha}, \qquad E_0 = \frac{\mu + \gamma}{\alpha} I_0, \qquad I_0 = \frac{\mu(Q - 1)}{\beta}$$
(1)

with

$$Q := rac{eta lpha}{(\mu + lpha)(\mu + \gamma)}.$$

For the endemic steady state solution to exist in the context of epidemiology, $I(t), S(t), E(t) \ge 0$ for all t. Thus, endemic steady state solution exists if and only if Q > 1. In either case, we interpret Q to be the *reproductive rate*, often denoted as R_0 : the average number of secondary cases produced by one infectious individual in a population of susceptible individuals in one infectious period [5].

Routine calculations show that the trivial steady state solution is stable when $Q \leq 1$ and unstable with Q > 1. In this latter case the endemic steady state is asymptotically stable.

2.3 Seasonally-Forced SEIR Model

Now, we adapt the basic SEIR model to incorporate seasonality of infections. In the context of measles, "seasonality" refers to the biennial cycles of high and low yearly incidence. Other infectious diseases, such as influenza and cholera, exhibit peaks and troughs in incidence throughout the year. In each of these contexts, seasonal forcing can be implemented in the same way by choosing an appropriate time scale. Here we focus on the implementation

Compartment	Description		
Susceptible	individuals capable of contracting the disease		
Exposed	individuals who are infected but not yet infectious		
Infectious	individuals capable of transmitting the disease		
Recovered	individuals who are immune		

Table 1: Compartments in the SEIR model [3,5].

Parameter	Description		
μ	natural birth and death rate		
β	contact rate		
1/lpha	mean latent period		
γ	recovery rate		

of seasonal forcing for the measles case and we adjust the contact rate β to be periodic with period one year:

$$\beta(t) = \beta_0 (1 + \delta \cos(2\pi t)), \tag{2}$$

where our unit of time is a year. Moving forward, the endemic state refers to (1) with $\beta = \beta_0$.

For measles, we set the parameters so that $1/\mu$ is 50 years, the average latent period measured by $1/(\mu + \alpha)$ and the average infectious period measured by $1/(\mu + \gamma)$ are between a few days to a week. We will continually use the fact that μ , $1/(\mu + \alpha)$, and $1/(\mu + \gamma)$ are of the same order of magnitude on the scale of $O(10^{-2})$. We define

$$\varepsilon := \beta_0 I_0 = \mu (Q - 1). \tag{3}$$

Then, there exist Δ_2, Δ_3 so that

$$\mu + \alpha = \frac{\Delta_2}{\varepsilon}$$
 and $\mu + \gamma = \frac{\Delta_3}{\varepsilon}$

and $0 < \varepsilon \ll 1$.

In order to make a dimension reduction, we will first make a change of variables. In particular, we define x, y, z so that

$$S = S_0(1+x),$$
 $E = E_0(1+y),$ $I = I_0(1+z),$

Using (1), (2), and (3) and the original SEIR model, we obtain the seasonally forced system:

$$\begin{split} \dot{x} &= \varepsilon [(\eta + \delta \cos(2\pi t))x + (1 + \delta \cos(2\pi t))(z + xz)] \\ \dot{y} &= \frac{\Delta_2}{\varepsilon} [\delta \cos(2\pi t) - y + (1 + \delta \cos(2\pi t))(x + z + xz)] \\ \dot{z} &= \frac{\Delta_3}{\varepsilon} (y - z), \end{split}$$

where $\eta = Q/(Q-1)$. By construction, the endemic steady state solution of the $(\dot{x}, \dot{y}, \dot{z})$ system with $\delta = 0$ occurs at (x, y, z) = (0, 0, 0).

2.4 Reduced System

To reduce the dimension of the model, we will make a change of variables so that the resulting linear part is close to its Jordan form when $\delta = 0$. To do this, we assume that δ is small; in particular we assume δ/ϵ is small.

Let us define our change of variables from (x, y, z) to $(\bar{x}, \bar{y}, \bar{z})$ as follows:

$$\bar{x} = \nu \left[\frac{x}{\varepsilon} - \varepsilon \frac{\Delta_3}{(\Delta_2 + \Delta_3)^2} (z - y) \right]$$
$$\bar{y} = \frac{\Delta_3 y + \Delta_2 z}{\Delta_2 + \Delta_3}$$
$$\bar{z} = z - y,$$

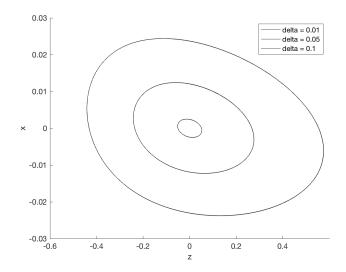


Figure 2: Phase portrait of the reduced system, $\bar{x}' = -\nu \bar{y}$, $\bar{y}' = \nu x(1+y)$. Periods vary between $2\pi/\nu$ near the origin to $+\infty$ near the nullcline y = -1.

where
$$\nu = \sqrt{\frac{\Delta_2 \Delta_3}{\Delta_2 + \Delta_3}}$$
.

When we do this change of variables, we simultaneously convert the non-autonomous system into an autonomous system by rewriting in terms of $\tau = t/\varepsilon$, adding the variable $\theta = \varepsilon \tau$, and taking the time-derivatives in terms of τ . For more information on this procedure, see [5].

Under this change of variables, with $\delta = \varepsilon = 0$, we obtain what we will refer to as the *reduced system*

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

In this reduced system, the origin is a center which is surrounded by periodic orbits (Figure 2).

3 Existence of *n*-Periodic Solutions

From the reduced system, we note that for every integer n such that $2\pi/\nu < n < \infty$, there is a periodic solution to the reduced system of at least period n [5]. This property leads us to expect a similar result for the unreduced system, which turns out to be the case.

Theorem 1 (Schwartz and Smith [5]) Let $(\bar{x}_n(t), \bar{y}_n(t)) = (\bar{x}_n(t+n), \bar{y}_n(t+n))$ denote a periodic solution of the reduced system, where $n > 2\pi/\nu$. Let

$$\gamma_2 := \nu^2 \int_0^n \bar{y}_n(t) \cos(2\pi t) dt \neq 0$$
$$\gamma_1 := \frac{-2}{\nu} \cdot \frac{\Delta_2 \Delta_3 - (\Delta_3 + \Delta_2)^2 \eta}{2(\Delta_3 + \Delta_2)^2},$$

and for $\alpha \in [0, n)$, $|\varepsilon| \ll 1$, $|\delta| \ll 1$, let

$$B(\alpha,\varepsilon,\delta) = -\gamma_1\varepsilon + \gamma_2\delta\cos(2\pi\alpha) + O(|\varepsilon| + |\delta|)^2$$

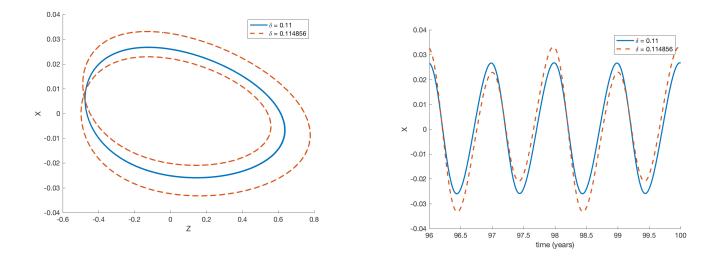


Figure 3: The seasonally forced system $(\dot{x}, \dot{y}, \dot{z})$ undergoes a period doubling bifurcation at $\delta \approx 0.114856$.

If (\bar{x}'_n, \bar{y}'_n) spans the n-periodic solutions of the variational equations of the reduced system about (\bar{x}_n, \bar{y}_n) , and $(\alpha, \varepsilon, \delta)$ is such that $B(\alpha, \varepsilon, \delta) = 0$, then the unreduced system $(\bar{x}', \bar{y}', \bar{z}')$ has an n-periodic solution $(\bar{x}, \bar{y}, \bar{z})$ given by

$$\bar{x}(t) = \bar{x}_n(t+\alpha) + O(|\varepsilon|(1+|\delta|))$$

$$\bar{y}(t) = \bar{y}_n(t+\alpha) + O(|\varepsilon|+|\delta|)$$

$$\bar{z}(t) = -\frac{\varepsilon\Delta_2}{\nu^2(\Delta_2+\Delta_3)}\bar{y}'(t+\alpha) + O(|\varepsilon|+|\delta|)^2.$$

4 Numerical Simulations

Using the measles-specific parameters listed in Table 3, we find that for $\delta < 0.114856$ period-1 orbits exist for the seasonally forced system

$$\begin{split} \dot{x} &= \varepsilon [(\eta + \delta \cos(2\pi t))x + (1 + \delta \cos(2\pi t))(z + xz)] \\ \dot{y} &= \frac{\Delta_2}{\varepsilon} [\delta \cos(2\pi t) - y + (1 + \delta \cos(2\pi t))(x + z + xz)] \\ \dot{z} &= \frac{\Delta_3}{\varepsilon} (y - z). \end{split}$$

In particular, the orbit starting at $(x_0, y_0, z_0) = (0.0243, -0.0364, -0.0669)$ undergoes a period-doubling bifurcation from a period-1 orbit to a period-2 orbit at $\delta \approx 0.114856$ (Figure 3). This orbit is close to the endemic steady state for $\delta = 0$ which occurs at (0, 0, 0).

Table 3: Parameter values for measles as given in [5].

μ	$0.02 \ (year)^{-1}$	β_0	$1575.0 (year)^{-1}$
α	$1/0.0279 \ (year)^{-1}$	Q	~ 15.73807
γ	$1/0.01 \ (year)^{-1}$	ε	~ 0.29476

5 Conclusion

Theorem 1 indicates that bifurcations into periodic solutions with larger periods occur near periodic solutions to the reduced system. Further analysis of this system would allow us to find such bifurcations. Before the licensing of the measles vaccine, measles outbreaks in the United States exhibited two year cycles, alternating years of high and low incidence. Thus, the period-2 orbits are of particular interest to this application.

By changing the disease-specific parameters, we can apply these methods to other diseases that exhibit periodic behavior, such as influenza in the United States and cholera in Bangladesh and India.

References

- [1] Centers for Disease Control and Prevention. (2017). Measles (Rubeola). Centers for Disease Control and Prevention, Published online: 3 Mar. 2017, www.cdc.gov/measles/about/history.html.
- [2] Hall-Baker, P.A., et al. (2007). Summary of Notifiable Diseases United States, 2007. Morbidity and Mortality Weekly Report (MMWR).
- [3] Hethcote, H. W. (2000). The mathematics of infectious diseases. SIAM review, 42(4), 599-653.
- [4] Porta, M. (Ed.). (2014). A dictionary of epidemiology. Oxford University Press.
- [5] Schwartz, I. B., & Smith, H. L. (1983). Infinite subharmonic bifurcation in an SEIR epidemic model. Journal of mathematical biology, 18(3), 233-253.
- [6] World Health Organization (1996). World health report 1996. Geneva, Switzerland: World Health Organization.