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## ANALYSIS OF DELAYED PULSE VACCINATION MODEL OF INFECTIOUS DISEASES

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### ABSTRACT

This study concerns the theoretical determination of the analysis of delayed pulse vaccination model of infectious diseases that affects children. In this study, a delayed SEIR epidemic model with impulsive effect and the global dynamic behaviors of the model will be analyzed. Using the discrete dynamical systems determined, it's shown that there exists an 'infection-free' periodic solution which is globally attractive when the period of impulsive effect is less than some critical value. The sufficient condition for the permanence of the epidemic model with pulse vaccination is given, which means the epidemic disease is to spread around. The study has concluded that time delay and pulse vaccination brings great effects of shortening 'infection period' on the dynamics of the model. The main feature of the study was to introduce time delay together with pulse into epidemic model, and investigate their effects on the dynamics of model. The results indicate that a large vaccination rate or a short period of pulsing leads to the eradication of the disease. Numerical simulation has been used together with the analytical results. The results shall be presented in tabular and graphical form.

### KEYWORDS

Basic reproduction, ratio- $R_0$ , Compartmental model, Infectious diseases, Disease-free Equilibrium, Mathematical modeling, Pulse vaccination, Time delay.

## Introduction

Infectious diseases are disorders caused by pathogenic microorganisms, such as bacteria, viruses, fungi or parasites. Many organisms live in and on our bodies. Most infectious diseases could be driven towards eradication, if adequate and timely steps (e.g. vaccination, treatment, educational and enlightenment campaign, etc.) are taken in the course of an epidemic. However, many of these diseases eventually become endemic in many societies due to lack of adequate policies and timely interventions to mitigate the spread of the diseases. Consequently, there is the need for proactive steps towards controlling the spread of infectious diseases, particularly those ones for which both vaccine and cure are available. Moreover, it's often cheaper to prevent the occurrence of a disease with vaccination than to cure it.

The ultimate goal of an epidemic model would be to closely follow and predict real-life disease outbreaks, with the aim of informing public policy and related government agencies. It will focus on looking at control methods, i.e. ways to keep the infective population low or to eradicate the infection altogether. One such control method is vaccination. Some vaccination campaigns are run continuously, for example with people of a certain age receiving their vaccine. Another way is to organize large campaigns in which a large proportion of the population is vaccinated over a short time; this technique is known as pulse vaccination, which has been considered in this study. There are many different ways to construct a compartmental model, depending on the relevant disease, some models may agree with reality more closely than others. Many models assume an exponential distribution of the time to move between compartments, but another way is to use delay differential equations. A constant delay will be used if the movement time (e.g. time until recovery or time until development of contagiousness) was known with reasonable certainty. Time-varying parameters will be used, or approximated by a constant.

In modeling of delayed pulse vaccination of infectious diseases, there are different ways to approach the vaccination problem of how to model such a situation. One way is to use probabilistic models, involving for example Markov chains and stochastic processes, while the other uses differential equations that dictate the time evolution of the system (deterministic modeling). In a probabilistic model, it only determines the probability of an outcome; a differential equation-based model in contrast will produce one particular outcome for any given set of parameters and initial conditions. It's important that this investigation is done to establish under what conditions a given agent can invade a partially vaccinated population, i.e., how large a fraction of the population is to be vaccinated to prevent the agent from establishing. Earn (2009) discussed the advantages and disadvantages of each type of models above. It's noted that deterministic models can be fitted very well to a particular outbreak, while they represent a simplified version of the events. This study focuses on deterministic models and dynamical systems used to model epidemics, using deterministic compartmental models, in which a given population is divided into compartments based on the disease status (susceptible, exposed etc.). The transfers between compartments, as well as the entrance to the population of new individuals

and the exit of others are modeled as terms in a differential equation governing the time-evolution of each compartmental value. After the infectious individuals lived through an infection period, they recover completely and transfer to the 'removed' class, R, so, the number of the death of the infectious should be considered during convalescence, which is called the phenomena of 'time delay'.

Pulse vaccination strategy (PVS), was first proposed by Agur *et al* (1993) which consists of periodical repetitions of impulsive vaccinations in a population, on all the age cohorts, differently from the traditional constant vaccination. At each vaccination time, a certain fraction of susceptible individuals is vaccinated. This kind of vaccination is called impulsive vaccination, since all the vaccine doses are applied in a time which is very short with respect to the dynamics of the disease. Pulse vaccination is gaining prominence as a strategy for the elimination of childhood viral infectious diseases such as measles, hepatitis, parotitis, smallpox and phthisis, and was considered in many literatures in D'Onofrio (2002, 2004) and Gao (2008). Known theoretical results showed that the pulse vaccination strategy can be distinguished from the conventional strategies in leading to disease eradication at relatively low value of vaccination. Therefore, this study will consider an epidemic model with impulsive vaccination and time delay and study their dynamic behaviors (the 'infection-free' periodic solution, the permanence and the global attractive behavior) under pulse vaccination. The main aim of this study is to introduce time delay, pulse vaccination in an epidemic model and to obtain some important qualitative properties and valid pulse vaccination strategy. First, let's look at what the researchers have done in this field of epidemic modeling as this would have given way to look at what has been done in the delayed pulse vaccination.

### **Related works/Literature survey**

In recent years, a large number of research analyses have been carried out on the epidemic modeling, involving the modeling of pulse vaccination of infectious diseases. Wencai *et al* (2015) researched on dynamical analysis of SIR epidemic model with non-linear pulse vaccination and lifelong immunity. In this study, due to the limited medical resources, vaccine immunization rate is considered as a nonlinear saturation function and their findings were enriching medical resources i.e. increase  $\theta$  or reduce the vaccination period i.e. decrease T, the disease will be in extinction, otherwise the disease will be permanent. Onyejekwe and Kebede (2015) studied the epidemiological modeling of measles infection with optimal control of vaccination and supportive treatment, in which they concluded that the optimal combination of the strategies required to achieve the set objective depend on the relative cost of each of the control measures and the resulting optimality system. The use of both vaccination and supportive treatment gives the highest possible rate to the control of epidemics.

Tongqian *et al* (2014), in their study SVEIRS a new epidemic disease model with time delays and impulsive effects realized that global dynamical behavior of the model with pulse

vaccination and impulsive population inputs effects at two different periodic moments, existence and global attractivity of the infection free periodic solution and also permanence of the model. Their results shows that time delay, pulse vaccination and pulse population input can exert a significant influence on the dynamics of the systems which confirms the availability of pulse vaccination strategy for the practical epidemic prevention. Shulgin *et al* (2014) considered a simple SIR model with pulse vaccination and have shown that if certain conditions regarding the magnitude of vaccination proportion and on the period of pulses are satisfied then the pulse vaccination leads to epidemic eradication.

Yanke and Rui (2010) investigated a delayed SIR epidemic model with nonlinear incidence rate and pulse vaccination, they noted that the global attractiveness of infection free periodic solution was analyzed and sufficient conditions are obtained for permanence of the system. Their results indicated that a large vaccination rate or a short period of pulsing leads to the eradication of the disease.

Heesterbeek (2005) discussed compartmental modeling and particularly discussed the use of the law of mass action for the bilinear incidence term in deterministic modeling. ODE model deals nominally with two compartments, SI, (a removed class is implied) in a homogeneously mixed population, with permanent removal and no control measures by Kermack (1927). The literature which followed branched into such areas as; Vaccination control measures, Heterogeneous populations (age-structured, infectious stages), spatial heterogeneity (PDEs), Constant latent/infectious/immune periods (DDEs), Distributed delay, stochastic effects and delayed pulse vaccination using DDEs.

An epidemic HIV/AIDS model with treatment has been investigated in the study by Cai *et al* (2009). The model allows some infected individuals to move from symptomatic phase to the asymptomatic phase by all kinds of treatments. The authors introduced the time delay to the model in order to investigate the effect of the time delay on the stability of the endemically infected equilibrium. This discrete time delay has also been used to the model to describe the time from the start of the treatment in the symptomatic stage until the treatment effects becomes clear. It was found that treatment can be used to make the disease free equilibrium ( $E_0$ ) stable when it would be unstable in the absence of treatment. On the other hand using the time delay can induce oscillation in the system. Biologically, this means that there is a critical value for the treatment-induced delay which determines the stability of the infected equilibrium  $E^*$ . That is, the infected equilibrium  $E^*$  is asymptotically stable when antiretroviral drugs on average show positive effects in patients within less than time delay.

The study on general forms of incidence, pulse vaccination campaigns, and delay differential equations were also looked at in which it was established that periodic vaccination campaigns plays a bigger part in compacting the outbreak of the infectious diseases. The mass-action

bilinear incidence term and the standard incidence term which takes into account varying population size, according to Shaoying *et al* (2009), Riu *et al* (2010). The contact rate still increases as  $I$  increases, but the growth is largest when  $I$  is very close to 0 and approaches a positive limit from below for large  $I$ .

Gao *et al* (2006) developed a model and a pulse vaccination strategy in which the repeated application of vaccine over a defined age range. It revealed it's an effective strategy for the elimination of infectious diseases. Gao *et al* (2008), the dynamics of an SEIR model with two delays and pulse vaccination were analyzed. They obtained that the infection free periodic solution is globally attractive if the pulse vaccination rate is larger than a critical value  $\theta^*$ . Zhao *et al* (2008) considered an SEIR model with delay and nonlinear incidence rate of the form  $\beta IS^q$  and they studied the dynamical behavior of the system under pulse vaccination.

Rost (2008) came up with a new SEIR model with distributed infinite delay. The author stated that the infectivity depends on the age of infection. The basic reproduction number  $R_0$ , which is a threshold quantity for the stability of equilibria, is calculated. If  $R_0 < 1$ , then the disease-free equilibrium is globally asymptotically stable and this is the only equilibrium. On the contrary, if  $R_0 > 1$ , then an endemic equilibrium appears which is locally asymptotically stable. Applying a permanence theorem for infinite dimensional systems, they obtained that the disease is always present when  $R_0 > 1$ .

D'Onofrio *et al* (2007) presented simple epidemiological models with information dependent vaccination functions which can generate sustained oscillations via Hopf bifurcation of the endemic state. The onset of these oscillations depends on the shape of the vaccination function. They used "global" approach to characterize the instability condition and identify classes of functions that always lead to stability/instability. The analysis allows the identification of an analytically determined "threshold vaccination function" having a simple interpretation: coverage functions lying always above the threshold always lead to oscillations, whereas coverage functions always below never lead to instability.

Psychological effects may cause contact rates to not just level off but to decline with respect to  $I$  for high levels of infectives, for example as individuals become wary of contact. Capasso and Serio (1978) modeled such effects in the incidence term in which without infection, there can be no transmission, and there can be no "negative" transmission (a susceptible contacting an infective cannot take away the disease). Alexander and Moghadas (2004), for example, use an incidence term  $\beta[I + f(I; v)]IS$  where  $f(I, 0) = 0$  and so  $v$  is a measure of the "departure from mass action". They find that under reasonable assumptions on  $f$ , multiple endemic equilibria can be possible even when the reproduction number is less than one ( $R_0 < 1$ ). Thus it's noted that, having a good empirical basis for the model structure chosen is very important, and also that

while simplifications can be very instructive, merely choosing a simple model may not explain phenomena that could be observed in real-life outbreaks.

Like Alexander and Moghadas (2004), Van den Driessche P and Watmough J (2000) also look at bifurcations, in their case with an *SIS* model with incidence term  $\lambda(I)SI$  where  $S = I - I$ . Korobeinikov (2006) uses the incidence term  $G(S, I, t) = f(S, I)$  where  $f$  satisfies the above physicality conditions and is concave down with respect to  $I$ . D'Onofrio (2005) dispenses with the parameter  $\nu$  but generalizes to non-autonomous systems using  $G(S, I, t) = g(I, t)S^q$  for  $q > 0$ . Adding the  $t$ -dependence complicates the results. D'Onofrio (2005) also considers pulse vaccination control measures and general incidence.

Gakkhar and Negi (2008) study bifurcations in an *SIRS* model with non-monotonic incidence in  $I$  of the form  $\kappa SI / (1 + \beta I + \alpha I^2)$ . Gao *et al* (2006), Wang *et al* (2009) and Xu and Ma (2010) use a saturation incidence in *SIRVS*, *SEIRS*, and *SEIR* models, respectively. Zhang and Teng (2008) and Meng *et al* (2007) analyze *SEIRS* models with saturation in  $S$ , that is, with incidence term  $\beta \frac{S}{1 + \alpha S} I$ ; Song *et al* (2009) use an *SVEIR* model with saturation in  $S$  and  $V$ . Zhang *et al* (2010) more recently use saturation in  $S$  in an *SIR* model. Wang *et al* (2009) and Luo *et al* (2011) study a  $\beta IS^q$  incidence in *SEIR* and *SIR* models respectively, while Hui and Chen (2004) study  $\beta I^p S^q$ . While more complicated incidence terms may lead to richer dynamics, accurate parameter estimation and the necessity of confidence in the model choice can raise issues. Looking at a more general form of the incidence function, may be more complicated but can lead to more widely applicable results. D'Onofrio in (2005) considers a general force of infection which is polynomial in  $S$  but a general function of  $I$  and  $t$ . The model is using pulse vaccination but with no delay from d'Onofrio (2000)  $V$  is the vaccinated compartment while  $R$  is for those who have recovered from the disease.

The compartments  $R$  and  $V$  do not directly affect the dynamics of  $S$  and  $I$ , so by assuming that recovery from the disease leads to the same strength of immunity as vaccination, and hence by setting  $\theta = 0$  (that is, no continuous at-birth vaccination) it can combine compartments  $R$  and  $V$ , assuming that the populations are continuous from the left, as opposed to from the right as will be seen later. This assumption does not affect the existence/uniqueness or form of solutions, and later it will use right-continuous differential equations in order to pick a method and be consistent. The general incidence  $g(I, t)$  is subject, as in D'Onofrio (2005), to the assumptions. As before, the first two assumptions are for physicality of the incidence. In the third assumption, it's noted that  $\lambda(t)$  from the restriction (It's not defining  $\lambda$  point wise in  $t$ , that is, it is not letting  $\lambda(t_1) > 0$  while  $\lambda(t_2) \geq 0$ ; rather, it is simply choosing an upper bound to  $\lambda(t_1)$  that is always nonzero. If  $\lambda(t_1)$  itself is always nonzero then we define  $\lambda(t)$  equal to it, otherwise it will lead to choosing a different function). It's also noted that, for the purposes of the proofs in D'Onofrio (2005),  $\lambda(t)$  must be periodic with period  $T$  which divides into the pulse vaccination interval  $\tau$  (i.e.  $\tau = nT$  for some  $n \in \mathbb{Z}$ ). This restriction decreases the generality of the model, but can make

physical sense in the sense that  $\lambda(t)$  could model seasonal variations with a period of one year, while the pulse vaccination campaign is led every few years. Thus restricting the  $g(I, t)$  incidence to one that grows at most linearly in  $I$ . This  $g(I, t)$ , however, does allow far more general incidence rates than the usual bilinear term, is the disease-free periodic solution.

Meng *et al* (2008) and Jin *et al* (2008) studied an SIR model with some people failing to obtain immunity after first dose but gained immunity after later doses. As it's known immunity to infectious diseases after being vaccinated against them might not be life long, so in this study it's assumed that the latent and immunity (not permanent) period are constants. In D'Onofrio (2005) eradication conditions are found; they also extend the results for this non-delay, time varying parameter pulse vaccination model to find conditions for disease permanence. For piecewise-constant contact rate bilinear incidence model using methods from Gao *et al* (2008) to tighten thresholds obtained in Liu and Stechlin (2011), and extend their work to find thresholds which guarantee uniform asymptotic stability under small delay. Then survey of the methods for time varying total population and the effects of such variation on the pulse vaccination schemes. They retain thresholds for eradication by considering the compartment populations as fractions of the total, instead of population numbers, as in Cooke *et al* (1996), Wang *et al* (1999) and extend the results to pulse vaccination models. The fraction technique is also applied to constant population delay systems. In spite of what has been done, the focus of this study is to determine the conditions for which the disease will be eradicated or otherwise become incurable in a population, hence the need to combine pulse vaccination with time delay.

In Rui (2010), the study of a delayed SIR epidemic model with nonlinear incidence rate and pulse vaccination, studied the dynamical behavior of the SIR model describing infection period. The study noted that if  $R_0 < 1$  the infectious population will vanish and the disease will die out. But if  $R_0 > 1$  the infectious population will persist and the disease will become endemic. This meant that to prevent the epidemic from becoming endemic is by increasing the vaccination or shortening the period of pulsing.

In Meng and Chen (2008), their study was the global dynamic behaviors for an SIR epidemic model with time delay and pulse vaccination, they only gave the 'relatively exact' sufficient and unnecessary conditions for global attractivity of 'infection-eradication' periodic solution (with  $R_1 < 1$ ) and uniform permanence of the epidemic disease (with  $R_2 > 1$ ).

The control of epidemics by vaccination, by Verriest *et al* (2011), they used recently developed results on optimal impulsive control for time delay systems in the problem of control of an epidemic through pulse vaccination. For added realism, delays are explicitly incorporated in the epidemiological model. It was shown that the conditions for optimality are easily amenable by an iterative gradient type numerical algorithm. They recommended future work to include multipulse strategies. They expected that current policies of *periodic* vaccination pulses can be

improved upon. This will then provide a 'proof of principle' with which more realistic models for disease may be attacked.

It's from these studies of constant vaccination, pulse vaccination, time delay and linear or nonlinear incidences that precipitated the study undertaken here.

The combination of pulse vaccination in an epidemic model with time delay is the main objective of this study, focusing on pulse vaccination. The study of the pulse vaccination model with delay as given by Gao (2009) will be the basis of this research.

### **Purpose of the study**

Infectious diseases have been a major concern in health sector, as it affects children and young borns adversely. Constant vaccination have been used mostly as a method of controlling infectious diseases e.g. measles, polio, etc. Pulse vaccination is the latest advancement in health sector. This research covers a comprehensive study on the effects of pulse vaccination. In this study we want to investigate the modeling of pulse vaccination of infectious diseases with time delay.

### **Objectives of the study**

The main objective of this study is to model the infectious diseases, come up with the control measures to enable their eradication and determine the effect of the various population parameters on the delayed pulse vaccination using delayed differential equations, also to:

- i. To determine and analyze contact rate parameters which are piecewise constant or time-varying of epidemiological modeling for the disease eradication or become incurable.
- ii. To determine the effects of delay and non-delay pulse vaccination models in the control of an epidemic outbreak.
- iii. To obtain the model for simulating delayed pulse vaccination of infectious diseases.
- iv. To obtain the threshold values for which an outbreak will die or persist in the population.
- v. To discuss the implications of the model for the management of the infectious diseases.

### **Methods/Discussion**

In this study we analyse the deterministic compartmental model of the infectious disease on the population. A deterministic compartmental model is one in which the individuals in a population are classified into compartments depending on their status with regard to the infection, the compartments are; Susceptible –  $S(t)$ , Exposed/latent but not yet infectious –  $E(t)$ , Infected –  $I(t)$  and the Removed –  $R(t)$  for *SEIR* model. There are many different compartmental epidemic



models for example we have *SEIR*, *SIR*, *SI* model and others. The differential equations (DE) will be formulated from figure 1.1; these equations will be assigned initial conditions (IC) and boundary conditions (BC) which will help to solve them. The time-varying or constant parameters will be determined for the dynamical system. The partial differential equations governing the deterministic models have been used. In mid-19th century, Xinzhi L and Peter S (2009) discussed different theorems of aiding in solving partial differential equations. These equations have been derived based on the fundamental governing equations of modeling different infectious diseases, these theorems are:

- (i) The existence and uniqueness theorem,
- (ii) The stability theorems, and
- (iii) The Comparison theorems.

In this section, these theorems on existence, uniqueness, and stability for differential equations (DEs) relevant to the epidemic modeling are presented. Section 2.2.1 discusses ordinary differential equations and Section 2.2.2 extends the results to delay DEs. Section 2.2.3 discusses hybrid systems and in particular the effects of discrete impulses on the preceding theorems.

After presenting theorems applicable to very general systems of differential equations, then apply them to the following systems based on the equations of D’Onofrio *et al* (2005).

**a) Non-delay SIR Model**

$$\left. \begin{aligned} \frac{dS}{dt} &= b(N(t) - S(t)) - \beta \frac{I(t)}{N(t)} S(t) \\ \frac{dI}{dt} &= \beta \frac{I(t)}{N(t)} S(t) - (\mu + \gamma) I(t) \\ \frac{dR}{dt} &= \gamma I(t) - \mu R(t) \end{aligned} \right\} \dots \dots \dots 2.1$$

**b) Delay SEIR Model:**

$$\left. \begin{aligned} \frac{dS}{dt} &= b(N(t) - S(t)) - \beta \frac{I(t)}{N(t)} S(t) \\ \frac{dE}{dt} &= \beta \frac{I(t)}{N(t)} S(t) - \beta e^{-\mu r} \frac{I(t-r)}{N(t-r)} S(t-r) - \mu E(t) \\ \frac{dI}{dt} &= \beta e^{-\mu r} \frac{I(t-r)}{N(t-r)} S(t-r) - (\mu + \gamma) I(t) \\ \frac{dR}{dt} &= \gamma I(t) - \mu R(t) \end{aligned} \right\} \dots \dots \dots 2.2$$

**2.2.1 Ordinary Differential Equations**

An ordinary differential equation (ODE) is an equation that involves some ordinary derivative of a function which can be solved by integration.

$$x'(t) = f(t, x) \dots\dots\dots 2.3$$

Here, theorems for a general ordinary differential equation (ODE) are discussed, which will be relevant to later analysis. This equation is non-autonomous since it depends explicitly on the time variable  $t$  in addition to the state variable  $x(t)$ . It's assumed that the ODE is subject to the initial condition (IC)

$$x(t_0) = x_0. \dots\dots\dots 2.4$$

Analyzing these models using results from Xinzhi (2009) (the theorems are commonly known but will be referenced to Xinzhi (2009) from which they were transcribed). They are then applied to the results to the sample model system (2.3). These theorems are:

**i. The Existence and uniqueness theorem**

**a) Local existence theorem**

Peano's existence theorem gives conditions for when a solution to equation 2.3 exists:

**Theorem 1: Peano's Existence Theorem:** Let  $f \in C(F, R^n)$ , that is,  $f$  is a continuous function from  $F$  to  $R^n$  where

$$F = \{(t, x) \in R \times R^n : |t - t_0| \leq a, \|x - x_0\| \leq c, a, c > 0\} \dots\dots\dots 2.5$$

and let,  $\|f(t, x)\| \leq M$  on  $F$  for some  $M > 0$ . Then the IVP (2.3-2.4) has at least one solution  $x(t)$  defined on  $[t_0 - \alpha, t_0 + \alpha]$  where  $\alpha = \min(a, \frac{c}{M})$ .

**b) Equal Birth and Death Rates**

If  $\mu = b$  and the population is normalized to  $N(t) = S(t) + I(t) + R(t) \equiv 1$ , equation (2.1) becomes:

$$\left. \begin{aligned} dS/dt &= \mu(1 - S(t)) - \beta I(t)S(t) \\ dI/dt &= \beta I(t)S(t) - (\mu + \gamma)I(t) \\ dR/dt &= \gamma I(t) - \mu R(t) \end{aligned} \right\}$$

Defining  $x = [S, I, R]^T$  and  $f(t, x) := [x^1, x^2, x^3]^T$ . Then (2.1) is equivalent to  $x'(t) = f(t, x)$ .

In this normalized case, the physical region is  $x \in \Omega_I := \{(S, I, R) \in [0, 1]^3 : S + I + R = 1\}$  since  $S, I$ , and  $R$ , are fractions of the population. This region is positively invariant.

Using the  $L_1$ -norm,

$$\begin{aligned} \|f(t, x)\| &= |\mu(1 - S) - \beta SI| + |\beta SI - (\gamma + \mu)I| + |\gamma I - \mu R| \\ &\leq |\mu(1 - S)| + |\beta SI| + |\beta SI| + |(\gamma + \mu)I| + |\gamma I| + |\mu R| \\ &\leq \mu + 2\beta SI + 2\gamma I + \mu(|S| + |I| + |R|) \end{aligned}$$

$$\leq 2\mu + 2(\beta + \gamma) = M_I,$$

Since  $S(t), I(t), R(t) \geq 0$  and  $S(t) + I(t) + R(t) = 1$ . Thus  $\|f(t, x)\| \leq M_I$  for all  $x \in \Omega_I$ . If we choose any compact region  $F = \{(t, x) \in R^+ \times \Omega_I: |t - t_0| \leq a, \|x - x_0\| \leq c\}$ , then we have  $f \in C(F, \Omega_I)$  and  $\|f(t, x)\| \leq M_I$  on  $F$ . Therefore by Peano's Existence Theorem, Equation (2.3) has at least one solution on  $[t_0 - \alpha, t_0 + \alpha]$ , where  $\alpha = \min(a, \frac{c}{M})$ . Notice that if we choose  $c \geq 3$  then  $\{x: \|x - x_0\| \leq c\} \supseteq \Omega_I$

### c) Allowance for Population Growth

If the birth and death rates are unequal,  $b \neq \mu$ , then the boundedness of the model is slightly more difficult to prove, since the population sizes may grow. The physical region of interest is now (potentially) unbounded; thus we define  $\Omega_N = R_+^3$  (where  $R^+ = [0, \infty)$ ). The region  $\Omega_N$  is positively invariant with respect to the DE 2.3:

$S(t) = 0 \Rightarrow S' = \mu > 0$        $I(t) = 0 \Rightarrow I' = 0$ :       $R(t) = 0 \Rightarrow R' = \gamma I(t) \geq 0$       so with these initial conditions in  $\Omega_N$ , the trajectory of the solution will never leave  $\Omega_N$ .

Now suppose we again take a compact region  $F = \{(t, x) \in R^+ \times \Omega^N: |t - t_0| \leq a, \|x - x_0\| \leq b\}$ .

Consider  $N(t) = S(t) + I(t) + R(t)$ . Notice from system (2.1) that

$$\begin{aligned} N' &= S' + I' + R' \\ &= [b(S(t) + I(t) + R(t)) - \beta \frac{S(t)}{N(t)} I(t) - \mu S(t)] + [\beta \frac{S(t)}{N(t)} I(t) - (\gamma + \mu) I(t)] + [\gamma I(t) - \mu R(t)] \\ &= b(S(t) + I(t) + R(t)) - \mu(S(t) + I(t) + R(t)) \\ \Rightarrow N' &= (b - \mu) N(t) \Rightarrow N(t) = N_0 e^{(b-\mu)(t-t_0)} \dots\dots\dots 2.6 \end{aligned}$$

So for now we find that  $N(t)$  varies exponentially with time, which means  $N(t)$  is bounded on the compact region  $F$  because,  $N(t) \leq N_0 e^{|b-\mu|a} =: N^M$ . Since all of  $S(t), I(t),$  and  $R(t)$ , are non-negative and  $N(t) = S(t) + I(t) + R(t)$  we must have  $S(t), I(t), R(t) \leq N(t) \leq N^M$  as well. Now we can show that  $\|f(t, x)\|$  is also bounded on  $F$  as follows, noting that all parameters and variables are positive and that

$$N(t) = S(t) + I(t) + R(t) \Rightarrow S(t)N(t) \leq 1 \text{ and } I \leq N:$$

$$\begin{aligned} \|f(t, x)\| &= |b(S + I + R) - \beta \frac{S}{N} I - \mu S| + |\beta \frac{S}{N} I - (\gamma + \mu) I| + |\gamma I - \mu R| \\ &\leq (|bN| + |\beta \frac{S}{N} I| + |\mu S|) + (|\beta \frac{S}{N} I| + |\gamma I| + |\mu I|) + (|\gamma I| + |\mu R|) \\ &\leq bN + 2\beta I + 2\gamma I + \mu(|S| + |I| + |R|) \\ &= (b + \mu)N + 2(\beta + \gamma)I \end{aligned}$$

$$\leq (b + \mu + 2\beta + 2\gamma)N(t) \leq (b + \mu + 2\beta + 2\gamma)N^M =: M.$$

Thus, we find on an arbitrary compact  $F \subset R_+ \times \Omega_N$  that  $f \in C(F, \Omega_N)$  and  $\|f(t, x)\| \leq M$  for all  $(t, x) \in F$ . Hence we find that the system (2.1) has, by Peano's Existence Theorem, at least one solution on  $[t_0 - \alpha, t_0 + \alpha]$ , where  $\alpha = \min\left(a, \frac{b}{M}\right)$ .

This analysis assumes the total population will undergo exponential growth or decay depending on the relative values of  $b$  and  $\mu$ .

**Table 2.1 variables and definitions of sub-populations used as variables**

Variable	Definition
S(t)	The number of susceptibles at time, t
E(t)	The number of Exposed at time, t
I(t)	The number of Infected at time, t
R(t)	The number of Removed at time, t

**Table 2.2 parameter and their definitions**

Parameter	Definition
B	Birth rate
$\mu$	Mortality rate
$\beta$	Contact rate
$\frac{1}{\sigma}$	Average latent rate
$\frac{1}{\gamma}$	Average infectious period
$\rho$	Proportion of those successively vaccinated at birth
$\delta$	Differential mortality due to measles
$\omega$	Proportion of those successively treated after being infected

### SEIR MODEL WITHOUT VACCINATION

The differential equations for this model are;

$$\frac{dS}{dt} = bN(t) - \beta S(t) \frac{I}{N} - \mu S(t) \quad (1)$$

$$\frac{dE}{dt} = \beta S(t) \frac{I}{N} - (\sigma + \mu) E(t) \quad (2)$$

$$\frac{dI}{dt} = \sigma E(t) - (\gamma + \mu + \delta) I(t) \quad (3)$$

$$\frac{dR}{dt} = \gamma I(t) - \mu R(t) \quad (4)$$

$$\frac{dN}{dt} = 0, \text{ and } N = S + E + I + R \text{ is thus constant.}$$

## Properties of the SEIR Model Equations

The basic properties of the model equations 1-4 are feasible solutions and positivity of solutions. The feasible solution shows the region in which the solution of the equations are biologically meaningful and the positivity of the solutions describe the non-negativity of the solutions of the equations 1-4.

### Feasible solution

The feasible solution set which is positively invariant set of the model is given by,

$$\emptyset = \left\{ (S, E, I, R) \in \mathbb{R} : S + E + I + R = N \leq \frac{b}{\mu} \right\} \quad \mathbb{R}_+^4$$

From the Model Equations 1-4 it will be shown that the region is positively invariant. Considering the steps below from the Model equations, the total population of individuals is given by

$N = S + E + I + R$ . Therefore adding the differential equations 1-4, the results becomes

$$\frac{dN}{dt} = (b - \mu)N$$

### Method of solution

A first-order linear differential equation of the form

$$\frac{dN}{dt} = (b - \mu)N. \text{ Thus } N(t) = Ce^{(b-\mu)t} \text{ at } t=0, N(0) = C$$

Hence the solution of the linear differential equation then becomes

$$N(t) = N(0)e^{(b-\mu)t} \text{ Therefore, } \emptyset \text{ is positively invariant.}$$

### Positivity of solutions

It can be proved that all the variables in the model equations 1-4 are non-negative.

Let the initial data set be  $(S, E, I, R)(0) \geq 0 \in \emptyset$ , then the solution set  $(S, E, I, R)(t)$

Of the equations 1-4 is positive for all  $t > 0$ .

**Proof:** from equation 1 we have that,  $S(t) \geq S(0)e^{-(\mu + \beta \frac{I}{N})t} \geq 0$ , since  $(\mu + \beta \frac{I}{N}) > 0$

From equation 2,  $E(t) \geq E(0)e^{(\mu + \sigma)t} \geq 0$ , since  $(\mu + \sigma) > 0$ .

From equation 3,  $I(t) \geq I(0)e^{-(\gamma + \mu + \delta)t}$  since  $(\gamma + \mu + \delta) > 0$

From equation 4, is obtained  $R(t) = \gamma \frac{I}{\mu} + R(0)e^{-\mu t} \geq 0$  since  $\mu > 0$ .

### **Existence of steady states of the system**

The equilibrium points of the system can be obtained by equating the rate of changes to zero.

$$\frac{dS}{dt} + \frac{dE}{dt} + \frac{dI}{dt} + \frac{dR}{dt} = 0$$

### **Global asymptotic stability of the model**

In proving the global stability of the SEIR Model, there is need to find the equilibrium points of the system 5-8.

Assuming that the birth rate,  $b$  is equal to death rate,  $\mu$  i.e.  $b = \mu$

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