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Analysis of Basic Reproduction Number in Epidemiological Model

Manaye Chanie[1*], Demeke Fisseha[2]

[1] Department of Mathematics, Jinka University, Jinka, Ethiopia
[2] Department of Mathematics, Debre Markos University, Debre Marqos, Ethiopia

Email Address

cmanaye88@gmail.com (Manaye Chanie)
*Correspondence: cmanaye88@gmail.com

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Abstract:

In this project we present analysis of basic reproduction number in epidemiological model. Epidemiological analysis and mathematical models are now essential tools in understanding the dynamics of infectious diseases and in designing public health strategies. The threshold for many epidemiological models is the basic reproduction number R_0. It reflects the average number of secondary infections produced by one infected individual put into completely susceptible host society. It is a threshold quantity which determines whether the epidemic will occur or not. We will discuss the general SIS, SIR and SEIR model with vital dynamics for the mathematical modeling of diseases. The reproduction number and the stabilities of both the disease-free and the endemic equilibrium will be calculated. Finally numerical simulations using Matlab Software will be conducted for SIR model with vital dynamics.

Keywords:

Mathematical Model, Reproduction Number, Deterministic (SIS/SIR/SEIR) Model, Disease-Free Equilibrium, Endemic Equilibrium, Simulation

1. Introduction

The introductory section gives a picture of the incitements for this project. In this chapter, a brief history of the basic reproduction number is given as well as the objectives of this master project together with the significance and organization will be discussed. Throughout the world numerous people die from infectious by serious disease like Black Death, smallpox, tuberculosis, etc. Although some of these fatal diseases are gradually disappearing from our lives, many widespread diseases still exist resulting in the death of millions of people. Medical workers and health authorities have devoted substantial efforts and resources into trying to predict and control the spread of diseases of many types. Here mathematicians can be of invaluable assistance and play an important role which will help to decide how resources are allocated. To prevent and to control infectious diseases more effectively, it is important to first fully understand the mechanism of the spread and the transmission dynamics of the diseases, and then provide useful predictions and guidance so that better strategies can be established. Mathematical epidemiology contributes to the understanding of the behavior of infectious diseases, its impacts on

possible future predictions about its spreading. Hence it is important to be able to predict how a disease will develop and spread. Mathematical investigations in the theory of epidemics are therefore important in predicting the development and spread of diseases.

The basic reproduction number, denoted $\boldsymbol{\mathcal{R}_0}$, pronounced as "R nought", is a key concept in epidemiology, and 'one of the foremost and most valuable ideas that mathematical thinking has brought to epidemic theory' [10]. The basic reproduction number was originally developed for the study of demographics [2,23,8,16] but was independently studied for vector born disease such as malaria [22,19] and directly transmitted human infections [15,26,6,13]. It is now widely used in the study of infectious disease, and more recently, in models of in host population dynamics. Two excellent surveys of the tangled history of $\mathcal{R}_0$ can be found in Dietz [7] and Heesterbeek [11]. An excellent overview of the demographic history can be found in Smith & Keyfitz [24].

Ongoing theoretical work has extended $\mathcal{R}_0$ for a range of complex models, including stochastic and finite systems [21], models with spatial structure [20,17] or age structure [1,4]. However, we restrict our attention to very simple deterministic models.

As a general definition, $\mathcal{R}_0$ is the expected number of secondary individuals produced by an individual in its lifetime? The interpretation of 'secondary' however, depends on context. In demographics and ecology, $\mathcal{R}_0$ is taken to mean the lifetime reproductive success of a typical member of the species. In epidemiology, we take $\mathcal{R}_0$ to mean the number of individuals infected by a single infected individual during his or her entire infectious period, in a population which is entirely susceptible. For in host dynamics, $\mathcal{R}_0$ gives the number of newly infected cells produced by one infected cell during its lifetime, assuming all other cells are susceptible.

From this definition, it is immediately clear that when $\mathcal{R}_0 < 1$, each infected individual produces, on average, less than one new infected individual, and we therefore predict that the infection will be cleared from the individual. If $\mathcal{R}_0 > 1$, the pathogen is able invade the susceptible population. This threshold behavior is the most important and useful aspect of the $\mathcal{R}_0$ concept. In an endemic infection, we can determine which control measures, and at what magnitude, would be most effective in reducing $\mathcal{R}_0$ below one, providing important guidance for public health initiatives.

1.1. General Objective

The main objective of this project is to present a precise definition of the basic reproduction number and also come up with the transmission of infection can be easily studied by epidemiological model.

1.2. Specific Objectives

The specific objectives of this project are:

To present the definition of mathematical modeling.

To find the basic reproductive number, the equilibrium states of the SIS, SIR and SEIR model with vital dynamics.

To present the limitation of the basic reproduction number.

1.3. Significance of the Project

The project will be significant to the society in the following ways:

It will help health professionals to understand the role of basic reproduction number in epidemiology and set strategies on how the diseases will decline and eventually die out.

It will provide useful information that will help to decide the stability of the disease free and endemic equilibrium points.

It may help in such studying issues furthermore.

1.4. Organization of the Project

The project consists of five main chapters. The first chapter is an introductory chapter that encompasses the background of the topic, objectives and significance.

In chapter two we introduce some mathematical preliminaries and basics that are important prerequisites to the study of epidemiological models. It includes definition of key terms and concepts, mathematical modeling, why epidemiological models, deterministic and stochastic approach to epidemiological models.

Chapter three provides the basic reproduction number. In this chapter, definition of the basic reproduction number and $\mathcal{R}_0$ values will be presented. We discuss the factors that affect the basic reproduction number. These are the contact rate, infectious period and mode of transmission. We will discuss the two methods used to calculate the basic reproduction number. These are the largest Eigenvalue of the Jacobian matrix and the next generation method. We discuss the importance and limitation of the basic reproduction number.

Chapter four presents deterministic epidemiological models. In this chapter, we will be presented the description, assumption, notation of variables and parameters, equations and equilibrium points of the SIS, SIR and SEIR models.

In Chapter five we will come up with the numerical simulation of SIR model with vital dynamics using ODE solvers coded in MATLAB programming language.

1.5. Source of Information

The project will be involved information obtain from some books, published journals, unpublished journals, which are available in the library and browsing internet. In addition to this, we discussed on the project topic with my colleagues at my work place and with my classmates in the school in order to get right information to make the data reliable and valuable. All the information obtained will be recorded in the project that will be carried out.

2. Mathematical Preliminaries and Basics

2.1. Definition of Infectious Diseases

Infectious diseases, also known as transmissible diseases or communicable diseases are a great human concern. Infectious diseases are caused by pathogenic microorganisms or simply \germs. Germs are tiny living things that can be found almost everywhere such as in the air or in water. An infectious disease is an illness due to a specific infectious agent or its toxic products that arises through transmission of that agent or its products from an infected person, animal or reservoir to a

susceptible host, either directly or indirectly through an intermediate plant or animal host, vector or inanimate environment. You can get infected by touching, eating, drinking or breathing something that contains a germ.

2.2. Modes of Transmission of Disease

The transmission can happen in a direct or indirect way.

Direct contact transmission occurs when there is physical contact between an infected person or animal and a susceptible person. Germs can pass from one person to another through physical contact, coughing, through a blood transfusion, or even through the exchange of body fluids from sexual contact. Also, a pregnant woman may pass germs that cause infectious diseases to her unborn baby. AIDS, Anthrax and Plagues are some examples of disease that spread by direct contact. (Figure 1)

Figure 1. *Disease transmission schematic with direct contact.*

Indirect contact transmission occurs when there is no direct contact between the holder of the disease and the one that this disease is transmitted to. Germs can be found on inanimate objects such as doorknobs. When you touch a doorknob after someone with the flu has touched it, you can pick up the germs he or she left behind, and you may become infected. Also, a disease can spread by airborne dispersal, like droplet transmission, when someone is sick and he sneezes, he expels droplets into the air around him; the droplets he expels contain the germ that caused his illness. A disease can also spread through food contamination or insect bites. Some germs use insects such as mosquitoes, fleas, lice or ticks to move from host to host [3]. Malaria and Tapeworm are some examples of disease that spread by indirect contact. (Figure 2)

Figure 2. *Disease transmission schematic with indirect contact.*

Infectious diseases are classified by frequency of occurrence; an infectious disease can be an epidemic, endemic or pandemic. An endemic is an infectious disease that is constantly present in a population. A disease that quickly and severely affects a large number of people and then subsides is an epidemic. For epidemics we have many cases of infection in a given area in short period. Seasonal influenza is an example of an epidemic. A pandemic disease is a world-wide epidemic that may affect entire continents or even the world. Influenza is occasionally pandemic, such as the pandemic of 1918. Throughout the Middle-Ages, successive pandemics of the plague killed millions. Thus, from an epidemiologist's point of view, the Black Death in Europe and AIDS in sub-Saharan Africa are pandemic rather than epidemics. (Table 1)

Table 1. *Infectious Diseases and how they are spread.*

Disease	Transmission
AIDS	Contact of body fluid with that of an infected person. Sexual contact and sharing of unclean
Hepatitis	Direct or indirect contact with infected person
Common cold	Direct or indirect contact with infected person
Gonorrhea	Sexual contact

Malaria	Mosquito bite
Measles	Direct or indirect contact with infected person

2.3. Some Key Terms to Describe Individuals

Most epidemic models are based on dividing the population into a small number of subclasses (compartments). Each containing individuals, that are identical in terms of their status with respect to the disease in question.

Here are some of the main compartments that a model can contain;

• Passive immune (M): is composed by newborns that are temporary passively immune due to antibodies transferred by their mothers;

• Susceptible (S): is the class of individuals who are susceptible to infection; this can include the passively immune ones who lost their immunity;

• Exposed or Latent (E): compartment refers to the individuals that despite being infected, do not exhibit obvious signs of infection and the abundance of the disease may be too low to allow further transmission. Individuals are exposed but not infectious.

• Infected (I): in this class, the level of parasite is sufficiently large within the host and there is a potential of transmitting the infection to other susceptible individuals;

• Recovered or Removal (R): includes all individuals who have been infected and have recovered from the disease and are immune for life.

Not all disease models will include all of these classes, and some models will include more. For example, there may be a vaccinated class; there may be waning immunity such that those individuals who have recovered steadily decay to a partially-susceptible class. We may also wish to sub-divide the classes further, such that the population is age-structured or sexually-structured. In general the choice of compartment to include in a model depends on the characteristics of the particular disease being modeled and the purpose of the model.

2.4. Stages of Infection /Timelines for Infection and Disease

The infection has different stages in a person and the duration and strength vary according to a person's immunity, age, health, previous exposure to the infection etc. A person who is not infected and has a chance of getting infected is said to be in susceptible stage. A person's immunity system may destroy the infectious organism. It may continue to stay inside a person's body depending upon his characteristics.

Different stages of infection are as follows:

• Latent Period

The latent period is the period between the exposure and the onset of infectiousness.

• Incubation Period

It is the time period between the infectious period and the onset of symptoms (the time from first infection to the appearances of symptoms).

• Symptomatic Period

Symptomatic period starts after the incubation period when the symptom shows up till the infected person stops infecting other. (Figure 3)

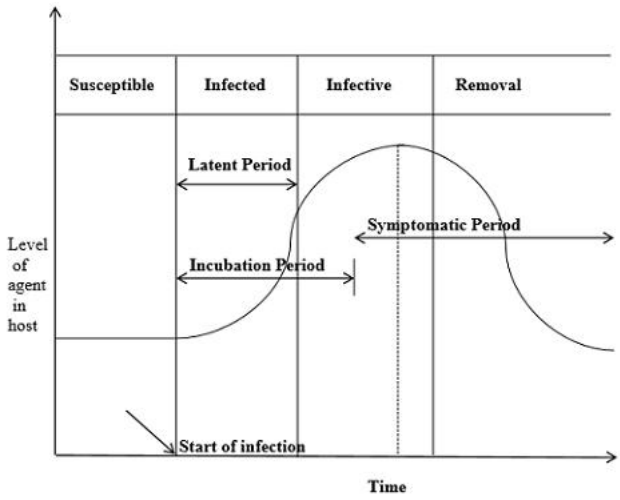

Figure 3. *Stages of Infection.*

2.5. Some Key Terms to Describe the Infectious Disease at the Population Level

Epidemic: The occurrence in a community or region of cases of an illness clearly in excess of normal expectancy.

Endemic: The constant presence/ habitual presence (usual occurrence) of a disease within a given geographical area.

Pandemic: An epidemic occurring over a very wide area, crossing international boundaries and usually affecting a large number of people.

2.6. Mathematical Modeling

Mathematical modeling is an activity of translating a real world situation into the abstract language of mathematics for subsequent analysis of the problem. A mathematical model is a mathematical description of the situation, typically in the form of a system of equations.

Each involvement in developing other sciences is a success for mathematics, and, for mathematicians, biology opens up many new branches of study. Biology provides interesting topics and mathematics provides models to help in understanding these topics. Mathematical modeling of infectious diseases is one of the interesting areas of mathematical biology. Mathematical modeling helps in the understanding of the spread of an infectious disease and provides a platform to study how to control the spread and thus control health problems.

The mathematical modeling of natural phenomena or disease modeling is one of the major research areas for mathematicians and biologist. The mathematical models of disease or natural phenomena often involved complexity and non-linearity. These complexities and non-linearity cannot be solved analytically. The models that present the epidemiology of a particular disease can be analyzed by studying their dynamical behavior, reproduction number, stability analysis, and their numerical results. By studying such properties of the epidemiological models, one can get reliable and useful information about the disease control and spread.

Mathematical models have become important tools in analyzing the spread and control of infectious diseases. The model formulation process clarifies assumptions,

variable, and parameters; moreover, models provide conceptual results such as thresholds, basic reproduction numbers and contact numbers.

Mathematical models and computer simulations are useful experimental tools for building and testing theories assessing quantitative conjectures, answering specific questions, determining sensitivities to changes in parameter values, and estimating key parameters from data. Understanding the transmission characteristics of infectious diseases in community, regions and countries can lead to better approaches to decreasing the transmission of diseases. Mathematical models are used in comparing, planning, implementing, evaluating, and optimizing various detection, prevention and control programs.

In order to make a model for a disease in a population, we divide the population into different classes and we study the variation in numbers in these classes with respect to time. The choice of these classes is related to the disease studied. The most used classes are, S, the number of susceptible individuals, E, the number of exposed individuals, I, the number of infected individuals and R, the number of recovered individuals. For example, if a model considers "flu" as disease, this model would be an SIS model because individuals recover with no immunity to the disease; that is, individuals are immediately susceptible once they have recovered. Some of the well-studied epidemic models are: SI, SIR, SIS, SEIR, SEIS (Table 2).

Table 2. *Different epidemiological models.*

Model name	Special Property	Example of a disease
SI	No recover (infectious hosts remain infectious for life)	Herpes, AIDS, plant infection
SIR	Permanent immunity after recovery	Influenza, Rubella, Mumps
SIS	No immunity after recovery	Gonorrhea, Syphilis
SEIR	Latent period where the infected is not infectious yet	Measles, Tuberculosis
SEIS	SIS + latent period	Malaria

Thus, some of the flow diagrams of epidemic models are as follows:

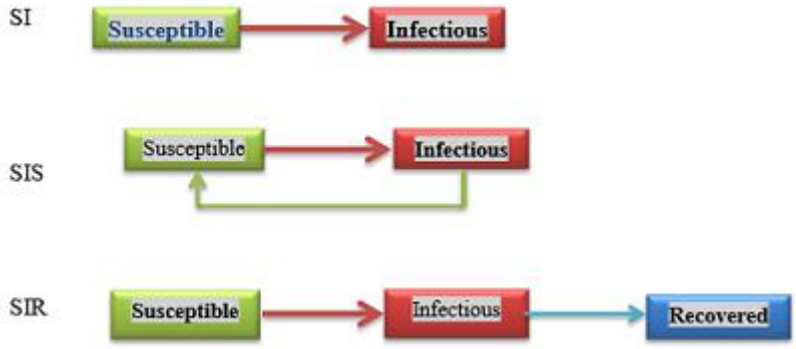

Figure 4. *The flow diagrams of epidemic models. Source: Deterministic Modeling of Infectious Diseases: Theory and Models. Trottier et al.*

2.7. Deterministic and Stochastic Approach to Mathematical Modeling

A first distinction within the wide variety of mathematical approaches mostly undertaken in infectious disease epidemiology can be made between deterministic and stochastic models. For instance, mathematical epidemiology uses models based on difference, differential, integral or functional differential equations. Deterministic models have had a very important role in the description of the spread of an infection.

Using for instance a system of differential equations, once the initial conditions and parameter values have been fixed, it is possible to obtain solutions as functions of time that are unique.

On the other hand, in stochastic models, there are transition probabilities at each step of moving from one population state to another. The same set of parameter values and initial conditions will lead to an ensemble of different output.

In simple deterministic models for epidemics, it is possible to obtain a precise threshold which allows determining whether an epidemic will occur or will not occur. Instead, a stochastic model may lead, for instance, to probabilities that a disease would occur or can give information as mean time of extinction. Thus the approach, concepts and appropriate questions are quite different for stochastic models.

Both deterministic and stochastic epidemiological models have other limitations besides being only approximations of reality. Obviously, the natural world is buffed by stochasticity. But, stochastic model are considerably more complicated.

Especially when the aim is to model a disease, deterministic models do not take into account the role of chance that the disease is subjected to. A set of initial conditions lead to exactly one solution in a deterministic model; thus no information is available on the reliability or the confidence in the results.

On the other hand, these changes are embedded in stochastic models, but it is harder to get analytical results for these models. Moreover, computational results are also harder since simulations could require many computer runs in order to detect patterns and get quantitative results. Deterministic model are rapid to simulate, relative easy to parameterize and capture the average of epidemic behavior, i.e. they can be considered a valid tool for predictions in large populations. On the other hand, stochastic approaches can be appropriate to model the spread of a disease in small populations.

The mathematical models we will consider in this project are deterministic compartmental models at population level. This type of model allows us to divide the entire population, involved in the transmission, into compartments that usually describe the infectious state.

2.8. Why do We Model Infectious Diseases?

Following Heesterbeek & Roberts (1995):

• Gain insight into mechanisms influencing disease spread, and link individual scale ‘clinical’ knowledge with population-scale patterns.

• Focus thinking: model formulation forces clear statement of assumptions, hypotheses.

• Derive new insights and hypotheses from mathematical analysis or simulation.

• Establish relative importance of different processes and parameters, to focus research or management effort.

• Thought experiments and “what if” questions, since real experiments are often logistically or ethically impossible.

• Explore management options.

2.9. Limitations of Mathematical Modeling

The following are some of the limitations of mathematical modeling.

• Mathematical model is not reality; it is an extreme simplification of reality.

• Deterministic models do not reflect the role of chance in disease spread and do not provide confidence interval on results.

• Models that incorporate randomness are harder to analyze than the corresponding deterministic models.

3. Basic Reproduction Number

Basic reproduction number: The basic reproduction number of an infectious disease is a pivotal concept in epidemiology. It is a famous result due to Kermack and McKendrick [15]. It is an important measure of transmissibility of the disease.

The basic reproduction number $\mathcal{R}_0$ is defined as the expected number of secondary cases produced in a completed susceptible population, by a typical infected individual during its entire period of infectiousness [1,4]. In the simple model which includes only one infected compartment, its value can be calculated as the product of the rate at which such an individual gives rise to infections and the duration of their infectious period. In turn, the infection rate is a product of the rate at which an infective meets susceptible individuals, i.e. the contact rate, and the per-contact probability of transmission. For complex models we use the so-called next generation matrix approach to compute or to estimate $\mathcal{R}_0$.

3.1. Methods for Calculating the Basic Reproduction Number

In this section, we identify the Jacobian and the next generation methods used to calculate $\mathcal{R}_0$. But, there are many other methods used to calculate $\mathcal{R}_0$ such as the survival function, constant term of the characteristic polynomial, the final size equation, etc. Many methods produce different values of $\mathcal{R}_0$ based on what the modeler considers to be appropriate.

It is important to understand that employing one of the methods at random does not guarantee the calculation represents the number of secondary infections arising from a single infected individual.

3.1.1. The Jacobian Method

The Jacobian is

• A matrix of partial derivatives.

• Created by differentiating every equation with respect to every variable.

Given n function $f_1(x_1,x_2,...,x_n)$, $f_2(x_1,x_2,...,x_n)$,...,$f_n(x_1,x_2,...,x_n)$, describing n the dynamics variables $x_1,x_2,...,x_n$ the Jacobian matrix J is defined as:

$$J = \begin{bmatrix} \frac{\partial f_1}{\partial x_1} & \frac{\partial f_1}{\partial x_2} & \cdots & \frac{\partial f_n}{\partial x_n} \\ \frac{\partial f_2}{\partial x_1} & \frac{\partial f_2}{\partial x_2} & \cdots & \frac{\partial f_n}{\partial x_n} \\ \vdots & \vdots & & \vdots \\ \frac{\partial f_n}{\partial x_1} & \frac{\partial f_n}{\partial x_2} & \cdots & \frac{\partial f_n}{\partial x_n} \end{bmatrix}$$

A predictive threshold is often found through the study of the eigenvalues of the jacobian at the disease-free equilibrium (for details, see Diekmann & Heesterbeek [4]). This is a simple, widely used method for ODE systems.

A method for determining stability:

(1). Calculate the disease free equilibrium

(2). Create the Jacobian matrix

(3). Evaluate the Jacobian at the equilibrium

(4). Find the eigenvalues

(5). If all eigenvalues < 0 ⇒ stable

If even one eigenvalue > 0 ⇒unstable

(6). Largest eigenvalue ⇒ 0-like threshold

The Jacobian method clearly allows us to derive a parameter that reflects the stability of the disease- free equilibrium. Around the disease free equilibrium, the linear systems will have the same stability properties as the nonlinear system if it is hyperbolic; that is, if no eigenvalues have zero real part. In particular, if all eigenvalues have negative real part, then the equilibrium is stable, whereas if there is an eigenvalue with positive real part, the equilibrium is unstable.

Usefulness of the Jacobian:

• The Jacobian can determine stability of equilibria

• It can also lead us to -like thresholds

• These determine whether an epidemic will persist or die out.

3.1.2. Next Generation Method

If the model contains several infected compartments, for instance, latent period and infection period, then cannot be determined directly from the definition as in section (3.1). In this case the next generation method, introduced by Diekman et al. [5], is the general method of deriving in such cases, encompassing any situation in which the population is divided into disjoint classes.

Consider the general compartment model in Equation (3.2) below, which models the dynamic of the transmission of a disease in a heterogeneous population in which the individuals can be distinguishable by the stage of the disease, spatial position, and age, but can be grouped into n homogeneous compartments according to stage of disease (see van den Driessche [25]).

$$\frac{dx_i}{dt} = f_i = \mathcal{F}_i(x) - \mathcal{V}^-(x) + \mathcal{V}^+(x), i = 1,2, \ldots n \qquad (3.2)$$

Regarding the system (3.2), let $x = (x_1, \ldots, x_n)'$ where $x_i \leq 0$ is the number of individuals in each compartment and also we assume that the first m compartments are related to infected individuals, so the m+1, ..., n correspond to those compartments free of disease. Let $X_q = \{x_i \geq 0 \mid x_i = 0 \text{ for } i = 1, \ldots, m\}$ be the set of disease free states (all compartment with absence of disease). Regarding the system (3.2), let $\mathcal{F}_i(x)$ be the rates of appearance of new infections into compartment i, $\mathcal{V}^-(x)$ be the rate of transfer of individuals out of compartment i and $\mathcal{V}^+(x)$ the rate of transfer of individuals into compartment i. Also we assume that all these functions are

continuous and differentiable at least twice in each variable (x_i) and also they satisfy the following five assumptions.

Assumption one: If $x \geq 0$, then $\mathcal{F}_i(x)$, $\mathcal{V}^-(x)$,$\mathcal{V}^+(x)$ are all non-negative since each of these functions describe the transition of individuals between compartments.

Assumption two: If $x_i = 0$ then $\mathcal{V}^-(x) = 0$. If the number of individuals in each compartment is equal to zero then there is no transfer of individuals out of the compartment. In particular if x is the number of individuals in disease state, then the rate of transfer of individual $\mathcal{V}^-(x)$ will be zero for infected compartments.

Assumption three: $\mathcal{F}_i(x) = 0$ if i > m. This means that the rate of appearance of new infections into the disease Free State is zero. Consider the model in system (3.1) with Assumptions one and two. If $x_i = 0$ then the system 3.1 will become $\frac{dx_i}{dt} = f_i = \mathcal{F}_i(x) + \mathcal{V}^+(x) \geq 0$.

Assumption four: If $x \in Xq$, then $\mathcal{F}_i(x) = 0$ and $\mathcal{V}^+(x) = 0$ for i = 1, ..., m this indicates that if the number of individual x is the set of disease free state there will be no transfer out to infected compartment, so in this case we will say that the disease free state is invariant because if the population is free of disease then the population will remain free of disease.

Assumption five: consider the system (3.1) restricted on the set of disease-free state Xq, we define the DFE and we subscript it by x_0 to be the local asymptotically stable equilibrium solution to our model restricted to Xq. If $\mathcal{F}_i(x) = 0$ all the eigenvalues of the Jacobian matrix $D f(x_0)(x - x_0)$ (which is calculated from system (3.1) around equilibrium point (x_0) have negative real part,

$$\frac{dx_i}{dt} = Df_i(x_0)(x - x_0) = D\boldsymbol{\mathcal{F}_i}(x_0) - D\boldsymbol{\mathcal{V}}_i(x_0) \tag{3.3}$$

Where

$(x_0) = \mathcal{V}^- - \mathcal{V}^+$.

For a disease-free equilibrium point, $D(x_0)$, of (3.1), where $D(x_0)$ and $f_i(x)$ satisfy assumptions (one to five), we define m × m matrices, F and V,

$$F = \left[\frac{\partial \boldsymbol{\mathcal{F}}(x_0)}{\partial x_j}\right] \quad \text{and} \quad V = \left[\frac{\partial \boldsymbol{\mathcal{V}}(x_0)}{\partial x_j}\right] \tag{3.4}$$

For $i \geq 1$ for the number of compartments, and $1 \leq j \leq m$ for the infected compartments only

According to Diekmann and Heesterbeek,

The next generation matrix is

$$K = FV^- \tag{3.5}$$

where F and V are transmission and transition matrices respectively.

The basic reproduction number is the eigenvalue of largest magnitude, or spectral radius of the next generation matrix, that is, the number of all new infectious host types in the next generation.

$$\mathcal{R}_0 = \rho(K) = \rho(FV^-) \tag{3.6}$$

where ρ denotes the spectral radius (dominant eigenvalue) of the matrix (FV^-).

3.2. $\mathcal{R}_0$ is a Threshold Criteria

One of the main goals of studying epidemiology models is to analyze the spread of a disease in order to try to understand its underlying principles. The reason for this is to be able to come to some conclusions about the severity and duration of the epidemic. Certainly, it is desired to be able to answer important questions such as: Will there be an epidemic? If so, how long will it last? How severe might it be? Can the disease be eradicated through some type of control scheme? Mathematically, most of these questions translate to studying the stability properties of the models' disease-free solution.

Thresholds that dictate the persistence or eradication of a disease are very important in epidemiology. Hence, one of the main goals of disease modeling is to establish criteria based on the parameters and structure of the system that will ensure disease eradication. This has been done in many of the classical models in the literature, and the basic reproduction number, $\mathcal{R}_0$ is one of the most effective threshold parameters, which describes the features of mathematical problems concerning infectious diseases. When $\mathcal{R}_0 < 1$, this simply implies that each infected individual can produce an average of less than one new infected individual during his/her entire period of infectiousness. In this situation the disease will not persist in the population and may be wiped out. But in a situation where $\mathcal{R}_0 > 1$, then each infected individual produces on average more than one new infection and the disease is spread in the population. Thus the basic reproduction number $\mathcal{R}_0$ is often considered as the threshold quantity that determines when an infection can invade and persist in a new host population. The larger the magnitude of $\mathcal{R}_0$, the faster the disease will spread, and presumably the more difficult it will be to control.

3.3. Factors that Affect $\mathcal{R}_0$

The following factors are taken into account to calculate $\mathcal{R}_0$ of a disease:

• Infectious period / disease duration/ :- Some diseases are contagious for longer periods than others. For example, according to the Centers for Disease Control and Prevention, adults with the flu are typically contagious for up to eight days, while children can be contagious for up to two weeks. The longer the infectious period of a disease, the more likely an infected person is to spread the disease to other people. A long period of infectiousness will contribute to a higher $\mathcal{R}_0$ value.

• Contact rate:- If a person who's infected with a contagious disease comes into contact with many people who aren't infected or vaccinated, the disease will spread more quickly. If that person remains at home, in a hospital, or otherwise quarantined while they're contagious, the disease will spread more slowly. A high contact rate will contribute to a higher $\mathcal{R}_0$ value.

• Modes of transmission:- The diseases that spread most quickly and easily are the ones that can travel through the air, such as the flu or measles. Physical contact with an infected person isn't necessary for the transmission of such conditions. You can catch the flu from breathing near someone who has the flu, even if you never touch them.

In contrast, diseases that are transmitted through bodily fluids, such as HIV, aren't as easy to catch or spread. This is because you need to come into contact with infected blood, saliva, or other bodily fluids to contract them. Airborne illnesses tend to have a higher value than those spread through contact.

3.4. Epidemiological Importance of $\mathcal{R}_0$

The following are the major important points of $\mathcal{R}_0$:

• It determines how fast an epidemic is growing.

• It determines the prevalence of an endemic infection.

• It determines the efficacy of an intervention program.

• Can be used to calculate the critical coverage rates of vaccines, or any intervention.

• Can be used for stability analysis (based on the values of $\mathcal{R}_0$, we can decide the stability of the disease free and endemic equilibrium points).

3.5. Limitation of $\mathcal{R}_0$

When calculated from mathematical models, particularly ordinary differential equations, what is often claimed to be $\mathcal{R}_0$ is, in fact, simply a threshold, not the average number of secondary infections.

• Suppose

$\mathcal{R}_0$ = 2, this implies infection will persist in the population, but it is not guaranteed that one infected individual will produce two secondary infections; it may be three, or 1000, or 1+ε. Similarly, if $\mathcal{R}_0$= 0.6, it is guaranteed that the infection will die out, but it is not necessarily true that one infected individual will produce an average of 0.6 secondary infections.

What these thresholds will do is determine whether a disease will die out (if $\mathcal{R}_0$< 1) or whether it may become epidemic (if $\mathcal{R}_0$ > 1), but they generally cannot compare different disease.

• Suppose

HIV has an $\mathcal{R}_0$ of 3

SARS has an $\mathcal{R}_0$ of 5

• Unless they were calculated using the same method, we don't know if SARS is worse than HIV

• All we know is that both will persist

4. Deterministic Epidemiological Models

The deterministic epidemiological models will be used in this chapter. This is where individuals in the population are assigned to different subgroups or compartments, each representing a specific stage of the epidemic. The transition rates from one class to another are mathematically expressed as derivatives, hence the model is formulated using differential equations. While building such models, it must be assumed that the population size in a compartment is differentiable with respect to time and that the epidemic process is deterministic. Deterministic epidemiological models form the simplest models in the mathematical study of infectious disease dynamics. Unlike stochastic models, deterministic epidemiological models consider the population level mean behavior of the system. In deriving and analyzing these models, we usually perform the following steps.

(1) Derive model and compartments.

(2) Write equations corresponding to these compartments.

(3) Derive parameter values from data/literature.

(4) Mathematically analyze equations.

• Evaluate equilibrium points.

• Determine stability of equilibrium points.

• Derive threshold conditions.

• Draw phase portraits.

We will use the terminology SIS to describe a disease with no immunity against re-infection, to indicate that the passage of individuals is from the susceptible class to the infective class and then back to the susceptible class. We would use the terminology SIR to describe a disease which confers immunity against re-infection, to indicate that the passage of individuals is from the susceptible class S to the infective class I to the removed class R. Usually, diseases caused by a virus are of SIR type while diseases caused by bacteria are of SIS type. In addition to SIS and SIR models, more complicated compartmental structure is possible. For example, SEIR model, with an exposed period between being infected and becoming infective. We shall describe such models in later sections.

4.1. SIS Model

The SIS model is a two-state deterministic model which assumes that a person can be in one of only two states, either susceptible (S) or infectious (I). These states are often called compartments and the corresponding models are called compartment model. Not all diseases are accurately described by a model with only two states, but a two-state model is useful in describing some classes of micro parasitic infections to which individuals never acquire a long lasting immunity. In a simple model for this process, individuals never enter a recovered state, but rather alternate between being susceptible and being infectious. Such a model is appropriate for diseases that commonly have repeat infections, for example, the common cold (rhinoviruses) or sexually transmitted diseases such as gonorrhea or syphilis.

In order to model such an epidemic we divide the host population being studied into two classes:

• The class of individuals who are healthy but can contract the disease. These are called susceptible individuals or susceptible. The size of this class is usually denoted by S

• The class of individuals who have contracted the disease and are now sick with it, called infected individuals. The size of the class of infected individuals is denoted by me.

In fact, there are two SIS models.-They describe either an SIS model without vital dynamics, the duration of the disease is assumed to be short compared to the time scale of the population dynamics, or they describe an SIS model with vital dynamics (a disease present in the population for a long period of time where the class of susceptible is being nourished by new income from births). However, we restrict our attention to SIS model with vital dynamics.

4.2. SIS Model with Vital Dynamics

4.2.1. Description of the Model

In a susceptible-infected-susceptible model to derive the differential equations, we consider how the classes change over time. When a susceptible individual enters into contact with an infectious individual, that susceptible individual becomes infected with a certain probability and moves from the susceptible class into the infected class. The susceptible population decreases in a unit of time by all individuals who become infected in that time. At the same time, the class of infectives increases by the same number of newly infected individuals.

Each individual can reside in exactly one compartment and can move from one compartment to another. Compartmental models are schematically described by a diagram often called a flowchart. Each compartment in a flowchart is represented by a box indexed by the name of the class. Arrows indicate the direction of movement of individuals. The movement arrows are typically labeled by the transition rates (see Figure 5).

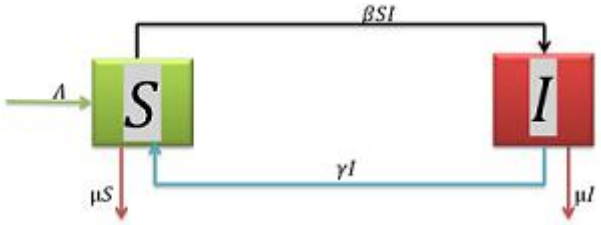

Figure 5. *Flow chart of the SIS model with vital dynamics.*

Table 3. *Description of state variables for SIS model.*

Variable	Name	Units	Meaning
S	Susceptible Individuals	Number of Individuals	Individuals susceptible to infection who can contract the disease if they are exposed to it
I	Infected Individuals	Number of Individuals	Individuals infected by infection who are capable of transmitting the infection to any susceptible individuals

Table 4. *Description of SIS model Parameters.*

Parameter	Name	Units	Meaning
Λ	Birth Rate	$\frac{birth}{day}$	Birth rate of newborns each year
μ	Death Rate	$\frac{death}{day}$	Death rate of susceptible and infected individuals each year
β	Transmission Rate (Susceptible to Infected)	$days^{-1}$	Rate at which susceptible individuals Become infected individuals and leave susceptible class and enter infected class
γ	Recovery Rate (Infected to Susceptible)	$days^{-1}$	Rate at which infected individuals leave infected class and enter susceptible class

4.2.2. Basic Assumptions of the SIS Model

To formulate a model, we have to make assumptions to simplify reality. The model is based on the following assumptions.

• The population size is constant during the epidemic period, hence the birth and natural death rates are equal (Λ = μ) and there are no disease-induced deaths

• Individuals are either susceptible or infectious.

• All susceptible individuals are equally susceptible and all infected ones are equally infectious.

• There is no latent period for the disease, i.e., the disease is transmitted instantaneously when the contact takes place.

• The size of each compartment is a differentiable function of time.

4.2.3. Differential Equations for SIS Model

Differential equations have been developed as mathematical models to study the dynamics of disease transmission for many communicable diseases. For SIS model the population is divided into two classes based on epidemiological status. Individuals are classified as either susceptible or infected. The sizes of these groups are represented by S, and I respectively. This description of the SIS model was made more mathematical by a formulated differential equation for the proportion of individuals in each class.

Susceptible

The rate at which people become susceptible starts with the birth rate, Λ and those people become recovered γ I. From that rate is subtracted the normal death rate of people that have not yet been infected to a disease, μS and those people become infected, βSI.

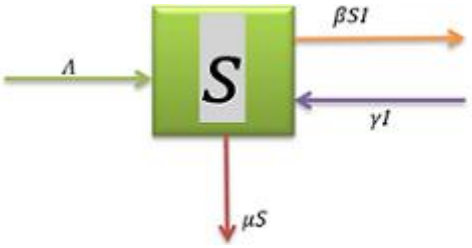

Figure 6. *An S (Susceptible) - compartment model from SIS.*

From what has just been discussed above, the rate of change of the susceptible class can be put into an equation form as below,

$$\frac{dS}{dt} = \Lambda + \gamma I - \mu S - \beta SI \tag{4.1}$$

Infected Component

The rate of change of the infected class is equal to the difference between infected members that moved from the susceptible into the infected class and the rate at which infected individuals die naturally and recover into the susceptible class.

Figure 7. *An (Infected) - compartment model from SIS.*

From what has just been discussed above, the rate of change of the infected class can be put into an equation form as below,

$$\frac{dI}{dt} = \beta SI - (\mu + \gamma)I \tag{4.2}$$

Thus, putting the two model equations together, this leads to the following formulations of the SIS model from the description, assumptions and compartmental diagram and was given as follows;

$$\begin{cases} \frac{dS}{dt} = \Lambda + \gamma I - \mu S - \beta SI \\ \frac{dI}{dt} = \beta SI - \mu I - \gamma I \end{cases} \quad (4.3)$$

The nonlinear system of differential equations formulated above has initial conditions

$$S(0) = S_0 > 0,\ I(0) = I_0 > 0,$$

Also, the rate of transmission, the recovery rate and the birth and death rate are all non-negative ($\beta > 0, \gamma > 0, \Lambda > 0$ and $\mu > 0$ respectivelly).

Hence $N(t) = S(t) + I(t)$ and

$$\frac{d}{dt}[S(t) + I(t)] = 0$$

Since $\frac{dN}{dt} = 0$ and thus $N = S + I$ is a constant.

Now all the state variables and parameters remain non-negative since they represent human population.

4.2.4. Stability Analysis of SIS Model

In this section we discuss the existence of equilibrium points, linearized system of equation (4.3) and by analyzing the eigenvalues of the Jacobian matrices of system (4.3), we show the stability analysis using the threshold value $\mathcal{R}_0$.

Finding the equilibrium points or steady states is one of the first steps in analyzing any dynamical system. Equilibrium is a state of a system which does not change with time. An equilibrium solution is a constant solution of the system, and is usually called a Critical point.

In epidemiology we have two types of equilibrium points; disease free-equilibrium (E_0) and endemic equilibrium (E^*).

i. Once a disease dies out, at I = 0, no new infectious individuals can develop for that particular outbreak. There are no infectious individuals left to infect anyone who is susceptible. This is known as the disease free equilibrium.

ii. An endemic equilibrium is when the number of infectious individuals in the population reaches a certain value and remains there. This usually occurs when the rate of infection equals the rate of recovery.

If the dynamics of a system is described by a differential equation (or a system of differential equations), then we can find the equilibrium points for a particular system of equations by setting each differential equation in the system equal to zero and solving to find the number of individuals in each compartment.

To find the equilibrium points of equation (4.3) the right-hand sides of each differential equation are set to zero. We have $\frac{dS}{dt} = \frac{dI}{dt} = 0$

That is,

$$\begin{cases} \Lambda + \gamma I - \mu S - \beta SI = 0 \\ \beta SI - \mu I - \gamma I = 0 \end{cases} \quad (4.4)$$

i. Disease-Free Equilibrium (E_0)

At disease-free equilibrium, it is assumed that there is no disease in the system, to do so we must set $I = 0$ into the above equations of (4.4) and solve.

Now solve the first equation of (4.4) for S by using $I = 0$.

$$\Lambda - \mu S = 0$$
$$\Rightarrow \Lambda = \mu S$$
$$\Rightarrow S = \frac{\Lambda}{\mu}$$

Now from the assumptions of the model birth rate is equal to death rate, i.e. $\Lambda = \mu$

$$\Rightarrow S = 1$$

Therefore, the disease-free equilibrium becomes:

$$E_0 = (1,0)$$

ii. Endemic Equilibrium (E^*)

At endemic equilibrium the disease cannot be totally eradicated but remains in the population. For the disease to persist in the population, the susceptible class and the Infectious class must not be zero at equilibrium. In other words, if $E^* = (S^*, I^*)$ is the endemic equilibrium, then $E^* = (S^*, I^*) \neq (0,0)$. In order to obtain the endemic equilibrium, we solve systems of differential equation (4.4) simultaneously taking into consideration the fact that $E^* = (S^*, I^*) \neq (0,0)$.

For $I \neq 0$, solve the second equation of (4.4) for S.

$$\beta SI - (\mu + \gamma)I = 0$$
$$\Rightarrow I(\beta S - (\mu + \gamma)) = 0$$
$$\Rightarrow I = 0 \text{ or } \beta S - (\mu + \gamma) = 0,$$

But

$$I = 0$$

is disease-free equilibrium.

$$\Rightarrow \beta S - (\mu + \gamma) = 0$$
$$\Rightarrow S = \frac{\mu + \gamma}{\beta}$$

Thus

$$S = S^* = \frac{\mu + \gamma}{\beta}$$

Substitute this in the first equation of (4.4).

$$\Lambda + \gamma I - \mu S - \beta SI = 0$$
$$\Rightarrow \gamma I - \beta SI = \mu S - \Lambda$$
$$\Rightarrow I(\gamma - \beta S) = \mu S - \Lambda$$

$$\Rightarrow \; I\left(\gamma - \beta\left(\frac{\mu+\gamma}{\beta}\right)\right) = \mu\left(\frac{\mu+\gamma}{\beta}\right) - \Lambda, since\, S = \frac{\mu+\gamma}{\beta}$$

$$\Rightarrow \; I(\gamma - \mu - \gamma) = \mu\left(\frac{\mu+\gamma}{\beta}\right) - \Lambda$$

$$\Rightarrow \; I(-\mu) = \mu\left(\frac{\mu+\gamma}{\beta}\right) - \Lambda$$

$$\Rightarrow \; I = \frac{\mu\left(\frac{\mu+\gamma}{\beta}\right) - \Lambda}{-\mu}$$

$$\Rightarrow \; I = \frac{\Lambda - \mu\left(\frac{\mu+\gamma}{\beta}\right)}{\mu}$$

$$\Rightarrow \; I = \frac{\Lambda}{\mu} - \frac{\mu\left(\frac{\mu+\gamma}{\beta}\right)}{\mu}$$

$$\Rightarrow \; I = \frac{\Lambda}{\mu} - \left(\frac{\mu+\gamma}{\beta}\right)$$

Since birth rate is equal to death rate, i.e.

Thus

$$I = I^* = 1 - \left(\frac{\mu+\gamma}{\beta}\right)$$

Now let us calculate the basic reproduction number for SIS model, we only have one infected class; i.e. the class.

Consider

$$\frac{dI}{dt}: \beta SI - \mu I - \gamma I \; = 0$$

$$\Rightarrow \beta SI - \mu I - \gamma I \; = 0$$

$$\Rightarrow I(\beta S - (\mu + \gamma)) = 0$$

This is satisfied when $I^* = 0$ or $S^* = \frac{\mu+\gamma}{\beta}$

Hence, at endemic equilibrium the fraction of susceptible in the population being the inverse of $\mathcal{R}_0$. Since $S^* = \frac{1}{\mathcal{R}_0}$ is the endemic prevalence of susceptible.

Therefore $\mathcal{R}_0 = \frac{\mu+\gamma}{\beta}$

($\mathcal{R}_0$ = transmission rate $*$ infectious period)

Therefore, the endemic equilibrium becomes:

$$E^* = \left(\frac{\mu+\gamma}{\beta}, 1 - \left(\frac{\mu+\gamma}{\beta}\right)\right)$$

$$= \left(\frac{1}{\mathcal{R}_0}, 1 - \frac{1}{\mathcal{R}_0}\right)$$

iii. Stability Analysis of the Equilibrium Points

Linearization is non-linear model change to linear model. One of linearization method is Jacobian methods. For the stability analysis of the disease-free and the endemic equilibrium points, we will find the Jacobian matrix of SIS model equations.

Equilibrium points at disease-free equilibrium and endemic equilibrium will be substituted into the Jacobian matrix. After this we will solve the matrix equations to obtain an expression for the characteristic equations which will be used in the stability analysis.

Thus, using equation (3.1) the Jacobian matrix of system (4.3) written as

$$J(S,I) = \begin{bmatrix} \frac{\partial\left(\frac{dS}{dt}\right)}{\partial S} & \frac{\partial\left(\frac{dS}{dt}\right)}{\partial I} \\ \frac{\partial\left(\frac{dI}{dt}\right)}{\partial S} & \frac{\partial\left(\frac{dI}{dt}\right)}{\partial I} \end{bmatrix} = \begin{bmatrix} \frac{\partial S'}{\partial S} & \frac{\partial S'}{\partial I} \\ \frac{\partial I'}{\partial S} & \frac{\partial I'}{\partial I} \end{bmatrix}$$

$$= \begin{bmatrix} -\beta I - \mu & \gamma - \beta S \\ \beta I & \beta S - \mu - \gamma \end{bmatrix} \quad (4.5)$$

and evaluated at the equilibrium points to decide on the stability, which is directly determined from the eigenvalues λ of: $|J(x) - \lambda I|$. Based on the eigenvalues λ of the linearized system will either be stable (all the eigenvalues of the Jacobian evaluated at the equilibrium point contain negative real parts) or unstable (at least one of the eigenvalues of the Jacobian evaluated at the equilibrium point has positive real part).

a. Stability Analysis of the Disease-Free Equilibrium

Evaluating the above Jacobian matrix (4.5) at the disease-free equilibrium, $E_0 = (1,0)$ and solving eigenvalue $\det|J - \lambda I| = 0$ the result we get

$$J_0 = J(E_0) = \begin{bmatrix} -\mu & \gamma - \beta \\ 0 & \beta - \mu - \gamma \end{bmatrix}$$

Where J_0 represent Jacobian matrix at disease-free equilibrium. From here, we begin solving the matrix equation $\det|J - \lambda I| = 0$, where I identity matrix of 2x2.

$$\begin{bmatrix} -\mu & \gamma - \beta \\ 0 & \beta - \mu - \gamma \end{bmatrix} = det|J_0 - \lambda I| = 0$$

$$\Rightarrow \begin{vmatrix} -\mu - \lambda & \gamma - \beta \\ 0 & \beta - \mu - \gamma - \lambda \end{vmatrix} = 0$$

The characteristics equation becomes

$$(-\mu - \lambda)(\beta - \mu - \gamma - \lambda) = 0$$

$$\Rightarrow (-\mu - \lambda) = 0 \; or \; (\beta - \mu - \gamma - \lambda) = 0$$

$$\Rightarrow \lambda = -\mu \; or \; = 0 \; or \lambda = \beta - \mu - \gamma$$

Therefore, a 2×2 matrix has 2 eigenvalues.

The eigenvalues are thus

$$\lambda = \{-\mu, \beta - \mu - \gamma\}$$

Now let $\lambda_1 = -\mu$ or or $\lambda_2 = \beta - \mu - \gamma$

Here, $\lambda_1 < 0$. Now, considering λ_2

-If $\lambda_2 < 0$ which means $\beta < \mu + \gamma$ or $\frac{\beta}{\mu+\gamma} < 1$ or $\mathcal{R}_0 < 1$

Then, the disease-free equilibrium point is stable as both the eigenvalues are negative. For any infectious disease, one of the most important concerns is its ability

to invade a population. This can be expressed by a threshold parameter $\mathcal{R}_0$. The infected individual in its entire period of infectivity will produce less than one infected individual on average if$\mathcal{R}_0 < 1$. In disease-free equilibrium point case, the system is stable. This shows that the disease will be wiped out of the population.

-If $\lambda_2 > 0$ which means $\beta > \mu + \gamma$ or $\frac{\beta}{\mu+\gamma} > 1$ or $\mathcal{R}_0 > 1$

Then, the disease-free equilibrium point is unstable because λ_1 is negative and λ_2 is positive and hence each infected individual in its entire infective period having contact with susceptible individual will produce more than one infected individual, which will then lead to the disease invading the susceptible population, and the disease-free equilibrium point will become unstable.

In general based on the Jacobian method, rearrange the largest eigenvalue implies $\mathcal{R}_0$-like threshold.

Eigenvalues $\{-\mu, \beta - \mu - \gamma\}$

$$\lambda_1 = -\mu < 0, \lambda_2 = \beta - \mu - \gamma$$

$\beta - \mu - \gamma < 0 \Leftrightarrow \frac{\beta}{\mu+\gamma} < 1$, stable, No epidemic

$-\mu - \gamma > 0 \Leftrightarrow \frac{\beta}{\mu+\gamma} > 1$, unstable, Epidemic

b. Stability Analysis of the Endemic Equilibrium

Evaluating the above Jacobian matrix (4.5) at the endemic equilibrium point $E^* = (S^*, I^*)$ and solving eigenvalue $det|J - \lambda I| = 0$ the result we get

$$J^* = J(E^*) = \begin{bmatrix} -\beta I^* - \mu & \gamma - \beta S^* \\ \beta I^* & \beta S^* - \mu - \gamma \end{bmatrix}$$

$$= \begin{bmatrix} -\beta\left(1 - \left(\frac{\mu+\gamma}{\beta}\right)\right) - \mu & \gamma - \beta\left(\frac{\mu+\gamma}{\beta}\right) \\ \beta\left(1 - \left(\frac{\mu+\gamma}{\beta}\right)\right) & \beta\left(\frac{\mu+\gamma}{\beta}\right) - \mu - \gamma \end{bmatrix}$$

$$= \begin{bmatrix} -\beta + \gamma & -\mu \\ \beta - \mu - \gamma & 0 \end{bmatrix}$$

Where J^* represent Jacobian matrix at endemic equilibrium. From here, we begin solving the matrix equation $\det|J^* - \lambda I| = 0$

$$det|J^* - \lambda I| = 0$$

$$\begin{vmatrix} -\beta + \gamma - \lambda & -\mu \\ \beta - \mu - \gamma & -\lambda \end{vmatrix} = 0$$

$$\Rightarrow (-\beta + \gamma - \lambda)(-\lambda) - (\beta - \mu - \gamma)(-\mu) = 0$$

The characteristics equation becomes

$$\lambda^2 + (\beta - \gamma)\lambda + \mu(\beta - \mu - \gamma) = 0$$

Note that coefficients $\beta - \gamma$ and $\mu(\beta - \mu - \gamma)$ are both positive.

The roots of the polynomial or the eigenvalues are:

$$\lambda = \frac{1}{2}\left[-(\beta - \gamma) \pm \sqrt{(\beta - \gamma)^2 - 4\mu(\beta - \mu - \gamma)}\right]$$

Since $\mu(\beta-\mu-\gamma)$ is positive, the quantity under the square root is either smaller than $(\beta-\gamma)^2$ or greater than $(\beta-\gamma)^2$. If $(\beta-\gamma)^2 < 4\mu(\beta-\mu-\gamma)$ then the eigenvalues are complex with the real part$-(\beta-\gamma)$, which is negative. If $(\beta-\gamma)^2 > 4\mu(\beta-\mu-\gamma)$ then the quantity under the square root must be smaller in absolute value than$(\beta-\gamma)^2$, but still the real part is negative. Either way, we conclude that the endemic equilibrium is stable since the real parts of both eigenvalues are negative. It shows that the endemic equilibrium point is stable i.e. both the susceptible and infected population will survive in either of the cases and the trajectories will approach to the endemic equilibrium point.

4.3. Limitations of the SIS Model

There are various limitations or shortcomings in this model, which are explained as follows:

• There should be a Recovered (sometimes Removed) class. These may or may not have the disease, but they can't become infected and they can't transmit the disease to others.

• There should be an Exposed (but not yet infected) class; people have to be exposed to the disease before they can be infected and consequently become infectious.

Therefore, the limitations and flaws in the SIS model can be modified and extended to the SIR and SEIR models.

4.4. SIR Model

The SIR model is one of a simple compartmental model, due to Kermack and McKendrick, of an epidemic of an infectious disease in a large population and many models are derivations of this basic form. We assume the population consists of three types of individuals, whose numbers are denoted by the letters S, I and R (which is why this is called an SIR model). S for the number susceptible; the susceptible are those who are capable of contracting the disease and becoming themselves infective, I for the number of infective; the infective are those who are infected and can transmit the disease, and R for the number recovered (sometimes removed); the removed are those individuals which, having contracted the diseases, have died or, if recovered, are permanently immune, or have been isolated, thus being unable to further transmit the disease. This model is reasonably predictive for infectious diseases which are transmitted from human to human, and where recovery confers lasting resistance, such as mumps and rubella.

These variables (S, I, and R) represent the number of people in each compartment at a particular time. To represent that the number of susceptible, infected and recovered individuals may vary over time (even if the total population size remains constant), we make the precise numbers a function of t (time): $S(t)$,$I(t)$and $R(t)$. For a specific disease in a specific population, these functions may be worked out in order to predict possible outbreaks and bring them under control. In fact, there are two SIR Models.- They describe either an SIR model without vital dynamics, sometimes called the classical epidemic model because the duration of the disease is assumed to be short compared to the time scale of the population dynamics, this model is good for acute diseases with relatively short lifespans, for example influenza or they describe an SIR model with vital dynamics (a disease present in the population for a long period of time where the class of susceptible is being nourished by new income from births or

recovered individuals who lost their temporal immunity). These two models are the foundations for the modern mathematical epidemiology and are still widely used in practice. However, we restrict our attention to SIR model with vital dynamics.

4.5. The SIR Model with Vital Dynamics

4.5.1. Description of the Model

The simplest and most common way of introducing demography into the SIR model is to assume there are a natural birth rate and the rate at which individuals, at any epidemiological compartment, suffer natural mortality. It is important to emphasize that natural mortality rate is independent of the disease and is not intended to reflect the pathogenicity of the infectious agent. The inclusion of vital dynamics may allow a disease to die out or persist in a population in the long term. For this reason it is important to explore what happens when the system is at equilibrium.

The compartmental model becomes

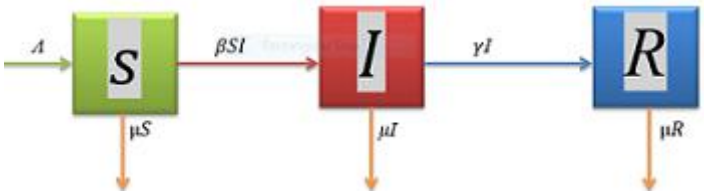

Figure 8. *Flow chart of the SIR model with vital dynamics.*

This model was initially studied in depth by Kermack and McKendrick in 1927 [15], has since been studied extensively, for example in [14,18].

Table 5. *Description of state variables for SIR model.*

Variable	Name	Units	Meaning
S	Susceptible Individuals	Number of Individuals	Individuals susceptible to infection who can contract the disease if they are exposed to it
I	Infected Individuals	Number of Individuals	Individuals infected by infection who are capable of transmitting the infection to any susceptible individuals
R	Recovered Individuals	Number of Individuals	Individuals recovered from infection who are temporarily immune from the infection

Table 6. *Description of SIR model Parameters.*

Parameter	Name	Units	Meaning
Λ	Birth Rate	$\frac{birth}{person}$	Birth rate of newborns each year
μ	Death Rate	$\frac{death}{person}$	Death rate of susceptible and infected individuals each year
β	Transmission Rate (Susceptible to Infected)	$days^{-1}$	Rate at which susceptible individuals Become infected individuals and leave susceptible class and enter infected class
γ	Recovery Rate (Infected to Susceptible)	$days^{-1}$	Rate at which infected individuals leave infected class and enter susceptible class

4.5.2. Basic Assumptions of the SIR Model

The SIR model is used in epidemiology to compute the amount of susceptible, infected, and recovered people in a population. It is important to note that this model does not work with all diseases. For the SIR model to be appropriate, once a person has recovered from the disease, they would receive lifelong immunity. This model is an appropriate one to use under the following assumptions:

• The death rate is assumed to be the same constant for all hosts, and the total death is balanced by total birth Λ, and there are no disease-induced deaths, hence the population is constant.

• The incubation period of the disease is negligible in length, hence when a susceptible is infected; they are immediately infectious and able to spread the disease.

• All individuals in the population mix homogeneously, so that every pair of individuals has an equal probability of coming into contact with one another.

• There is no vertical transmission, meaning that parents cannot transmit the disease to their children (unlike AIDS for example). Therefore, all newborns enter the susceptible compartment.

• The size of each compartment is a differentiable function of time.

4.5.3. Differential Equations for SIR Model

For SIR model the population is divided into three classes based on epidemiological status. Individuals are classified as either susceptible, infected or recover. The sizes of these groups are represented by S, I and R respectively. This description of the SIR model was made more mathematical by a formulated differential equation for the proportion of individuals in each class.

Susceptible:

The rate at which people become susceptible starts with the birth rate, Λ. From that rate is subtracted the normal death rate of people that have not yet been infected to a disease, μS and those people become infected βSI.

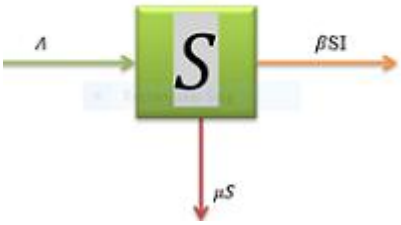

Figure 9. *An (Susceptible) - compartment model from SIR.*

From what has just been discussed above, the rate of change of the susceptible class can be put into an equation form as below,

$$\frac{dS}{dt} = \Lambda - \mu S - \beta SI \qquad (4.6)$$

Infected Component:

From the model number of people leaving the susceptible class for the infectious class is denoted by βSI and leaving the infected class for recover class is denoted by γI. Some of the infectious individuals die naturally is denoted by μI.

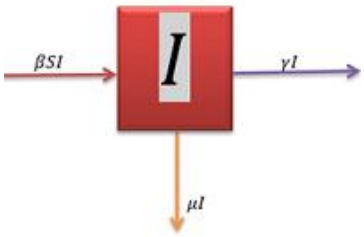

Figure 10. *An (Infected) - compartment model from SIR.*

From what has just been discussed above, the rate of change of the infected class can be put into an equation form as below,

$$\frac{dI}{dt} = \beta SI - \mu I - \gamma I \tag{4.7}$$

Recovered Component

The rate of change of the recover class is equal to the number of people leaving the infected class for the recovered class is denoted by γI. Some of the infectious individuals die naturally denoted by μR.

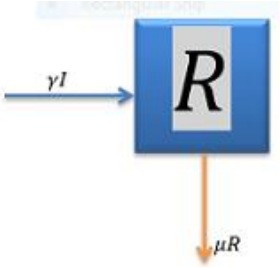

Figure 11. *An (Recovered) - compartment model from SIR.*

What has just been discussed above, the rate of change of the recovered class can be put into an equation form as below,

$$\frac{dR}{dt} = \gamma I - \mu R \tag{4.8}$$

Thus, putting the three model equations together, we obtain the following system of nonlinear ordinary differential equations:

$$\begin{cases} \frac{dS}{dt} = \Lambda - \mu S - \beta SI \\ \frac{dI}{dt} = \beta SI - \mu I - \gamma I \\ \frac{dR}{dt} = \gamma I - \mu R \end{cases} \tag{4.9}$$

The nonlinear system of differential equations formulated above has initial conditions $S(0) = S_0 > 0$, $I(0) = I_0 > 0$, and $R(0) = R_0 > 0$ to make the problem biologically interesting.

Also, the rate of transmission, the recovery rate and the birth and death rate are all non-negative ($\beta > 0, \gamma > 0, \Lambda > 0$ and $\mu > 0$ respectively).

Hence $N(t) = S(t) + I(t) + R(t)$ and

$$\frac{d}{dt}[S(t) + I(t) + R(t)] = 0$$

Since $\frac{dN}{dt} = 0$ and thus $N = S + I + R$ is a constant.

4.5.4. Stability Analysis of SIR Model

To find the equilibrium points of equation (4.9) the right-hand sides of each differential equation are set to zero, leading to the system.

We have $\frac{dS}{dt} = \frac{dI}{dt} = \frac{dR}{dt} = 0$

That is,

$$\begin{cases} \Lambda - \mu S - \beta SI = 0 \\ \beta SI - \mu I - \gamma I = 0 \\ \gamma I - \mu R = 0 \end{cases} \quad (4.10)$$

i. Disease-Free Equilibrium (E_0)

At disease-free equilibrium, it is assumed that there is no disease in the system, therefore substituting $I = 0$ into the above equations of (4.10).

From the third equation of (4.10), if $I = 0$ implies that $R = 0$.

Now solve the first equation of (4.10) for S by using $I = 0$.

$$\Lambda - \mu S = 0$$

$$\Rightarrow \Lambda = \mu S$$

$\Rightarrow S = \frac{\Lambda}{\mu}$, but from the assumptions of the model the birth and natural death rates are equal ($\Lambda = \mu$). Hence $s = 1$

Therefore, the disease-free equilibrium becomes:

$$E_0 = (1,0,0)$$

ii. Endemic Equilibrium E^*

At endemic equilibrium the disease cannot be totally eradicated but remains in the population. For the disease to persist in the population, the susceptible class, the Infectious class and the Recovered class must not be zero at equilibrium. In other words, if $E^* = (S^*,I^*,R^*)$ is the endemic equilibrium, then $E^* = (S^*,I^*,R^*) \neq (0,0,0)$. In order to obtain the endemic equilibrium, we solve systems of differential equation (4.10) simultaneously taking into consideration the fact that $E^* = (S^*,I^*,R^*) \neq (0,0,0)$.

For $I \neq 0$, solve the second equation of (4.10) for S.

$$\beta SI - \mu I - \gamma I = 0$$

$$\Rightarrow I(\beta S - \mu - \gamma) = 0$$

By the zero product rule either $I = 0$ or $\beta S - \mu - \gamma = 0$, but $I = 0$ is disease-free equilibrium.

$$\beta S - \mu - \gamma = 0$$

$$\Rightarrow \beta S = \mu + \gamma$$

$$\Rightarrow S = \frac{\mu+\gamma}{\beta}$$

Substitute this in the first equation of (4.10).

$$\Lambda - \mu S - \beta SI = 0$$

$$\Rightarrow \beta SI = \Lambda - \mu S$$

$$\Rightarrow \beta\left(\frac{\mu+\gamma}{\beta}\right) I = \Lambda - \mu\left(\frac{\mu+\gamma}{\beta}\right), \quad \text{Since } S = \frac{\mu+\gamma}{\beta}$$

$$\Rightarrow (\mu+\gamma) I = \Lambda - \mu\left(\frac{\mu+\gamma}{\beta}\right),$$

$$\Rightarrow I = \frac{\Lambda - \mu\left(\frac{\mu+\gamma}{\beta}\right)}{(\mu+\gamma)}$$

$$\Rightarrow I = \frac{\Lambda}{\mu+\gamma} - \frac{\mu}{\beta}$$

$$\Rightarrow I = \frac{\beta\Lambda - \mu(\mu+\gamma)}{\beta(\mu+\gamma)} = \left(\frac{\mu}{\beta}\right)\left(\frac{\beta-\mu-\gamma}{\mu+\gamma}\right)$$

From the third equation of (4.10), we have

$$\mu R = \gamma I$$

$$\Rightarrow R = \frac{\gamma}{\mu} I$$

$$\Rightarrow R = \frac{\gamma}{\mu}\left(\frac{\beta\Lambda - \mu(\mu+\gamma)}{\beta(\mu+\gamma)}\right) = \left(\frac{\gamma}{\beta}\right)\left(\frac{\beta-\mu-\gamma}{\mu+\gamma}\right)$$

Now let us calculate the basic reproduction number for SIR model, we only have one infected class; i.e. the I class.

Consider

$$\frac{dI}{dt}: \beta SI - \mu I - \gamma I = 0$$

$$\Rightarrow \beta SI - \mu I - \gamma I = 0$$

$$\Rightarrow I(\beta S - (\mu + \gamma)) = 0$$

This is satisfied when $I^* = 0$ or $S^* = \frac{\mu+\gamma}{\beta}$

Hence, at endemic equilibrium the fraction of susceptible in the population being the inverse of $\mathcal{R}_0$.

Since $S^* = \frac{1}{\mathcal{R}_0}$

Therefore $\mathcal{R}_0 = \frac{\beta}{\mu+\gamma}$

($\mathcal{R}_0$ = transmission rate $*$ infectious period)

Therefore, the endemic equilibrium point becomes:

$$E^* = \left(\frac{\mu+\gamma}{\beta}, \left(\frac{\mu}{\beta}\right)\left(\frac{\beta-\mu-\gamma}{\mu+\gamma}\right), \left(\frac{\gamma}{\beta}\right)\left(\frac{\beta-\mu-\gamma}{\mu+\gamma}\right)\right)$$

$$= \left(\frac{1}{\mathcal{R}_0}, \left(\frac{\mu}{\beta}\right)\left(\frac{\beta-\mu-\gamma}{\mu+\gamma}\right), \left(\frac{\gamma}{\beta}\right)\left(\frac{\beta-\mu-\gamma}{\mu+\gamma}\right)\right)$$

$$= \left(\frac{1}{\mathcal{R}_0}, \left(\frac{\mu}{\beta}\right)\left(\frac{\beta}{\mu+\gamma} - \frac{(\mu+\gamma)}{\mu+\gamma}\right), \left(\frac{\gamma}{\beta}\right)\left(\frac{\beta}{\mu+\gamma} - \frac{(\mu+\gamma)}{\mu+\gamma}\right)\right)$$

$$= \left(\frac{1}{\mathcal{R}_0}, \left(\frac{\mu}{\beta}\right)(\mathcal{R}_0 - 1), \left(\frac{\gamma}{\beta}\right)(\mathcal{R}_0 - 1)\right)$$

iii. Stability Analysis of the Equilibrium Points

In this section we discuss the stability of the equilibrium points (disease-free and endemic which will be characterized using the threshold value $\mathcal{R}_0$).

To determine the stability of each equilibrium point we find the Jacobian matrix. The Jacobian matrix for the SIR model in equation (4.10) is given by

$$J(S,I,R) = \begin{bmatrix} \frac{\partial S'}{\partial S} & \frac{\partial S'}{\partial I} & \frac{\partial S'}{\partial R} \\ \frac{\partial I'}{\partial S} & \frac{\partial I'}{\partial I} & \frac{\partial I'}{\partial R} \\ \frac{\partial R'}{\partial S} & \frac{\partial R'}{\partial I} & \frac{\partial R'}{\partial R} \end{bmatrix}$$

$$= \begin{bmatrix} -\mu-\beta I & -\beta S & 0 \\ \beta I & \beta S-\mu-\gamma & 0 \\ 0 & \gamma & -\mu \end{bmatrix} \quad (4.11)$$

a. Stability Analysis of the Disease-Free Equilibrium

Evaluating the above Jacobian matrix (4.11) at the disease-free equilibrium, $\mathrm{E}_0 = (1,0,0)$ and solving eigenvalue $\det|\mathrm{J}-\lambda\mathrm{I}| = 0$ the result we get

$$J_0 = J(E_0) = \begin{bmatrix} -\mu & -\beta & 0 \\ 0 & \beta-\mu-\gamma & 0 \\ 0 & \gamma & -\mu \end{bmatrix}$$

where J_0 represents Jacobian matrix at disease-free equilibrium. From here, we begin solving the matrix equation $det|J_0-\lambda I| = 0$,where I identity matrix of $3x3$.

$$\begin{bmatrix} -\mu-\lambda & -\beta & 0 \\ 0 & \beta-\mu-\gamma-\lambda & 0 \\ 0 & \gamma & -\mu-\lambda \end{bmatrix} = det|J_0-\lambda I| = 0$$

$$\Rightarrow \begin{bmatrix} -\mu-\lambda & -\beta & 0 \\ 0 & \beta-\mu-\gamma-\lambda & 0 \\ 0 & \gamma & -\mu-\lambda \end{bmatrix} = 0$$

$$\Rightarrow(-\mu-\lambda)\begin{vmatrix} \beta-\mu-\gamma-\lambda & 0 \\ \gamma & -\mu-\lambda \end{vmatrix} - (-\beta)\begin{vmatrix} 0 & 0 \\ 0 & -\mu-\lambda \end{vmatrix} + 0\begin{vmatrix} 0 & \beta-\mu-\gamma-\lambda \\ 0 & \gamma \end{vmatrix}$$

$$\Rightarrow(-\mu-\lambda)\big[(\beta-\mu-\gamma-\lambda)(-\mu-\lambda)\big] - (-\beta)(0) + 0$$

$$\Rightarrow(-\mu-\lambda)\big[(\beta-\mu-\gamma-\lambda)(-\mu-\lambda)\big] = 0$$

The characteristics equation becomes

$$(-\mu-\lambda)^2(\beta-\mu-\gamma-\lambda) = 0$$

$$\Rightarrow (-\mu-\lambda)^2 = 0 \; or \; (\beta-\mu-\gamma-\lambda) = 0$$

$$\Rightarrow \lambda = -\mu \; or \; \lambda = \beta-\mu-\gamma$$

Therefore, a 3×3 matrix has 3 eigenvalues.

The eigenvalues are thus

$$\lambda = \{-\mu, -\mu, \boldsymbol{\beta - \mu - \gamma}\}$$

Now let $\lambda_1 = -\mu$, $\lambda_2 = -\mu$ and $\lambda_3 = \beta - \mu - \gamma$

Here, λ_1 and λ_2 are negative. Now, considering λ_3,

If $\lambda_3 < 0$, which means $\beta < \mu - \gamma$ or $\frac{\beta}{\mu+\gamma} < 1$ or $\mathcal{R}_0 < 1$

Then, all the eigenvalues are negative and hence there is no epidemic and the trajectories will approach to disease-free equilibrium point. In disease-free equilibrium point case, the system is stable. This shows that the disease will be wiped out of the population.

If $\lambda_3 > 0$, which means $\beta > \mu - \gamma$ or $\frac{\beta}{\mu+\gamma} > 1$ or $\mathcal{R}_0 > 1$

Hence, the disease -free equilibrium point is unstable.

In general based on the Jacobian method, rearrange the largest eigenvalue $\Rightarrow \mathcal{R}_0$ - like threshold Eigenvalues $\{-\mu, -\mu, \beta - \mu - \gamma\}$

$$\lambda_1 = -\mu < 0$$

$$\lambda_2 = -\mu < 0$$

$$\lambda_3 = \beta - \mu - \gamma$$

$\beta - \mu - \gamma < 0 \Leftrightarrow \frac{\beta}{\mu+\gamma} < 1$, stable, No epidemic

$\beta - \mu - \gamma < 0 \Leftrightarrow \frac{\beta}{\mu+\gamma} > 1$, unstable, Epidemic

b. Stability Analysis of the Endemic Equilibrium

Evaluating the above Jacobian matrix (4.11) at the endemic equilibrium point $E^* = (S^*, I^*, R^*) = \left(\frac{\mu+\gamma}{\beta}, \left(\frac{\mu}{\beta}\right)\left(\frac{\beta-\mu-\gamma}{\mu+\gamma}\right), \left(\frac{\gamma}{\beta}\right)\left(\frac{\beta-\mu-\gamma}{\mu+\gamma}\right)\right)$ and solving eigenvalue $\det|J - \lambda I| = 0$ the result we get

$$J^* = J(E^*) = \begin{bmatrix} -\mu - \beta I^* & -\beta S^* & 0 \\ \beta I^* & \beta S^* - \mu - \gamma & 0 \\ 0 & \gamma & -\mu \end{bmatrix}$$

$$= \begin{bmatrix} -\mu - \beta\left(\frac{\mu}{\beta}\right)\left(\frac{-\mu-\gamma}{\mu+\gamma}\right) & -\beta\left(\frac{\mu+\gamma}{\beta}\right) & 0 \\ \beta\left(\frac{\mu}{\beta}\right)\left(\frac{-\mu-\gamma}{\mu+\gamma}\right) & \beta\left(\frac{\mu+\gamma}{\beta}\right) - \mu - \gamma & 0 \\ 0 & \gamma & -\mu \end{bmatrix}$$

$$= \begin{bmatrix} -\mu - \mu\left(\frac{\beta-\mu-\gamma}{\mu+\gamma}\right) - \lambda & -\mu - \gamma & 0 \\ \mu\left(\frac{\beta-\mu-\gamma}{\mu+\gamma}\right) & -\lambda & 0 \\ 0 & \gamma & -\mu - \lambda \end{bmatrix}$$

Where J^* represent Jacobian matrix at endemic equilibrium. From here, we begin solving the matrix equation $\det|J^* - \lambda I| = 0$

$$det|J^* - \lambda I| = 0$$

$$\begin{vmatrix} -\mu - \mu\left(\frac{\beta-\mu-\gamma}{\mu+\gamma}\right) - \lambda & -\mu-\gamma & 0 \\ \mu\left(\frac{\beta-\mu-\gamma}{\mu+\gamma}\right) & -\lambda & 0 \\ 0 & \gamma & -\mu-\lambda \end{vmatrix} = 0$$

$$\Rightarrow\left(-\mu-\mu\left(\tfrac{\beta-\mu-\gamma}{\mu+\gamma}\right)-\lambda\right)\begin{vmatrix} -\lambda & 0 \\ \gamma & -\mu-\lambda \end{vmatrix} - (-\mu-\gamma)\begin{vmatrix} \mu\left(\frac{\beta-\mu-\gamma}{\mu+\gamma}\right) & 0 \\ 0 & -\mu-\lambda \end{vmatrix} + 0\begin{vmatrix} \mu\left(\frac{\beta-\mu-\gamma}{\mu+\gamma}\right) & -\lambda \\ 0 & \gamma \end{vmatrix} = 0$$

The above matrix equation reduce to

$$\left[\left(-\mu-\mu\left(\frac{\beta-\mu-\gamma}{\mu+\gamma}\right)-\lambda\right)(-\lambda(-\mu-\lambda))\right] - \left[(-\mu-\gamma)\left(\mu\left(\frac{\beta-\mu-\gamma}{\mu+\gamma}\right)(-\mu-\lambda)\right)\right] = 0$$

The characteristics equation becomes

$$(-\mu-\lambda)\left[\lambda^2+\mu(1+\left(\tfrac{\beta-\mu-\gamma}{\mu+\gamma}\right)\lambda+\mu(\beta-\mu-\gamma)\right] = 0 \Rightarrow (-\mu-\lambda) = 0 \; or \; \lambda^2+\mu(1+\left(\tfrac{\beta-\mu-\gamma}{\mu+\gamma}\right)\lambda+\mu(\beta-\mu-\gamma) = 0$$

On solving this equation we get the following eigenvalues:

$$\lambda_1 = -\mu$$

$$\lambda_2 = \frac{1}{2}\left[-\mu\left(1+\left(\frac{\beta-\mu-\gamma}{\mu+\gamma}\right)\right) \pm \sqrt{\mu^2\left(1+\left(\frac{\beta-\mu-\gamma}{\mu+\gamma}\right)\right)^2 - 4\mu(\beta-\mu-\gamma)}\;\right]$$

$$= \frac{1}{2}\left[-\mu\left(1+\frac{\beta}{\mu+\gamma}-\frac{(\mu+\gamma)}{\mu+\gamma}\right) \pm \sqrt{\mu^2\left(1+\frac{\beta}{\mu+\gamma}-\frac{(\mu+\gamma)}{\mu+\gamma}\right)^2 - 4\mu(\beta-\mu-\gamma)}\;\right]$$

$$= \frac{1}{2}\left[-\mu\left(1+\frac{\beta}{\mu+\gamma}-\frac{(\mu+\gamma)}{\mu+\gamma}\right) \pm \sqrt{\mu^2\left(1+\frac{\beta}{\mu+\gamma}-\frac{(\mu+\gamma)}{\mu+\gamma}\right)^2 - 4\mu(\beta-\mu-\gamma)}\;\right]$$

$$= \frac{1}{2}\left[-\mu(1+\mathcal{R}_0-1) \pm \sqrt{\mu^2(1+\mathcal{R}_0-1)^2 - 4\mu(\beta-\mu-\gamma)}\;\right]$$

$$= \frac{1}{2}\left[-\mu\mathcal{R}_0 \pm \sqrt{\mu^2{\mathcal{R}_0}^2 - 4\mu(\beta-\mu-\gamma)}\;\right]$$

Since $\mu(\beta-\mu-\gamma)$ is positive, the quantity under the square root is either smaller than $\mu^2{\mathcal{R}_0}^2$ or it is greater. If greater, then the solutions are complex with real part $-\mu\mathcal{R}_0$ which is negative. Otherwise, the square root must be smaller in absolute value than $\mu^2{\mathcal{R}_0}^2$, but still the real part of the eigenvalue is negative. Either way, we conclude that the endemic equilibrium is stable since the real parts of both eigenvalues are negative and λ_1 is also negative.

4.6. Limitations of the SIR Model

There are various limitations or shortcomings in this model, which are explained as follows:

There should be an Exposed (but not yet infected) class; people have to be exposed to the disease before they can be infected and consequently become infectious. In fact, these are the case for the measles, tuberculosis, etc. In such case a patient becomes infectious only after the infected person develops the symptoms. Therefore, the limitations and flaws in the SIR model can be modified and extended to the SEIR model.

4.7. SEIR Model

Many diseases have a latent phase during which the individual is infected but not yet infectious. This delay between the acquisition of infection and the infectious state can be incorporated within the SIR model by adding a latent (exposed) population, E and letting infected (but not yet infectious) individuals move from S to I and from E to I.

4.7.1. Description of the Model

The model we present here is an SEIR model, where the total population size is divided into four distinct epidemiological subclasses (compartments) of individuals which are susceptible, exposed, infectious, and recovered. Compartments with labels S, E, I, R are used for epidemiological classes as shown in Figure 12. The class S is the class of susceptible individuals; that is, those who can become infected. When there is an adequate contact of a susceptible with an infective so that transmission occurs, the susceptible enters the exposed class E of those in the latent period, who are infected but not yet infectious. At the end of the latent period, the individual enters the class I of infective, who are capable of transmitting the infection (that is, infectious). At the end of the infectious period, the individual enters the recovered class R. At time t, there are S(t) susceptible, E(t) exposed, I(t) infectious and R(t) recovered individuals in the population of constant size, N. The model assumes that all new-born are susceptible i.e., no vertical transmission to the infection and are recruited at rate Λ. The susceptible are exposed to the infection once in contact with an infectious individual. The exposed become infected at rate αE and the infectious individuals recover from the infection at rate γI .

The compartmental model becomes

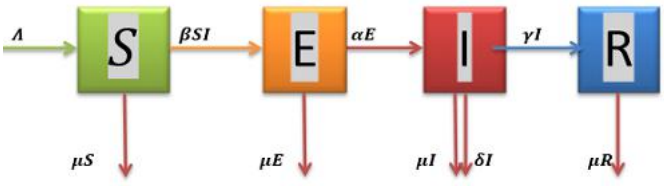

Figure 12. *Flow chart of the SEIR model.*

Table 7. *Description of state variables for SEIR model.*

Variable	Name	Units	Meaning
S	Susceptible Individuals	Number of Individuals	Individuals susceptible to infection who can contract the disease if they are exposed to it
E	Exposed individual	Number of Individuals	Individuals exposed to infection who are infected but have not yet become

			infectious and cannot pass the infection to other susceptible individuals
I	Infected Individuals	Number of Individuals	Individuals infected by infection who are capable of transmitting the infection to any susceptible individuals
R	Recovered Individuals	Number of Individuals	Individuals recovered from infection who are temporarily immune from the infection

Table 8. *The parameter definitions for SEIR model.*

Parameter	Name	Units	Meaning
Λ	Birth Rate	$\frac{birth}{person}$	Birth rate of newborns each year
μ	Death Rate	$\frac{death}{person}$	Death rate of susceptible and infected individuals each year
β	Transmission Rate (Susceptible to Infected)	$days^{-1}$	Rate at which susceptible individuals Become infected individuals and leave susceptible class and enter infected class
α	Latency rate	$days^{-1}$	Rate at which exposed individuals become infected by incubating infection and leave exposed class and enter infected class
γ	Recovery Rate (Infected to Susceptible)	$days^{-1}$	Rate at which infected individuals leave infected class and enter susceptible class
δ	Disease related death rate	$days^{-1}$	Rate at which infected individuals leave infected class by disease induced mortality

4.7.2. Assumptions of the Model

The model assumptions for the SEIR model are as follows:

The natural birth rate Λ and death rates μ are assumed to be different rate.

Each individual in the population is considered as having an equal probability of contacting the disease with a contact rate β.

The number of infected individuals move from the exposed compartment per unit time is αE at time t.

The number of recovered individuals move from the infected compartment per unit time is γI at time t.

The rate of susceptible, exposed, infected and recovered individual removed from each compartments through natural death and disease induced death are μS, μE, μI, μR and I respectively.

4.7.3. Differential Equations for SEIR Model

The differential equations for SEIR model using the description, assumptions and compartmental diagram above is described as follows:

The rate at which people become susceptible starts with the birth rate, Λ. From that rate is subtracted the normal death rate of people that have not yet been exposed to disease, μS, with infective and become exposed, βSI.

Therefore the rate of susceptible becomes

$$\frac{dS}{dt} = \Lambda - \mu S - \beta SI \tag{4.12}$$

Beside the number of individuals leave S and enter E , a fraction of exposed E move to infectious group I with a latent rate α,αE an individual's move from exposed to infectious and some of the exposed group die through natural death rate μ, μE to an individual's move from exposed to death. The rate of exposed becomes

$$\frac{dE}{dt} = \beta SI - \alpha E - \mu E \tag{4.13}$$

As the number of individuals leave E and enter I, fraction of infected individuals leaves I and enter into the recovered group with latent rate α and recovery rate γ respectively. This gives rate of infective and recovered as;

$$\frac{dI}{dt} = \alpha E - \delta I - \mu I - \gamma I \tag{4.14}$$

$$\frac{dR}{dt} = \gamma I - \mu R \tag{4.15}$$

Thus, putting the four model equations together, we obtain the following system of nonlinear ordinary differential equations:

$$\begin{cases} \frac{dS}{dt} = \Lambda - \mu S - \beta SI \\ \frac{dE}{dt} = \beta SI - \mu E - \alpha E \\ \frac{dI}{dt} = \alpha E - \delta I - \mu I - \gamma I \\ \frac{dR}{dt} = \gamma I - \mu R \end{cases} \tag{4.16}$$

The nonlinear system of differential equations formulated above has initial conditions $S(0) = S_0 > 0$, $I(0) = I_0 > 0$,$E(0) = E_0 > 0$ and $R(0) = R_0 > 0$ to make the problem biologically interesting.

Also, the rate of transmission, the recovery rate and the birth and death rate are all non-negative ($\beta > 0$,$\gamma > 0$, $\Lambda > 0$,$\mu > 0$, and $\delta > 0$ respectively).

Hence $N(t) = S(t) + E(t) + I(t) + R(t)$

This implies $\frac{dN}{dt} = \frac{dS}{dt} + \frac{dE}{dt} + \frac{dI}{dt} + \frac{dR}{dt}$

$$= \Lambda - \mu S - \beta SI + \beta SI - \mu E - \alpha E + \alpha E - \delta I - \mu I - \gamma I + \gamma I - \mu R$$

$$= \Lambda - \delta I - \mu S - \mu E - \mu I - \mu R$$

$$= \Lambda - \delta I - \mu(S + E + I + R)$$

$$= \Lambda - \delta I - \mu N, since\ N = S + E + I + R$$

Therefore summing the differential equations (4.16), leads to the equation

$$\frac{dN}{dt} = \Lambda - \delta I - \mu N \tag{4.17}$$

Here, it is important to note that in the absence of the disease, equation (4.17) become $N(t) \to \frac{\Lambda}{\mu}$

The population size $N(t)$ declines exponentially to zero if $\Lambda < \mu$, may approach zero, remain finite, or grow exponentially to infinity, depending on the infective I(t), if $\Lambda > \mu$.

Since R does not appear in the first three differential equations, most of the times the last equation is omitted, indeed,

$$N(t)R(t) = N(t) - S(t) - E(t) - I(t) \tag{4.18}$$

Equation (4.16) can be written as a standard way

$$\begin{cases} \frac{dS}{dt} = \Lambda - \mu S - \beta SI \\ \frac{dE}{dt} = \beta SI - \mu E - \alpha E \\ \frac{dI}{dt} = \alpha E - \delta I - \mu I - \gamma I \\ \frac{dN}{dt} = \Lambda - \delta I - \mu N \end{cases} \tag{4.19}$$

With initial condition

$S(0) = S_0 > 0,\ I(0) = I_0 > 0, E(0) = E_0 > 0\ ,\ N(0) = N_0 > 0$

The SEIR model has two infected compartments; the exposed-E and the infected class-I, so let us calculate the basic reproduction number using the method of the next generation matrix.

The next generation matrix is

$K = FV^{-1}$, where F and V are transmission and transition matrices, respectively, as presented (in equation 3.5).

The basic reproduction number is the eigenvalue of largest magnitude, or spectral radius of the next generation matrix, that is, the number of all new infectious host types in the next generation.

$\mathcal{R}_0 = \rho(K) = \rho(FV^{-1})$ where ρ denotes the spectral radius (dominant eigenvalue) of the matrix FV^{-1} , as presented (in equation3.6).

The vector of disease states from the equation (4.19) is the exposed and infectious compartment, can be written as

$$\begin{cases} \frac{dE}{dt} = \beta SI - (\mu + \alpha)E \\ \frac{dI}{dt} = \alpha E - (\delta + \mu + \gamma)I \end{cases} \tag{4.20}$$

Note that equation (4.20) is made of two compartments E and I which are the exposed and the infected class respectively. These are used for the determination of $\mathcal{R}_0$.

Then we have matrix F= $\begin{pmatrix} \beta SI \\ 0 \end{pmatrix}$ and V = $\begin{pmatrix} (\mu+\alpha)E \\ (\delta+\mu+\gamma)I - \alpha E \end{pmatrix}$

$$F = \begin{pmatrix} F_1 \\ F_2 \end{pmatrix} \text{ and } V = \begin{pmatrix} V_1 \\ V_2 \end{pmatrix}$$

The derivatives of F and V are given as (see equation 3.4):

$$F=\begin{pmatrix}\frac{\partial F_1}{\partial E} & \frac{\partial F_1}{\partial I}\\ \frac{\partial F_2}{\partial E} & \frac{\partial F_2}{\partial I}\end{pmatrix} \text{ and } V=\begin{pmatrix}\frac{\partial V_1}{\partial E} & \frac{\partial V_1}{\partial I}\\ \frac{\partial V_2}{\partial E} & \frac{\partial V_2}{\partial I}\end{pmatrix}$$

The derivatives of F and V are given by:

$$F=\begin{pmatrix}\frac{\partial(\beta SI)}{\partial E} & \frac{\partial(\beta SI)}{\partial I}\\ \frac{\partial(0)}{\partial E} & \frac{\partial(0)}{\partial I}\end{pmatrix}$$

$$=\begin{pmatrix}0 & \beta\\ 0 & 0\end{pmatrix}$$

and similarly

$$V=\begin{pmatrix}\frac{\partial((\mu+\alpha)E)}{\partial E} & \frac{\partial((\mu+\alpha)E)}{\partial I}\\ \frac{\partial((\delta+\mu+\gamma)I-\alpha E)}{\partial E} & \frac{\partial((\delta+\mu+\gamma)I-\alpha E)}{\partial I}\end{pmatrix}$$

$$V=\begin{pmatrix}(\mu+\alpha) & 0\\ -\alpha & (\delta+\mu+\gamma)\end{pmatrix}$$

Therefore, matrix F and V at the disease-free equilibrium are

$$F=\begin{pmatrix}0 & \beta\\ 0 & 0\end{pmatrix},\ V=\begin{pmatrix}(\mu+\alpha) & 0\\ -\alpha & (\delta+\mu+\gamma)\end{pmatrix}$$

Then, we need to find the next generation matrix

$$K=FV^{-1}$$

$$F=\begin{pmatrix}0 & \beta\\ 0 & 0\end{pmatrix},\ V=\begin{pmatrix}(\mu+\alpha) & 0\\ -\alpha & (\delta+\mu+\gamma)\end{pmatrix}$$

Now V is 2×2 matrix, then $V^{-1}=\frac{\text{adjoint of V}}{|V|}$

$$\Rightarrow V^{-1}=\frac{\begin{pmatrix}(\delta+\mu+\gamma) & 0\\ \alpha & \mu+\alpha\end{pmatrix}}{(\mu+\alpha)(\delta+\mu+\gamma)}$$

Then

$$FV^{-1}=\begin{pmatrix}0 & \beta\\ 0 & 0\end{pmatrix}\begin{pmatrix}\frac{(\delta+\mu+\gamma)}{(\mu+\alpha)(\delta+\mu+\gamma)} & \frac{0}{(\mu+\alpha)(\delta+\mu+\gamma)}\\ \frac{\alpha}{(\mu+\alpha)(\delta+\mu+\gamma)} & \frac{(\mu+\alpha)}{(\mu+\alpha)(\delta+\mu+\gamma)}\end{pmatrix}$$

$$=\begin{pmatrix}0\times\frac{(\delta+\mu+\gamma)}{(\mu+\alpha)(\delta+\mu+\gamma)}+\beta\times\frac{\alpha}{(\mu+\alpha)(\delta+\mu+\gamma)} & 0\times\frac{0}{(\mu+\alpha)(\delta+\mu+\gamma)}+\beta\times\frac{(\mu+\alpha)}{(\mu+\alpha)(\delta+\mu+\gamma)}\\ 0\times\frac{(\delta+\mu+\gamma)}{(\mu+\alpha)(\delta+\mu+\gamma)}+0\times\frac{\alpha}{(\mu+\alpha)(\delta+\mu+\gamma)} & 0\times\frac{0}{(\mu+\alpha)(\delta+\mu+\gamma)}+0\times\frac{(\mu+\alpha)}{(\mu+\alpha)(\delta+\mu+\gamma)}\end{pmatrix}$$

$$= \begin{pmatrix} \frac{\beta\alpha}{(\mu+\alpha)(\delta+\mu+\gamma)} & \frac{\beta(\mu+\alpha)}{(\mu+\alpha)(\delta+\mu+\gamma)} \\ 0 & 0 \end{pmatrix}$$

$$= \begin{pmatrix} \frac{\beta\alpha}{(\mu+\alpha)(\delta+\mu+\gamma)} & \frac{\beta}{(\delta+\mu+\gamma)} \\ 0 & 0 \end{pmatrix}$$

Thus, the next generation matrix is

$$K = FV^{-1} = \begin{pmatrix} \frac{\beta\alpha}{(\mu+\alpha)(\delta+\mu+\gamma)} & \frac{\beta}{(\delta+\mu+\gamma)} \\ 0 & 0 \end{pmatrix} \quad (4.21)$$

Then, by using this matrix (K),

We need to find the spectral radius by using $\det|K - \lambda I| = 0$, where identity matrix of 2×2 and λ is the eigenvalues.

Thus,

$$\det|K - \lambda I| = 0$$

$$\Rightarrow \begin{vmatrix} \frac{\beta\alpha}{(\mu+\alpha)(\delta+\mu+\gamma)} - \lambda & \frac{\beta}{(\delta+\mu+\gamma)} \\ 0 & 0 - \lambda \end{vmatrix} = 0$$

The characteristics equation becomes

$$\left(\frac{\beta\alpha}{(\mu+\alpha)(\delta+\mu+\gamma)} - \lambda\right)(-\lambda) = 0$$

$$\Rightarrow \frac{\beta\alpha}{(\mu+\alpha)(\delta+\mu+\gamma)} - \lambda = 0 \text{ or } -\lambda = 0$$

$$\Rightarrow \lambda = \frac{\beta\alpha}{(\mu+\alpha)(\delta+\mu+\gamma)} \text{ or } \lambda = 0$$

The basic reproduction number is the eigenvalue of largest magnitude, or spectral radius of the next generation matrix.

The basic reproduction number for the model equation (4.19):

$$\mathcal{R}_0 = \frac{\beta\alpha}{(\mu+\alpha)(\delta+\mu+\gamma)} \quad (4.22)$$

5. Numerical Simulation

We are going to perform numerical simulations of the SIR model with vital dynamics. In solving the systems of differential equations, we employed the fourth order RungeKutta method. The algorithms for the analysis were implemented using MATLAB R2007b.

5.1. Simulations of SIR Model with Vital Dynamics

In order to solve the system (4.9) we need the numeric values of the physical parametersμ,β and γ which in turn gives the reproductive number. For the SIR model with vital dynamics we use the estimated parameters in Table 9.

Table 9. *Parameter values for the SIR model with vital dynamics.*

Description	Parameter	Value

Birth rate	Λ	0.000003
Natural death rate	μ	0.000003
Infectious rate	β	0.001
Recovered rate	γ	0.1

The values of these physical parameters as well as the initial data are taken from [9]. For the simulations here, in [9] $S(0) = 500$, $I(0) = 1$, $R(0) = 0$, $\mu = 0.000003$,$\beta = 0.001$ and $\gamma = 0.1$.

We perform numerical simulations on the SIR model using the data we have

M-files 'sus_inf_rec.png'

```
function output=susceptible_infected_recovered( )

t0 = 0;

tf =100;

y0_SIR=                                                    [500 1 0]
[ty_Susceptible_Infected_Recovered]=ode45(@Susceptible_Infected_Recovered,[t0
tf],y0_SIR);
plot(t,y_Susceptible_Infected_Recovered(:,1),'g',t,y_Susceptible_Infected_Recovered
(:,2),'r+',t,y_Susceptible_Infected_Recovered(:,3),'b.','linewidth',2);
set(gca,'FontSize',20)

legend('susceptible','infected','recovered')

xlabel('time')

ylabel('population')

 saveas(gcf,'sus_inf_rec.png','png')

% y1 -- susceptible popn,

% y2 -- infected popn

% y3 -- recovered popn

function dy =Susceptible_Infected_Recovered(t,y)

dy = zeros(3,1);

dy(1) = 0.000003 -0.000003*y(1) -0.001*y(1)*y(2);

dy(2) = 0.001*y(1)*y(2)-0.000003*y(2)-0.1*y(2);

dy(3) = 0.1*y(2)-0.000003*y(3);
```

Observing Figure 13 carefully, The Susceptible population decreases as time increases. This decrease may be possibly because of the transmission rate parameter, since the transmission rate parameter depends on the contact rate and the probability of transmission occurring during a contact. The higher the rates of contact, the more rapid the spread of the disease, it is also observed that as the contact rate decreases, the fraction of individuals infected decreases at a faster rate as would be expected logically. The population of infected individuals at the very beginning rise sharply as the rate increases and then falls uniformly as time increases. This graph also demonstrates that the contact rate has large impact on the spread of the disease through population. If the contact rate is observed to be high then the rate of infection of the disease will also be high as would be expected logically. However, there exists

another parameter to consider, as more individuals are infected with the disease and I(t) grows, some individuals are also leaving the infected class by being cured and then join the Recovered class. The recovered individual rise up steadily for some number of years and then drops and remains nearly a constant. This could be due to the greater number of infectious individuals who have been treated and also acquired education about the disease transmission.

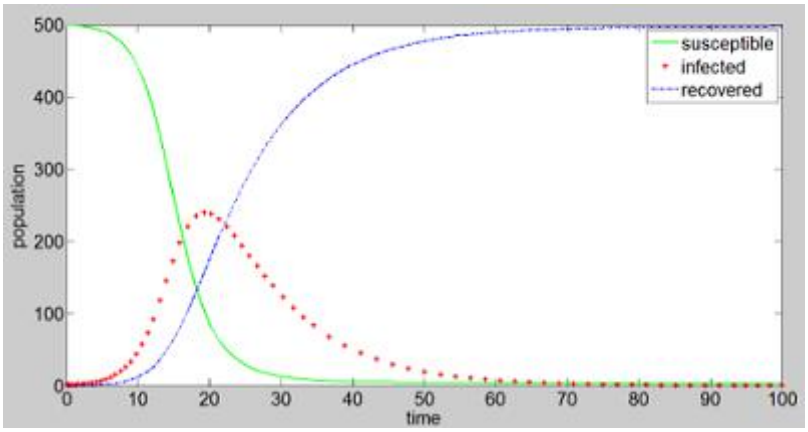

Figure 13. *Matlab Simulink solutions for the SIR model with vital dynamics.*

5.2. Effects of Initial Infective on the Various Compartments

Experiments were performed to verify the effect of varying initial infectives on the dynamics of the susceptible, infective, and recovered populations. Table 10 contains the various instances considered for the initial number of infectives. The number of susceptible varies appropriately with change in the number of infectives.

Table 10. *Varying the initial number of infectives.*

Susceptible	Infectives	Recovered
500	1	0
399	101	0
299	201	0
199	301	0
99	401	0

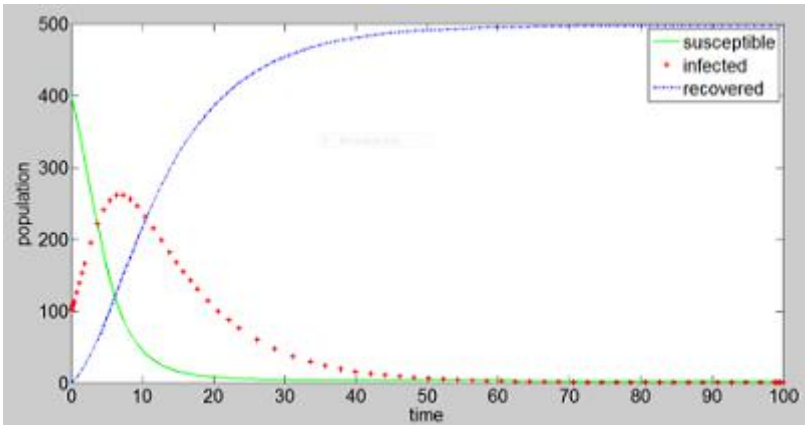

Figure 14. *S (0) = 399, I (0) = 101, R (0) = 0.*

To see the effect of initial data on the results, we performed simulations using different values of initial data. We fixed the values of $\mu = 0.000003, \beta = 0.001$ and $\gamma = 0.1$ as given in [9] and observed the effect of initial data. It can be seen from the Figs. (5.2) – (5.5) that when the initial infective is increased to 101,201,301and 401,

the susceptible declined from an initial value of 399,299 and199 to a minimum value of 99.

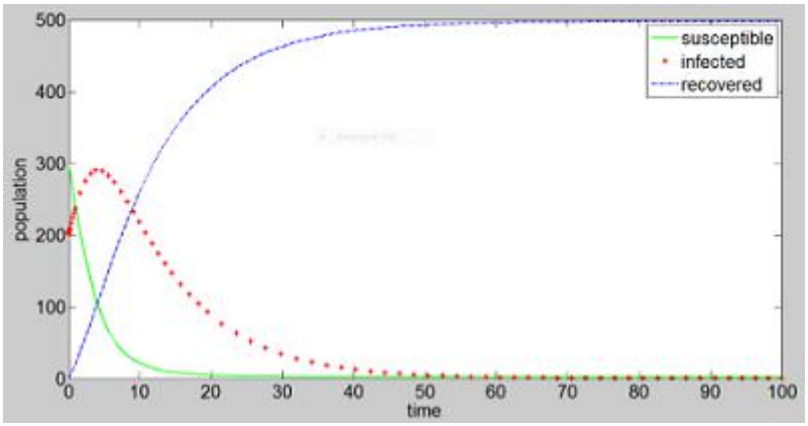

Figure 15. *S (0) = 299, I (0) = 201, R (0) = 0.*

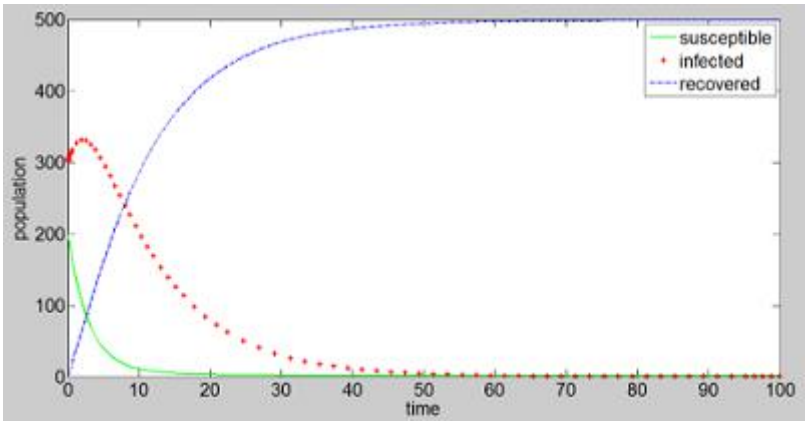

Figure 16. *S (0) = 199, I (0) = 301, R (0) = 0.*

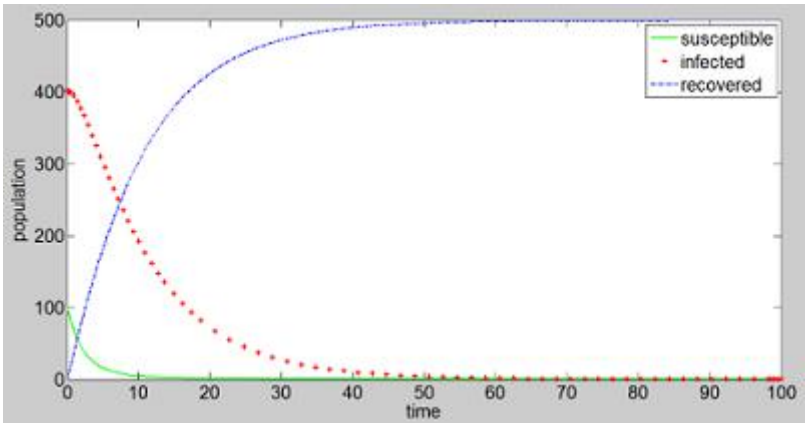

Figure 17. *S (0) = 99, I (0) = 401, R (0) = 0.*

5.3. Stability Analysis of the SIR Model with Parameter Values

We now look at the stability of the disease-free equilibrium point $E_0 = (1,0,0)$ and the eigenvalues $\lambda_1 = -\mu$, $\lambda_2 = -\mu$ and $\lambda_3 = \beta - \mu - \gamma$. By substituting the parameter values in Table 9 into these eigenvalues, the eigenvalues corresponding to the disease-free equilibrium are $\lambda_1 = -0.000003$, $\lambda_2 = -0.000003$ and $\lambda_3 = -0.099003$. Since the eigenvalues are all negative, it implies the disease free equilibrium is stable.

The endemic equilibrium point occurs at a time where all the compartments of the population coexist in the population. The introduction of an infected person will infect others, therefore changing the health condition of a lot of people. Substituting the parameter values in Table 9 into $\lambda_1 = -\mu$ and $\lambda_{2,3} = \frac{1}{2}[-\mu\mathcal{R}_0 \pm \sqrt{\mu^2\mathcal{R}_0{}^2 - 4\mu(\beta-\mu-\gamma)}\,]$, we obtain the eigenvalues corresponding to the endemic equilibrium. This is given by

$$\lambda_1 = -0.000003$$

$$\lambda_{2,3} = \frac{1}{2}\left[-\mu\mathcal{R}_0 \pm \sqrt{\mu^2\mathcal{R}_0{}^2 - 4\mu(\beta-\mu-\gamma)}\;\right]$$

$$= \frac{1}{2}[-(0.000003)(0.00999970001) \pm \sqrt{(0.000003)^2(0.00999970001)^2 - 4(0.000003)(-0.099003)}\;]$$

$$= \frac{1}{2}[-0.00000003 \pm 0.00000118804\,]$$

$$\lambda_2 = 0.00054 \text{ and } \lambda_2 = -0.00054$$

Since the two eigenvalues are both negative and the other one is positive, it implies the endemic equilibrium is unstable

5.4. Simulation of SIR Model in Terms of $\mathcal{R}_0$

From equation (4.9), we obtained the reproductive number $\mathcal{R}_0 = \frac{\beta}{\mu+\gamma}$. Now we perform simulations on the SIR model using the data in [9] in terms of $\mathcal{R}_0$.

M-file

```
function output=susceptible_infected_recovered()
global mu beta gamma
 %parameters mu=0.0002;
beta=0.001; gamma=0.0001;
R0=beta/(gamma+mu);
%R0=basic reproduction number
t0 = 0;
 tf =100;
y0 = [500 1 0]
[t  y]  = ode45 (@Susceptible_Infected_Recovered,[t0 tf],y0);
 plot(t,y(:,2),'r-','linewidth',2); set(gca,'FontSize',20)
 xlabel('time')
ylabel('Infected population')
% y1 -- susceptible popn,
% y2 -- infected popn
% y3 -- recovered popn
```

```
function dy =Susceptible_Infected_Recovered(t,y)
dy = zeros(3,1);
dy(1) = 0.0002 -0.0002*y(1) -0.001*y(1)*y(2);
dy(2) = 0.001*y(1)*y(2)-0.0002*y(2)-0.0001*y(2);
dy(3) = 0.0001*y(2)-0.0002*y(3);
```

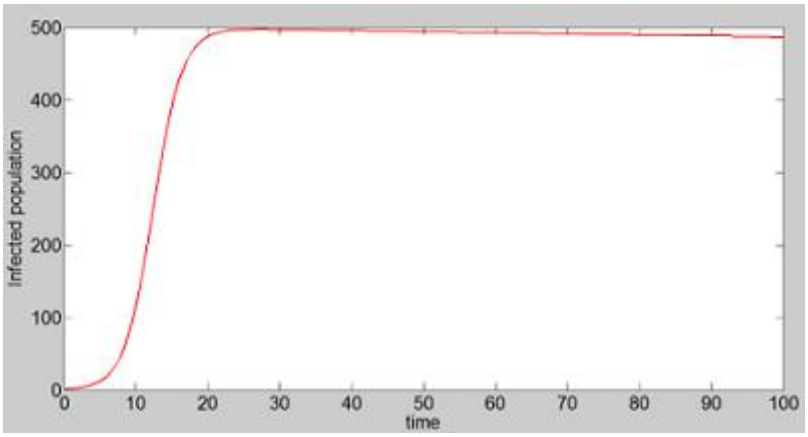

Figure 18. *(a)*$\mathcal{R}_0 = 3.333 > 1$*, where* $\beta = 0.001$*,* $\mu = 0.0002$ *and* $\gamma = 0.0001$.

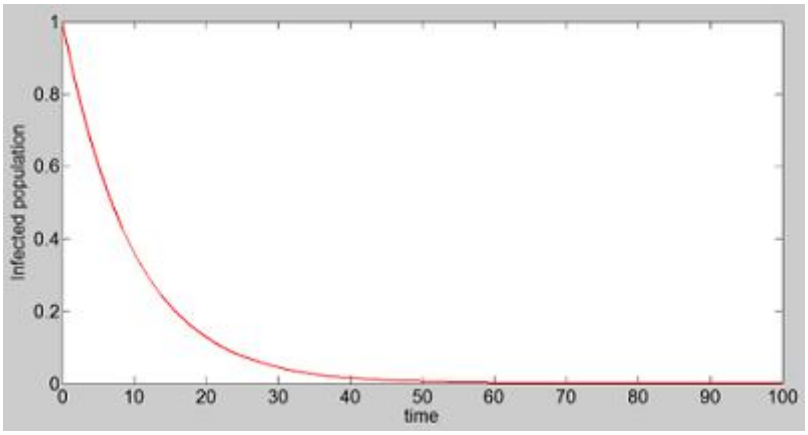

Figure 19. *(b)*$\mathcal{R}_0 = 0.0016 < 1$*, where* $\beta = 0.001$*,* $\mu = 0.000003$ *and* $= 0.6$.

Figure 19 Infected population for different values of $\mathcal{R}_0$. Note that for $\mathcal{R}_0 > 1$ the disease persist. Whereas, for $\mathcal{R}_0 > 1$ the disease could be eliminated. The parameter values in the syntax are chosen for the purpose of illustration of different $\mathcal{R}_0$ values. Carefully selection (considering the biology and other factors) of parameters is however necessary.

6. Conclusions

We did not consider a mathematical model to represents some special disease in this project, but our main goal was to give idea that the transmission of infection can be easily studied by epidemiological model. Analysis of the model showed that there are two equilibrium points one is disease-free equilibrium and the other one is endemic equilibrium. The dynamics of the proposed model are determined by the basic reproduction number $\mathcal{R}_0$ which depends on the parameter values. We also presented that for $\mathcal{R}_0 < 1$ the disease-free equilibrium is stable while for $\mathcal{R}_0 > 1$ the endemic equilibrium exists.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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