UNIVERSITY OF CAPE COAST

MATHEMATICAL MODEL FOR THE CONTROL OF MALARIA

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A MATHEMATICAL MODEL FOR THE CONTROL OF MALARIA

BY

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DECLARATION

Candidate's Declaration

I hereby declare that this thesis is the result of my own original work and that no part of it has been presented for an other degree in this university or elsewhere.

Candidate's signature ..... Date .....

Name .....

Supervisors' Declaration

We hereby declare that the preparation and presentation of the thesis were supervised in accodance with the guidelines o n supervision of thesis laid down by the University of Cape Coast.

Principal Supervisor's Signature ..... Date .....

Name .....

Co-Supervisor's Signature ..... Date .....

Name .....

ABSTRACT

Many infectious diseases including malaria are preventable, yet they remain endemic in many communities due to lack of proper, adequate and timely control policies.

Strategies for controlling the spread of any infectious disease include a rapid reduction in both the infected and susceptible populations. (if a cure is available) as well as a rapid reduction in the susceptible class if a vaccine is available. For diseases like malaria where there is no vaccine, it is still possible to reduce the susceptible class through a variety of control measures.

In this dissertation, we have developed a mathematical model for the transmission of malaria. We have shown that the model has a unique disease-free and endemic equilibria.

The disease-free equilibrium ls locally and globally asymptotically stable, if $R_0 \leq 1$, and that the endemic equilibrium exist provided $R_0 > 1$.

Simulation of the model clearly shows that, with a proper combination of treatment and a concerted effort aimed at prevention, malaria can be eliminated from our community.

It is not necessary (or impossible) to kill all mosquitoes in order to eliminate malaria.

In fact, effective treatment offered to about 50% of the infected population, together with about 50% prevention rate is all that is required to eliminate the disease.

ACKNOWLEDGEMENTS

There are many people that I would like to thank for making this dissertation possible. First and foremost, I would like to express my sincere gratitude, and deepest appreciation to my supervisor, Professor Francis Benyah, for his deep understanding, and guidance. His in depth understanding in Mathematical Biology has helped me build a solid background in Epidemiological Modelling.

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DEDICATION

To

In honour of my loving grand mother, Dorcas Yanney.

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CHAPTER ONE

INTRODUCTION

Background

This chapter considers the background to the study. It also outlines the purpose of the study. We also look at what others have done under literature review.

Infectious diseases such as malaria, AIDS and cholera continue to claim millions of lives around the world, Busenberg and Cooke (1993). Global eradication programs of these infectious diseases have been implemented for many years with some considerable success. Long term solutions to combating some of these diseases have eluded researchers, because some of these diseases have no cure. Malaria, an infection of the red blood cells, caused by Plasmodium, is spread by the bite of an infected female anopheles mosquito and is endemic to tropical areas where the climatic and weather conditions allow continuous breeding of the mosquito.

There is no vaccine that can provide permanent immunity against malaria. However, certain preventive drugs can be taken in advance before entering a malaria high-risk area to prevent or reduce the possibility of infection. No drug therapy has been found to be completely effective in preventing the infection. Moreover the drug therapy depends largely on which type of malaria an individual has.

The factors that have influence the resurgence and spread of malaria include:

(i) mosquito resistance to the usual insecticides.

(ii) resistance of some parasite strains to the commonly used anti malaria drugs and

(iii) economic factors that influence the financing of malaria control operations.

Most malaria high-risk areas are located in developing countries where

(a) the level of education is generally low and

(b) drugs can be purchased without prescriptions.

A combination of (a) and (b) generally results in maladministration of the drugs. A number of studies modeling the effects of vaccination as a disease control mechanism have been carried out by many authors such as Hill and Longini Jr (2003). Kribs-Zaleta and Velasco-Hernandez (2000) considered a simple vaccination model in which they found that vaccination without behavior change and indecency of vaccines may fail to achieve the desired objective of eradicating the epidemic. This conclusion is supported by Blower and Mclean (2002) and by Hadeler and Castillo (1995). Most of the studies exhibited the bifurcation phenomena. The concept of bifurcation which arose in studies by Kribs-Zaleta and Velasco-Hernandez (2000), Dushoff *et al.* (1998), Greenhalgh *et al.* (2000), van den Driessche and Watmough (2000) have important implications in the behavior of the disease in a population.

Purpose of Study

The purpose of the study is as follows:

(1) To develop an epidemic model for the transmission of malaria.

(2) Remove the inoculation parameter and determine the reproduction number.

(3) Include the inoculation parameter and determine the reproduction number.

(4) Use the method of linearization to determine the stability conditions for the model with the inoculation parameter.

(5) Perform simulations on the model to determine the effects of various control strategies.

(6) To make appropriate recommendations.

Literature Review

Mathematical modeling of malaria began in 1911 with Ross' model (1911) and major extensions are described in Macdonald's (1957) book. This Ross-Macdonald model is defined as

$$\frac{\mathrm{dx}}{\mathrm{dt}} = (\mathrm{abM/N})\mathrm{y}(1-\mathrm{x}) - \mathrm{rx} \tag{1.1}$$

$$\frac{\mathrm{dy}}{\mathrm{dt}} = \mathrm{ax}(1-\mathrm{y}) - \mu\mathrm{y} \tag{1.2}$$

where x is the fraction of infectious humans; y is the fraction of infectious female mosquitoes; a is the number of bites on humans by a single female mosquito per unit time, usually day; b is the probability of transmission of infection from an infected mosquito to a susceptible human per bite; M is the size of the total female mosquito population; N is the size of the total human population; r is the rate of recovery for infectious humans ; and μ is the death rate of the female mosquito population. In a survey,

Aron and May (1982) describe the properties of this model, including the derivation of the reproductive number, $\mathcal{R}_0$, as

$$\mathcal{R}_0 = \frac{\mathrm{Ma^2b}}{\mathrm{N}\mu\mathrm{r}}$$

The reproductive number, $\mathcal{R}_0$, is defined as the number of secondary infections that one infectious person would produce in a fully susceptible population through the entire duration of the infectious period. The idea is derived from the idea of a reproductive number in population dynamics which is defined as the expected number of offspring that one organism will produce over its lifespan. Heesterbeek in (2002) conducts a review on the history of $\mathcal{R}_0$.

For simple homogeneous models, the reproductive number can be defined as the product of the number of contacts that one individual has per unit time, the probability of transmission per contact and the duration of the infectious period. For Ross model 1.1, $\mathcal{R}_0$ is defined as the product of the number of mosquitoes that one infectious human infects and the number of humans that one infectious mosquito infects, through the duration of their infectious periods. The number of contacts with mosquitoes that one human has per unit time is (aM/N). The probability of transmission from an infectious human to a susceptible mosquito is assumed to be 1; and $1/r$ is the average duration of the infectious period of the human. Thus, (M/N)(a/r) is the number of mosquitoes that one human infects over the entire infectious period. Similarly, a is the number of contacts with humans that one mosquito has per unit time; b is the probability of transmission from an infectious mosquito to a susceptible human; and $1/\mu$ is the average duration of the infectious period of the mosquito (female mosquitoes are infectious till death). Thus, (abμ) is the number of humans that one mosquito infects through its infectious lifetime. The product of the two, (M/N)($\mathrm{a^2b} = (\mathrm{r}\mu)$) forms the reproductive number. It is the number of

humans that one infectious human will infect, through a generation of infectious mosquitoes. Aron and May (1982) continue their review by adding various characteristics of malaria to the model, such as an incubation period in the mosquito, a periodically fluctuating density of mosquitoes, superinfection and a period of immunity in humans.

They also include a continuum model for immunity where the dynamical variables are the population of asexual blood stages of Plasmodium in humans, the population of gametocytes (sexual stages of Plasmodium in humans), and the level of human immunity. In this system of partial differential equations, the variables depend on both time and age. The mosquitoes are modeled through V , the vectorial capacity, which is proportional to the mosquito density. This model is a significant deviation from the Ross-Macdonald model 1.1 as it does not keep track of the number of infected humans and mosquitoes. Instead, this continuum model measures the number of parasites and level of immunity in the average human. This is useful for malaria because there can be a large difference in the parasitemia load in different humans, that the Ross-Macdonald model ignores.

In a later review, Anderson and May (1991) revisited many of the ideas discussed by Aron and May. Anderson and May in this addition, compile numerous data sets for parameter values, including the latent period in mosquitoes and humans, the rate of recovery for humans, the expected adult lifespan of mosquitoes and malaria prevalence data across age distributions for humans. Anderson and May also studied the effect of adding age structure to the basic Ross-Macdonald model 1.1. Finally, they looked at different control strategies, discussing the effects of a vaccine and the reduction of transmission rates on the malaria age-prevalence profile of the human population.

Other reviews on mathematical modeling in malaria include Nedelman (1985) and Koella (1991). Nedelman surveys various data sets to statistically approximate parameters such as inoculation rates, rates of recovery and loss of immunity in humans, human-biting rates of mosquitoes and infectivity and susceptibility of humans and mosquitoes. Koella also begins with the Ross-Macdonald model 1.1 with an additional latent stage for the mosquitoes. He then studies the effect of variability of the parameters and adds an infection-rate dependent period of immunity. Using this model with immunity, he studies the effects of vaccines, comparing those that act on asexual blood stages and those that block transmission, to show that the asexual blood stage vaccines are more effective. An important advance for the mathematical modeling of malaria was the inclusion of acquired immunity in the model proposed by Dietz, Molineaux and Thomas in 1974. Dietz *et al.* proposed a model with two different classes of humans: one without immunity to malaria and one class with some immunity. As the non-immune class falls sick, some people recover with immunity. The immune class can get infected, but does not fall clinically ill and cannot be infectious. The model by Dietz *et al.* also included superinfection, a phenomenon usually associated with macroparasites. As also described by Aron and May (2003) and Anderson and May 1991), superinfection is a significant increase of the parasite load, when an infected person is reinfected from the outside. This is usually modeled by making the recovery rate (r in the above equation 1.1 a (usually monotonically non increasing) function of the inoculation rate . Various models, with superinfection, for the recovery rate, r, include:

$$\begin{aligned} \text{Ross}(1911) : r &= \gamma \\ \text{Dietz}(1974) : \text{r} &= \gamma \, [\text{e}^{(\lambda/\gamma)} - 1] \end{aligned}$$

and

$$\text{Macdonald}(1957) : \text{r} = \begin{cases} \gamma - \lambda & \gamma > \lambda \\ 0 & \gamma \leq \lambda \end{cases}$$

where λ is the inoculation rate (defined in 1.1 as $\lambda = (abM = N)y$) and γ is the reinfection-free rate of recovery, i.e. $1/\gamma$ is the average duration of the infectious period in the absence of further infection. The model for superinfection by Dietz is also described by Bailey (1957).

Another important feature of malaria is the transient nature of acquired immunity. Aron (1982) reviews the compartmental and continuous models for temporary immunity in humans. In compartmental models, an additional recovered class is added. In the usual Susceptible-Infectious-Recovered-Susceptible (SIRS) or Susceptible-Exposed-Infectious-Recovered-Susceptible
(SEIRS) model, the rate of loss of immunity, ρ, is a constant parameter. However, sustained immunity to malaria requires continuous reinfection; thus in the absence of reinfection, immunity is lost quickly, while in the presence of a high infection rate, immunity is long-lived. This non-constant period of immunity can be modeled by making the rate of loss of immunity, ρ a function of the inoculation rate as shown below.

$$\rho(\lambda) = \frac{\lambda \text{e}^{(-\lambda\tau)}}{1 - \text{e}^{(-\lambda\tau)}} \tag{1.3}$$

where λ is again the inoculation rate and τ is the average duration of the immune period in the absence of infection.

Some of the more recent papers on the mathematical modeling of malaria have included environmental effects. Yang (2000) describes a compartmental model where humans follow an SEIRS-type (with more than one

immune class for humans) pattern and mosquitoes follow a Susceptible-Exposed-Infectious (SEI) pattern. Additionally, some of the parameters related to mosquitoes are now a function of temperature. These include the time taken for mosquito eggs to develop into adults and the time taken for Plasmodium gametocytes ingested by the mosquito to develop into sporozoites and migrate to the salivary glands (the incubation time in the mosquito). Yang defines a reproductive number, $\mathcal{R}_0$ for this model and shows, through linear stability analysis, that the disease-free equilibrium is stable for $\mathcal{R}_0 < 1$. He also derives an expression for an endemic equilibrium that is biologically relevant only when $\mathcal{R}_0 > 1$. He uses numerical simulations to support his proposition that for$\mathcal{R}_0 > 1$, the disease-free equilibrium is unstable and the endemic equilibrium is stable.

Yang and Ferreira (2000) use the model by Yang (2000) to study the effects of global warming. Using the estimated increase in temperature of $1.0^0C - 3.5^0C$ by the year 2100, they show that it is possible in some areas of the world for $\mathcal{R}_0$ to increase above 1; for areas to change from a stable disease-free endemic state to one with low levels of endemicity and for other areas to change from low levels of endemicity to high levels. They do, however, conclude by saying that economic and social effects are still more important than temperature effects and a good health care system with good malaria control techniques can overcome the negative effects of an increase in temperature.

Li *et al.* (2002) derive a model where humans move through multiple Susceptible Exposed-Infectious-Recovered (SEIR) stages, where a history is kept of previous infections. They include a submodel for the mosquito population with subdivisions for juveniles and adults. They use the steady state value for the adult mosquito population, from this submodel, as the input into their model for malaria transmission. They introduce dependence of

the parameters for the mosquito population submodel on an environmental parameter (eg. temperature or rainfall) and calculate the dependence of the reproductive number, for the full malaria model, on this environmental parameter.

Other recent models have included the spread of drug-resistant Plasmodium, Koella and Anita (2003) and of the evolution of immunity. Koella and Antia (2003) discuss a model where, starting with the Ross-Macdonald model 1.1 and moving to more complicated models, they include a strain of disease that is resistant to treatment. Their results show that in their simplest models, there is a threshold value of fraction of infectious humans treated, below which there is no resistance to drugs, and above which, resisistance to treatment spreads. In the more complicated models, this kind of resistance is usually not fixed, but there is some level of sensitivity to drugs that is maintained in the population. Koella and BoËte (2003) study a host-parasite evolution model of malaria where the host invests in its immune system over time and the parasite invests in its ability to evade the host's immune response.

The model for malaria transmission that we analyze, is an extension of the equations introduced by Ngwa and Shu (2000). In the Ngwa and Shu model, humans follow an SEIRS-like pattern and mosquitoes follow a SEI pattern, similar to that described by Yang (2000) but with only one immune class for humans. Humans move from the susceptible to the exposed class at some probability when they come into contact with an infectious mosquito, and then to the infectious class, as in conventional SEIRS models. However, infectious people can then recover with, or without, a gain in immunity; and either return to the susceptible class, or move to the recovered class. A new feature of this model is that although individuals in the recovered class are assumed to be "immune", in the sense that they do not suffer from serious

illness and do not contract clinical malaria, they still have low levels of Plasmodium in their blood stream and can pass the infection to susceptible mosquitoes. After some period of time these recovered individuals return to the susceptible class.

Susceptible mosquitoes get infected and move to the exposed class, at some probability when they come into contact with either infectious humans or recovered humans (albeit at a much lower probability). They then pass on to the infectious class.

Both humans and mosquitoes leave the population through a density dependent natural death rate. This allows the model to account for changing human and mosquito populations. Variations in mosquito populations are crucial to the dynamics of malaria, and constant population models do not account for this. The model also includes human disease-induced death as mortality for malaria in areas of high transmission can be high, especially in infants.

Ngwa and Shu analyze this model assuming a linear per capita death rate. They convert the system to dimensionless quantities and in these new variables, define a reproductive number, $\mathcal{R}_0$.

They show that when $\mathcal{R}_0 > 1$, there exists an endemic equilibrium (nonnegative solution distinct from the disease-free equilibrium), and furthermore, with no disease-induced death, this endemic equilibrium is unique. Using linear analysis, they also show that the disease-free equilibrium is locally asymptotically stable when $\mathcal{R}_0 \leq 1$ and the unique endemic equilibrium (for no disease-induced death) is locally asymptotically stable when $\mathcal{R}_0 > 1$. They conclude by using numerical simulations to support their proposition that the endemic equilibrium is stable for $\mathcal{R}_0 > 1$.

In a second paper, Ngwa (2004) rewrites the reproductive number in terms of the original (with dimension) parameters. He also includes a

small disease induced death rate, using perturbation analysis to evaluate a first order approximation to the endemic equilibrium with disease induced death. Finally, he conducts some numerical simulations on a stochastic expansion of the model.

This profusion of models has been driven by the need to understand different aspects of the complex malaria epidemiology. In the model we analyze, we aim to capture some of the more important aspects of this epidemiology while still keeping it mathematically tractable. Some of the important factors that we include are the presence of an exposed state in mosquitoes and dynamically changing human and mosquito populations, including human immigration and disease-induced death.

Outline of the Study

This section outlines the contents within each of the six chapters of the thesis, and gives a brief description of these contents.

The Introduction is the first chapter of the study. It looks at the background to the study. The objectives of the study is stated. A Literature Review of the contributions by other researchers follows next. The final section, gives a brief Outline of the Study.

Chapter two discusses the Dynamical Systems and their Stability. The chapter looks at the Basic Definitions and Notations. Under chapter two critical analyses of Linear and Nonlinear systems. It again considers the Routh-Hurwitz Criteria, Phase Portrait Analysis and Gershgorin Theorem. Finally, we consider Bifurcation Theorems with examples.

Chapter three considers Basic Epidemic models. We study, the dynamics of the compartmental models, SIR, SIS, SIRS. We also study the effect of vaccination on a generic SIR model.

In chapter four, Vector-Host Models are looked at into details. The Compartmental Model for the Vector-Host Model together with the Differential Equation are drawn up. Two Species are considered for the Vector-Host Model. We show that changing the boundaries condition and some of the parameter values do not affect the stability of the system.In the same chapter, we consider a very important concept called Basic Reproduction Number. This concept is a determining factor as to whether a disease dies out becomes endemic. The Derivation of the reproduction Number leads us to the Next Generation Matrix. This shows the approach in finding the Basic Reproduction Number. Lastly we consider the Application of the Next Generation Matrix in solving models such as TB Treatment, Multi Strain, Vector-Host Model and SLIAR Model. The rest are Simple Vaccination Model.

Chapter five considers Vector-Host Models. The Compartmental Model for the Vector-Host Model together with the Differential Equation are drawn up. Two Species are considered for the Vector-Host Model. We show that changing the boundaries condition and some of the parameter values do not affect the stability of the system. Conclusion conclude chapter four.

A mathematical Analysis of the Effects of Control Strategies on the Transmission Dynamics of Malaria in a Human Host and Mosquito Vector with Temporary Immunity is looked at in chapter six. This chapter is my contribution to literature and an effort aimed at fighting malaria. This chapter start with and introduction . It then reviews works on malaria. For illustrative purposes, an SIR model is used to show the effect of inoculation. Five-state compartmental model is drawn and the differential equations explicitly defined. Chapter five then looks at the Determination of $\mathcal{R}_0$. The Existence of Equilibrium Solutions for disease-free and

the endemic equilibria are examined. We again, examine the global stability of the disease-free equilibrium. The effects of control strategies on infected humans and infected mosquitoes are discussed. We conclude on the chapter.

In Chapter Six, we make a summary of all the various observations that have emerged from the study. We then discuss some of these observations. Finally, we draw appropriate conclusions and make few recommendations based on the result of the study.

CHAPTER TWO

STABILITY ANALYSIS OF DYNAMICAL SYSTEMS

Systems Of ODES

A wide variety of natural phenomena can be modelled by a system of two first-order **autonomous system** of ordinary differential equations of the form

$$\begin{aligned} \frac{\mathrm{dx}}{\mathrm{dt}} &= \mathrm{f(x,y)} \\ \frac{\mathrm{dy}}{\mathrm{dt}} &= \mathrm{g(x,y)} \end{aligned} \tag{2.1}$$

where f and g are differential functions in some region R of the xy-plane, called the **phase plane** of the system 2.1.

Then, given t_0 and any initial point (x_0, y_0) of R, there is a unique solution $\mathrm{x = x(t), y = y(t)}$ of 2.1 that is defined on some open interval (a, b) containing t_0 and satisfied the initial conditions

$$\mathrm{x(t_0) = x_0}, \qquad \mathrm{y(t_0) = y_0} \tag{2.2}$$

The equations $\mathrm{x = x(t), y = y(t)}$ then describes a parametrized solution curve in the phase plane. Any such a solution curve is called a **trajectory** of the system in 2.1.

A **critical point** of the system in 2.1 is a point (x_*, y_*) such that

$$\mathrm{f(x_*, y_*) = g(x_*, y_*) = 0} \tag{2.3}$$

For any critical point (x_*, y_*) of the system, the constant-valued functions

$$\mathrm{x}(\mathrm{t}) \equiv \mathrm{x}_*, \qquad \mathrm{y}(\mathrm{t}) \equiv \mathrm{y}_* \tag{2.4}$$

satisfy equation 2.1. Such a constant-valued solution is called an equilibrium solution of the system. The trajectory of the equilibrium solution consists of the single point (x_*, y_*).

Equilibrium solutions are of the greatest importance in many practical situations. For instance, suppose that the system $x' = f(x, y)$, $y' = g(x, y)$ is a model for two species $x(t), y(t)$ that live in the same environment, then a critical point (x_*, y_*) of the system denotes constant populations $x(t) = x_*$ and $y(t) = y_*$ that can coexist with one another in the environment.

Example 2.1. For example, the critical points of the system

$$\begin{aligned} \frac{\mathrm{dx}}{\mathrm{dt}} &= 30\mathrm{x} - 5\mathrm{x}^2 - 3\mathrm{xy} \\ \frac{\mathrm{dy}}{\mathrm{dt}} &= 8\mathrm{y} - \mathrm{y}^2 - \mathrm{xy} \end{aligned} \tag{2.5}$$

are given by $(0, 0), (0, 8), (6, 0), (3, 5)$.

If $x(t)$ and $y(t)$ denote populations of two species of animals sharing the same environment, then the critical point $\mathrm{x}(\mathrm{t}) \equiv 3$, $\mathrm{y}(\mathrm{t}) \equiv 5$, gives the number of each of the species that can co-exiting together. The other critical points can be interpreted analogously.

Nature of a Critical Point

Definition 2.1 (Node)**.** A critical point $(\mathrm{x}_*, \mathrm{y}_*)$ of an autonomous system is called a **node** if

(a) Either every trajectory approaches (x_*, y_*) as $t \to \infty$ or every trajectory recedes from (x_*, y_*) as $t \to \infty$, and

(b) Every trajectory is tangent at (x_*, y_*) to some straight line through the critical point

Definition 2.2. A node is said to be a **sink** if all trajectories approach the critical point, and a **source** if all trajectories emanate (recede) from it. See Figures 2 and 2.

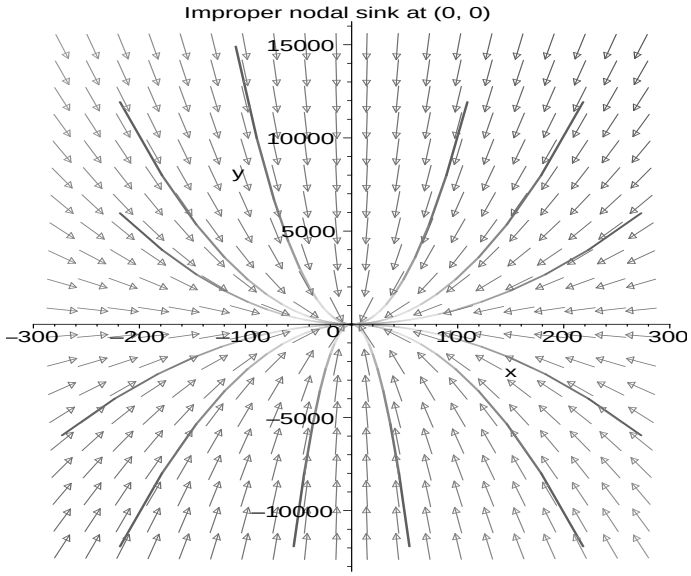

Figure 1: A Nodal Sink at $(0, 0)$ for $x' = -x$, $y' = -2y$

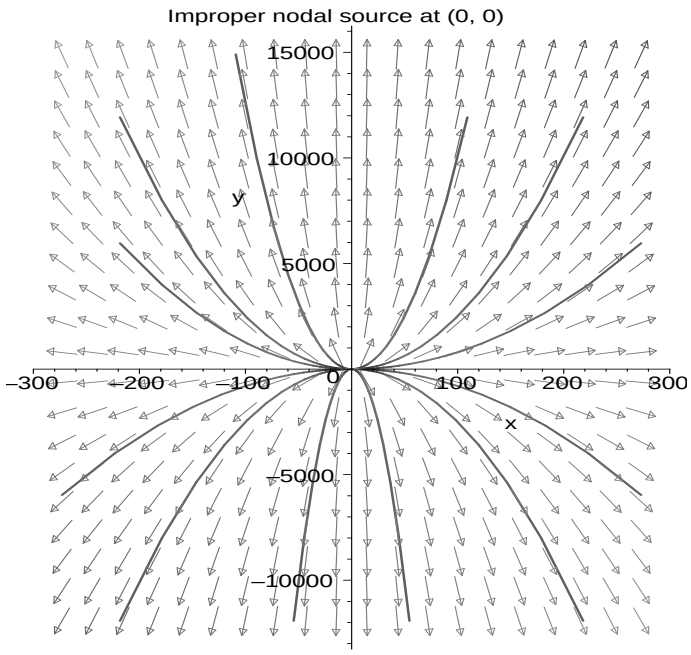

Figure 2: A Nodal Source at $(0, 0)$ for $x' = x$, $y' = 2y$

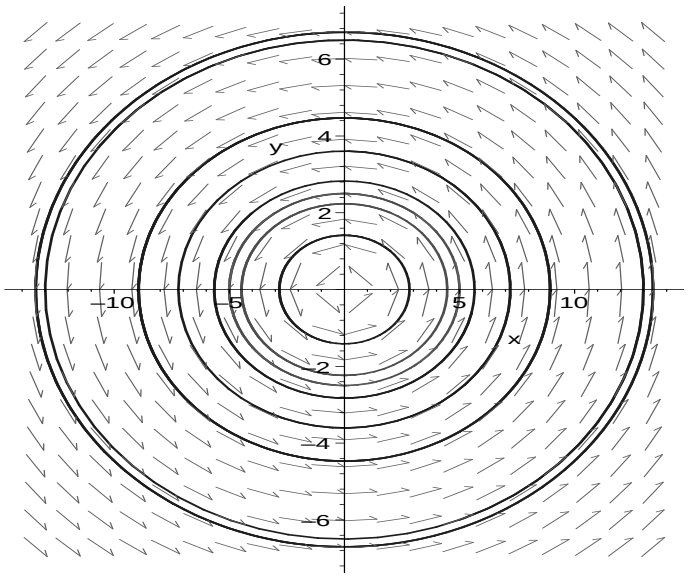

Figure 3: A Stable Centre at $(0, 0)$ for $x' = -y$, $y' = \frac{1}{4}x$

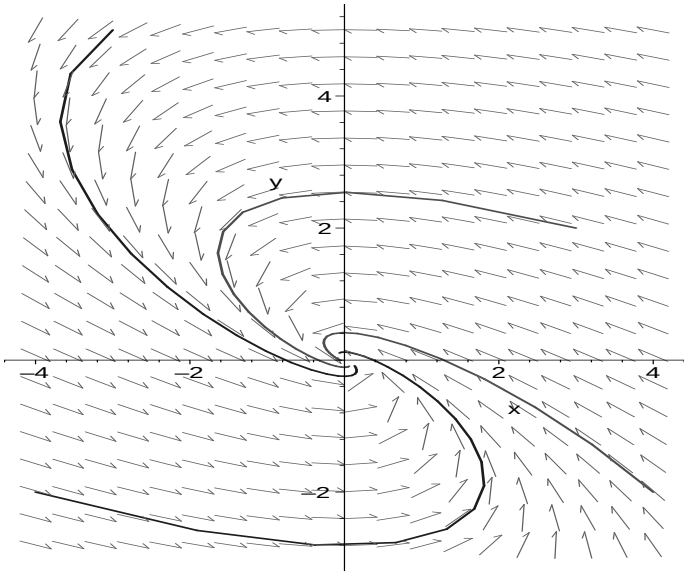

Figure 4: Spiral Sink at $(0,0)$ for $x' = -2x - 2y$, $y' = x$

Stability of Linear and Non-Linear Systems

This section deals with the stability of linear and non-linear systems.

Stability of a Critical Point

In many applications the stability of an equilibrium point is often of utmost importance. If $(\mathrm{x}_*, \mathrm{y}_*)$ is a critical point, then the equilibrium solution
$\mathrm{x(t)} \equiv \mathrm{x}_*, \mathrm{y(t)} \equiv \mathrm{y}_*$ is called **stable** or **unstable** depending on the nature of the critical point.

Definition 2.3. A critical point $(\mathrm{x}_*, \mathrm{y}_*)$ of the autonomous system 2.1 is said to be stable, provided that if the initial point (x_0, y_0) is sufficiently close to $(\mathrm{x}_*, \mathrm{y}_*)$ then $(\mathrm{x(t)}, \mathrm{y(t)})$ remains close to $(\mathrm{x}_*, \mathrm{y}_*)$ for all $\mathrm{t} \geq 0$.

Let $\mathbf{x} = (\mathrm{x(t)}, \mathrm{y(t)}), \mathbf{x}_0 = (\mathrm{x}_0, \mathrm{y}_0)$, and $\mathbf{x}_* = (\mathrm{x}_*, \mathrm{y}_*)$.

Then the critical point $\mathbf{x}_*$ is **stable** provided that, for each $\epsilon > 0$, there exists $\delta > 0$ such that

$$\|\mathbf{x}_0 - \mathbf{x}_*\| \quad < \quad \delta \quad \Rightarrow \quad \|\mathbf{x}(\mathrm{t}) - \mathbf{x}_*\| \quad < \quad \epsilon \quad \text{for all} \quad \mathrm{t} > 0. \qquad (2.6)$$

Obviously, the condition given in 2.6 also holds in the case of a nodal sink, where $\mathbf{x}(t) \to \mathbf{x}_*$ as $t \to \infty$. Thus, the origin $(0, 0)$ in Figures 2 and 2 are stable nodes.

The critical point (x_*, y_*) is called **unstable** if it is not stable. The saddle point $(0, 0)$ in Figure 2 is an unstable critical point since the point $(x(t),\, y(t))$ tends to infinity as t tends to infinity.

Asymptotic Stability

A critical point (x_*, y_*) is called **asymptotically stable** if it is stable and, every trajectory that starts sufficiently close to (x_*, y_*) also approaches (x_*, y_*) as $t \to \infty$. That is, there exists $\delta > 0$ such that

$$\|\mathbf{x}_0 - \mathbf{x}_*\| \quad < \quad \delta \quad \Rightarrow \quad \lim_{\mathrm{t}\to\infty} \mathbf{x}(\mathrm{t}) = \mathbf{x}_* \tag{2.7}$$

where $\mathbf{x}_0 = (\mathrm{x}_0, \mathrm{y}_0),\ \mathbf{x}_* = (\mathrm{x}_*, \mathrm{y}_*)$, and $\mathbf{x}(\mathrm{t}) = (\mathrm{x}(\mathrm{t}),\, \mathrm{y}(\mathrm{t}))$ is a solution with with starting point $\mathbf{x}(0) = \mathbf{x}_0$.

Remark 2.1. suppose that $(\mathrm{x}(\mathrm{t}),\, \mathrm{y}(\mathrm{t}))$ represents populations coexisting in the same environment with a critical point $(\mathrm{x}_*, \mathrm{y}_*)$ which is asymptotically stable. If the initial point $(x_0 y_0)$ which is sufficiently close to $(\mathrm{x}_*, \mathrm{y}_*)$ then we should have $\lim_{\mathrm{t}\to\infty} \mathrm{x}(\mathrm{t}) = \mathrm{x}_* \quad \text{and} \quad \lim_{\mathrm{t}\to\infty} \mathrm{y}(\mathrm{t}) = \mathrm{y}_*$.

That is, the populations $x(t)$ and $y(t)$ approaches the equilibrium populations x_* and y_* as $t \to \infty$.

Stability of Linear Systems

The linear system $\dot{\mathbf{x}} = \mathbf{A}\mathbf{x}$, given by

$$\begin{bmatrix} \dot{\mathrm{x}} \\ \dot{\mathrm{y}} \end{bmatrix} = \begin{bmatrix} \mathrm{a} & \mathrm{b} \\ \mathrm{c} & \mathrm{d} \end{bmatrix} \begin{bmatrix} \mathrm{x} \\ \mathrm{y} \end{bmatrix} \tag{2.8}$$

has only one critical point, $(0, 0)$. The stability of this critical point depends on the nature of the eigenvalues of the coefficient matrix. The eigenvalues λ_1 and λ_2 of the coefficient matrix

$$\texttt{det}(\mathbf{A} - \lambda\mathbf{I}) = \begin{vmatrix} a - \lambda & b \\ c & d - \lambda \end{vmatrix} = 0 \tag{2.9}$$

Definition 2.4 (Isolated Critical Point)**.** A **critical point** is called **isolated** if some neighbourhood of it contains no other critical point.

Example 2.2. Consider the linear system

$$\begin{bmatrix} \dot{\mathrm{x}} \\ \dot{\mathrm{y}} \end{bmatrix} = \begin{bmatrix} -1 & 2 \\ 2 & -4 \end{bmatrix} \begin{bmatrix} \mathrm{x} \\ \mathrm{y} \end{bmatrix} \tag{2.10}$$

It can be verified that the critical point $(0, 0)$ of the system is not an isolated critical point. In fact, every point of the form $(2s, s)$, $s \in \mathbb{R}$, is a critical point of the system. Thus, every neighbourhood of $(0, 0)$ contains a critical point of the system. For the linear system in 2.8 to have an isolated critical point, the determinant $ad - bc \neq 0$. That is, both eigenvalues must be nonzero.

Nature of the Critical Point of a Linear System

The nature of the isolated critical point $(0, 0)$ depends on whether the two nonzero eigenvalues λ_1 and λ_2 of $\mathbf{A}$ are

1. real and unequal with the same sign
2. real and unequal with opposite signs
3. real and equal
4. complex conjugates with nonzero real parts, or

5. pure imaginary

We examine these five cases separately.

Unequal Eigenvalues with the Same Sign

In this case the matrix $\mathbf{A}$ has linearly independent eigenvectors $\mathbf{v}_1$ and $\mathbf{v}_2$, and the general solution of 2.8 is of the form $\mathbf{x}(t) = [x(t)\ x(t)]^T$ where

$$\mathbf{x}(t) = c_1\mathbf{v}_1 e^{\lambda_1 t} + c_2\mathbf{v}_2 e^{\lambda_2 t} \tag{2.11}$$

where λ_1 and λ_2 are either both positive or both negative.

Case 1: $\boldsymbol{\lambda_1 < \lambda_2 < 0}$

Then $\mathbf{x}(t) \to \mathbf{0}$ as $t \to \infty$ regardless of the values of c_1 and c_2. In other words, all solutions approach the the critical point $(0, 0)$ as $t \to \infty$. If a solution starts with an initial point on the line through $\mathbf{v}_1$, then $c_2 = 0$; the solution remains on that line t, and approaches the origin as $t \to \infty$. similarly, if a solution starts on the line through $\mathbf{v}_2$, then it approaches the origin along that line.

Suppose that the initial starting point (x_0, y_0) does not lie on either of the vectors $\mathbf{v}_1$ and $\mathbf{v}_2$. Then we can express Equation 2.11 in the form

$$\mathbf{x}(\mathrm{t}) = \mathrm{e}^{\lambda_2 \mathrm{t}} \left[\mathrm{c}_1\mathbf{v}_1\mathrm{e}^{(\lambda_1-\lambda_2)\mathrm{t}} + \mathrm{c}_2\mathbf{v}_2\right] \tag{2.12}$$

Then, since $\lambda_1 - \lambda_2 < 0$, the term $c_2\mathbf{v}_2$ dominates the term $c_1\mathbf{v}_1 e^{(\lambda_1-\lambda_2)t}$ if $c_2 \neq 0$. Therefore, as $t \to \infty$, the trajectory not only approaches the critical point $(0, 0)$ but also tends towards the line through $\mathbf{v}_2$. Hence, all solution curves approach the critical point tangent to $\mathbf{v}_2$ at the origin, except those that start on the line through $\mathbf{v}_1$.

Example 2.3. The matrix

$$\mathbf{A} = \begin{bmatrix} -4 & 3 \\ 0 & -1 \end{bmatrix}$$

has eigenvalues $\lambda_1 = -4,\ \lambda_2 = -1$ ($\lambda_1 < \lambda_2 < 0$), with corresponding eigenvectors $\mathbf{v}_1 = [1\ 0]^T$ and $\mathbf{v}_2 = [1\ 1]$. The solution of the linear system is $\mathbf{x}' = \mathbf{A}\mathbf{x}$ is given by

$$\mathbf{x}(t) = c_1\mathbf{v}_1 e^{-4t} + c_2\mathbf{v}_2 e^{-t} = e^{-t}\left[c_1\mathbf{v}_1 e^{-3t} + c_2\mathbf{v}_2\right]$$

and $\mathbf{x}(t) \to \mathbf{v}_2$ as $t \to \infty$. Trajectories starting from any initial point (apart from lines through $\mathbf{v}_1$) tends towards $\mathbf{v}_2 = [1\ 1]^T$ as t increases. The critical point $(0, 0)$, is therefore a nodal sink.

Example 2.4. Case 2: $\boldsymbol{\lambda_2 > \lambda_1 > 0}$.

The matrix

$$\mathbf{B} = -\mathbf{A} = \begin{bmatrix} 4 & -3 \\ 0 & 1 \end{bmatrix}$$

has eigenvalues $\lambda_1 = 1,\ \lambda_2 = 4$, with the same eigenvectors $\mathbf{v}_1 = [1\ 1]^T$ and $\mathbf{v}_2 = [1\ 0]$.

The solution of the corresponding linear system $\mathbf{x}' = \mathbf{B}\mathbf{x}$ is given by

$$\mathbf{x}(t) = c_1\mathbf{v}_1 e^{t} + c_2\mathbf{v}_2 e^{4t} = e^{4t}\left[c_1\mathbf{v}_1 e^{-3t} + c_2\mathbf{v}_2\right]$$

Trajectories starting from any initial point (apart from lines through $\mathbf{v}_1$) move away from the origin (0, 0) towards lines parallel to $\mathbf{v}_2 = [1\ 0]^T$ as t increases.

The critical point $(0, 0)$ of the linear system $\mathbf{x}' = \mathbf{B}\mathbf{x}$ is therefore a nodal source.

Unequal Real Eigenvalues with Opposite Signs

The general solution is

$$\mathbf{x} = c_1\mathbf{v}_1 e^{\lambda_1 t} + c_2\mathbf{v}_2 e^{\lambda_2 t} \tag{2.13}$$

where $\lambda_2 < 0 < \lambda_1$. If the solution starts at an initial point on the line through $\mathbf{v}_1$ then it follows that $c_2 = 0$. Consequently the solution stays on the line through $\mathbf{v}_1$ for all t. Since $\lambda_1 > 0, \|\mathbf{x}\| \to \infty$ as $t \to \infty$. On the other hand, if the solution starts at an initial point on the line through $\mathbf{v}_2$ then it stays on that line for all t, however in this case, $\|\mathbf{x}\| \to 0$ as $t \to \infty$ since $\lambda_2 < 0$.

The positive exponential term is the dominant term in 2.13 the expression A solution starting from other initial points follow a trajectory that lie on a hyperbola asymptotic to the lines through the lines determined by $\mathbf{v}_1$ and $\mathbf{v}_2$. The only solution that passes through the critical point $(0, 0)$ are those that start on the line determined by $\mathbf{v}_1$. Figure 2 shows some typical trajectories.

Example 2.5. *The matrix*

$$\mathbf{A} = \begin{bmatrix} 2 & 1 \\ 1 & 2 \end{bmatrix}$$

has eigenvalues $\lambda_1 = -1,\ \lambda_2 = 3$, with corresponding eigenvectors $\mathbf{v}_1 = [1\ 1]^T$ and $\mathbf{v}_2 = [-1\ 1]$. The system $\mathbf{x}' = \mathbf{A}\mathbf{x}$ has only one critical point $(0, 0)$.

A phase portrait of the system in Figure 2 shows that the linear trajectories point in the same direction of the two eigenvectors, while the non-linear trajectories are hyperbolas in the $\mathbf{v}_1\mathbf{v}_2$-coordinate system.

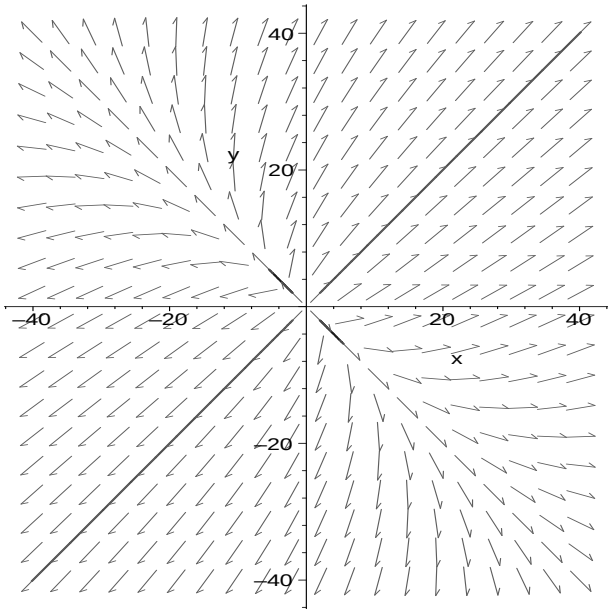

Figure 5: A saddle point at $(0, 0)$ for the system $\mathbf{x}' = \mathbf{A}\mathbf{x}$ of Example 2.5

Equal Real Roots

Here, we have $\lambda_1 = \lambda_2 = \lambda$. The nature of the critical point $(0, 0)$ depends on whether or not the matrix $\mathbf{A}$ has two linearly independent eigenvectors.

(a) **Two linearly independent eigenvectors:** The general solution in this case is

$$\mathbf{x} = \mathrm{c}_1\mathbf{v}_1\mathrm{e}^{\lambda \mathrm{t}} + \mathrm{c}_2\mathbf{v}_2\mathrm{e}^{\lambda_2 \mathrm{t}} \tag{2.14}$$

where $\mathbf{v}_1$ and $\mathbf{v}_2$ are the two linearly independent eigenvectors. The ratio x_2/x_1 is independent of t, but depends on the components of $\mathbf{v}_1$ and $\mathbf{v}_2$ and on the arbitrary constants c_1 and c_2. Thus every trajectory lies on the straight line through the origin. The critical point in this case is called a **proper node** or sometimes called a **star point**.

Example 2.6. The matrix

$$\mathbf{A} = \begin{bmatrix} -1 & 0 \\ 0 & -1 \end{bmatrix}$$

has eigenvalues $\lambda_1 = -1 = \lambda_2$, with two linearly independent eigenvectors $\mathbf{v}_1 = [1\ 0]^T$ and $\mathbf{v}_2 = [0\ 1]^T$. the system $\mathbf{x}' = \mathbf{A}\mathbf{x}$ has a nodal sink at the critical point $(0, 0)$.

Example 2.7. The matrix

$$\mathbf{B} = -\mathbf{A} = \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}$$

has eigenvalues $\lambda_1 = 1 = \lambda_2$, with the same eigenvectors $\mathbf{v}_1 = [1\ 0]^T$ and $\mathbf{v}_2 = [0\ 1]^T$. The system $\mathbf{x}' = \mathbf{B}\mathbf{x}$ has a nodal source at the critical point $(0, 0)$.

(b) **One independent eigenvector:** If the matrix $\mathbf{A}$ is **defective**, then the eigenvalues $\lambda_1 = \lambda_2 = \lambda$ has only one corresponding eigenvector $\mathbf{v}$. In this case we have solution of the form

$$\mathbf{x} = c_1\mathbf{x}e^{\lambda t} + c_2\left(t\mathbf{v}e^{\lambda t} + \mathbf{u}e^{\lambda t}\right) \tag{2.15}$$

where $\mathbf{v}$ is the eigenvector corresponding to λ, and $\mathbf{u}$ is the generalized eigenvector associated with the repeated eigenvalue. ($\mathbf{u}$ is a solution of $(\mathbf{A} - \lambda\mathbf{I})\,\mathbf{u} = \mathbf{v}$.)

For a large t the term $c_2 t\mathbf{v}e^{\lambda t}$ dominates the other terms in 2.15. Hence, as $t \to \infty$, every trajectory approaches the origin tangent to the line through the eigenvector $\mathbf{v}$. Even if $c_2 = 0$, then the solution $\mathbf{x} = c_1\mathbf{v}e^{\lambda t}$ lies on this line. Similarly, for large negative values of t, the term $c_2\mathbf{v}e^{\lambda t}$ dominates, and so as $t \to \infty$, each trajectory is asymptotic to the line parallel to $\mathbf{v}$.

When a double eigenvalue has only one independent eigenvector, the critical point is called an **improper node** or a **degenerate node**.

(i) If $\lambda_1 = \lambda_2 = \lambda < 0$, then the critical point is an **improper nodal sink**.

Example 2.8. The matrix

$$\mathbf{A} = \begin{bmatrix} -2 & 0 \\ 1 & -2 \end{bmatrix}$$

has a repeated eigenvalue $\lambda_1 = \lambda_2 = -2$, corresponding to the eigenvector $\mathbf{v} = [0,\, 1]^T$, and a generalized eigenvector is given by $\mathbf{u} = [-1,\, 1]^T$. The linear system $\mathbf{x}' = \mathbf{A}\mathbf{x}$ has only one critical point $(0, 0)$, which is a **nodal sink**, since the eigenvalue(s) are negative. The trajectories approach the critical point $(0, 0)$ tangent to the line through $\mathbf{v} = [0\ 1]^T$.

(ii) On the other hand if, $\lambda_1 = \lambda_2 = \lambda > 0$, then the critical point is an **improper nodal source**.

Complex Eigenvalues with Non-zero Real Parts

Suppose that the matrix $\mathbf{A}$ has eigenvalues $\lambda_1 = a + bi$ and $\lambda_2 = a - bi$, ($a \neq 0$, $b > 0$). Any linear system with eigenvalues $a \pm ib$ can be represented by

$$\begin{bmatrix} x' \\ y' \end{bmatrix} = \begin{bmatrix} a & b \\ -b & a \end{bmatrix} \begin{bmatrix} x \\ y \end{bmatrix} \tag{2.16}$$

In scalar form we have

$$\mathrm{x}' = \mathrm{ax} + \mathrm{by}, \qquad \mathrm{y}' = -\mathrm{bx} + \mathrm{ay} \tag{2.17}$$

Using polar coordinates $(r,\ \theta)$ where

$$\mathrm{r}^2 = \mathrm{x}^2 + \mathrm{y}^2, \qquad \tan(\theta) = \frac{\mathrm{y}}{\mathrm{x}}.$$

Taking the derivatives with respect to t give

$$\mathrm{rr}' = \mathrm{xx}' + \mathrm{yy}' \tag{2.18}$$

$$(\sec^2\theta)\theta' = \frac{\mathrm{xy}' - \mathrm{yx}'}{\mathrm{x}^2} \tag{2.19}$$

Substituting for x' and y' from Equation 2.17 into 2.18 gives

$$\mathrm{r}' = \mathrm{ar} \tag{2.20}$$

with solution

$$\mathrm{r} = \mathrm{r}_0\mathrm{e}^{\mathrm{at}}, \qquad (\mathrm{r}_0 \text{ a constant}) \tag{2.21}$$

Similarly, substituting for x' and y' from Equation 2.17 into 2.19 gives

$$\theta' = -\mathrm{b} \tag{2.22}$$

with solution

$$\theta = -\mathrm{bt} + \theta_0, \qquad (\theta_0 = \theta(0)) \tag{2.23}$$

Equations 2.21 and 2.23 are the parametric equations in polar coordinates, of the trajectories of the solution of Equation 2.17. From 2.23, we deduce that θ decreases as $t \to \infty$, so the direction of motion is clockwise. Similarly, from 2.21, we deduce that $r \to 0$ if $a < 0$, and $r \to \infty$ if $a > 0$. Therefore, the trajectories are **spirals** which recede from the origin if $a > 0$, and approach the origin if $a < 0$. The critical point $(0, 0)$ is therefore called a **spiral sink** if $a < 0$, and a **spiral source** if $a > 0$.

Example 2.9. The matrix

$$\mathbf{A} = \begin{bmatrix} 1 & 2 \\ -2 & 1 \end{bmatrix}$$

has eigenvalues $\lambda = 1 \pm 2i$ with a positive real part, and so $(0, 0)$ is a spiral source. Figure 2 shows the direction field with typical trajectories receding from the origin as $t \to \infty$.

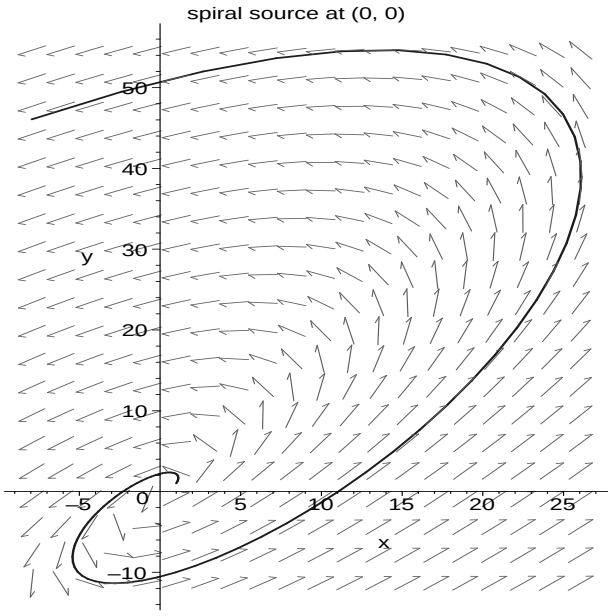

Figure 6: A spiral source at $(0, 0)$ for the system $\mathbf{x}' = \mathbf{A}\mathbf{x}$ of Example 2.9

Pure Imaginary Eigenvalues

Suppose the matrix $\mathbf{A}$ has eigenvalues $\lambda = \pm bi$ Then Equation 2.16 with $a = 0$ becomes

$$\begin{bmatrix} x' \\ y' \end{bmatrix} = \begin{bmatrix} 0 & b \\ -b & 0 \end{bmatrix} \begin{bmatrix} x \\ y \end{bmatrix} \tag{2.24}$$

Then Equations 2.20 and 2.22) become respectively,

$$\mathrm{r}' = 0, \qquad \theta' = -\mathrm{b} \tag{2.25}$$

with solutions

$$\mathrm{r} = \mathrm{c}, \qquad \theta = -\mathrm{bt} + \theta_0 \tag{2.26}$$

where c and θ_0 are constants. The trajectories are circles with centre at the origin, traversed in a clockwase direction if $b > 0$, and couter-clockwise if $b < 0$. A complete cirsuit about the origin is made in the time interval $2\pi/b$, and so all solutions are periodic with period $2\pi/b$. The critical point in this case is called a **center**. In general, when the eigenvalues a pure imaginary, then the trajectories are **ellipses** centered at the origin.

Example 2.10. The matrix

$$\mathbf{A} = \begin{bmatrix} 0 & 2 \\ -2 & 0 \end{bmatrix}$$

has eigenvalues $\lambda = \pm 2i$, and so $(0, 0)$ is a stable centre. Figure (2) shows the direction field with typical elliptical trajectories surrounding $(0, 0)$.

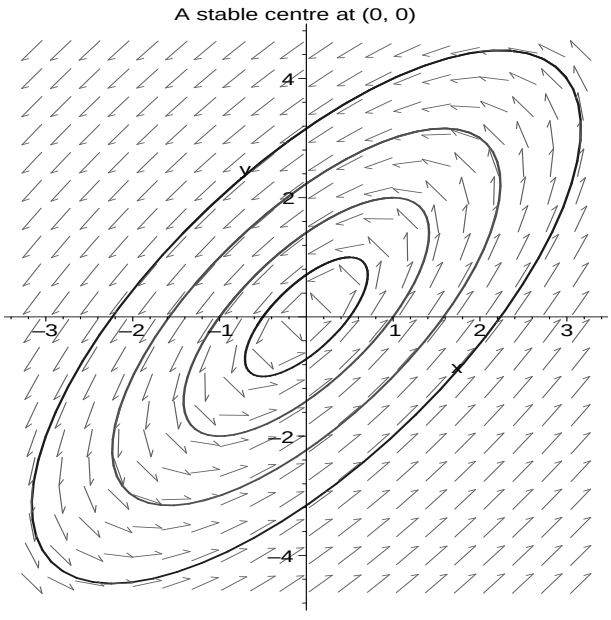

Figure 7: Trajectories of the system in Example 2.10 showing a `stable centre`

Theorem 2.1 (Stability of Linear Systems)**.** Let λ_1, λ_2 be the eigenvalues of the coefficient matrix $\mathbf{A} = \begin{bmatrix} a & b \\ c & d \end{bmatrix}$ of the two-dimensional autonomous linear system

$$\begin{aligned} \frac{dx}{dt} &= ax + by \\ \frac{dy}{dt} &= cx + dy \end{aligned} \tag{2.27}$$

with ad − bx ≠ 0. Then the critical point $(0, 0)$ is:

1. Asymptotically stable if the eigenvalues λ_1 and λ_2 are real and negative, or have negative real parts.

2. Stable but not asymptotically stable if λ_1 and λ_2 are pure imaginary, that is, $\lambda_1, \lambda_2 = \pm bi$.

3. Unstable if either λ_1 or λ_2 are real and positive of have positive real parts.

The Routh-Hurwitz Conditions for Linear Systems

The Routh-Hurwitz conditions give the necessary and sufficient conditions for all roots of the characteristic polynomial to have negative parts, thus implying asymptotic stability.

Theorem 2.2 (Routh-Hurwitz Conditions)**.** Let $\mathbf{A}$ be the coefficient matrix of the linear system in 2.27. Then the critical point (0, 0) is stable if

$$\texttt{trace}(\mathbf{A}) < 0 \quad \text{and} \quad \texttt{det}(\mathbf{A}) > 0 \tag{2.28}$$

Otherwise, it is unstable.

The trace of an n × n matrix $\mathbf{A}$, is the sum of the diagonal entries of $\mathbf{A}$. Thus, trace $(\mathbf{A}) = \mathrm{a}_{11} + \mathrm{a}_{22} + \cdots + \mathrm{a}_{\mathrm{nn}}$.

Stability of Non-Linear Systems

We examine the behaviour of the solutions of the autonomous system

$$\begin{aligned} \frac{\mathrm{dx}}{\mathrm{dt}} &= \mathrm{f(x,\ y)} \\ \frac{\mathrm{dy}}{\mathrm{dt}} &= \mathrm{g(x,\ y)} \end{aligned} \tag{2.29}$$

near an isolated critical point $(x_*,\ y_*)$ where $f(x_*,\ y_*) = g(x_*,\ y_*) = 0$.

The first step in investigating the behaviour of trajectories of the system 2.29 near a critical point $(x_*,\ y_*)$ is by approximating the nonlinear system with an appropriate linear system, whose trajectories are easy to investigate. The crucial question is whether the trajectories of the linearized system are good approximations to those of the nonlinear system.

First, we explain what is meant by a nonlinear system being close to a linear system.

We assume that the functions f and g are continuously differentiable in a neighbourhood of $(x_*,\ y_*)$. Then the Taylor Formula for f and g about the critical point $(x_*,\ y_*)$ gives

$$\begin{aligned} \frac{\mathrm{dx}}{\mathrm{dt}} &= \mathrm{f_x(x_*,\ y_*)(x - x_*) + f_y(x_*,\ y_*)(y - y_*) + F(x - x_*,\ y - y_*)} \\ \frac{\mathrm{dy}}{\mathrm{dt}} &= \mathrm{g_x(x_*,\ y_*)(x - x_*) + g_y(x_*,\ y_*)(y - y_*) + G(x - x_*,\ y - y_*)} \end{aligned} \tag{2.30}$$

Let

$\mathrm{u = x - x_*}$, $\mathrm{v = y - y_*}$, so that $\mathrm{dx/dt = du/dt}$, and $\mathrm{dy/dt = dv/dt}$.

Then, in matrix form, 2.30 becomes

$$\begin{bmatrix} \dot{u} \\ \dot{v} \end{bmatrix} = \begin{bmatrix} \mathrm{f_x(x_*,\ y_*)} & \mathrm{f_y(x_*,\ y_*)} \\ \mathrm{g_x(x_*,\ y_*)} & \mathrm{g_y(x_*,\ y_*)} \end{bmatrix} \begin{bmatrix} u \\ v \end{bmatrix} + \begin{bmatrix} \mathrm{F(u,\ v)} \\ \mathrm{G(u,\ v)} \end{bmatrix} \tag{2.31}$$

The matrix

$$\mathbf{J} = \begin{bmatrix} f_x(x_*, y_*) & f_y(x_*, y_*) \\ g_x(x_*, y_*) & g_y(x_*, y_*) \end{bmatrix} \tag{2.32}$$

is the **Jacobian matrix** of the system in 2.29, evaluated at the critical point (x_*, y_*).

Definition 2.5. The autonomous system 2.29 is called **almost linear** at the point (x_*, y_*) provided that it can be put in the form

$$\begin{aligned} \frac{dx}{dt} &= a(x - x_*) + b(y - y_*) + F(x - x_*, y - y_*) \\ \frac{dy}{dt} &= c(x - x_*) + d(y - y_*) + G(x - x_*, y - y_*) \end{aligned} \tag{2.33}$$

where $a = f_x(x_*, y_*)$, $b = f_y(x_*, y_*)$, $c = g_x(x_*, y_*)$, $d = g_y(x_*, y_*)$,, $F(x - x_*, y - y_*)$ and $G(x - x_*, y - y_*)$

have the property that

$$\lim_{\|(x,y)-(x_*,y_*)\|\to 0} \frac{\|F(x - x_*, y - y_*)\|}{\|(x, y) - (x_*, y_*)\|} =$$

$$\lim_{\|(x,y)-(x_*,y_*)\|\to 0} \frac{\|G(x - x_*, y - y_*)\|}{\|(x, y) - (x_*, y_*)\|} = 0. \tag{2.34}$$

That is, in the neighbourhood of (x_*, y_*), the expressions

$$\|F(x - x_*, y - y_*)\| \quad \text{and} \quad G\|(x - x_*, y - y_*)\|$$

are small in comparison with $\|(x, y) - (x_*, y_*)\|$ which is itself small.

Thus, when (x, y) is near the point (x_*, y_*) the nonlinear system in 2.29 is "close" to the **linearized** system

$$\begin{aligned} \frac{dx}{dt} &= ax + by \\ \frac{dy}{dt} &= cx + dy \end{aligned} \tag{2.35}$$

The system in 2.31 is called the **linearization** of 2.29 about the critical point (x_*, y_*).

Linearisation involves approximating a complicated system of equations with a simpler linear system. Then the behaviour of the nonlinear system can be determined through an analysis of the behaviour of its linearisation. We expect that the nonlinear system in 2.29 behaves at least locally at (x_*, y_*), like its linearisation in 2.35 at (0, 0).

Example 2.11. The system

$$\begin{array}{rcl} \dfrac{dx}{dt} & = & x + x^2 - 3xy \;=\; x(1 + x - 3y) \\ \dfrac{dy}{dt} & = & 3y - y^2 - xy \;=\; y(3 - x - y) \end{array} \tag{2.36}$$

has a critical point $(x_*, y_*) = (2, 1)$. Then a linearization of 2.36 about the critical point $(2, 1)$ can be obtained by evaluating the Jacobian matrix of the system at the equilibrium point $(2, 1)$.

Stability of Almost Linear Systems

The effects of the small nonlinear terms $F(x - x_*, y - y_*)$ and $G(x - x_*, y - y_*)$ in 2.33 is equivalent to the effects of small perturbations in the coefficients of the associated linear system in 2.35. This is stated, without proof in the following Theorem.

Theorem 2.3 (Stability of Almost Linear Systems)**.** Let λ_1 and λ_2 be the eigenvalues of the coefficient matrix **A**, of the linear system in 2.35 of the autonomous system in 2.33. Then

1. If $\lambda_1 = \lambda_2$ are equal real eigenvalues, then the critical point $(0, 0)$ of 2.33 is either a **node** of a **spiral point**, and is asymptotically if $\lambda_1 = \lambda_2 < 0$, unstable if $\lambda_1 = \lambda_2 > 0$.

2. If λ_1 and λ_2 are pure imaginary, then $(0, 0)$ is either a **centre** or a **spiral point**; It may be either asymptotically stable, stable or unstable.

3. Otherwise (that is, unless λ_1 and λ_2 are either real and equal, or pure imaginary), the critical point $(0, 0)$ of the almost linear system in 2.33 is of the same type and stability as the critical point of the associated linear system in 2.27.

The Routh-Hurwitz Conditions for Almost Linear Systems

The stability of a critical point (x_*, y_*) of the almost linear system

$$\begin{aligned} \frac{\mathrm{dx}}{\mathrm{dt}} &= \mathrm{f(x,\, y)} \\ \frac{\mathrm{dy}}{\mathrm{dt}} &= \mathrm{g(x,\, y)} \end{aligned} \tag{2.37}$$

can be determined from the following Theorem.

Theorem 2.4 (Routh-Hurwitz Conditions)**.** Let

$$\mathbf{J} = \begin{bmatrix} \mathrm{f_x}(\mathrm{x_*}, \mathrm{y_*}) & \mathrm{f_y}(\mathrm{x_*}, \mathrm{y_*}) \\ \mathrm{g_x}(\mathrm{x_*}, \mathrm{y_*}) & \mathrm{g_y}(\mathrm{x_*}, \mathrm{y_*}) \end{bmatrix}$$

be the Jacobian matrix of the almost linear system given in 2.37 evaluated at the critical point (x_*, y_*). Then the critical point (x_*, y_*) is stable if

$$\mathtt{trace}(\mathbf{J}) < 0 \quad \text{and} \quad \mathtt{det}(\mathbf{J}) > 0$$

Otherwise, it is unstable.

Qualitative Analysis: Nullclines

For most nonlinear autonomous systems, it is impossible to obtain analytical solutions. We can use numerical techniques to obtain approximate

solutions; however, qualitative analysis may provide answers to some questions much faster than numerical techniques, for example, questions related to the long term behavior of solutions.

Definition 2.6. Nullclines Given an n-dimensional system of differential equations

$$\frac{\mathrm{d}\mathbf{x}}{\mathrm{dt}} = \mathbf{f}(\mathbf{x}),$$

the x_i **nullcline** is the set of points where $\frac{\mathrm{dx_i}}{\mathrm{dt}} = \mathrm{f_i}(\mathbf{x}) = 0$.

For example, in the following system

$$\begin{aligned} \frac{\mathrm{dx}}{\mathrm{dt}} &= \mathrm{f}(\mathrm{x},\mathrm{y}) \\ \frac{\mathrm{dy}}{\mathrm{dt}} &= \mathrm{g}(\mathrm{x},\mathrm{y}) \end{aligned}$$

the **x-nullcline** consisits of the set of points satisfying $\frac{\mathrm{dx}}{\mathrm{dt}} = \mathrm{f}(\mathrm{x},\mathrm{y}) = 0$, so called because at each point on these clines, $\frac{\mathrm{dx}}{\mathrm{dt}} = 0$. Similarly, the **y-nullcline** consisits of the set of points satisfying $\frac{\mathrm{dy}}{\mathrm{dt}} = \mathrm{g}(\mathrm{x},\mathrm{y}) = 0$.

Nullclines plays a central role in the qualitative approach. The first step in performing a qualitative analysis, (or a **phase-plane analysis**) in the case of a two-dimensional system) is to obtain the equilibrium points, which are the intersenction of the nullclines.

Example 2.12. The following system

$$\begin{aligned} \frac{\mathrm{dx}}{\mathrm{dt}} &= \mathrm{ax} - \mathrm{ex}^2 - \mathrm{bxy} = \mathrm{x}(\mathrm{a} - \mathrm{ex} - \mathrm{by}) \\ \frac{\mathrm{dy}}{\mathrm{dt}} &= -\mathrm{cy} + \mathrm{dxy} = \mathrm{y}(-\mathrm{c} + \mathrm{dx}) \end{aligned} \tag{2.38}$$

has equilibrium points (0, 0), $\left(\frac{\mathrm{a}}{\mathrm{e}}, 0\right)$ and $\left(\frac{\mathrm{c}}{\mathrm{d}}, \frac{\mathrm{ad}-\mathrm{ec}}{\mathrm{bd}}\right)$. The location and type of equilibrium points depends on the sign of $(\mathrm{ad}-\mathrm{ec})/\mathrm{bd}$. We consider two cases, namely,

1. **Case 1:** $(\mathrm{ad} - \mathrm{ec})/\mathrm{bd} < 0 \Rightarrow \dfrac{\mathrm{a}}{\mathrm{e}} < \dfrac{\mathrm{c}}{\mathrm{d}}$: the critical is not in the first quadrant. The only equilibrium points that a bilogically meaningful are $(0, 0)$ and $(\frac{a}{e}, 0)$. The null clines are shown in Fugure 1. These nullclines divide the first quadrant into three regions namely, I, II and III. From the direction of the arrows we notice that solutions starting in region I move into region II, and solutions starting in region II move into region III, or end up at the equilibrium point $(\frac{a}{e}, 0)$. We note also, that region III is invariant, and all solution curves starting from there are directed towards the equilibrium point $(\frac{a}{e}, 0)$.

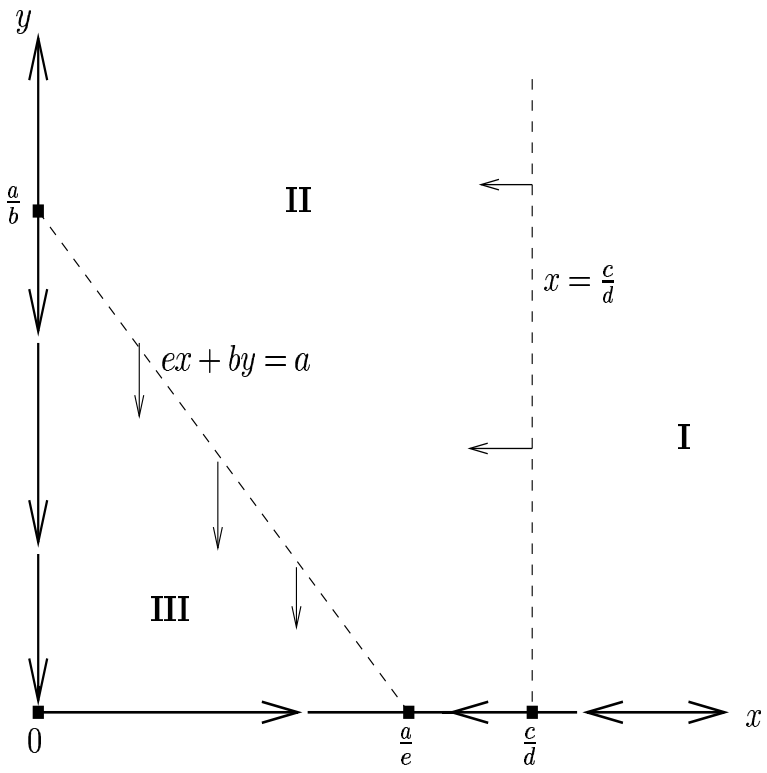

Figure 8: The nullclines for Case 1 of Equation 2.38

2. **Case 2:** $(\mathrm{ad} - \mathrm{ec})/\mathrm{bd} > 0 \Rightarrow \dfrac{\mathrm{a}}{\mathrm{e}} > \dfrac{\mathrm{c}}{\mathrm{d}}$: the critical point is in the first quadrant; all the three equilibrium points are of interest. The nullclines are shown in Figure (2). We observe that solution curves move from region I to region II to region III to region IV, and back to region I. Thus, the solution curves spirals around the the equilibrium

point $(\frac{\mathrm{c}}{\mathrm{d}}, \frac{\mathrm{ad}-\mathrm{ec}}{\mathrm{bd}})$. It can be shown that this equilibrium point is **asymptotically stable**, and that all solution curves tend to this equilibrium point. Thus, the predator and prey populations coexist.

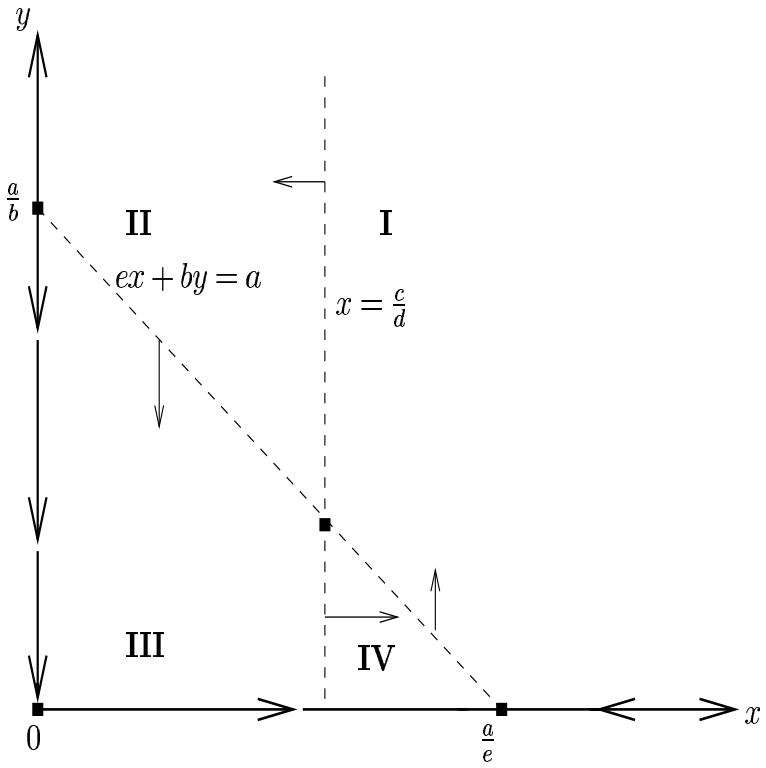

Figure 9: The nullclines for Case 2 of Equation 2.38

The Routh-Hurwitz Criteria

The Routh-Hurwitz criteria are used to determine asymptotic stability of an equilibrium for nonlinear sys tem of differential equation. The Routh-Hurwitz criteria give the necessary and sufficient conditions for all roots of the characteristic polynomial to have negative parts, thus implying asymptotic stability.

Theorem 2.5. Routh-Hurwitz Conditions Assume the polynomial

$$\mathrm{p}(\lambda) = \lambda^{\mathrm{n}} + \mathrm{a}_1\lambda^{\mathrm{n}-1} + \cdots + \mathrm{a}_{\mathrm{n}-1}\lambda + \mathrm{a}_{\mathrm{n}}$$

where the coefficients a_i are real constants, $i = 1, \ldots, n$, define the n Hurwitz matrices using t he coefficients a_i of the characteristic polynomial:

$$H_1 = (a_1), \quad H_2 = \begin{pmatrix} a_1 & 1 \\ a_3 & a_2 \end{pmatrix}, \quad H_3 = \begin{pmatrix} a_1 & 1 & 0 \\ a_3 & a_2 & a_1 \\ a_5 & a_4 & a_3 \end{pmatrix},$$

and

$$H_n = \begin{pmatrix} a_1 & 1 & 0 & 0 & \dots & o \\ a_3 & a_2 & a_1 & 1 & \dots & 0 \\ a_5 & a_4 & a_3 & a_2 & \dots & 0 \\ \vdots & \vdots & \vdots & \vdots & \dots & \vdots \\ 0 & 0 & 0 & 0 & \dots & a_n \end{pmatrix}$$

where $a_i = 0$ if $j > n$. All of the roots of the polynomial $P(\lambda)$ are negative or have negative real part if and only if the determinants of all Hurwitz matrices are positive:

$$detH_j > 0, \quad j = 1, 2, \dots, n.$$

When $n = 2$, the Routh-Hurwitz criteria simplify to $detH_1 = a_1 > 0$ and

$$detH_2 = det \begin{pmatrix} a_1 & 1 \\ 0 & a_2 \end{pmatrix} = a_1 a_1 > 0$$

or $a_1 > 0$ or $a_2 > 0$. The Routh-Hurwitz criteria are summarized below for polynomials of degree $n = 2, 3, 4$.

$$\begin{bmatrix} n = 2 : a_1 > 0 \, and \, a_2 > 0. \\ n = 3 : a_1 > 0, a_3 > 0, \text{ and } a_1 a_2 > a_3. \\ n = 4 : a_1 > 0, a_3 > 0, a_4 > 0, \text{ and } a_1 a_2 a_3 > a_3^2 + a_1^2 a_4 \end{bmatrix}$$

Corollary 2.1. Suppose the coefficients of the characteristic polynomial are real. If all of the roots of the characteristic polynomial

$$P(\lambda) = \lambda^2 a_1 \lambda^{n-1} + a_2 \lambda^{n-2} + \cdots + a_n$$

are negative or have negative real part, then the coefficients $a_i > 0$ for $i = 1, 2, \dots, n$.

Example 2.13. Consider the linear differential equation

$$\frac{\mathrm{d}^3\mathrm{x}}{\mathrm{dt}^3} + 6\frac{\mathrm{d}^2\mathrm{x}}{\mathrm{dt}^2} + \frac{\mathrm{dx}}{\mathrm{dt}} + \mathrm{ax} = 0.$$

The characteristic polynomial becomes

$$\mathrm{P}(\lambda) = \lambda^3 + 6\lambda^2 + \lambda + \mathrm{a}.$$

For the roots to have negative real part and the solution to approach zero, Routh-Hurwitz criteria indicates that the coefficients must satisfy $\mathrm{a}_1 > 0,\ \mathrm{a}_3 > 0, \mathrm{a}_1\mathrm{a}_2 > \mathrm{a}_3$. Nonetheless, $\mathrm{a}_1 = 6, \mathrm{a}_2 = 1,$ and $\mathrm{a}_3 = \mathrm{a},$ thus a must satisfy $6 > \mathrm{a} > 0$

Gershgorin's Theorem

The Gershgorin's theorem provides sufficient conditions for the eigenvalues to lie in the left halve of t he complex plane.

Theorem 2.6. Gershgorin's Theorem Let A be an $n \times n$ matrix. Let D_i be the disk in the complex plane with centre at a_{ii} and radius $\mathrm{r_i} = \sum_{\mathrm{j=1,j\neq i}}^{\mathrm{n}} |\mathrm{a_{ii}}|$. Then all eigenvalues of the matrix A lie in the union of th e disks,

$$\mathrm{D_i}, \mathrm{i} = 1, 2, \ldots, \mathrm{n}, \cup_{\mathrm{i=1}}^{\mathrm{n}} \mathrm{D_i}.$$

In particular, if λ is an eigenvalue of A, then for some $i = 1, 2, \ldots, n$,

$$|\lambda - \mathrm{a_{ii}}| \leq \mathrm{r_i}$$

Proof

Let λ be any eigenvalue of A and $V = (v_1, \ldots, v_n)^T$ an eigenvector corresponding to this eigenvalue. Then $AV = \lambda V$ which implies that $\lambda v_i = \sum_{j=1}^{n} a_{ij} v_j$ or

$$\lambda v_i - a_{ii} v_i = \sum_{j=1, j\neq i} n a_{ij} v_i \quad i = 1, \ldots, n.$$

Let v_k denotes the elements of of the eigenvector V with the greatest magnitude $|v_k| \geq |v_j|, j \neq k$. Then $|\frac{v_j}{v_k}| \leq 1$ for all $j = 1, \ldots,$ and

$$|\lambda - a_{kk}| \leq \sum_{j=1, j\neq i}^{n} |a_{kj}| \left|\frac{v_j}{v_k}\right| \leq \sum_{j=1, j\neq i}^{n} |a_{kj}|.$$

Hence, λ lies in the disk D_k. The conclusion of the theorem follows.

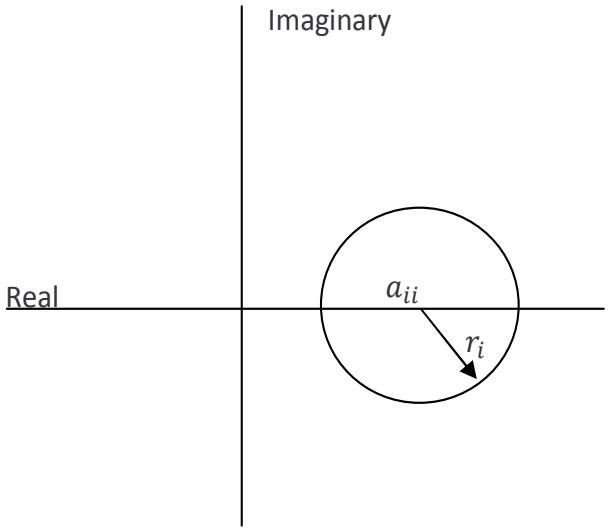

Figure 10: Gershgorin's disk in a complex plane

Gershgorin's theorem applies to real and complex matrices A. When the entries of A are real, it follows from Gershgorin's theorem that the disk lie in the left half of the complex if

$$r_i + a_{ii} < 0 \quad \text{i.e.} \quad \mathrm{a_{ii}} < -\mathrm{r_i}$$

for $i = 1, 2, \ldots, n$. The strict inequality guarantees that the Gershgorin disk lies entirely in the left half of the complex plane.

Corollary 2.2. Let A be an $n \times n$ matrix with real entries. If the diagonal elements of A satisfy

$$\boxed{a_{ii} < -r_i, \quad where \quad r_i = \sum_{j=1, j\neq i}^{n} |a_{ij}|}$$

for $i = 1, 2, \ldots, n$, then eigenvalues of A are negative or have negative real part.

Example 2.14. Apply Gershgorin's theorem to determine sufficient conditions on the parameters a, b and c such that the eigenvalues of A are negative or have negative real part.

(a)

$$\mathrm{A} = \begin{pmatrix} a & -1 & 0 \\ -1 & b & 1 \\ 0 & -2 & c \end{pmatrix}$$

(b)

$$\mathrm{A} = \begin{pmatrix} a & -b \\ c & -2 \end{pmatrix}$$

Solution

(a) $a_{11} = a, a_{22} = b$ and $a_{33} = c$. Now, $r_1 = 1, r_2 = 2$ and $r_3 = 2$. Therefore, the values of the parameters a, b and c for which the eigenvalues of A are negative or have negative real part are: $a < -1$, $b < -2$ and $c < -2$.

(b) Similarly, $a_{11} = a$ and $a_{22} = -2$ whiles $r_1 = b$ and $r_2 = c$. Hence, for A to have negative or negative real part, $a < -|b|$ and $-2 < -|c|$ or $|c| < 2$.

The corollary illustrates sufficient condition but not necessary.

Example 2.15. Assume the matrix

$$K = \begin{pmatrix} -3 & 1 & 1 \\ 1 & -3 & -1 \\ 2 & 1 & -3 \end{pmatrix}.$$

For this matrix, $r_1 = 2 = r_2$ and $r_3 = 3$ and so $a_{11} < -2$, $a_{22} < -2$ but $a_{33} = -3$. Nevertheless, the eigenvalues of K : $\lambda_{1,2} = -2, -\frac{7}{2} \pm \frac{\sqrt{5}}{2}$

Introduction to Bifurcation Theory

The qualitative structure of the flow on the vector field under investigation can change as parameters are varied: in particular, FPs can be created or destroyed, or their stability can change. These qualitative changes in the dynamics are called bifurcations, and the parameter values at which they occur are called bifurcation points. The types of bifurcation under discussion include: saddle node, pitchfork, transcritical, and Hopf bifurcations. The first three types of bifurcations occur in scalar and in systems of differential equations. The fourth, Hopf bifurcation, involves a change to periodic solution. Scalar autonomous differential equation cannot have periodic solution.

First-Order Equations

Firstly, we consider the first three bifurcations in the case of differential equations. Consider the scalar differential equation

$$\frac{dx}{dt} = f(x, r).$$

The value r is the bifurcation parameter and $\bar{x}$ is an equilibrium solution which depends on r. There exist three types of bifurcation. Namely,

(I) saddle-node

(II) pitchfork

(III) transcritical

At the bifurcation value $\bar{r}$, it is the case that the equilibrium changes stability. In particular for $r = \bar{r}$ and $x = \bar{x}(\bar{r})$,

$$\left.\frac{\mathrm{df(x,r)}}{\mathrm{dx}}\right|_{(\mathrm{x,r})=(\bar{\mathrm{x}}(\bar{\mathrm{r}}),\bar{\mathrm{r}})} = 0. \tag{2.39}$$

In a saddle-node bifurcation, as the bifurcation parameter passes through the bifurcation point, two equilibria disappear so that there are no equilibria afterward. One of the two equilibria is stable and the other is unstable before they disappear.

In a pitchfork bifurcation, there are two stable equilibria separated by an unstable equilibrium. A system where there two different stable equilibria is said to have a property of **bistability**. When bifurcation point is passed, there is only one stable equilibrium. This bifurcation is referred to as **supercritical pitchfork** bifurcation. On the other hand, if the stability of supercritical pitchfork bifurcation is reversed, subcritical pitchfork bifurcation is obtained where there are two unstable equilibria separated by stable equilibrium, until the bifurcation point is passed.

In transcritical bifurcation, there two equilibria, one stable and the other unstable. When the bifurcation point is passed, there is an exchange of stability; the unstable equilibrium become stable and the stable equilibrium becomes unstable. As the initially negative parameter r increases the two fixed points at $(0, r)$ coalesce and form a half-stable fixed points when $r = 0$. When further increasing r to positive values the two fixed points split again, but now they have switched stability.

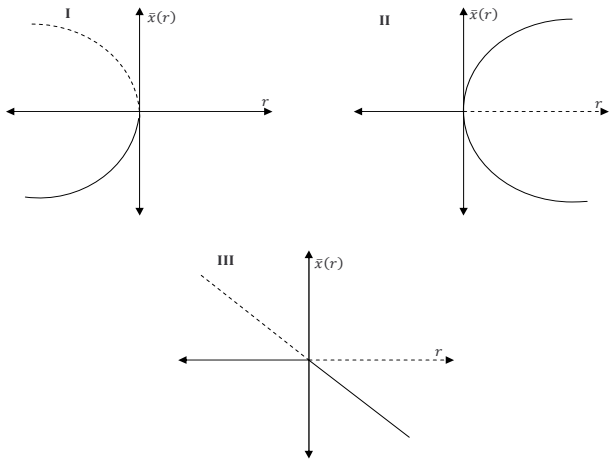

Figure 11: Stability in the $\tau - \delta$ plane.

Figure 2 represents the bifurcation diagram corresponding to the three bifurcation types I, II and III. Dashed curves denote unstable equilibria and solid curves denotes stable equilibria.

The prototypical example of a saddle-node bifurcation is given by

$$\frac{dx}{dt} = r \pm x^2.$$

For demonstration purposes, let $\frac{dx}{dt} = r + x^2$.

1. As $r < 0$, there are two fixed points, stable at $x = r$ and unstable at $x = -r$.

2. As r increases the two fixed points move towards each other and coalesce into a half-stable fixed point at $x = 0$.

3. This fixed point is destroyed as r increase to become positive.

Pitchfork bifurcation is related to symmetries in the system. For example in systems having a spatial symmetry between left and right fixed points tend to appear and disappear in symmetrical pairs (think for instance of a buckling beam). The normal form is

$$\frac{\mathrm{dx}}{\mathrm{dt}} = \mathrm{rx} \pm \mathrm{x}^3 \tag{2.40}$$

The minus sign gives supercritical pitchfork bifurcation. The name implies that there can exist a fixed point above bifurcation.

Consider, the example

$$\frac{\mathrm{dx}}{\mathrm{dt}} = \mathrm{rx} + \mathrm{x}^3 \tag{2.41}$$

From the bifurcation Equations, we find that there are three branches of equilibria: $\mathrm{x}_0 = 0$, $\mathrm{x}_0 = \sqrt{-\mathrm{r}}$, and $\mathrm{x}_0 = -\sqrt{-\mathrm{r}}$. The non-zero fixed points ($\mathrm{x}_0 = \pm\sqrt{-\mathrm{r}}$) are unstable.

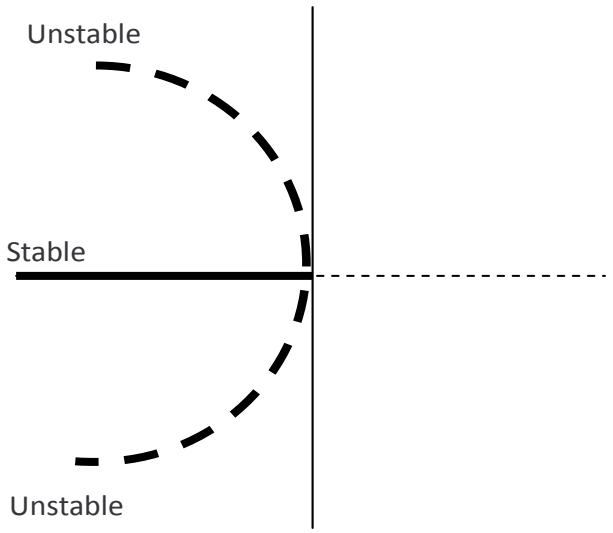

Figure 12: Pitchfork bifurcation.

Consider the transcritical bifurcation

$$\frac{\mathrm{dx}}{\mathrm{dx}} = \mathrm{rx} - \mathrm{x}^2. \tag{2.42}$$

The bifurcation equation becomes $rx - x^2 = 0$. This gives two branches of equilibria $x_0 = 0$; and $x_0 = r$. For the branch $x_0 = 0$; we have $f_x(x, r) = r$ and thus the stability changes from stable to unstable as r increases cross 0; and $r_0 = 0$ is the bifurcation point. For the second branch, $x_0 = r$; we have $f_x(x, r) = r$. Therefore, this branches changes stability in the opposite direction to the first branch, and the bifurcation point is also $r_0 = 0$. The transcritical bifurcation can be described as two branches of equilibria intersect and exchange stability type at the bifurcation point.

Hopf Bifurcation Theorem

One new bifurcation that can occur in a two-dimensional system is the so-called Andronov-Hopf bifurcation, mostly just referred to as Hopf bifurcation, van Voorn 2006. This Hopf bifurcation theorem states sufficient conditions for the existence of periodic solution. As one parameter is varied, the dynamics of the system change from a stable spiral to center to

an unstable spiral. The eigenvalues of the linearized system change from having negative real part to zero real part to positive real part. Under certain conditions, there exist periodic solutions.

Consider a system of autonomous differential Equations given by 2.43

$$\frac{\mathrm{dx}}{\mathrm{dt}} = \mathrm{f(x, y, r)} \quad \text{and} \quad \frac{\mathrm{dy}}{\mathrm{dt}} = \mathrm{g(x, y, r)} \tag{2.43}$$

where the functions f and g depend on the bifurcation parameter r. Suppose that there is an existence of equilibrium of the system 2.43. Suppose again that this equilibrium occurs at $(x(r), y(r))$ and the Jacobian matrix evaluated at the equilibrium has eigenvalues $\Re(r) \pm \Im(r)$. Again assume a change in stability occurs at $r = r^*$, where $\Re(r^*) = 0$. If $\Re(r) < 0$ for values of r closer to r^* but for $r < r^*$ and if $\Re(r) > 0$ for all values of r closer to r^* but for $r > r^*$ holding that $\Im(r^*) \neq 0$, then the equilibrium changes from stable spiral to an unstable spiral as r passes through r^*. The Hopf Bifurcation Theorem states that there exists a periodic orbit near $r = r^*$ for any neighbourhood of the equilibrium in $\mathbf{R}^2$. The value r is the *bifurcation parameter* and r^* is the *bifurcation value*. The bifurcation theorem is valid only when the bifurcation parameter has a value close to the bifurcation value.

Example 2.16. Consider the linear system

$$\begin{aligned} \frac{\mathrm{dx}}{\mathrm{dt}} &= \mathrm{rx} - \mathrm{y} \\ \frac{\mathrm{dy}}{\mathrm{dt}} &= \mathrm{x} + \mathrm{ry} \end{aligned} \tag{2.44}$$

The origin is an equilibrium. The trace and determinant of the Jacobiam matrix evaluated at the origin are $2r$ and $r^2 + 1$ respectively. Since the discriminant of the Jacobian matrix is negative,

$$[Tr(J)]^2 - 4[det] = (2r)^2 - 4(r^2 + 1) = -4.$$

The eigenvalues are $r = \pm i$. If $r < 0$ the origin is a stable spiral. If $r = 0$ the origin is a center, and if $r > 0$, it is an unstable spiral. The bifurcation value is $r = r^* = 0$. In Figure 2, the stability diagram is graphed as a function of trace τ and determinant δ. The bifurcation in this example occurred because r crossed the δ-axis where $\delta > 0$. A Hopf bifurcation occurs. As the bifurcation parameter r increases through the bifurcation value $r^* = 0$, the equilibrium $(0, 0)$ changes from stable spiral to neutral center to an unstable spiral. There are infinitely many periodic solutions at the bifurcation value $r^* = 0$. Solutions to $dx/dt = -y$ and $dy/dt = x$ are of the form $x^2(t) + y^2(t) = C$, where C is a constant that depends on the initial conditions.

The linear example illustrate the change instability as the bifurcation parameter r is varied. In general, at a Hopf bifurcation, as r passes through the bifurcation value r^*, there three possible dynamics that may occur.

(i) At the bifurcation value r^* infinitely many neutrally stable concentric closed orbits encircle the equilibrium.

(ii) A stable spiral changes to a stable limit cycle for values of the parameter close to r^* (supercritical bifurcation).

(iii) A stable spiral and unstable limit cycle change to an unstable spiral for values for values of the parameter close to r^* (subcritical bifurcation).

Example 2.16 illustrate a change of stability. Figure 2 illustrate a supercritical and subcritical bifurcation in $x - y - r$ space. Stable solutions are identified by solid curves and unstable unstable solutions by dashed curves.

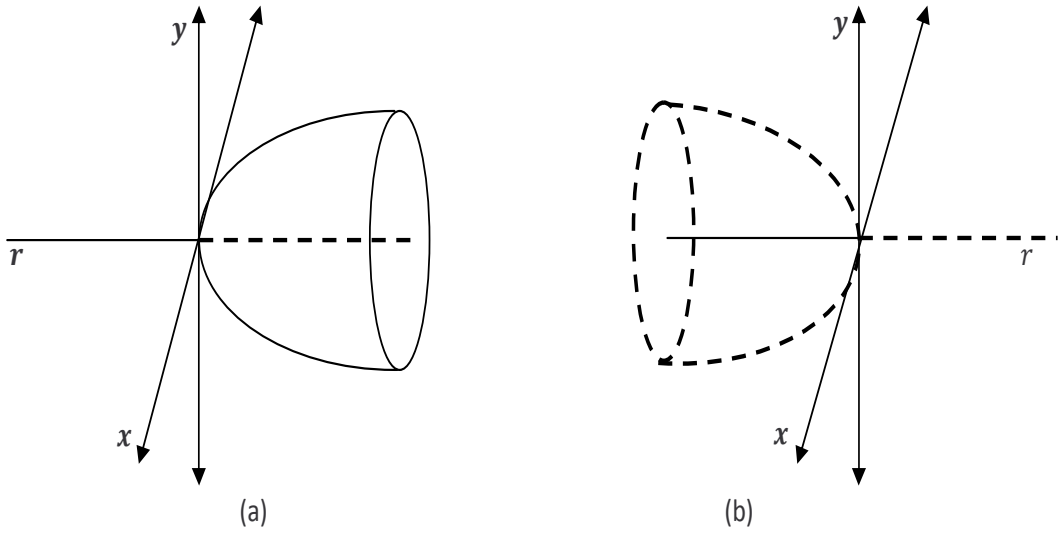

Figure 13: Types of Hopf Bifurcation.

In Figure 2, (a) supercritical and (b) subcritical bifurcation in $x-y-r$ space. Solid curves circling or on the r axis are stable. Dashed curves are on unstable.

First the system is transformed so that the equilibrium is at the origin and the parameter r at $r^* = 0$ gives purely imaginary eigenvalues. System 2.43 can be written as :

$$\begin{aligned} \frac{dx}{dt} &= a_{11}(r)x + a_{12}(r)y + f_1(x, y, r) \\ \frac{dy}{dt} &= a_{21}(r)x + a_{22}(r)y + g_1(x, y, r) \end{aligned} \tag{2.45}$$

The linearization of the system 2.45 about the origin is given by $dZ/dt = J(r)Z$, where $Z = (x, y)^T$ and

$$\mathrm{J(r)} = \begin{pmatrix} a_{11}(r) & a_{12}(r) \\ a_{21}(r) & a_{22}(r) \end{pmatrix} \tag{2.46}$$

is the Jacobian matrix evaluated at the origin.

Theorem 2.7. Hopf Bifurcation Theorem Let f_1 and g_1 in the system 2.45 have continuous third-order derivatives in x and y. Assume that the origin $(0, 0)$ is an equilibrium of 2.45 and that the Jacobian matrix $J(r)$,

defined in 2.46, is valid for all sufficiently $|r|$. In addition, assume that the eigenvalues of the matrix $J(r)$ are $\Re(r) \pm \Im(r)$ with $\Re(0) = 0$ and $\Im(0) \neq 0$ such that the eigenvalues cross the imaginary axis with nonzero speed (transversal),

$$\left.\frac{d\Re}{dr}\right|_{r=0} \neq 0.$$

Then, in any open set U containing the origin in $\mathbf{R}^2$ and for any $r_0 > 0$, there exists a value $\bar{r}$, $|\bar{r}| < r_0$ such that the system of differential Equations 2.45 has a periodic solution for $r = \bar{r}$ in U (with approximate period $T = 2\pi/\Im(0)$).

Example 2.17. Consider the system in Example 2.16 with bifurcation parameter r. We want to show that the conditions of Hopf Bifurcation Theorem holds.

$$\begin{aligned} \frac{\mathrm{dx}}{\mathrm{dt}} &= \mathrm{rx} - \mathrm{y} \\ \frac{\mathrm{dy}}{\mathrm{dt}} &= \mathrm{x} + \mathrm{ry} \end{aligned} \tag{2.47}$$

In this instance $f_1 = 0 = g_1$. The Jacobian matrix is

$$\mathrm{J(r)} = \begin{pmatrix} r & -1 \\ 1 & r \end{pmatrix}$$

with eigenvalues equal to $r \pm 1$. Since $\Re(0) = 0$, $\Im(0) \neq 0$ and $d\Re/dr = 1 \neq 0$. The conditions of Hopf Bifurcation Theorem hold. In fact there exists a periodic solution for $r = 0$ in every neighbourhood of the origin.

Example 2.18. Consider another example,

$$\begin{aligned} \frac{\mathrm{dx_1}}{\mathrm{dt}} &= \mathrm{rx_1} + \mathrm{x_2} - \mathrm{x_1 x_1^2} + \mathrm{x_2^2} \\ \frac{\mathrm{dx_2}}{\mathrm{dt}} &= -\mathrm{x_1} + \mathrm{rx_2} - \mathrm{x_2 x_1^2} + \mathrm{x_2^2} \end{aligned} \tag{2.48}$$

The system has one equilibrium point $(0, 0)$. the linearized system is

$$\begin{pmatrix} \dot{x_1} \\ \dot{x_2} \end{pmatrix} = \begin{pmatrix} r & 1 \\ -1 & r \end{pmatrix} \begin{pmatrix} x_1 \\ x_2 \end{pmatrix}.$$

The characteristic equation is

$$\lambda^2 - 2\mathrm{r}\lambda + \mathrm{r}^2 + 1 = 0.$$

The eigenvalues are

$$\lambda_{1,2} = \frac{2\mathrm{r} \pm \sqrt{4\mathrm{r}^2 - 4(\mathrm{r}^2 + 1)}}{2} = \mathrm{r} \pm \mathrm{i}.$$

(i) If $r < 0$, the origin is a stable spiral.

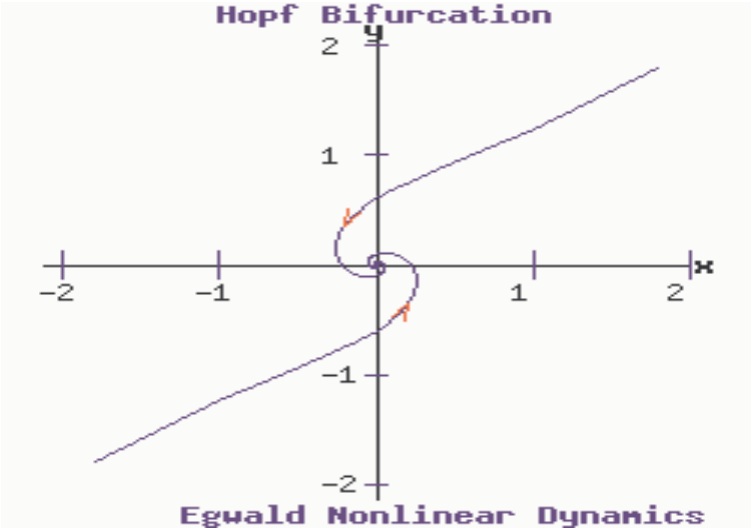

Figure 14: Catastrophic behaviour: $r = -1 < 0$.

(ii) If $r = 0$ then the origin is a center. It is not asymptotically stable.

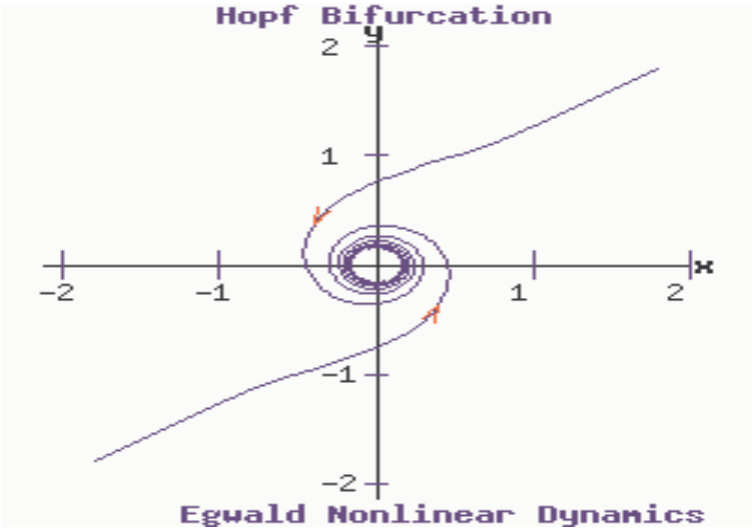

Figure 15: Catastrophic behaviour: $r = 0$.

(iii) If $r > 0$, then the origin is an unstable spiral which is surrounded by stable limit cycle. This case is an example of Hopf bifurcation because it generate a limit cycle.

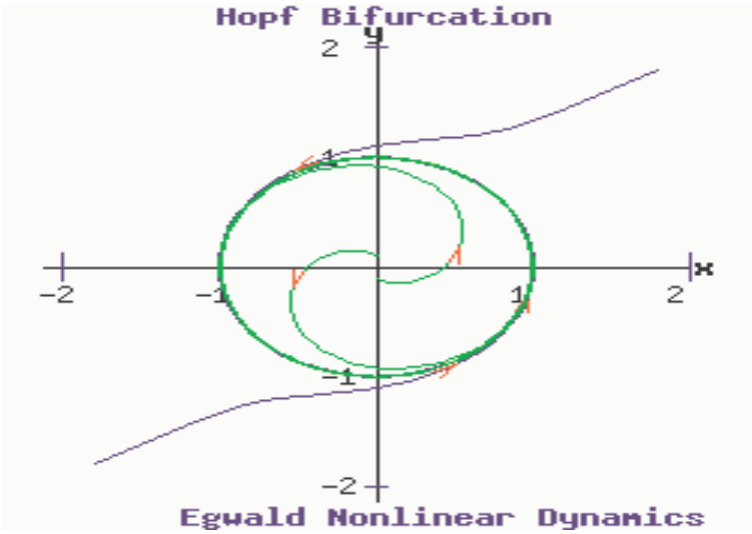

Figure 16: Catastrophic behaviour: $r > 0$.

CHAPTER THREE

BASIC EPIDEMIC MODELS

Introduction

Chapter three deals with basic Epidemic models. It talks about the use of the basic of the basic reproduction number. Finally, this chapter looks at the effect of vaccination on some of the models.

SIR Epidemic Model Without Vital Dynamics

This model was proposed by Kermack and McKendrick in 1927. This model can be used for diseases that persist in a population for short period of time. Examples of such diseases are measles, mumps, and chicken pox. The disease only persists for a short period of time (usually within a year), the vital dynamics are not taken into account.

The compartmental model for the SIR model is demonstrated in figure 3.

Figure 17: The basic SIR model

The assumptions for this model are the same as the assumptions for the SIR, but in addition we have the following:

- Individuals recover from the disease at a rate proportional to the

number of infective, with constant of variation γ. This constant is called **the recovery removal rate**. $\mathbf{1}/\gamma$ is the average period of infectivity.

- The disease confers permanent immunity on every infected victim.

Let

- S(t)/N, be the proportion of susceptible in the population.
- I(t)/N, be the proportion of susceptible in the population.
- R(t)/N, be the proportion of susceptible in the population.

The basic SIR model for frequency-dependent transmission is given by;

$$\begin{aligned}\frac{\mathrm{dS}}{\mathrm{dt}} &= \frac{-\beta}{\mathrm{N}}\mathrm{SI}\\ \frac{\mathrm{dI}}{\mathrm{dt}} &= \frac{\beta}{\mathrm{N}}\mathrm{SI}-\gamma\mathrm{I}=\mathrm{I}\left(\frac{\beta}{\mathrm{N}}\mathrm{S}-\gamma\right)\\ \frac{\mathrm{dR}}{\mathrm{dt}} &= \gamma\mathrm{I}\end{aligned}$$

Where $\mathrm{S}(0)>0, \quad \mathrm{I}(0)>0, \quad \mathrm{R}(0)\geq 0$, and so $\mathrm{S}(0)+\mathrm{I}(0)+\mathrm{R}(0)=\mathrm{N}$. Thus $\mathrm{S(t)}+\mathrm{I(t)}+\mathrm{R(t)}=\mathrm{N}$. Since $R(t)$ can be obtained from $S(t)$ and $I(t)$, It is sufficient to consider only the variables S and I. Note that Equation 3.1 can now be written as Equation 3.1.

$$\begin{aligned}\frac{\mathrm{dS}}{\mathrm{dt}} &= \frac{-\beta\mathrm{SI}}{\mathrm{N}}\\ \frac{\mathrm{dI}}{\mathrm{dt}} &= \frac{\beta\mathrm{SI}}{\mathrm{N}}-\gamma\mathrm{I}.\end{aligned} \tag{3.1}$$

Dividing through the above Equation 3.1 by N, we obtain Equation 3.2.

$$\begin{aligned}\frac{\mathrm{dS}}{\mathrm{dt}} &= -\beta\mathrm{SI}\\ \frac{\mathrm{di}}{\mathrm{dt}} &= \beta\mathrm{SI}-\gamma\mathrm{I}\end{aligned} \tag{3.2}$$

It is clear that when $\mathrm{s}<\frac{\gamma}{\beta}$ and $\frac{\mathrm{di}}{\mathrm{dt}}<0$, i(t) decreases and the disease dies out. On the other hand, when $\mathrm{s}>\frac{\gamma}{\beta}$ then $\frac{\mathrm{di}}{\mathrm{dt}}>0$, i(t) increases resulting in an epidemic.

From the Equation 3.2, dividing $\frac{\mathrm{di}}{\mathrm{dt}}$ by $\frac{\mathrm{ds}}{\mathrm{dt}}$ gives

$$\frac{\mathrm{di}}{\mathrm{ds}} = -1 + \frac{\gamma}{\beta \mathrm{s}} \tag{3.3}$$

Let $\boldsymbol{\sigma}$ denote $\frac{\boldsymbol{\gamma}}{\boldsymbol{\beta}}$ then the Equation above can be integrated to obtain

$$\mathrm{i(t)} + \mathrm{s(t)} - \sigma \ln \mathrm{s(t)} = \mathrm{i}_0 + \mathrm{s}_0 - \sigma \ln \mathrm{s}_0$$

Therefore maximum value of i occurs when $s = \frac{\gamma}{\beta}$. Therefore

$$\mathrm{i}_{\max} = \mathrm{i}_0 + \mathrm{s}_0 - \frac{\gamma}{\beta} \ln \mathrm{s}_0 - \frac{\gamma}{\beta} + \frac{\gamma}{\beta} \ln \frac{\gamma}{\beta}.$$

Now, $\mathrm{s} < \frac{\gamma}{\beta} \implies \frac{\beta}{\gamma}\mathrm{s} < 1$. The quantity $\frac{\beta}{\gamma}\mathrm{s}$, is therefore, an important **epidemic threshold** for the SIR model. It is called the **replacement number**, and is usually denoted by $\mathrm{R} = \frac{\beta}{\gamma}s$. It determines when an infection dies out, or when it becomes an epidemic.

The **basic reproduction number** $\mathcal{R}_0$ is the threshold quantity for many epidemiological models. It is defined as the average number of secondary infections produced when one infected individual is introduced into a host population where everyone is susceptible.

When $\mathcal{R}_0 <$ then the infection will die out. On the other hand if $\mathcal{R}_0 > 1$, then there is some possibility that an epidemic will occur. Thus, the basic reproduction number $\mathcal{R}_0$ is often as the threshold quantity that determines whether or not an infectious disease will spread through a population. The basic reproduction number for the SIR model in Equation 3.1 is given by

$$\mathcal{R}_0 = \frac{\beta}{\gamma}.$$

The $S-$ and $-I$ nullclines of Equation 3.1 is depicted in Figure 3.

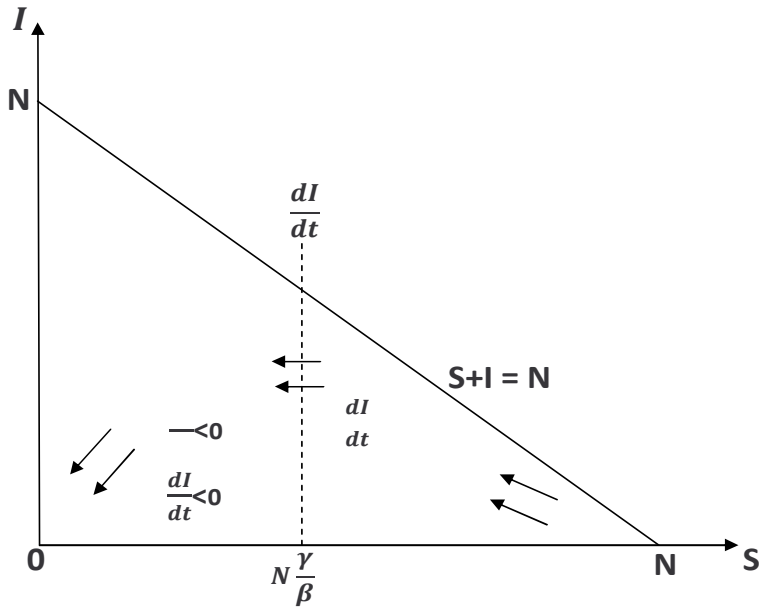

Figure 18: S- and- I nullclines of the system in 3.1

The basic reproduction number is affected by a number of factors including:

1. the duration of infectivity of the affected patients.

2. the infectiousness of the organism, and

3. the number of susceptible people in the population that the affected patients get into contact with.

Remark

Note that the three quantities $\mathrm{R}_0, \frac{\beta}{\gamma}$, and R are all equal at the beginning of the spread of the infectious disease when the entire population is susceptible $s_0 = 1$ except the infective invader.Although R_0 is only defined at the time of invasion, $\frac{\beta}{\gamma}$ and R are defined at all time. For most models, the contact number $\frac{\beta}{\gamma}$ remains constant as the infection spreads, so it is always equal to the basic reproduction number$\mathcal{R}_0$. In these models $\frac{\beta}{\gamma}$ andR_0 can be used interchangeably and invasion theorems can be stated in

terms of either quantity. However, after invasion, the susceptible fraction is less than 1, so that not all adequate contacts results in a new case. Thus the replacement number R is always less than the contact number $\frac{\beta}{\gamma}$ after the invasion. Combining these results leads to $\mathcal{R}_0 \geq \frac{\beta}{\gamma} \geq \mathrm{R}$ with equality of the three models at the time of invasion. Note that $\mathrm{R}_0 = \frac{\beta}{\gamma}$ for most models, and $\frac{\beta}{\gamma} > \mathrm{R}$ after the invasion for all models.

Effect of Treatment Without Inoculation in Infected Population

To illustrate the effect of vaccination on an SIS model, let's consider the model

$$\begin{aligned} \dot{\mathrm{S}} &= \mu - \beta \mathrm{SI} - \mu \mathrm{S} \\ \dot{\mathrm{I}} &= \beta \mathrm{SI} - \mu \mathrm{I} - \gamma \mathrm{I} \\ \dot{\mathrm{R}} &= \gamma \mathrm{I} - \mu \mathrm{R}. \end{aligned} \tag{3.4}$$

In this regard an attempt is made at increasing the quality of clinical treatment. The parameter γ, which represents the treatment level is increased from 20%, 40% , 60% up to 80%. The effect is demonstrated in the Figure 3.

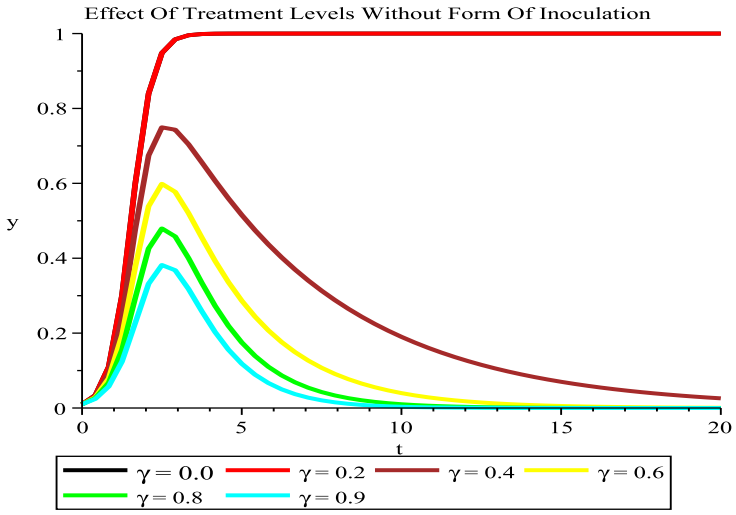

Figure 19: Increasing the Quality of Clinical Treatment without Inoculation

The effect is that when there was no treatment of any form, the disease invades the whole population. The disease in this case is malaria and so everyone gets the disease. When there was level of treatment of $\gamma = 0.2$, the disease could affect at least 75% of the population or more. The quality of treatment was then increased to 0.4. The resulting effect was that about 60% become infected. This approach was continued until about 40% became infected. This result was achieved for 90% treatment level. Thus increasing the quality of treatment can have a positive impact on the number number of individuals who become ill. It must be emphasised that the rate of treatment as pertained in the country may not be 40% efficient. In addition any effort made in this direction will not eventually eradicate the disease. Thus a more efficient approach must be found to militate the malaria and it effects.

Treatment in addition to reducing the number of susceptibles.

Another way of controlling the disease apart from curing is to have a programme of reducing the number of susceptibles. The SIR in this situation is different since there is an effort at reducing the number of susceptibles by way of inoculation. The dynamics is given by Equation 3.5.

$$\begin{aligned} \dot{\mathrm{S}} &= \mu - \beta \mathrm{SI} - \mu \mathrm{S} - \alpha \mathrm{S} \\ \dot{\mathrm{I}} &= \beta \mathrm{SI} - \mu \mathrm{I} - \gamma \mathrm{I} \\ \dot{\mathrm{R}} &= \gamma \mathrm{I} - \mu \mathrm{R} + \alpha \mathrm{S}. \end{aligned} \tag{3.5}$$

This Equation has disease-free equilibrium as

$$\mathbf{DFE} = (\mathrm{S}_0,\, \mathrm{I}_0,\, \mathrm{R}_0) = \left(\frac{\mu}{\mu + \alpha},\, 0,\, \frac{\alpha}{\mu + \alpha} \right).$$

The endemic equilibrium is also by

$$\mathbf{EE} = \begin{Bmatrix} S_e \\ I_e \\ R_e \end{Bmatrix} = \begin{Bmatrix} \dfrac{\mu+\gamma}{\beta} \\ \dfrac{-\mu\beta+\mu^2+\mu\gamma+\alpha\mu+\alpha\gamma}{\beta(\mu+\gamma)} \\ -\dfrac{-\beta\gamma+\mu\gamma+\gamma^2-\alpha\gamma-\alpha\mu}{\beta(\mu+\gamma)} \end{Bmatrix}. \tag{3.6}$$

Again, we showcase the importance of control strategy in the form of "inocuation" aimed at reducing the level of susceptibility , using the generic SIR model. We replicate the method employed in previous subsection. The effect will then be juxtaposed to control , by increasing the quality of treatment rate without a reduction in susceptible class. The simulation for model in Equation 3.5 can be found in Figure 3.

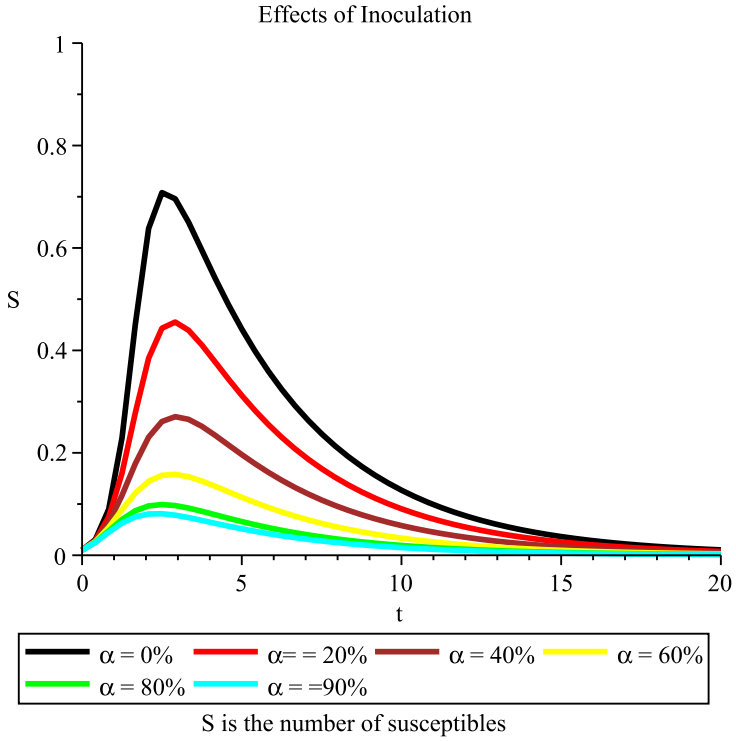

Figure 20: Clinical Treatment with Control.

In this approach, the susceptible class is reduced from 100% to 10% via 20%, 40%, 60% and 80% and maybe 90%. It can clearly be observed that the infective class decreased with an increased rate.

The effect of mass vaccination programs can be seen in the basic epi-

demic model above. Vaccination reduces or eliminate the incidence of infection directly or indirectly. Vaccinated individuals are removed or protected from direct infection, and fewer susceptible individuals leads to a decreased likelihood that an unvaccinated susceptible will come in contact with the disease. This latter indirect effect is referred to as herd immunity.

For vaccination program to be effective, the fraction p immunised must be such that the remaining population $(1 - \mathrm{p})\mathrm{N}$ will be less than the the threshold level necessary for the disease to continue. To prevent an epidemic

$$\mathcal{R}_0(1 - \mathrm{p}) < 1.$$

An estimate for the minimum value of p is found by solving $\mathcal{R}_0(1 - \mathrm{p}) = 1$ or

$$\mathrm{p} = \frac{\mathcal{R}_0 - 1}{\mathcal{R}_0}.$$

For example, in England and Wales(1956-1968), the value of R_0 estimated for measles was ($R_0 \approx 13$), May, (1983). For this value of $\mathcal{R}_0$, to prevent an epidemic, it would have been necessary to vaccinate at least

$$\mathrm{p} = \frac{13 - 1}{13} = \frac{12}{13} \approx 92\%$$

Vaccination is a preventive strategy. However, during an outbreak, if there are no vaccines or treatment available for the disease, quarantine of suspected cases or isolation of those diagnosed with the disease are alternative strategies. Such control strategies were used of new diseases in 2003, **SARS**-Severe Acute Respiratory Syndrome.

An SIS With Vital Dynamics

When a disease persists in a population for a long period of time, births and deaths must be taken into consideration. The model will be the same as the Basic SIS Model, with additional inflow of newborns into the susceptible class, and death-removal from both the susceptible and the infected

classes. We assume that births balances deaths, so the population size remains constant. The following assumptions must be taken into account.

1. Susceptible and infected individuals die at a rate proportional to the number susceptible and infected individuals, with constant of proportionality $\boldsymbol{\mu}$ called the daily death removal rate; the number $\dfrac{\mathbf{1}}{\boldsymbol{\mu}}$ is the **average lifetime or life expectancy**

2. There is an inflow of newborns into the susceptible class at the rate of $\boldsymbol{\mu}N$

With the notions given above, the classic SIS model with vital dynamics is given by Equation 3.7.

$$\begin{aligned} \frac{\mathrm{dS}}{\mathrm{dt}} &= \frac{-\beta \mathrm{SI}}{\mathrm{N}} + \gamma \mathrm{I} + \mu \mathrm{N} - \mu \mathrm{S} \quad \mathrm{S}(0) = \mathrm{S}_0 \\ \frac{\mathrm{dI}}{\mathrm{dt}} &= \frac{\beta \mathrm{SI}}{\mathrm{N}} - \gamma \mathrm{I} - \mu \mathrm{I} \quad \mathrm{I}(0) = \mathrm{I}_0 \end{aligned} \tag{3.7}$$

To verify that $\mathrm{S(t)} + \mathrm{I(t)} = \mathrm{N}$, the total population, let

1. $\mathrm{s(t)} = \mathrm{S(t)/N}$ be the proportion of the of susceptibles in the population.

2. $\mathrm{i(t)} = \mathrm{I(t)/N}$ be the proportion of the infectives in the population.

Dividing through Equation 5.10 by N gives Equation 3.8.

$$\begin{aligned} \frac{\mathrm{ds}}{\mathrm{dt}} &= -\beta \mathrm{si} + \gamma \mathrm{i} + \mu - \mu \mathrm{s} \quad \mathrm{s}(0) = \mathrm{s}_0 \\ \frac{\mathrm{di}}{\mathrm{dt}} &= \beta \mathrm{si} - \gamma \mathrm{i} - \mu \mathrm{i} \quad \mathrm{i}(0) = \mathrm{i}_0 \end{aligned} \tag{3.8}$$

with $\mathrm{s(t)} + \mathrm{i(t)} = 1$ so that $\mathrm{s(t)} = 1 - \mathrm{i(t)}$

The system above has critical points

- **disease free equilibrium** is given by $(\mathrm{s}_1, \mathrm{i}_1) = (1, 0)$,
- **endemic equilibrium** $(\mathrm{s}_2, \mathrm{i}_2) = (\dfrac{\gamma + \mu}{\beta}, -\dfrac{-\beta + \gamma + \mu}{\beta})$

Let $\sigma = \dfrac{\beta}{\gamma + \mu}$, then

- when s$\sigma < 1$ then $i(t)$ decreases.
- when s$\sigma > 1$ then $i(t)$ increases.

The replacement number R, is given by $R = s\sigma$

If we assume that everyone is susceptible, then at $t = 0, s_0 = 1$, then $R = s_0\sigma = \sigma$, the contact number.

The contact number σ, is given by $\sigma = \dfrac{\beta}{\gamma + \mu} = \mathrm{R}_0$, the basic production number.

Theorem 3.1. Theorem

Let $(s(t), i(t))$ be a solution of Equation 3.8, and $\sigma = \dfrac{\beta}{\gamma + \mu}$. Then

- All solution paths approach the disease-free equilibrium point$(1, 0)$ if $\sigma \leq 1$.
- All solution paths approach the endemic equilibrium point $(\dfrac{1}{\sigma}, 1 - \dfrac{1}{\sigma})$ if $\sigma > 1$

An SIR Model With Vital Dynamics

When a disease persists in a population for a long period of time, births and deaths must be taken into consideration. In addition to assumptions and notation given under Basic SIR Model, we assume that susceptible and infected individuals die at a rate proportional to to the number of susceptible and infected individuals, with constant of proportionality μ, called the daily death removal rate; the number $\dfrac{1}{\mu}$, is the average lifetime or life expectancy

The SIR model with vital dynamics is given by Equation 3.9.

$$\begin{aligned}
\frac{\mathrm{dS}}{\mathrm{dt}} &= \frac{-\beta \mathrm{SI}}{\mathrm{N}} + \mu \mathrm{I} - \mu \mathrm{S} \quad \mathrm{S}(0) = \mathrm{S}_0 \\
\frac{\mathrm{dI}}{\mathrm{dt}} &= \frac{\beta \mathrm{SI}}{\mathrm{N}} - \gamma \mathrm{I} - \mu \mathrm{I} \quad \mathrm{I}(0) = \mathrm{I}_0 \\
\frac{\mathrm{dR}}{\mathrm{dt}} &= \mu \mathrm{R} \quad \mathrm{R}(0) = \mathrm{R}_0
\end{aligned} \tag{3.9}$$

This model can be used to model diseases that are **endemic** to the population; those diseases that persists in the population for a long periods of time (usually ten years or more). One such example is small pox which was endemic until it was eradicated in 1977.

Here, $s(t), i(t)$ and $r(t)$ are proportions susceptible, infected and recovered individuals. Since $s(t) + i(t) + r(t) = 1$, we can find r by putting $r(t) = 1 - s(t) - i(t)$, we know $s(t)$ and $i(t)$ from the reduced system:

$$\begin{aligned}
\frac{\mathrm{ds}}{\mathrm{dt}} &= -\beta \mathrm{si} + \mu - \mu \mathrm{s} \quad \mathrm{s}(0) = \mathrm{s}_0 \\
\frac{\mathrm{di}}{\mathrm{dt}} &= \beta \mathrm{si} - \gamma \mathrm{i} - \mu \mathrm{i} \quad \mathrm{i}(0) = \mathrm{i}_0
\end{aligned} \tag{3.10}$$

Since, $\mathrm{R(t)} = 1 - \mathrm{S(t)} - \mathrm{I(t)};\ \mathrm{S(t)} + \mathrm{I(t)} \leq 1$ the equilibrium solutions can be found by solving the Equation 3.10.

The equilibrium solutions of 3.10 are:

1. a disease-free equilibrium is at $(1, 0;)$
2. an endemic equilibrium is at $\left(\frac{\gamma + \beta}{\beta}, \frac{\mu[\beta - (\gamma + \mu)]}{\beta(\gamma + \mu)}\right)$

For the endemic equilibrium to exists $\frac{\mathrm{di}}{\mathrm{dt}} = \beta \mathrm{si} - \gamma \mathrm{i} - \mu \mathrm{i} > 0$. This implies that $\mathrm{i}(\beta \mathrm{s} - \gamma - \mu) > 0$. Eventually we obtain $\frac{\beta \mathrm{s}}{\mu + \gamma} > 1$

At the equilibrium $S = S(0) = 1$. Therefore,

$$\frac{\beta}{\mu + \gamma} > 1$$

is the condition for endemicity to exists.

Limitation of the Classic SIR model

The simple generic SIR models discussed above have obvious limitations. They unrealistically assume that the population is uniform and homogeneously mixing. In fact, it is known that depends on many factors including age (Children usually have more adequate contacts per unit time than adults). Moreover, different geographic and socio-economic groups have different contact rates. Despite these limitations, the classic SIR model can be used to obtain some useful estimates.

CHAPTER FOUR

VECTOR-HOST MODELS

Background

Some diseases are contracted by humans from sources such as mosquitoes, birds, rodents other than from human to human. Example of such diseases are malaria and dengue fever. **Vector-host models** are used to describe the spread of a disease between and within two populations.

The model below is an example of a vector host model. Here S, I, R are respectively, susceptible, Infected and recovered (with partial immunity) humans; V, M are the susceptible and infected vectors. It is assumed that infected vectors remain infected for life, and that the infection is not harmful to them. The recruitment rates for humans and vectors are b_1 and b_2 respectively, γ is the rate of recovery for humans.

This model has more than one disease compartments, and so the method for determining the *basic reproduction number* requires the use of the *next generation matrix*, defined and described below.

$$\begin{aligned}
\dot{\mathrm{S}} &= \mathrm{b}_1 - \beta_1 \mathrm{SI} - \beta 2\mathrm{SV} - \mathrm{dS} + \rho \mathrm{R} \\
\dot{\mathrm{I}} &= \beta_1 \mathrm{SI} + \beta 2\mathrm{SV} - \mathrm{dI} - \gamma \mathrm{I} \\
\dot{\mathrm{R}} &= \gamma \mathrm{I} - \mathrm{d}_\mathrm{R} - \rho \mathrm{R} \\
\dot{\mathrm{V}} &= \mathrm{b}_2 - \beta_3 \mathrm{IV} - \mathrm{dV} \\
\dot{\mathrm{M}} &= \beta_3 \mathrm{IV} - \mathrm{dM}
\end{aligned} \tag{4.1}$$

The basic Reproduction number

The basic reproductive ratio, $\mathcal{R}_{\prime}$, is a key concept in epidemiology, and is inarguably one of the foremost and most valuable ideas that mathematical thinking has brought to epidemic theory Heesterbeek and Dietz (1996). The basic reproduction number ($\mathcal{R}_0$) of an infection is defined by Diekmann and Heesterbeek (2000) as the 'expected number of secondary cases per primary case in a virgin population'. The roots of the basic reproduction concept can be traced through the work of Alfred Lotka, Ronald Ross, and others, but its first modern application in epidemiology was by George MacDonald in 1952, who constructed population models of the spread of malaria. In epidemiology, the basic reproduction number (sometimes called basic reproductive rate or basic reproductive ratio) of an infection is the mean number of secondary cases a typical single infected case will cause in a population with no immunity to the disease in the absence of interventions to control the infection. It is often denoted by ($\mathcal{R}_0$). This metric is useful because it helps determine whether or not an infectious disease will spread through a population. The roots of the basic reproduction concept can be traced through the work of Alfred Lotka, Ronald Ross, and others, but its first modern application in epidemiology was by George MacDonald in 1952, who constructed population models of the spread of malaria. If the reproduction number ($\mathcal{R}_0$) < 1, then the disease free equilibrium is locally asymptotically stable, and the disease cannot invade the population. On the other hand, if ($\mathcal{R}_0$) > 1, then the disease will eventually invade the the population, Hethcote (1975). A more recent review of the formulation, estimation and use of ($\mathcal{R}_0$) in deterministic models is attributed to Heffernan *et al.* (2005). Diekmann *et al.* (2000) defines ($\mathcal{R}_0$) as the spectral radius of of the next generation matrix.

The Next Generation Matrix

A rich history in the literature addresses the derivation of ($\mathcal{R}_0$), or an equivalent threshold parameter, when more than one class of infectives is involved (Rushton and Mautner (1955); Hethcote (1978); Nold 1980; Hethcote and Thieme (1985)) .

The next generation method, introduced by Diekmann *et al.* (1990), is a general method for deriving ($\mathcal{R}_0$) in such cases, encompassing any situation in which the population is divided into discrete, disjoint classes. The next generation operator can thus be used for models with underlying age structure or spatial structure, among other possibilities. For typical implementations, continuous variables within the population are approximated by a number of discrete classes. This approximation assumes that transmission probabilities between states are constant, or equivalently, that the distribution of residence times in each state is exponential. The next generation operator is fully
described in Diekmann and Heesterbeek (2000) and a number of salient cases are elucidated in van den Driessche and Watmough (2002).

In the next generation method, ($\mathcal{R}_0$) is defined as the **spectral radius of the next generation matrix**. The formation of the matrix involves determining two compartments, infected and non-infected, from the model. In this section, we outline the steps needed to find the next generation operator in matrix notation (assuming only finitely many types), and then employ this method for a susceptibleexposed infectiousrecovered (SEIR) model and a model of malaria. (For a detailed explanation on the formation of the next generation operator when there are infinitely many types. Diekmann and Heesterbeek (2000).)

For clarity we sort the compartments so that the first m compartments correspond to infected individuals. The basic reproduction number can not be determined from the structure of the mathematical model alone, but depends on the definition of infected and uninfected compartments. We define $\mathbf{X_s}$ to be the set of all disease free states. That is

$$\boldsymbol{X}_{\mathrm{s}} = \{\mathrm{x} \geq 0 | \mathrm{x_i} = 0, \mathrm{i} = 1, \ldots, \mathrm{m}\}.$$

In order to compute $\mathcal{R}_0$, it is important to distinguish new infections from all other changes in population. Let

- $\mathcal{F}_{\mathrm{i}}(\mathrm{x})$ be the rate of appearance of new infections in compartment i,
- $\mathrm{V_i^+(x)}$ be the rate of transfer of individuals into compartment i by all other means, and
- $V_i^-(x)$ be the rate of transfer of individuals out of compartment i.

It is assumed that each function is continuously differentiable at least twice in each variable. The disease transmission model consists of nonnegative initial conditions together with the following system of equations:

$$\dot{\mathrm{x}}_{\mathrm{i}} = f_{\mathrm{i}}(\mathrm{x}) = \mathcal{F}_{\mathrm{i}}(\mathrm{x}) - \mathcal{V}_{\mathrm{i}}(\mathrm{x}),\ \mathrm{i} = 1, \ldots, \mathrm{n}, \tag{4.2}$$

where $\mathcal{V}_{\mathrm{i}} = \mathcal{V}_{\mathrm{i}}^- - \mathcal{V}_{\mathrm{i}}^+$ and the functions satisfy assumptions (A1) through (A5) described below. Since each function represents a directed transfer of individuals, they are all nonnegative. Thus,

(A1) if $x \geq 0$, then $\mathcal{F}_{\mathrm{i}}, \mathcal{V}_{\mathrm{i}}^+, \mathcal{V}_{\mathrm{i}}^- \geq 0$ for $\mathrm{i} = 1, \ldots, \mathrm{n}$. If a compartment is empty, then there can be no transfer of individuals out of the compartment by death, infection, nor any other means. Thus,

(A2) if $x_i = 0$ then $\mathcal{V}_i^- = 0$. In particular, if $x \in \boldsymbol{X}_s$ then $\mathcal{V}_i^- = 0$ for $i = 1, \ldots, m$. Consider the disease transmission model given by Hethcote (2000) with $f_i(x)$, $i = 1, \ldots, n$, satisfying conditions $(A1)$ and $(A2)$. If $x_i = 0$, then $f_i(x) \geq 0$ and hence, the nonnegative cone $(x_i \geq 0,\ i = 1, \ldots, n)$ is forward invariant; swiggins (1990).

The next condition arises from the simple fact that the incidence of infection for uninfected compartments is zero.

(A3) $\mathcal{F}_i = 0$ if $i > m$.

To ensure that the disease free subspace is invariant, we assume that if the population is free of disease then the population will remain free of disease. That is, there is no (density independent) immigration of infectives. This condition is stated as follows:

(A4) if $\mathrm{x} \in \boldsymbol{X}_\mathrm{s}$ then $\mathcal{F}_\mathrm{i}(\mathrm{x}) = 0$ and $\mathcal{V}_\mathrm{i}^+(\mathrm{x}) = 0$ for $\mathrm{i} = 1, \ldots, \mathrm{m}$.

The remaining condition depends on the derivatives of f near a DFE. Consider a population near the DFE x_0. If the population remains near the DFE (i.e., if the introduction of a few infective individuals does not result in an epidemic) then the population will return to the DFE according to the linearized system,

$$\dot{\mathrm{x}} = \mathrm{D}f(\mathrm{x}_0)(\mathrm{x} - \mathrm{x}_0) \tag{4.3}$$

where $\mathrm{D}f(\mathrm{x}_0)$ is the derivative $[\partial f_\mathrm{i}/\partial \mathrm{x}_\mathrm{j}]$ evaluated at the DFE, x_0 (i.e., the Jacobian matrix). Here, and in what follows, some derivatives are one sided, since x_0 is on the domain boundary. We restrict our attention to systems in which the DFE is stable in the absence of new infection. That is

(A5) If $\mathcal{F}(x)$ is set to zero, then all eigenvalues of $Df(x_0)$ have negative real parts.

The conditions listed above allow us to partition the matrix $Df(x_0)$ as shown by the following lemma.

lemma

If x_0 is a disease-free equilibrium (DFE) and $f_i(x)$ satisfies $A1 - A5$ then the derivatives $\mathrm{D}\mathcal{F}(\mathrm{x}_0)$ and $D\mathcal{V}(x_0)$ are partitioned as

$$\mathrm{D}\mathcal{F}(\mathrm{x}_0) = \begin{pmatrix} \mathrm{F} & 0 \\ 0 & 0 \end{pmatrix}, \quad \mathcal{V}(\mathrm{x}_0) = \begin{pmatrix} \mathrm{V} & 0 \\ \mathrm{J}_3 & \mathrm{J}_4 \end{pmatrix} \tag{4.4}$$

where F and V and the $m \times m$ matrix is given by

$$\mathrm{F} = \left[\frac{\partial \mathcal{F}(\mathrm{x}_0)}{\partial \mathrm{x}_\mathrm{j}}\right] \quad \text{and} \quad \mathrm{V} = \left[\frac{\partial \mathcal{V}(\mathrm{x}_0)}{\partial \mathrm{x}_\mathrm{j}}\right] \tag{4.5}$$

with $1 \leq i \leq m$. F is non-negative and V is a is non-singular M-matrix and all eigenvalues of J_4 have positive real part.

Proof

Let $\mathrm{x}_0 \in \boldsymbol{X}_\mathrm{s}$ denote disease-free equilibrium. By assumptions A3 and A4, $\dfrac{\partial \mathcal{F}_\mathrm{i}}{\partial \mathrm{x}_\mathrm{j}}(\mathrm{x}_0) = 0$ if either $i > m$ or $j > m$.

Similarly, by A2 and A4, if $\mathrm{x} \in \boldsymbol{X}_\mathrm{s}$ then $\mathcal{V}_i = 0$ for $i \leq m$. Hence, $\dfrac{\partial \mathcal{V}}{\partial \mathrm{x}_\mathrm{j}}(\mathrm{x}_0) = 0$ for $\mathrm{i} \leq \mathrm{m}$ and $\mathrm{j} > \mathrm{m}$. This shows the stated partition and zero blocks. The nonnegativity of F follows from $A1$ and $A4$.

Let $\{e_j\}$ be the Euclidean basis vectors. That is , e_j is the j^th column of $n \times n$ identity matrix. Then, for $j = 1, \ldots, m$,

$$\left(\frac{\partial \mathcal{V}}{\partial \mathrm{x}_\mathrm{j}}\right)(\mathrm{x}_0) = \lim_{\mathrm{h} \to 0^+} \left(\frac{\mathcal{V}(\mathrm{x}_0 + \mathrm{he}_\mathrm{j}) - \mathcal{V}_\mathrm{i}(\mathrm{x}_0)}{\mathrm{h}}\right)$$

To show that V is nonsingular M-matrix, note that if x_0 is DFE, then by assumption A2 and A4, $\mathcal{V}(x_0) = 0$ for $i = 1, \ldots, m$ and if $i \neq j$, then the

i^{th} component of $\mathrm{x_0 + he_j} = 0$ and $\mathcal{V}(\mathrm{x_0 + he_j}) \leq 0$ by A1 and A2. Hence, $\dfrac{\partial \mathcal{V}_\mathrm{i}}{\partial \mathrm{x_j}} \leq 0$ for $i \leq 0$ and $j \neq i$ and V has real Z sign pattern. (For example, if a matrix B has the Z sign pattern and $s(B) > 0$, then B is a nonsingular M-matrix. s(A) be the maximum real part of the eigenvalues of A).

Additionally, by A5, all eigenvalues of V have positive real parts. These two conditions imply that V is a nonsingular M-matrix. Finally, assumption A5 also implies that the eigenvalues of J_4 have positive real part.

What is a Generation?

In demography, $\mathcal{R}_0$ represents the ratio of total population size from the start to the end of a generation, which is, roughly, the mean age of child-bearing. $\mathcal{R}_0 = e^{rT}$, where r is the instantaneous rate of increase of the population. Generations in epidemic models are the waves of secondary infection that flow from each previous infection. So, the first generation of an epidemic is all the secondary infections that result from infectious contact with the index case, who is of generation zero. If $\mathcal{R}_i$ denotes the reproduction number of the i_{th} generation, then $\mathcal{R}_0$ is simply the number of infections generated by the index case, i.e., generation zero. Now, these numbers are typically small and are therefore susceptible to random sampling error. Consequently, we talk about expected (i.e., averaged over many epidemics) numbers of secondary cases produced by generation zero.

The Basic Reproduction Number

The next generation matrix, $\mathrm{K = FV^{-1}}$, is nonnegative and therefore has a nonnegative eigenvalue, $\mathcal{R}_0 = \rho(\mathrm{FV^{-1}})$, such that there are no other eigenvalues of K with modulus greater than $\mathcal{R}_0$ and there is a nonnegative eigenvector ω associated with $\mathcal{R}_0$, Berman and Plemmons (1979). This eigenvector is in some sense the distribution of infected individuals that

produces the greatest number, $\mathcal{R}_0$, of secondary infections per generation. Thus, $\mathcal{R}_0$ and the associated eigenvector ω suitably define a **typical** infective and the basic reproduction number can rigorously be defined as the spectral radius of the next generation matrix, K. The spectral radius of a matrix K, denoted $\rho(K)$, is the maximum of the moduli of the eigenvalues of K. If K is irreducible, then $\mathcal{R}_0$ is a simple eigenvalue of K. However, if K is reducible, which is often the case for diseases with multiple strains, then K may have several positive real eigenvectors corresponding to reproduction numbers for each competing strain of the disease.

Therefore,

$$\mathcal{R}_0 = \rho(\mathrm{FV}^{-1}) \tag{4.6}$$

where FV^{-1} the next generation matrix for the model and we shall set $\mathcal{R}_0$ as equal to the spectral radius FV^{-1} and $\rho(\mathrm{A})$ denotes the spectral radius of the matrix A.

Application of the Next Generation Matrix

The first three examples are obtained from van den Driessche and Watmough (2002).

TB treatment Model

Consider a model where the population is divided into four compartments, namely, individuals susceptible to tuberculosis (S), exposed individuals (E), infectious individuals (I) and treated individuals (T). Susceptible and treated individuals enter the exposed compartment at rates $\beta_1\mathrm{I/N}$ and $\beta_2\mathrm{I/N}$,
respectively, where $\mathrm{N} = \mathrm{E} + \mathrm{I} + \mathrm{S} + \mathrm{T}$. Exposed individuals progress to the

infectious compartment at the rate ν. All newborns are susceptible, and all individuals die at the rate $d > 0$. Thus, the core of the model is an SEI model using standard incidence. The treatment rates are r_1 for exposed individuals and r_2 for infectious individuals. However, only a fraction q of the treatments of infectious individuals are successful. Unsuccessfully treated infectious

individuals re-enter the exposed compartment ($\mathrm{p} = 1 - \mathrm{q}$). The disease transmission model consists of the following differential equations together with nonnegative initial conditions:

$$\begin{aligned}
\frac{\mathrm{dS}}{\mathrm{dt}} &= \mathrm{bN} - \mathrm{dS} - \beta_1 \frac{\mathrm{SI}}{\mathrm{N}} && (4.7)\\
\frac{\mathrm{dE}}{\mathrm{dt}} &= \beta_1 \frac{\mathrm{SI}}{\mathrm{N}} + \beta_2 \frac{\mathrm{TI}}{\mathrm{N}} - (\mathrm{d} +_\nu + \mathrm{r}_1)\mathrm{E} + \mathrm{pr}_2\mathrm{I} && (4.8)\\
\frac{\mathrm{dI}}{\mathrm{dt}} &= \nu\mathrm{E} - (\mathrm{d} + \mathrm{r}_2)\mathrm{I} - \mathrm{qr}_2\mathrm{I} && (4.9)\\
\frac{\mathrm{dT}}{\mathrm{dt}} &= \mathrm{r}_1\mathrm{E} + \mathrm{qr}_2\mathrm{I} - \mathrm{dT} - \beta_2 \frac{\mathrm{TI}}{\mathrm{N}} && (4.10)
\end{aligned}$$

Rearranging the equations so that we start with infective classes, we obtain

$$\begin{aligned}
\frac{\mathrm{dE}}{\mathrm{dt}} &= \beta_1 \frac{\mathrm{SI}}{\mathrm{N}} + \beta_2 \frac{\mathrm{TI}}{\mathrm{N}} - (\mathrm{d} +_\nu + \mathrm{r}_1)\mathrm{E} + \mathrm{pr}_2\mathrm{I} && (4.11)\\
\frac{\mathrm{dI}}{\mathrm{dt}} &= \nu\mathrm{E} - (\mathrm{d} + \mathrm{r}_2)\mathrm{I} - \mathrm{qr}_2\mathrm{I} && (4.12)\\
\frac{dS}{dt} &= bN - dS - \beta_1 \frac{SI}{N} && (4.13)\\
\frac{dT}{dt} &= r_1 E + qr_2 I - dT - \beta_2 \frac{TI}{N} && (4.14)
\end{aligned}$$

In this case $m = 2$ (Two infected compartments). Thus from 4.11 the following equations are obtained.

$$\mathcal{F} = \begin{pmatrix} \beta_1 \dfrac{\mathrm{SI}}{\mathrm{N}} + \beta_2 \dfrac{\mathrm{TI}}{\mathrm{N}} \\ 0 \\ 0 \\ 0 \end{pmatrix}, \quad \mathcal{V} = \mathcal{V}_{\mathrm{i}}^{-} - \mathcal{V}_{\mathrm{i}}^{+} = \begin{pmatrix} (\mathrm{d} + \nu + \mathrm{r}_1)\mathrm{E} - \mathrm{pr}_2\mathrm{I} \\ (\mathrm{d} + \mathrm{r}_2)\mathrm{I} + \mathrm{qr}_2\mathrm{I} - \nu\mathrm{E} \\ \mathrm{dS} + \beta_1 \dfrac{\mathrm{SI}}{\mathrm{N}} - \mathrm{bN} \\ \mathrm{dT} - \mathrm{r}_1\mathrm{E} - \mathrm{qr}_2\mathrm{I} + \beta_2 \dfrac{\mathrm{TI}}{\mathrm{N}} \end{pmatrix}$$

The disease free equilibrium point of the system Equation 4.11 is

$$(\mathrm{E}_0, \mathrm{I}_0, \mathrm{S}_0, \mathrm{T}_0) = (0, 0, 1, 0).$$

Now, $\mathcal{F}$ and $\mathcal{V}$ evaluated at the disease-free equilibrium is given by

$$\mathrm{F} = \begin{pmatrix} 0 & \beta_1 \\ 0 & 0 \end{pmatrix} \text{ and } \mathrm{V} = \begin{pmatrix} d + \nu + r_1 & -pr_2 \\ -\nu & d + r_2 \end{pmatrix}$$

respectively. Since $\mathcal{R}_0 = \rho(\mathrm{FV}^{-1})$, we need to find V^{-1}.

$$\mathrm{V}^{-1} = \frac{1}{(\mathrm{d} + \nu + \mathrm{r}_1)(\mathrm{d} + \mathrm{r}_2) - \nu\mathrm{pr}_2} \begin{pmatrix} d + r_2 & pr_2 \\ \nu & d + \nu + r_1 \end{pmatrix}.$$

Hence, the reproduction number of the model above is

$$\mathcal{R}_0 = \frac{\nu\beta_1}{(\mathrm{d} + \nu + \mathrm{r} - 1)(\mathrm{d} + \mathrm{r}_2) - \nu\mathrm{pr}_2}.$$

Multi-Strain

Consider the model

$$\begin{aligned} \frac{\mathrm{dI}_1}{\mathrm{dt}} &= \beta_1\mathrm{SI}_1 - (\mathrm{b} + \gamma)\mathrm{I}_1 + \nu\mathrm{I}_1\mathrm{I}_2 \\ \frac{\mathrm{dI}_2}{\mathrm{dt}} &= \beta_2\mathrm{I}_2\mathrm{S} - (\mathrm{d} + \mathrm{r}_2)\mathrm{I}_2 - \nu\mathrm{I}_1\mathrm{I}_2 \\ \frac{\mathrm{dS}}{\mathrm{dt}} &= \mathrm{b} - \mathrm{bS} + \nu_1\mathrm{I}_1 + \mathrm{r}_2\mathrm{I}_2 - (\beta_1\mathrm{I}_1 + \beta_2\mathrm{I}_2)\mathrm{S} \end{aligned}$$

The disease-free equilibrium is calculated to be

$$(I_1, I_2, S) \quad = \quad (0,\ 0,\ 1)$$

and the derivatives of F and V of $\mathcal{F}$ and $\mathcal{V}$ are respectively.

$$\mathrm{F} = \begin{pmatrix} 0 & \beta_1 \\ 0 & \beta_2 \end{pmatrix} \quad \text{and} \quad \mathrm{V} = \begin{pmatrix} b + r_1 & 0 \\ 0 & b + r_2 \end{pmatrix}.$$

Therefore,

$$\mathrm{R_i} = \frac{\beta_\mathrm{i}}{\mathrm{b} + \beta_\mathrm{i}}, \quad \mathrm{i} = 1, 2.$$

Hence,

$$\mathcal{R}_0 = \max_{\mathrm{i}=\{1,2\}} \mathrm{R_i}. \tag{4.15}$$

Vector-Host Model

This example was proposed by Feng and Valesco-Hernández (1997) for Dengue fever. An SIS model is udes for the hosts, while an SI model is used for the vectors. The four compartments correspond to infected hosts (I), infected vectors (V), susceptible hosts (S) and susceptible vectors (M). Hosts are infected by contacts with infected vectors, and vectors are in turn infected by contacts with infected hosts. These infection rates are given by the two terms $\beta_s SV$ and $\beta_m MI$. The dynamics of the model is as follows:

$$\begin{aligned} \frac{\mathrm{dI}}{\mathrm{dt}} &= \beta_\mathrm{s}\mathrm{SV} - (\mathrm{b} + \gamma)\mathrm{I} \\ \frac{\mathrm{dV}}{\mathrm{dt}} &= \beta_\mathrm{m}\mathrm{MI} - \mathrm{cV} \\ \frac{\mathrm{dS}}{\mathrm{dt}} &= \mathrm{b} - \mathrm{bS} + \gamma\mathrm{I} - \beta_\mathrm{s}\mathrm{SV} \\ \frac{\mathrm{dM}}{\mathrm{dt}} &= \mathrm{c} - \mathrm{cM} - \beta_\mathrm{m}\mathrm{MI} \end{aligned}$$

The birth and death rates are $b > 0$ for the host, and $c > 0$ for the vector. The dynamical system has a disease-free equilibrium point as $E_0 = (0, 0, 1, 1)$, and an endemic equilibrium point

$$\mathrm{E_1} =$$

$$\left(-\frac{-\beta_s\beta_m + bc + c\gamma}{(b+\gamma+\beta_s)\beta_m}, -\frac{-\beta_s\beta_m + bc + c\gamma}{\beta_s(\beta_m + c)}, \frac{(b+\gamma)(\beta_m + c)}{(b+\gamma+\beta_s)\beta_m}, \frac{c(b+\gamma+\beta_s)}{\beta_s(\beta_m + c)}\right)$$

.

The derivatives of F and V at the disease-free equilibrium point are

$$F = \begin{pmatrix} 0 & \beta_s \\ \beta_m & 0 \end{pmatrix} \quad \text{and} \quad V = \begin{pmatrix} b+\gamma & 0 \\ 0 & c \end{pmatrix},$$

where V is nonsingular. The basic reproduction number is given by

$$\mathcal{R} = \sqrt{\frac{\beta_s\beta_m}{c(b+\gamma)}}. \tag{4.16}$$

Near the disease free equilibrium, each infected host produces $\frac{\beta_m}{c}$ new infected vectors over its expected infectious period, and each infected vector produces $\frac{\beta_s}{b+\gamma}$ new infected hosts over its expected infectious period. The square rot arises from the two generations required for an infected vector or host to reproduce itself.

The SLIAR Model

The SLIAR model for influenza consists of five compartments: susceptible (S), latent (L), infectious (I), asymptomatic (A) and removed (R). Only the middle three of these are considered disease states, so $x = (L, I, A)$. Infection and progression through the disease states is summarized in the following diagram.

The model consists of the following system of differential equations, together with nonnegative initial conditions:

$$\dot{\mathrm{S}} = -\beta \mathrm{S}(\epsilon \mathrm{L} + \mathrm{I} + \delta \mathrm{A}) \tag{4.17}$$

$$\dot{\mathrm{L}} = \beta \mathrm{S}(\epsilon \mathrm{L} + \mathrm{I} + \delta \mathrm{A}) - \kappa \mathrm{L} \tag{4.18}$$

$$\dot{\mathrm{I}} = \mathrm{p}\kappa \mathrm{L} - \alpha \mathrm{I} \tag{4.19}$$

$$\dot{\mathrm{A}} = (1 - \mathrm{p})\kappa \mathrm{L} - \eta \mathrm{A} \tag{4.20}$$

$$\dot{\mathrm{R}} = \alpha \mathrm{I} + \eta \mathrm{A} \tag{4.21}$$

New infections occur during contacts between susceptible individuals and individuals in any of the infected compartments, L, I or A. The incidence term is a sum of products of S with L, I and A, with ϵ and δ being the relative infectiousness of latent and asymptomatic infections. Technically, the term latent only applies if $\epsilon = 0$; otherwise, with $0 < \epsilon < 1$, L represents a first, partially infectious stage, and I a later, fully infectious stage.

The matrix V is given by

$$\mathrm{V} = \begin{pmatrix} \kappa & 0 & 0 \\ -\mathrm{p}\kappa & \alpha & 0 \\ -(1-\mathrm{p})\kappa & 01/\eta & \end{pmatrix}.$$

Now F and V^{-1} are given by

$$\mathrm{F} = \begin{pmatrix} \epsilon\beta S_0 & \beta S_0 & \delta\beta S_0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \qquad \mathrm{V}^{-1} = \begin{pmatrix} 1/\kappa & 0 & 0 \\ \mathrm{p}/\alpha & 1/\alpha & 0 \\ (1-\mathrm{p})/\eta & 0 & 1/\eta \end{pmatrix}.$$

Hence, the basic reproduction number is given by $\rho(FV^{-1})$ that is

$$\mathcal{R}_0 = \beta \mathrm{S}_0 \left(\frac{\epsilon}{\kappa} + \frac{\mathrm{p}}{\alpha} + \frac{\delta(1-\mathrm{p})}{\eta} \right).$$

The reproduction number is a sum of products of the infection rates $\epsilon\beta S_0$, βS_0 and $\delta\beta S_0$ and the sojourn times $1/\kappa$, p/α and $(1-p)/\eta$. The

factors p and $(1-p)$ appear since these are the fractions of infected individuals that progress to the symptomatic and asymptomatic stages, respectively. That is, the expected time an infected individual spends in the I compartment is p/α, since a fraction p spend on average $1/\alpha$ times units in compartment I.

A simple SI Vaccination Model

Consider the following SI vaccination model proposed by Gandon *et al.* (2003).

$$\begin{aligned}
\dot{\mathrm{S}} &= (1-\mathrm{p})\Pi - \mu\mathrm{S} - (\beta\mathrm{I} + \beta_{\mathrm{v}}\mathrm{I_v})\mathrm{S} \\
\dot{\mathrm{S}}_{\mathrm{v}} &= \mathrm{p}\Pi - \mu\mathrm{S_v} - (1-\mathrm{r})(\beta\mathrm{I} + \beta_{\mathrm{v}}\mathrm{I_v})\mathrm{S_v} \\
\dot{\mathrm{I}} &= (\beta\mathrm{I} + \beta_{\mathrm{v}}\mathrm{I_v})\mathrm{S} - (\mu+\nu)\mathrm{I} \\
\dot{\mathrm{I}}_{\mathrm{v}} &= (1-\mathrm{r})(\beta\mathrm{I} + \beta_{\mathrm{v}}\mathrm{I_v})\mathrm{S_v} - (\mu+\nu_{\mathrm{v}})\mathrm{I_v}.
\end{aligned}$$

S, I, $\mathrm{S_v}$ and $\mathrm{I_v}$ denote the subpopulations in the unvaccinated susceptible, unvaccinated infectious, vaccinated susceptible and vaccinated infectious compartments, respectively. Susceptible individuals are recruited at a rate Π and a fraction, p, of these recruits are vaccinated immediately. Individuals leave the population at a rate μ, with additional disease-induced host mortality at the rates ν and ν_v. Vaccination of infectious individuals reduces the transmission rate from β to β_v and vaccination of susceptible individuals reduces the probability of transmission by a fraction r.

The system has a unique disease-free equilibrium, given by $S_0 = (1-p)N_0$ and $S_{v0} = pN_0$, where $N_0 = \Pi/\mu$. The disease compartments are I and I_v, V is the diagonal matrix

Here,

$$V = \begin{pmatrix} \mu + \nu & 0 \\ 0 & \mu + \nu_v \end{pmatrix},$$

and F is rank one matrix that can be expressed as a product of two vectors $\omega = (\mathrm{S}_0,\, (1 - \mathrm{r})\mathrm{S}_{\mathrm{v}0})^{\mathrm{T}}$ and $\beta = (\beta, \beta_{\mathrm{v}})^{\mathrm{T}}$ as follows:

$$\mathrm{F} = \omega\beta^{\mathrm{T}} = \begin{pmatrix} \beta \mathrm{S}_0 & \beta_{\mathrm{v}} \mathrm{S}_0 \\ (1 - r)\beta S_{vo} & (1 - r)\beta_v S_{v0} \end{pmatrix}. \tag{4.22}$$

Since F has rank one, the next generation matrix also has rank one. The spectral radius of a rank one matrix is its trace. Therefore,

$$\mathcal{R}_{\mathrm{c}} = \rho(\mathrm{F}\mathrm{V}^{-1}) = \beta^{\mathrm{T}}\mathrm{V}^{-1}\omega = \frac{\beta \mathrm{S}_0}{\mu + \nu} + \frac{(1 - \mathrm{r})\beta_{\mathrm{v}}\mathrm{S}_{\mathrm{v}0}}{\mu + \nu}.$$

The simplest interpretation to place on this number is that it is the sum of the number of secondary infections of unvaccinated susceptible individuals produced by an index case in I and the number of secondary infections of vaccinated susceptible individuals produced by an index case in I_v. This simple interpretation is misleading. The correct, although not immediately obvious, interpretation is that $\mathcal{R}_c$ is the number of secondary infections, both vaccinated and unvaccinated, produced by an "index case", ω, distributed in both infectious compartments, with one part in I and $(1 - r)S_{v0}/S_0$ parts in I_v. Quite simply, $\mathcal{R}_c$ is the eigenvalue of K with largest modulus and ω is an associated eigenvector.

This simple vaccination model assumes the effects of the vaccine on susceptible and infectious individuals are separable, which leads to a rank one next generation matrix and a simple expression for $\mathcal{R}_c$. Replacing the four incidence parameter combinations $\beta, \beta_v, (1 - r)\beta$ and $(1 - r)\beta_v$, with the four parameters β_{uu}, β_{uv}, β_{vu} and β_{vv} respectively, leads to the next generation matrix

$$\mathbf{K} = \begin{pmatrix} \frac{\beta_{uu} S_0}{\mu + \nu} & \frac{\beta_{uv} S_0}{\mu + \nu} \\ \frac{\beta_{vu} S_{0v}}{\mu + \nu} & \frac{\beta_{vv} S_{0v}}{\mu + \nu} \end{pmatrix}. \tag{4.23}$$

Denoting the four entries of K as $\mathcal{R}_{\mathrm{uu}}$, $\mathcal{R}_{\mathrm{uv}}$, $\mathcal{R}_{\mathrm{vu}}$ and $\mathcal{R}_{\mathrm{vv}}$, the spectral radius of K is

$$\mathcal{R}_{\mathrm{c}} = \frac{\mathcal{R}_{\mathrm{uu}} + \mathcal{R}_{\mathrm{vv}}}{2} + \frac{1}{2}\sqrt{(\mathcal{R}_{\mathrm{uu}} + \mathcal{R}_{\mathrm{vv}})^2 - 4\mathcal{R}_{\mathrm{uu}}\mathcal{R}_{\mathrm{vv}} + 4\mathcal{R}_{\mathrm{uv}}\mathrm{R}_{\mathrm{vu}}} \tag{4.24}$$

Although this expression defies interpretation as anything other than the spectral radius of K, the threshold condition

$$R_c < 1$$

is equivalent to the pair of conditions

$$\frac{1}{2}(\mathcal{R}_{\mathrm{uu}} + \mathcal{R}_{\mathrm{vv}}) < 1,$$

$$\mathcal{R}_{\mathrm{uu}} + \mathcal{R}_{\mathrm{vv}} + \mathcal{R}_{\mathrm{uv}}\mathcal{R}_{\mathrm{vu}} - \mathcal{R}_{\mathrm{uu}}\mathcal{R}_{\mathrm{vv}} < 1$$

Note that these conditions only hold for nonnegative matrices and differ slightly from the more general Jury conditions. Several authors like Cherry *et al.* (1998), Hsieh *et al.*,(2004) have interpreted the left hand side of the second inequality as the reproduction number for the model. The danger in this interpretation is that the magnitude of this expression does not give any insight into the solutions of the model. As Roberts and Heesterbeek (2003) point out, this distinction is important if $\mathcal{R}_c$ is used as a measure of the effectiveness of disease control measures.

Conclusion

The review of the practical use of $\mathcal{R}_0$ has focused largely on the work of P. van den Driessche and James Watmough, Reproduction numbers

and sub-threshold endemic equilibria for compartmental models of disease transmission. The number of papers included here-and our own review was by no means exhaustive-thus testifies to the relevance of this important concept in epidemiology. $\mathcal{R}_0$ was estimated by using the novel next generation method for deterministic models.

The vector-Host Model

Since this vector-host model is based on the SIR model, it will consists of six equations.

Assumption

We make the following assumptions:

- The population size is relatively large and constant.
- The population is constant in that we do not consider population dynamics and emigration or immigration of species.
- There is no incubation period.
- There is homogeneous mixing between and within species.
- The recovery rate of humans and the removal rate of vectors is constant.
- The recovered individual becomes immune to the disease.
- The infection rate is proportional to the number of infectives.

These assumptions imply that

$$\begin{aligned} N_H &= S_H(t) + I_H(t) + R_H(t) \\ N_v &= S_v(t) + I_v(t) + R_v(t) \end{aligned} \tag{4.25}$$

Explanation of Variables

This vector-host model is based on the SIR Model, it has a very similar setup, but expanded for two species or populations. It thus consists of six variables, instead of three.

- S_H is the number of individuals in the human population susceptible to the disease.
- I_H is the number of infected and infectious individuals in the human population.
- R_H is the recovered individuals in the human population.
- S_v is the number of individuals in the vector population susceptible to the disease.
- I_v is the number of infected individuals in the vector population.
- R_v is the number of individuals removed from the vector population.

Parameters Used in the Model

- N_H is the human population size.
- N_v is the vector population size.
- β is the fixed number of contacts per day per individual (regardless of species) sufficient to spread the disease (where $\beta S(t)$ is the number of new infected individuals of either species per day).
- γ is the fraction of the human infected group that will recover during any given day.
- ρ is the proportion of infection that occurs between the human and vector populations.

- λ is the proportion of infection that occurs between (rather than within) human and vector populations.

The System of Differential Equations

Since we now have two populations in our model, the rate of change of the number of susceptibles and infectives in each population depends on how many hosts and vectors have already been infected. We thus arrive at the following differential equations.

$$\begin{aligned}
\dot{S}_H(t) &= -\beta S_H(t)[I_H(t)(1-\rho) + \rho I_v(t)] \\
\dot{I}_H(t) &= \beta S_H(t)[I_H(t)(1-\rho) + \rho I_v(t)] - \gamma I_H(t) \\
\dot{R}_H(t) &= \gamma I_H(t) \\
\dot{S}_v(t) &= -\beta S_v(t)[I_v(t)(1-\rho) + \rho I_H(t)] \\
\dot{I}_v(t) &= \beta S_v(t)[I_v(t)(1-\rho) + \rho I_H(t)] - \lambda I_v(t) \\
\dot{R}_v(t) &= \lambda I_v(t)
\end{aligned} \tag{4.26}$$

It can be verified from the system of Equations 4.26 that

$$\begin{aligned}
N_H &= S_H(t) + I_H(t) + R_H(t) \\
N_v &= S_v(t) + I_v(t) + R_v(t).
\end{aligned} \tag{4.27}$$

Solving the System of Equations 4.26

The system of Equations 4.26 presented in this system is clearly nonlinear. Here the solution is difficult compared to the three state SIR model. Mathematical software like Maple does not usually come up with an explicit answer because it does not have enough memory. To avoid this problem, we write a program in Maple that will use numerical methods to graph the solution. Thereby making it possible to identify whether or not they are asymptotically stable.

We are finally ready to examine the solutions. For the sake of conciseness, we will only look at cases in which the change of parameters significantly influences the solution and summarize the effects of all the parameters in the conclusion.

No Infected Humans Recover, No Infected vectors Removed ($\gamma = 0 = \lambda$)

In this situation, we reduce the system of equations to the following equations:

$$\begin{aligned} \dot{I}_H(t) &= \beta(N_H - I_H)[I_H(1-\rho) + \rho I_v] \\ \dot{I}_v(t) &= \beta(N_v - I_v)[I_v(1-\rho) + \rho I_H] \end{aligned} \tag{4.28}$$

Before presenting graphical solutions to the system, we will determine its stability and critical points. We find that

$$(I_H, I_v) = (0,0), (N_H, N_v)$$

are the only two critical points. We can now determine the stability of each by linearizing the system, and looking at the determinant and trace of the Jacobean evaluated at the critical points.

We first let **J0** be the Jacobean of the system in 4.28 and evaluate it at (0,0). This results in the equation below.

$$\mathbf{J0} = \begin{pmatrix} \frac{\dot{I}_h(t)}{dI_h} & \frac{\dot{I}_h(t)}{dI_v} \\ \frac{\dot{I}_v(t)}{dI_h} & \frac{\dot{I}_v(t)}{dI_v} \end{pmatrix} = \begin{pmatrix} \beta N_H(1-\rho) & \beta N_H \rho \\ \beta N_v \rho & \beta N_v(1-\rho) \end{pmatrix} \tag{4.29}$$

The trace and the determinant are calculated as:

$$\begin{aligned} \det(\mathbf{J0}) &= \beta^2 N_H N_v(1-2\rho) \\ \text{trace}(\mathbf{J0}) &= \beta(1-\rho)[N_H + N_v] \end{aligned} \tag{4.30}$$

It is clearly evident that $det(\mathbf{J0}) > 0$ if $\rho < 0.5$ and the $det(\mathbf{J0}) < 0$ if $\rho > 0.5$ and the $trace(\mathbf{J0}) > 0$ for all values of β, ρ N_H and N_v. This indicates that there is always at least one positive eigenvalue. This means that $(0, 0)$ is an unstable node for all values of the parameters.

The Jacobian of the system is evaluated at $(\mathrm{I_H}, \mathrm{I_v}) = (\mathrm{N_H}, \mathrm{N_v})$ is given by

$$\mathbf{JE} = \begin{pmatrix} -\beta[\mathrm{N_H}(1-\rho) + \rho\mathrm{N_v}] & 0 \\ 0 & -\beta[\mathrm{N_v}(1-\rho) + \rho\mathrm{N_H}] \end{pmatrix} \tag{4.31}$$

The determinant and the trace of the Jacobian matrix are:

$$\begin{aligned} \det(\mathbf{JE}) &= \beta^2[\mathrm{N_H}(1-\rho) + \rho\mathrm{N_v}][\mathrm{N_v}(1-\rho) + \rho\mathrm{N_v}] > 0 \\ \mathrm{trace}(\mathbf{JE}) &= -\beta(\mathrm{N_H} + \mathrm{N_v}) < 0 \end{aligned} \tag{4.32}$$

Since $\det(\mathbf{JE}) > 0$ for all values of the parameters, $(\mathrm{N_H} + \mathrm{N_v})$ is a stable critical point.

Graphical Solutions

We will now show graph the solutions to demonstrate the above results, which predict that I_H will approach N_H and move away from zero, and I_v will approach N_v and also move away from 0. In order for Maple to graph the solutions, we must give numerical values to each of the parameters. For the sake of this example, let:

Table 1: Numerical Values for Parameters

Parameters	Numerical Values
N_H	20000
N_v	10000
β	0.05
ρ	0.5
γ	0
λ	0

Altering these parameters above will not change the stability of the critical points. Let's assume the following conditions: $I_H(0) = 2$, $I_v(0) = 3$, $R_H(0) = 0$ and $R_v(0) = 0$. So initially, we 2000 humans infected and 3000 vectors infected. There is none recoveries for humans and vectors. The solutions are plotted using Maple. The following graphs 4 and 4are attained:

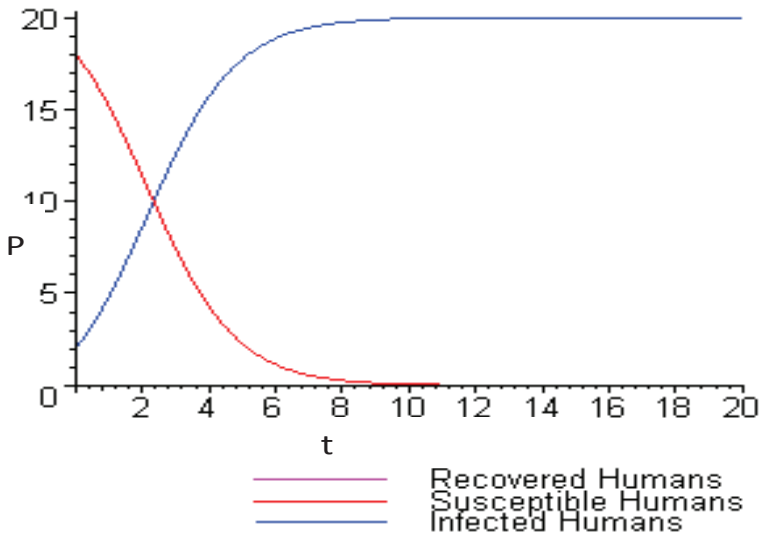

Figure 21: Solutions for Human Population.

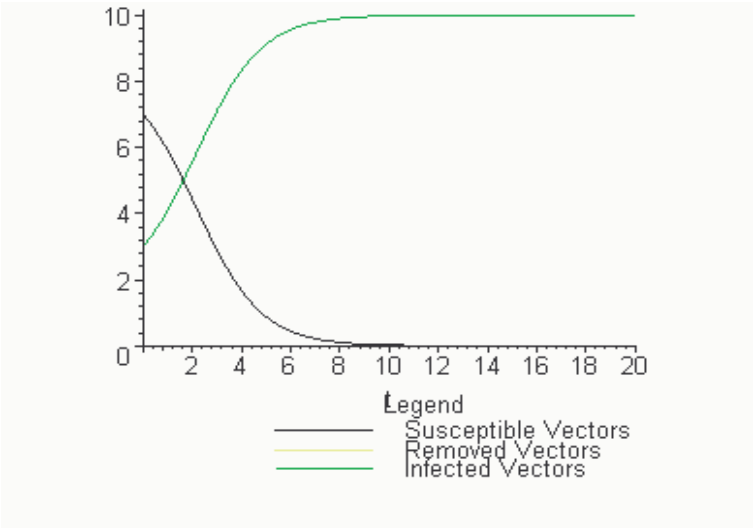

Figure 22: Solutions for Vector Population.

It can clearly be seen that the stable critical point exists at $(I_H, I_v) = (20, 10)$. The phase portrait at $(0, 0)$ in 4is an unstable node.

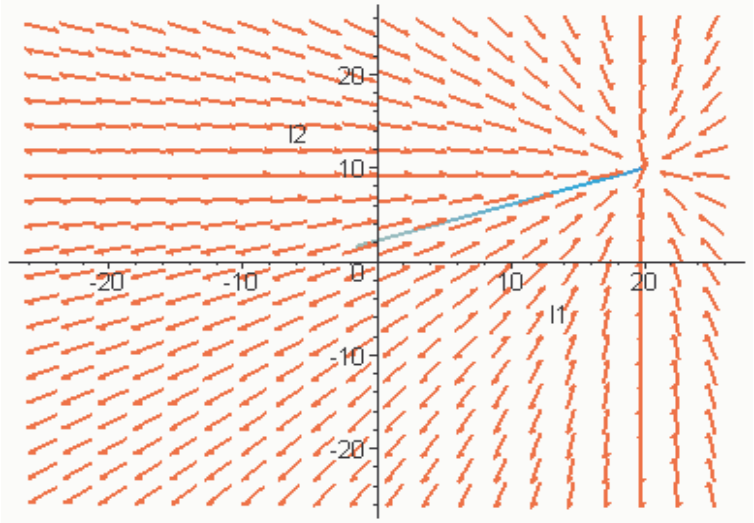

Figure 23: Phase Portrait of I_H vs. I_v.

As long as no humans or vectors are removed, everyone from both populations will eventually become infected. In other words, $S(t)$ asymptotically approaches N and $I(t)$ asymptotically approaches zero regardless of the size of each population, or the values of β and ρ. This is exactly what is expected, and is consistent with the simple SI model for one population.

Infected Humans Recover, No Infected Vectors Removed

($\lambda > 0, \gamma = 0$)

The model is slightly changed here and slightly more complicated. Consider the model where $\lambda > 0$, $\gamma = 0$.

$$\begin{aligned}
\frac{\partial \mathrm{I_H}}{\partial \mathrm{t}} &= \beta(\mathrm{N_H} - \mathrm{I_H} - \mathrm{R_H})[\mathrm{I_H}(1-\rho) + \mathrm{I_v}\rho] - \lambda \mathrm{I_H} \\
\frac{\partial \mathrm{I_v}}{\partial \mathrm{t}} &= \beta(\mathrm{N_v} - \mathrm{I_v})[\mathrm{I_v}(1-\rho) + \mathrm{I_H}\rho] \\
\frac{\partial \mathrm{R_H}}{\partial \mathrm{t}} &= \lambda \mathrm{I_H}
\end{aligned}$$

Solving Equation 4 gives the critical solution points as

$$(\mathrm{I_H}.\mathrm{I_v}, \mathrm{R_H}) = (0, 0, \mathrm{R_H}),\ (0, \mathrm{N_v}, \mathrm{N_H}).$$

We consider the following cases.

Case I: $(\mathrm{I_H}, \mathrm{I_v}, \mathrm{R_H}) = (0, 0, \mathrm{R_H})$, where $\mathrm{R_H}$ is arbitrary

Clearly, we notice that this case can be dismissed as trivial in this particular model. Since, in order to get this critical point, we must set I_v equal to zero for all values of the parameters and other variables, the model becomes almost identical to an original SIR model. In other words, this model accounts for only one species in the system. Since we have a solution to a very similar system looked at in Section 4.2), we simply take the limit as n approaches infinity to get the critical points.

$$\lim_{\mathrm{t}\to\infty} \mathrm{S(t)} = \lim_{\mathrm{t}\to\infty} \mathrm{S(0)} \exp \frac{-\beta}{\lambda}[\mathrm{R(t)} - \mathrm{R(0)}] = \mathrm{S(0)} \exp \frac{-\beta}{\lambda}[\mathrm{R}(\infty) - \mathrm{R(0)}] \tag{4.33}$$

Note that the critical points depend on the stability of R(t), as well as the values of β, λ, $R(0)$ and $S(0)$. It should be noted that exact stability cannot always be determined from a simple analysis of the critical points or even the solution of a system, because of potential dependency on other variables and parameters.

Case II: $(\mathrm{I_H}, \mathrm{I_v}, \mathrm{R_H}) = (0, \mathrm{N_v}, \mathrm{N_H})$

Equation 4.34 gives the Jacobian of the system of Equations 4 evaluated at $(0, N_H, N_v)$.

$$\mathbf{J} = \begin{pmatrix} -\beta \mathrm{N_v}\rho - \lambda & 0 & -\beta \mathrm{N_v}\rho \\ 0 & -\beta \mathrm{N_v}(1-\rho) & 0 \\ \gamma & 0 & 0 \end{pmatrix} \tag{4.34}$$

The determinant and trace of the matrix are found to be

$$\begin{aligned} \det(\mathbf{J}) &= -\lambda\beta^2 \mathrm{N_v^2}\rho(1-\rho) < 0 \\ \mathrm{trace}(\mathbf{J}) &= -\beta \mathrm{N_v} - \lambda < 0 \end{aligned}$$

The trace($\mathbf{J}$) and the det($\mathbf{J}$) are less than zero for all values of the parameters. This implies the eigevalues of this system are negative, which again implies $(0, N_v, N_H)$ is a stable node.

Grapical Simulation

Let's consider the following parameters.

Table 2: Numerical Values for Parameters

Parameters	Numerical Values
N_H	20000
N_v	10000
β	0.05
ρ	0.5
γ	0
λ	0.4

The following graphs are generated based on the initial conditions:

$I_H(0) = 2$, $I_v(0) = 3$, $R_H(0) = 0$ and $R_v(0) = 0$. All these values are in thousand.

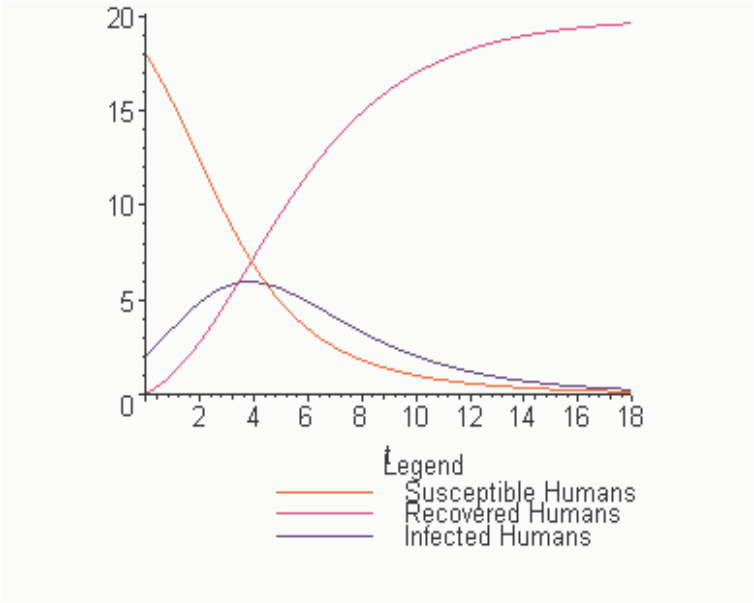

Figure 24: Human Population

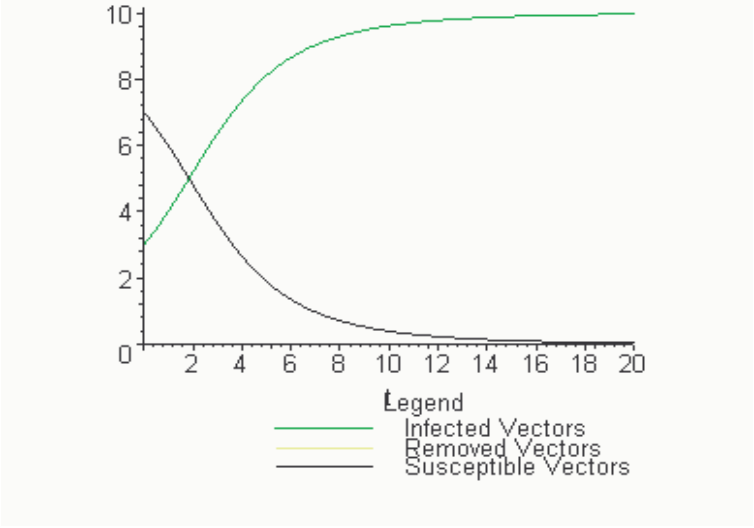

Figure 25: Vector Population

These graphs demonstrate exactly what we predicted. Because no vectors are removed, all vectors eventually become infected, yet since humans can recover and eventually become immune to the disease, the number of human infectives goes to zero.

To further justify these results, it is useful to display a Phase Portrait.

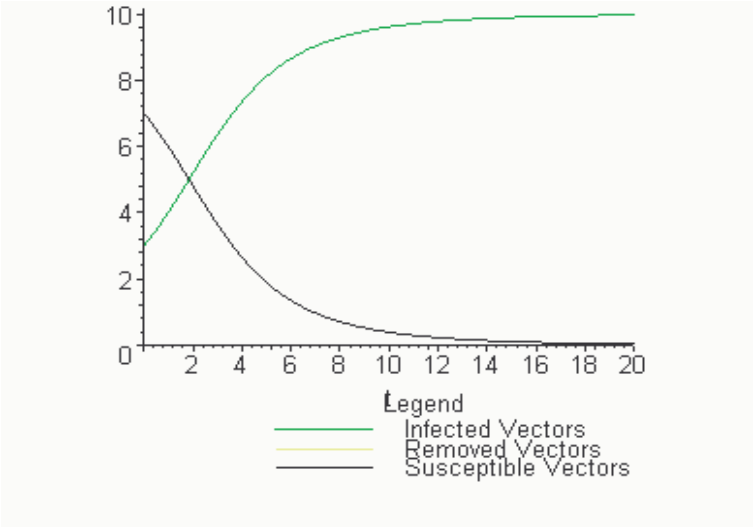

Figure 26: Phase Portrait of I_H and I_v

It can be seen that the solution is an arc, with a stationary point at $(I_H, I_v) = (0, 10)$, as we calculated above. This result is consistent with the other figures we have examined above.

Infected Humans Recover and Infected Vectors Removed.

I.e. $\lambda > 0, \gamma > 0$

Let's consider a model by assuming that a fixed proportion of the infected vectors is removed and a fixed proportion of infected humans recover. The following parameters are defined as follows.

Table 3: Numerical Values for Parameters

Parameters	Numerical Values
N_H	20000
N_v	10000
β	0.05
ρ	0.5
γ	0 .5
λ	0.3

We calculate for the critical points of Equation 4.26. We find that there is only one critical point. at

$$(\mathrm{I_H}, \mathrm{I_v}, \mathrm{R_H}, \mathrm{R_v}) = (0, 0, \mathrm{R_H}, \mathrm{R_v})$$

where R_H and R_v are arbitrary. To do the stability analysis, we first find the Jacobian of the system and evaluate at the critical point.

$$\mathbf{J} = \begin{pmatrix} \beta(\mathrm{N_H} - \mathrm{R_H})(1-\rho) - \lambda & \beta(\mathrm{N_H} - \mathrm{R_H})\rho & 0 & 0 & \\ \beta(\mathrm{N_v} - \mathrm{R_v})\rho & \beta(\mathrm{N_v} - \mathrm{R_v})(1-\rho) - \gamma & 0 & 0 & \\ \lambda & 0 & 0 & 0 & 0 \\ 0 & \gamma & 0 & 0 & \end{pmatrix}$$

From the Jacobian matrix $\mathbf{J}$, the determinant and the trace are:

$$\det(\mathbf{J}) = 0 \tag{4.35}$$

$$\mathrm{trace}(\mathbf{J}) = \beta(\mathrm{N_H} - \mathrm{R_H})(1-\rho) - \lambda + \beta(\mathrm{N_v} - \mathrm{R_v})(1-\rho) - \gamma \tag{4.36}$$

The fact that the determinant of the Jacobean matrix is zero means that there is at least one constant solution. This implies that the critical

point is most likely stable. However, the value of the trace depends on R_H and R_v, which are arbitrary yet indirectly dependent on the values of the other parameters. Such a critical point is very similar to those of the original SIR model, which depended on the initial conditions as well as the other parameters, as was shown in 4.33. We can therefore predicts that I_H and I_v will eventually go to zero, whereas R_H, R_v, S_H and S_v will stabilize at some point between 0 and N, approaching constant asymptotes.

The solutions are represented graphically in Figure 4 and 4 respectively.

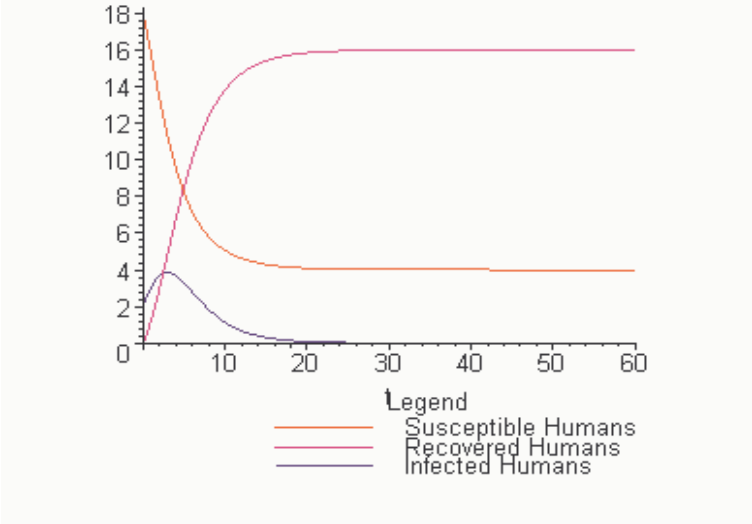

Figure 27: Human Population

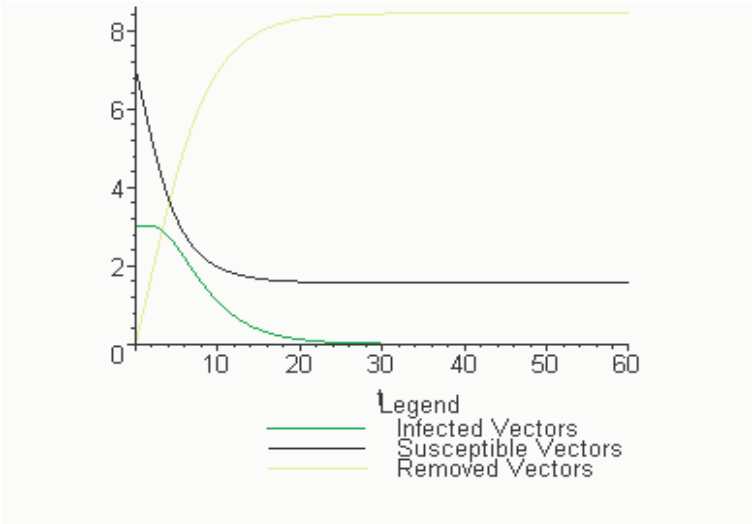

Figure 28: Vector Population

Although it is clear that I_H and I_v approach zero, it is unclear from the graph what asymptotes S(t) and R(t) approach. We can find them by using Maple.

Using Maple and a sequence write out, the stationary points are found to be $R_H = 16$, $S_H = 4$, $S_v = 8.45$, and $R_v = 1.55$. Figures 4 and 4 are the phase portraits of the nodes.

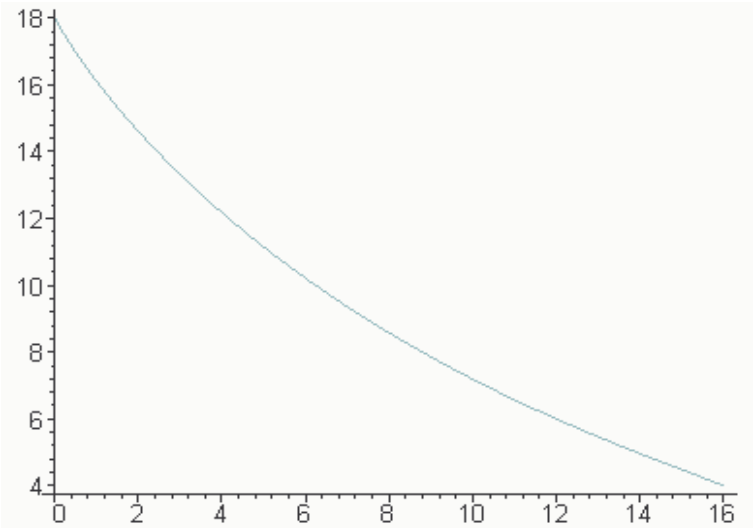

Figure 29: Phase Portrait of R_H against S_H

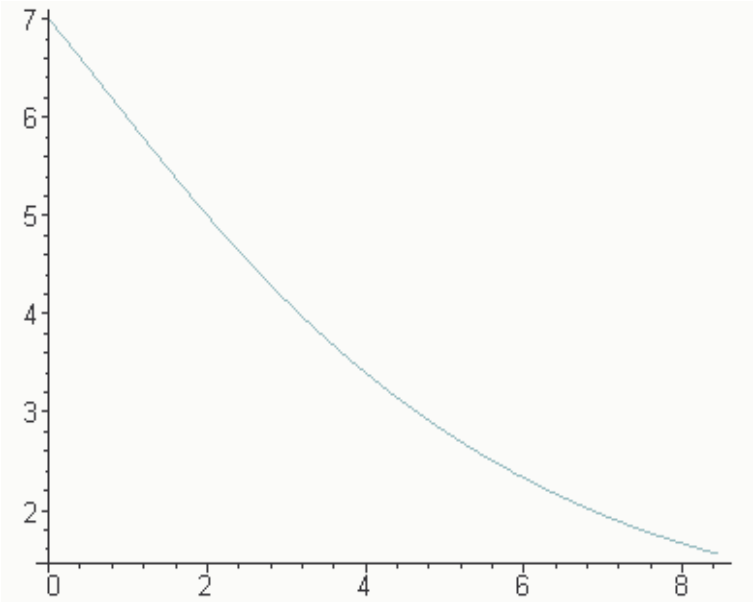

Figure 30: Phase Portrait of R_v against S_v

Changing the Boundary Conditions $I_H(0) = 0$ and $I_v(0) > 0$

In this example, the boundary conditions are changed as follows:

$$\mathrm{I_H}(0) = 0, \mathrm{I_v}(0) = 2, \mathrm{R_H}(0) = 0, \quad \text{and} \quad \mathrm{R_v}(0) = 0.$$

All these values are in thousand. The parameter values are tabled below.

Table 4: Numerical Values for Parameters

Parameter	Value
N_H	20 (in thousand)
N_v	10 (thousand)
ρ	0.5
λ	0.5
γ	0.3

The assumption here is that there are no infected humans initially, but there are some infected vectors. Since the disease can be spread from humans to vectors, our model should illustrate the spread of the disease from one population to the other. As in the previous case, the solutions should be stable, but approach a different asymptote since the initial conditions have been changed.

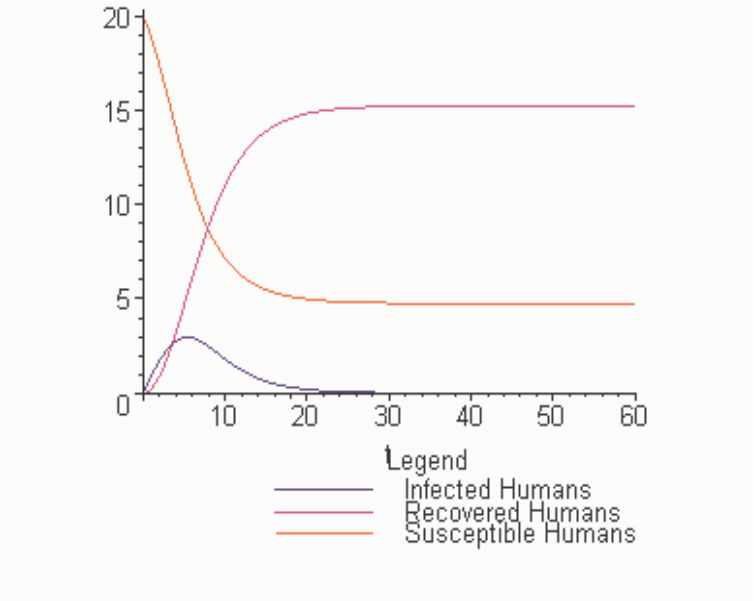

Figure 31: Human Population

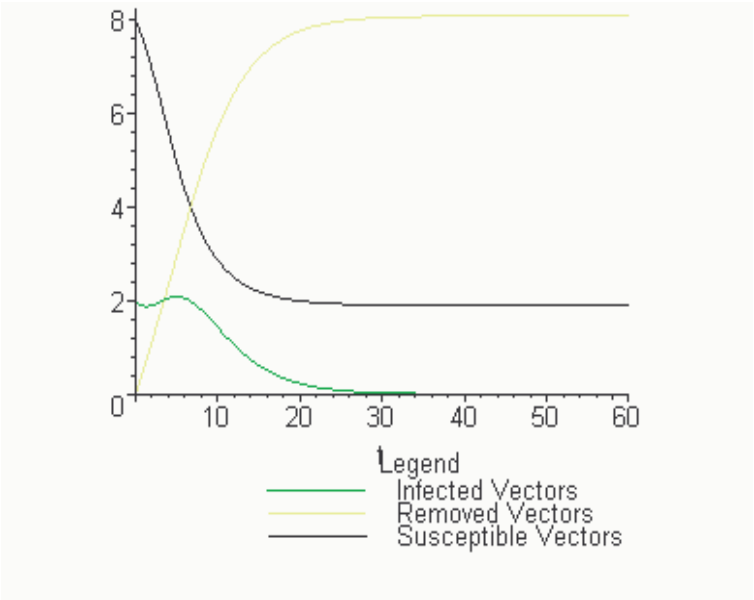

Figure 32: Vector Population

Even though, only one species contracted the disease initially, it ultimately spreads to the other species as well. Because the infected humans can recover and the infected vectors are removed, the number of infectives ultimately goes to zero and the other variables also stabilize. As before, this model makes it impossible for the entire population to become infected.

Changing the Other Parameters

It has become evidently clear that changing the parameters does not change a stable critical point into an unstable one. However, it does change the asymptote that the curves approach, as well as the rate at which they approach it. When the value β is increased , or λ or h are decreased, we find that the value $R(t)$ approaches asymptotically increases. Consequently, the value $S(t)$ approaches asymptotically decreases, because of the relationship between the two variables. This makes sense intuitively: more people have to recover as β, the fixed number of contacts per day sufficient to spread the disease increases and as less infectives of either population are allowd to get better or are removed. The opposite is true when we decrease β or increase λ or γ. Changing ρ influences the slopes of the graphs, but does not contribute to stability. Because the systems for humans and vectors are symmetrical, it does not matter whether N_H or N_v is greater.

Conclusions

Although the vector-host model presented in this paper demonstrates the same kind of stability one might expect after studying the original SIR model, it is important to note that many simplifications have been made. First, the recovery and removal rate are probably influenced by more than the proportion of infectives in each population. Depending on the nature of the disease, it can be difficult, if not impossible, to determine exactly how many infectives there are in a population, especially when the vector population is non-human. Many of the other parameters are also unknown in real life except after the epidemic has done its damage. It should be noted that our vector-host model, as well as the original SIR model, assumes that no one has died from the disease as it is spreading. This is clearly an unrealistic assumption. To further improve the model,

one might want to add another equation to the system in order to account for the death rate of infected individuals.

Despite these and other simplifications, this particular vector-host model is consistent with the original SIR model and useful in predicting overall trends. As we have shown, regardless of the value of each parameter, the variables ultimately stabilize, demonstrating consistency in the overall populations. Like the SIR model, our model makes it impossible for the entire population to become infected, unless no humans recover and no vectors are removed. However, it also demonstrates that it is enough for only one population to possess the disease initially for it to spread to both species, which makes it a superior model. Despite its simplicity, models such as our vector-host model enable officials to make important decisions about public health policy regarding some modern day diseases, such as the AIDS epidemic in Africa. As a result, they can gain a much better understanding of population dynamics, making it possible for something as unpredictable as an epidemic to be controlled and stabilized.

CHAPTER FIVE

MODEL FOR THE CONTROL OF MALARIA

Introduction

Plasmodium falciparum malaria is a major cause of mortality and morbidity in the tropical and subtropical areas of the globe, where around 200 million persons are at constant risk of infection, with some parts of Africa being the worst affected. WHO revealed that malaria kills at least one million people annually in sub-Saharan Africa with the potential to significantly increase in response to climate change (due to the role of temperature and rainfall in the population dynamics of its mosquito vector). Since malaria increases morbidity and mortality, it continues to inflict major public health and socio-economic burdens in developing countries.

In Africa, more than one million children mostly under five years die each year and at least one child dies every 30 second, WHO (2000). Another group who are particularly at risk from malaria are pregnant women. Pregnancy lowers the mothers immunity to malaria, making them more susceptible to infection.

Malaria slows economic growth in Africa by up to 1.3% according to WHO (2000) each year . Its devastating impact has increased massive research efforts to find an effective vaccine that would stop the progression and transmission of malaria. Although there is some optimism about

developing a malaria vaccine, malaria control currently, relies heavily on personal protection. Africa is the worst affected continent in the world.

Malaria cases are also being exacerbated by the high levels of HIV infection, that weaken the immune system rendering people with HIV more susceptible to contracting the disease and it also increases mortality in advanced HIV patients by a factor of about 25% in non-stable malaria areas. It's devastating impact has increased research efforts to find an effective solution(s) that

would stop the progression and transmission of malaria.

Personal protection measures are the first line of defense against mosquito-borne diseases. One of the methods of personal protection is the use of mosquito repellents. These are substances applied to exposed skin or to clothing to prevent human mosquito contact. These only repel but do not kill mosquitoes. The use of insecticide- treated bed nets **(ITNs)** for individuals against malaria has been shown to reduce morbidity of childhood malaria (below five years of age) by 50% and global child mortality by 20-30%. When used on a large scale ITNs are considered to represent efficient tools for malaria vector control. There is however a limiting factor of resistance in the insecticides used for impregnated nets. Resistance of the most important African malaria vector Anopheles **gambiae** to **pyrethroid** is already widespread in several West African countries and most especially Ghana. Government intervention comes in many forms. Some have already been mentioned. Other attempt on the governmental level includes mass spraying to reduce the basic reproduction number below one, and mass spraying of endemic areas to reduce the biting rate of mosquitoes. An adult female mosquito disperses from the water body where she was born and begins a life cycle which is maintained throughout the rest of life, alternating between obtaining a blood meal and **ovipositing** in a water body. Transmission of the malaria parasite to human hosts involves only adult mosquitoes since the larval stages are aquatic and do not feed on

humans.

Human malaria is caused by one of the four species of the genus Plasmodium a protozoan parasite transmitted by the bite of an infected female Anopheles mosquito. The following Plasmodium species are causative agents for malaria in humans: **Plasmodium falciparum**, the most deadly of the human parasites, is the most widespread in the tropics. **Plasmodium vivax** is a major cause of clinical malaria, but rarely fatal. **Plasmodium malariae** infrequently causes clinical malaria, especially in Africa. It can persist as low-grade **parasitaemia** for several decades. **Plasmodium ovale** causes clinically significant but non-fatal disease, but might be found in mixed infections with other species. The infection takes place when an infected mosquito injects **sporozoites** into a human host, which are carried through the blood to the liver within 30 minutes. They invade **hepatocytes** and undergo a process of asexual replication **exoerythrocytic schizogony** to give rise to $10 - 40$ thousand **merozoites** per sporozoite. Up to this point, the infection is non-pathogenic and clinically silent. After about $7 - 9$ days, the liver **schizonts** rupture to release the **merozoites** into the blood. Each merozoite invades an erythrocyte and divides to form an **erythrocytic schizont** containing about 16 daughter merozoites . These merozoites either reinfect fresh erythrocytes, giving rise to cyclical blood-stage infection with a periodicity of $48 - 72h$, depending on the Plasmodium species, or differentiate into sexual transmission stages called gametocytes. The factors that induce gametocyte production are unknown but it has been suggested that merozoites convert into gametocytes when micro-environmental conditions become unfavourable to parasite multiplication.

Partial immunity to malaria confers protection against severe illness without eliminating chronic, mild infections. In endemic areas, children

younger than five years have repeated and often serious attacks of malaria. The survivors develop and maintain partial immunity that reduces the severity of the disease but does not prevent subsequent infections. Thus in these areas older children and adults often have a **symptomatic parasitaemia**, that is, presence of Plasmodia in the blood stream without clinical manifestation. In endemic areas, some people often acquire immunity due to frequent exposure. Epidemiological evidence of immunity to P. falciparum malaria comes from areas with intense transmission. In areas of low malaria transmission, immunity develops slowly and malaria affects all age groups. Incomplete immunity to malaria complicates disease control strategies as the partially immune individuals suffer only mild infections and therefore might not seek medical attention but continue to transmit the parasite in the community. Malaria parasites have different **epitopes** hence partial immunity to one species does not confer immunity to the other species. Even with the same species the various stages exhibit different epitopes such that immunity could be partially conferred against one stage only.

It is important to establish the transmission dynamics of an epidemic in order to understand and predict it. Mathematical models are particularly helpful as experimental tools with which to evaluate and compare control procedures and preventive strategies, and to investigate the relative effects of various sociological, biological and environmental factors on the spread of diseases. These models have played a very important role in the history and development of vector-host epidemiology. Several authors have used mathematical models to analyse the transmission and spread of malaria. Mathematical models of malaria transmission that include both mosquito and human populations have been reviewed and discussed in detail by various authors. Nedelman (1985), did some further work on malaria model of

Dietz *et al.* (1974), and showed that the "inoculation" rate depends on a **pseudoequilibrium** approximation to the differential equation describing the mosquito dynamics in the malaria model.

The aim of this study is to use mathematical modelling to gain some insights into the transmission dynamics of malaria in the population and to explore the various impact of intervention strategies. Details of the formulation of the model are explicitly stated. A diagram of the compartmental model which shows the dynamics of the human and mosquito populations is also included. Conditions for the existence of an endemic equilibrium are established is also given. The reproduction number of the model is determined.The local and global stability of the disease-free equilibrium is carried out. The different cases of strategies are explained in detail. Finally, we give a summary and discuss the results of the study.

The infected humans either acquire some immunity or are susceptible again since immunity to malaria needs continuous exposure to reinfection. They may also die from the disease. Thus our model is based on the susceptible-infective-immune SIRS in human population and SI for the mosquito vector population. The recovery rate corresponds to how quickly parasites are cleared from the human host due to treatment. Thus we have an endemic model to study the dynamics of malaria over long periods as there is a renewal of susceptible humans due to births and immunity loss.

Formulation of the Model

We formulate a model for the spread of malaria in the human and mosquito population with the total population size at time t given by $N_h(t)$ and $N_v(t)$, respectively. These are further compartmentalized into epidemiological classes shown below. The vector component of the model does not include immune class as mosquitoes never recover from infection, that is,

their infective period ends with their death due to their relatively short life-cycle. Thus the immune class in the mosquito population is negligible and death occurs equally in all groups.

Our model has the following variables and parameters:

Table 1: Variables and parameters of the model

Variables and Parameters	Description
S_h	number of susceptible hosts
I_h	the number of infected hosts
R_h	the number of recovered hosts
S_v	the number of susceptible mosquitoes
I_v	the number of infected mosquitoes
b_h	host recruitment rate
b_v	vector recruitment rate
β_h	host contact rate
β_v	vector contact rate
δ_h	disease-induced death rate
d_h	natural death rate of host
d_v	natural death rate of vector
ρ_h	the rate of treatment
ω	rate of loss of immunity in hosts
α	the rate of "inoculation"

Assumptions

The following assumptions are made in order to formulate the equations of the model:

- The development of malaria starts when the infectious female mosquito bites the human host.

- Longevity of the vector is unaffected by the infection.
- The infective population recovers with temporary immunity with clinical treatment.
- Mosquitoes do not die from the infection.
- There is no super infection of the disease.
- All newborns are susceptible to infection.

Schematic Diagram For Malaria Transmission

Figure 1 is a schematic diagram for malaria transmission.

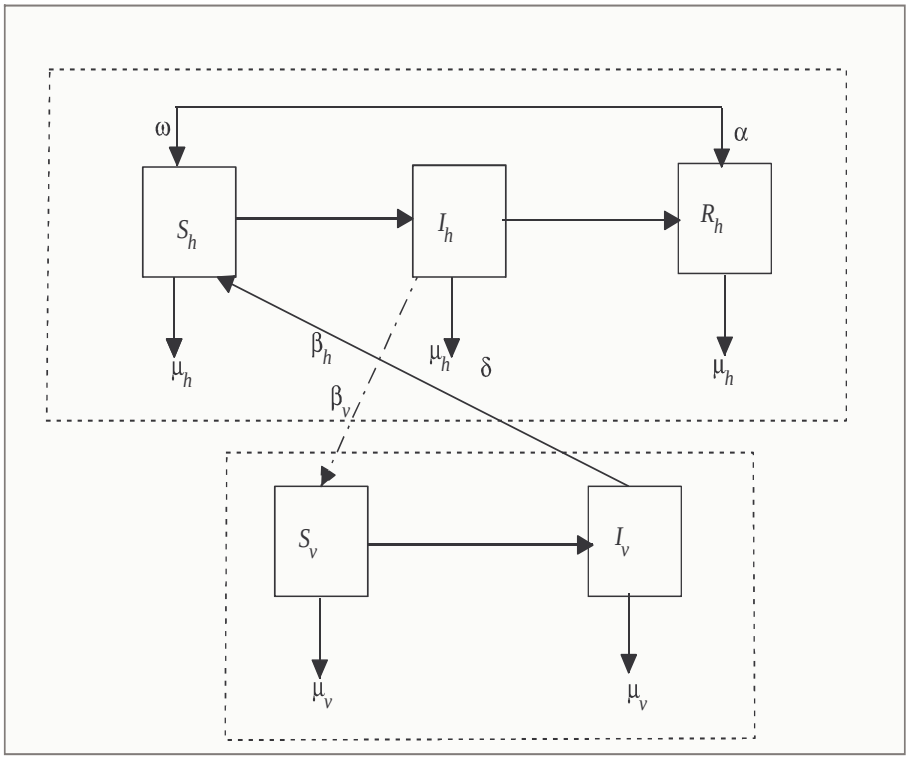

Figure 33: The Compartmental Model for Malaria Transmission.

In the schematic diagram, S_h is the susceptible humans. Susceptible individuals become infected at certain probability when they are bitten by infectious mosquitoes. They then progress through the infected class, I_h, and the recovered class, R_h, before reentering the susceptible class.

Susceptible mosquitoes, S_v, get infected at certain probability when they bite an infectious human. They then move to the infectious, I_v, class. Both species follow a logistic model for their population growth, with humans having additional and disease-induced death.

Equations of the Model

Applying the assumptions, definitions of variables and parameters and description of terms above, the differential equations which describe the dynamics of malaria in the human and mosquito populations are formulated below:

$$\begin{aligned}
\dot{\mathrm{S_h}} &= \mathrm{b_h} - \beta_\mathrm{h}\mathrm{S_h}\mathrm{I_v} - \mathrm{d_h}\mathrm{S_h} + \omega\mathrm{R_h} - \alpha\mathrm{S_h} \\
\dot{\mathrm{I_h}} &= \beta_\mathrm{h}\mathrm{S_h}\mathrm{I_v} - \mathrm{d_h}\mathrm{I_h} - \rho_\mathrm{h}\mathrm{I_h} - \delta_\mathrm{h}\mathrm{I_h} \\
\dot{\mathrm{R_h}} &= \rho_\mathrm{h}\mathrm{I_h} - \mathrm{d_h}\mathrm{R_h} - \omega\mathrm{R_h} + \alpha\mathrm{S_h} \\
\dot{\mathrm{S_v}} &= \mathrm{b_v} - \beta_\mathrm{v}\mathrm{S_v}\mathrm{I_h} - \mathrm{d_v}\mathrm{S_v} \\
\dot{\mathrm{I_v}} &= \beta_\mathrm{v}\mathrm{S_v}\mathrm{I_h} - \mathrm{d_v}\mathrm{I_v}
\end{aligned} \tag{5.1}$$

The total population sizes N_h and N_v can be determined by $\mathrm{S_h} + \mathrm{I_h} + \mathrm{R_h} = \mathrm{N_h}$ and $\mathrm{S_v} + \mathrm{I_v} = \mathrm{N_v}$, or from the following differential equations:

$$\begin{aligned}
\frac{\mathrm{dN_h}}{\mathrm{dt}} &= \mathrm{b_h} - \mathrm{d_h}\mathrm{N_h} - \delta_\mathrm{h}\mathrm{I_h} \\
\frac{\mathrm{dN_v}}{\mathrm{dt}} &= \mathrm{b_v} - \mathrm{d_v}\mathrm{N_v}
\end{aligned}$$

In the model, the term $\beta_h S_h I_v$ denotes the rate at which the susceptible host, S_H become infected by infected mosquitoes, I_v and $\beta_v S_v I_v$ refers to the rate at which the susceptible mosquitoes S_v are infected by infected human hosts I_h. It is important to note that the rate of infection of susceptible host, S_h by infected vector, I_v is dependent on the total number of humans N_h available per infected vector, Ngua and Shu (2000).

The system of Equation 5.1 has a disease-free equilibrium given by

$$\mathbf{E_0} = (\mathrm{S_h^0},\, \mathrm{I_h^0},\, \mathrm{R_h^0},\, \mathrm{S_v^0},\, \mathrm{I_v^0}) = \left(\frac{\mathrm{b_h}(\mathrm{d_h}+\omega)}{\mathrm{d_h}(\mathrm{d_h}+\omega+\alpha)},\, 0,\, \frac{\mathrm{b_h}\alpha}{\mathrm{d_h}+\omega+\alpha},\, \frac{\mathrm{b_v}}{\mathrm{d_v}},\, 0\right). \tag{5.2}$$

and an endemic equilibrium $\mathrm{EE} = \{\mathrm{S_h^1}, \mathrm{I_h^1}, \mathrm{R_h^1}, \mathrm{S_v^1}, \mathrm{I_v^1}\}$ given by

$$\begin{aligned}
\mathrm{S_h^1} &= \frac{\mathrm{A}}{\mathrm{B}} \\
\mathrm{I_h^1} &= \frac{\mathrm{C}}{\mathrm{B}}(\mathcal{R}-1) \\
\mathrm{R_h^1} &= \frac{\mathrm{C}}{\mathrm{B}}\left(\mathrm{G} + \rho\left\{\frac{\mathcal{R}}{\mathrm{d_h}+\omega} - \frac{1}{\mathrm{d_h}+\omega+\alpha}\right\}\right) \\
\mathrm{S_v^1} &= \frac{\mathrm{D}}{\mathrm{E}} \\
\mathrm{I_v^1} &= \frac{\mathrm{C}(\mathcal{R}-1)}{\mathrm{E}}
\end{aligned}$$

where

$$\mathcal{R} = \frac{\beta_\mathrm{h}\beta_\mathrm{v}\mathrm{b_h}\mathrm{b_v}(\mathrm{d_h}+\omega)}{\mathrm{d_h}\mathrm{d_v^2}(\mathrm{d_h}+\omega+\alpha)(\mathrm{d_h}+\rho_\mathrm{h}+\delta_\mathrm{h})}.$$

and

$$\begin{aligned}
\mathrm{A} &= \mathrm{d_v}(\mathrm{d_h}+\rho_\mathrm{h}+\delta)(\mathrm{d_h}\mathrm{d_v}\delta + \mathrm{d_h}\mathrm{d_v}\omega + \mathrm{d_v}\delta\omega \\
&\quad + \mathrm{b_h}\beta_\mathrm{v}\mathrm{d_h} + \mathrm{b_h}\beta_\mathrm{v}\omega + \mathrm{d_h^2}\mathrm{d_v} + \mathrm{d_h}\mathrm{d_v}\rho_\mathrm{h}) \\
\mathrm{B} &= (\mathrm{d_h^3}\mathrm{d_v} + \mathrm{d_h^2}\mathrm{d_v}\rho_\mathrm{h} + \mathrm{d_h^2}\mathrm{b_v}\beta_\mathrm{h} + \alpha\mathrm{d_v}\mathrm{d_h^2} + \mathrm{d_h}\mathrm{b_v}\rho_\mathrm{h}\beta_\mathrm{h} \\
&\quad + \alpha\mathrm{d_v}\mathrm{d_h}\rho_\mathrm{h} + \mathrm{d_h^2}\mathrm{d_v}\omega + \mathrm{d_h}\mathrm{d_v}\rho_\mathrm{h}\omega + \mathrm{d_h^2}\mathrm{d_v}\delta \\
&\quad + \alpha\mathrm{d_v}\mathrm{d_h}\delta + \mathrm{d_h}\delta\mathrm{b_v}\beta_\mathrm{h} + \mathrm{d_h}\omega\mathrm{b_v}\beta_\mathrm{h} + \\
&\quad \omega\delta\mathrm{b_v}\beta_\mathrm{h} + \mathrm{d_h}\mathrm{d_v}\delta\omega)\beta_\mathrm{v} \\
\mathrm{C} &= \mathrm{d_h}\mathrm{d_v^2}(\mathrm{d_h}+\delta+\rho_\mathrm{h})(\alpha+\omega+\mathrm{d_h}) \\
\mathrm{D} &= \mathrm{d_h^3}\mathrm{d_v} + \mathrm{d_h^2}\mathrm{d_v}\rho_\mathrm{h} + \mathrm{d_h^2}\mathrm{b_v}\beta_\mathrm{h} + \alpha\mathrm{d_v}\mathrm{d_h^2} + \mathrm{d_h}\mathrm{b_v}\rho_\mathrm{h}\beta_\mathrm{h} \\
&\quad + \alpha\mathrm{d_v}\mathrm{d_h}\rho_\mathrm{h} + \mathrm{d_h^2}\mathrm{d_v}\omega + \mathrm{d_h}\mathrm{d_v}\rho_\mathrm{h}\omega
\end{aligned}$$

$$
\begin{aligned}
& +\mathrm{d_h^2 d_v}\delta + \alpha \mathrm{d_v d_h}\delta + \mathrm{d_h}\delta \mathrm{b_v}\beta_\mathrm{h} \\
& +\mathrm{d_h}\omega \mathrm{b_v}\beta_\mathrm{h} + \omega\delta \mathrm{b_v}\beta_\mathrm{h} + \mathrm{d_h d_v}\delta\omega \\
\mathrm{E} &= \beta_\mathrm{h}(\mathrm{d_h d_v}\delta + \mathrm{d_h d_v}\omega + \mathrm{d_v}\delta\omega + \mathrm{b_h}\beta_\mathrm{v}\mathrm{d_h} + \mathrm{b_h}\beta_\mathrm{v}\omega \\
& +\mathrm{d_h^2 d_v} + \mathrm{d_h d_v}\rho_\mathrm{h}) \\
\mathrm{G} &= \frac{\alpha(\mathrm{d_v}\delta + \mathrm{d_h d_v} + \beta_\mathrm{v}\mathrm{b_h})}{\mathrm{d_h d_v}(\alpha + \omega + \mathrm{d_h})}
\end{aligned}
$$

Determination of Reproduction Number.

For computation of $\mathcal{R}_0$, it is important to distinguish new infections from all other changes in the population. We let $\mathcal{F}_\mathrm{i}\,(\mathrm{x})$ be the rate of appearance of new infections in compartment i, $\mathcal{V}_\mathrm{i}^{+}$ be the rate of transfer of individuals into compartment i and $\mathcal{V}_\mathrm{i}^{-}\,(\mathrm{x})$ be the rate of transfer of individuals out of compartment i. $\mathrm{D}\mathcal{F}(\mathrm{x}_0)$ is the derivative $\left[\dfrac{\partial \mathcal{F}_\mathrm{i}}{\partial \mathrm{x_j}}\right]$ evaluated at Disease-Free Equilibrium, E_0. In the five-states model 5.1, the disease states are $\mathrm{I_H}$ and $\mathrm{I_v}$.

$$
\mathcal{F} = \begin{bmatrix} \beta_\mathrm{h}\mathrm{S_h I_v} \\ \beta_\mathrm{v}\mathrm{S_v I_h} \end{bmatrix} \text{ and } \begin{bmatrix} (\mathrm{d_h} + \rho_\mathrm{h} + \delta_\mathrm{h})\mathrm{I_h}) \\ \mathrm{d_v I_v} \end{bmatrix}
$$

The differentials of the disease states, $(\mathcal{F})$ and the transfer states, $\mathcal{V}$ with respect to E_0 gives us

$$
\mathcal{DF}(\mathrm{E}_0) = \mathrm{F} = \begin{bmatrix} 0 & \dfrac{\beta_\mathrm{h}(\mathrm{d_h} + \omega)}{\beta_\mathrm{h}(\mathrm{d_h} + \omega + \alpha)} \\ \dfrac{\beta_\mathrm{v}\mathrm{b_v}}{\mathrm{d_h}} & 0 \end{bmatrix}
$$

and

$$
\mathrm{D}\mathcal{V}(\mathrm{E}_0) = \mathrm{V} = \begin{bmatrix} \mathrm{d_h} + \rho_\mathrm{h} + \delta_\mathrm{h} & 0 \\ 0 & \mathrm{d_v} \end{bmatrix}.
$$

The inverse of V is determined as

$$\mathrm{V}^{-1} = \begin{bmatrix} \dfrac{1}{d_h + \rho_h + \delta_h} & 0 \\ 0 & \dfrac{1}{d_v}. \end{bmatrix}.$$

The matrix FV^{-1} is defined as the next generation matrix and usually denoted by the letter K. The spectral radius, $\rho(\mathrm{FV}^{-1})$, is the biggest nonnegative eigenvalue of the next generation matrix . Thus, the basic reproduction number is given by

$$\mathcal{R}_0 = \rho(\mathrm{FV}^{-1}).$$

Thus,

$$\mathcal{R}_0 = \frac{\beta_\mathrm{h}\beta_\mathrm{v}\mathrm{b_h}\mathrm{b_v}(\mathrm{d_h} + \omega)}{\mathrm{d_h}\mathrm{d_v^2}(\mathrm{d_h} + \omega + \alpha)(\mathrm{d_h} + \rho_\mathrm{h} + \delta_\mathrm{h})}.$$

The basic reproduction number, $\mathcal{R}_0$, is an important threshold quantity. It is the expected number of secondary infections that one infectious individual would create over the duration of the infectious period. It is a determining factor as to whether a disease dies out or assumes endemicity.

Existence and Stability of Equilibrium Solutions

In this section, we establish that the disease-free equilibrium E_0 exists if $\mathcal{R}_0 < 1$. We also establish that the endemic equilibrium, E_e exists for $\mathcal{R}_0 > 1$.

Existence and Stability of Disease-Free Equilibrium

Disease-free equilibrium was calculated as

$$\mathbf{E_0} = (\mathrm{S_h^0}, \mathrm{I_h^0}, \mathrm{R_h^0}, \mathrm{S_v^0}, \mathrm{I_v^0}) = \left(\frac{\mathrm{b_h}(\mathrm{d_h} + \omega)}{\mathrm{d_h}(\mathrm{d_h} + \omega + \alpha)}, 0, \frac{\mathrm{b_h}\alpha}{\mathrm{d_h} + \omega + \alpha}, \frac{\mathrm{b_v}}{\mathrm{d_v}}, 0\right). \tag{5.3}$$

The disease-free equilibrium, E_0 exists for all nonnegative values of its parameters.

Theorem 5.1. The disease-free equilibrium E_0 in 5.2 is locally asymptotically stable if and only if, $R_0 \leq 1$, Li *et al.* (1999).

The Jacobian matrix of the system in 5.1 is given by.

$$\mathbf{J} = \begin{bmatrix} -\beta_{\mathrm{h}}\mathrm{I_v} - \mathrm{d_h} - \alpha & 0 & \omega & 0 & -\beta_{\mathrm{h}}\mathrm{S_h} \\ \beta_{\mathrm{h}}\mathrm{I_v} & -\mathrm{d_h} - \rho_h - \delta_h & 0 & 0 & \beta_{\mathrm{h}}\mathrm{S_h} \\ \alpha & \rho_h & -\mathrm{d_h} - \omega & 0 & 0 \\ 0 & -\beta_{\mathrm{v}}\mathrm{S_v} & 0 & -\beta_{\mathrm{v}}\mathrm{I_h} - \mathrm{d_v} & 0 \\ 0 & \beta_{\mathrm{v}}\mathrm{S_v} & 0 & \beta_{\mathrm{v}}\mathrm{I_h} & -\mathrm{d_v} \end{bmatrix}. \tag{5.4}$$

The Jacobian,**J**, evaluated at the disease-free equilibrium is represented in the array 5.5.

$$\mathbf{J}(E_0) = \begin{bmatrix} -\mathrm{d_h} - \alpha & 0 & \omega & 0 & -\dfrac{\beta_{\mathrm{h}}\mathrm{b_h}(\mathrm{d_h} + \omega)}{\mathrm{d_h}(\mathrm{d_h} + \omega + \alpha)} \\ 0 & -\mathrm{d_h} - \rho_{\mathrm{h}} - \delta_{\mathrm{h}} & 0 & 0 & \dfrac{\beta_{\mathrm{h}}\mathrm{b_h}(\mathrm{d_h} + \omega)}{\mathrm{d_h}(\mathrm{d_h} + \omega + \alpha)} \\ \alpha & \rho_h & -\mathrm{d_h} - \omega & 0 & 0 \\ 0 & -\dfrac{\beta_{\mathrm{v}}\mathrm{b_v}}{\mathrm{d_v}} & 0 & -\mathrm{d_v} & 0 \\ 0 & \dfrac{\beta_{\mathrm{v}}\mathrm{b_v}}{\mathrm{d_v}} & 0 & 0 & -\mathrm{d_v} \end{bmatrix}. \tag{5.5}$$

The stability of the disease-free equilibrium state can be obtained from studying the eigenvalues of $\mathbf{J}(E_0)$. If all the eigenvalues have negative real parts, then the equilibrium point is locally asymptotically stable.

The five eigenvalues of $\mathbf{J}(E_0)$ are

- $\lambda_1 = \lambda_4 = -\mathrm{d_h} < 0$
- $\lambda_2 = \mathrm{K}(-\mathrm{B} + \sqrt{\mathrm{C}})$. This may be either negative or positive.

- $\lambda_3 = -\mathrm{K}(\mathrm{B} + \sqrt{\mathrm{C}}) < 0$
- $\lambda_5 = -\mathrm{d_h} - \alpha - \omega < 0$

where

$$\mathrm{K} = \frac{1}{2}\frac{1}{\mathrm{d_v d_h}(\mathrm{d_h} + \omega + \alpha)}, \tag{5.6}$$

$$\begin{aligned}
\mathrm{B} \;=\; & -\alpha \mathrm{d_v d_h}\delta_\mathrm{h} - \mathrm{d_h d_v}\rho_\mathrm{h}\omega - \alpha \mathrm{d_v d_h}\rho_\mathrm{h} - \mathrm{d_h d_v}\delta_\mathrm{h}\omega \\
& -\alpha \mathrm{d_v d_h^2} - \mathrm{d_h^2 d_v}\rho_\mathrm{h} - \mathrm{d_h^2 d_v}\delta - \mathrm{d_h^2 d_v}\omega - \alpha \mathrm{d_v^2 d_h} - \mathrm{d_v^2 d_h^2} \\
& -\mathrm{d_h d_v^2}\omega - \mathrm{d_h^3 d_v}
\end{aligned}$$

and

$$\begin{aligned}
\mathrm{C} = \; & (4\mathrm{d_h^2 d_v}\alpha \mathrm{b_v}\beta_\mathrm{h}\mathrm{b_h}\beta_\mathrm{v} + 4\mathrm{d_h d_v}\omega^2 \mathrm{b_v}\beta_\mathrm{h}\mathrm{b_h}\beta_\mathrm{v} + 8\mathrm{d_h^2 d_v b_v}\beta_\mathrm{h}\mathrm{b_h}\beta_\mathrm{v}\omega \\
& +2\mathrm{d_h^5 d_v^2}\rho_\mathrm{h} - 4\mathrm{d_h^4 d_v^3}\omega + \mathrm{d_h^4 d_v^2}\omega^2 + 2\mathrm{d_h^5 d_v^2}\delta + \alpha^2 \mathrm{d_v^4 d_h^2} - 2\mathrm{d_h^4 d_v^3}\delta \\
& +4\mathrm{d_h^3 d_v b_v}\beta_\mathrm{h}\mathrm{b_h}\beta_\mathrm{v} + 2\alpha \mathrm{d_v^4 d_h^3} + 2\mathrm{d_h^5 d_v^2}\omega + 2\alpha^2 \mathrm{d_v^2 d_h^3}\delta_\mathrm{h} \\
& -2\alpha^2 \mathrm{d_v^3 d_h^3} - 4\alpha \mathrm{d_v^3 d_h^4} + \mathrm{d_h^4 d_v^2}\rho_\mathrm{h}^2 + 2\alpha \mathrm{d_v^2 d_h^5} - 2\mathrm{d_h^4 d_v^3}\rho_\mathrm{h} + \alpha^2 \mathrm{d_v^2 d_h^2}\delta^2 \\
& +2\mathrm{d_h^2 d_v^2}\rho_\mathrm{h}\omega^2\delta_\mathrm{h} + 4\mathrm{d_h^3 d_v^2}\rho_\mathrm{h}\omega\alpha + 4\mathrm{d_h^3 d_v^2}\rho_\mathrm{h}\omega\delta_\mathrm{h} \\
& -4\mathrm{d_h^2 d_v^3}\rho_\mathrm{h}\omega\alpha + 4\alpha \mathrm{d_v^2 d_h^2}\delta_\mathrm{h}\rho_\mathrm{h}\omega + \mathrm{d_h^2 d_v^4}\omega^2 - 2\alpha^2 \mathrm{d_v^3 d_h^2}\delta \\
& -4\alpha \mathrm{d_v^3 d_h^3}\delta + 4\alpha \mathrm{d_v^2 d_h^4}\delta + \mathrm{d_h^2 d_v^2}\rho_\mathrm{h}^2\omega^2 + 2\mathrm{d_h^3 d_v^2}\rho_\mathrm{h}^2\omega \\
& +4\mathrm{d_h d_v}\alpha \mathrm{b_v}\beta_\mathrm{h}\mathrm{b_h}\beta_\mathrm{v}\omega + 2\mathrm{d_h^3 d_v^2}\rho_\mathrm{h}\omega^2 + 2\alpha \mathrm{d_v^4 d_h^2}\omega \\
& +\alpha^2 \mathrm{d_v^2 d_h^4} + 2\mathrm{d_v^4 d_h^3}\omega + 2\alpha^2 \mathrm{d_v^2 d_h^2}\delta_\mathrm{h}\rho_\mathrm{h} + 2\alpha \mathrm{d_v^2 d_h^2}\delta^2\omega \\
& +4\alpha \mathrm{d_v^2 d_h^3}\delta_\mathrm{h}\rho_\mathrm{h} + 4\alpha \mathrm{d_v^2 d_h^3}\delta_\mathrm{h}\omega - 4\alpha \mathrm{d_v^3 d_h^2}\delta\omega \\
& +2\alpha \mathrm{d_v^2 d_h^3}\delta^2 + 2\mathrm{d_h^4 d_v^2}\rho_\mathrm{h}\delta - 4\alpha \mathrm{d_v^3 d_h^3}\rho_\mathrm{h} + 4\alpha \mathrm{d_v^2 d_h^4}\rho_\mathrm{h} + \mathrm{d_h^2 d_v^2}\delta^2\omega^2 \\
& +2\mathrm{d_h^3 d_v^2}\delta^2\omega + 2\mathrm{d_h^3 d_v^2}\delta\omega^2 - 4\mathrm{d_h^3 d_v^3}\delta\omega - 2\mathrm{d_h^2 d_v^3}\delta\omega^2 \\
& +4\mathrm{d_h^4 d_v^2}\delta_\mathrm{h}\omega + 2\alpha \mathrm{d_v^2 d_h^4}\omega - 4\alpha \mathrm{d_v^3 d_h^3}\omega + 4\mathrm{d_h^4 d_v^2}\rho_\mathrm{h}\omega \\
& +\alpha^2 \mathrm{d_v^2 d_h^2}\rho_\mathrm{h}^2 + 2\alpha^2 \mathrm{d_v^2 d_h^3}\rho_\mathrm{h} + 2\alpha \mathrm{d_v^2 d_h^3}\rho_\mathrm{h}^2 - 2\alpha^2 \mathrm{d_v^3 d_h^2}\rho_\mathrm{h} - 2\mathrm{d_h^3 d_v^3}\omega^2 \\
& +2\mathrm{d_h^2 d_v^2}\rho_\mathrm{h}^2\omega\alpha - 4\mathrm{d_h^3 d_v^3}\rho_\mathrm{h}\omega - 2\mathrm{d_h^2 d_v^3}\rho_\mathrm{h}\omega^2 + \mathrm{d_h^4 d_v^2}\delta^2 \\
& +\mathrm{d_v^4 d_h^4} - 2\mathrm{d_v^3 d_h^5} + \mathrm{d_h^6 d_v^2})^{\frac{1}{2}}
\end{aligned} \tag{5.7}$$

The condition for λ_2 to be negative is that $-B + \sqrt{C} < 0$, that is

$$\mathrm{B}^2 - \mathrm{C} > 0. \tag{5.8}$$

Equation 5.8 simplifies to

$$4(\mathrm{d_h} + \omega + \alpha)\mathrm{d_h}\mathrm{d_v}\{\mathrm{d_h}\mathrm{d_v^2}(\mathrm{d_h} + \rho_\mathrm{h} + \delta_\mathrm{h}) - \mathrm{b_v}\mathrm{b_h}\beta_\mathrm{h}\beta_\mathrm{v}(\mathrm{d_h} + \omega + \alpha)\} > 0. \tag{5.9}$$

Further simplification leads to

$$\frac{\mathrm{b_v}\mathrm{b_h}\beta_\mathrm{v}\beta_\mathrm{h}(\mathrm{d_h} + \omega)}{\mathrm{d_h}\mathrm{d_v^2}(\mathrm{d_h} + \delta_\mathrm{h} + \rho_\mathrm{h})(\alpha + \omega + \mathrm{d_h})} < 1. \tag{5.10}$$

The expression on the LHS of Equation 5.10 is $\mathcal{R}_0$, the basic reproduction number. Therefore,

$$\mathcal{R}_0 = \frac{\mathrm{b_v}\mathrm{b_h}\beta_\mathrm{v}\beta_\mathrm{h}(\mathrm{d_h} + \omega)}{\mathrm{d_h}\mathrm{d_v^2}(\mathrm{d_h} + \delta_\mathrm{h} + \rho_\mathrm{h})(\alpha + \omega + \mathrm{d_h})} < 1. \tag{5.11}$$

From theorem 5.1, it has been proven that the disease-free equilibrium is asymptotically stable if $R_0 < 1$.

Existence of the Endemic Equilibrium

Theorem 5.2. The endemic equilibrium, E_e exists if $\mathcal{R}_0 > 1$.

Proof. The endemic equilibrium point given in Equation 5.3 from which theorem follows. We examine the following cases to establish the existence of the endemic equilibrium.

- **Case I:**

  Invoking the positivity condition in the case of $\mathrm{I_h^1}$ and $\mathrm{I_v^1}$, it can clearly be verified that $R > 1$.

- **Case II:**

  In the case of R_h^1, we have a different situation. Here

  $$\frac{\mathrm{R}_0}{\mathrm{d_h}+\omega}-\frac{1}{\mathrm{d_h}+\omega+\alpha}>0.$$

  If $\mathrm{R}=1$, $\dfrac{1}{\mathrm{d_h}+\omega}>\dfrac{1}{\mathrm{d_h}+\omega+\alpha}$. If $R>1$, the inequality still holds. Therefore, the endemic equilibrium exists if $R>1$. Clearly, the components of R are the same as $\mathcal{R}_0$. Thus, the endemic equilibrium exists if $\mathcal{R}_0>1$.

□

Global Asymptotic Stability of the Disease-Free Equilibrium Point

Theorem 5.3. The disease-free equilibrium, E_0 is globally asymptotically stable if $\mathcal{R}_0 \leq 1$

Given that $\mathcal{R}_0 \leq 1$, then there exist only the disease-free equilibrium.

Proof

At the disease-free equilibrium, E_0, the following conditions hold.

$$\begin{aligned}
\mathrm{b_h} &= \beta_\mathrm{h}\bar{\mathrm{S}}_\mathrm{h}\bar{\mathrm{I}}_\mathrm{v}-\mathrm{d_h}\bar{\mathrm{S}}_\mathrm{h}+\omega\bar{\mathrm{R}}_\mathrm{h}-\alpha\bar{\mathrm{S}}_\mathrm{h}\\
\alpha\bar{\mathrm{S}}_\mathrm{h}+\rho_\mathrm{h}\bar{\mathrm{I}}_\mathrm{h} &= (\mathrm{d_h}+\omega)\bar{\mathrm{R}}_\mathrm{h}\\
\mathrm{b_h}-\delta_\mathrm{h}\bar{\mathrm{I}}_\mathrm{h} &= \mathrm{d_h}\bar{\mathrm{N}}_\mathrm{h}\\
\beta_\mathrm{h}\bar{\mathrm{S}}_\mathrm{h}\bar{\mathrm{I}}_\mathrm{v} &= (\mathrm{d_h}+\rho_\mathrm{h}+\delta_\mathrm{h})\bar{\mathrm{I}}_\mathrm{h}\\
\mathrm{b_v} &= \beta_\mathrm{v}\bar{\mathrm{S}}_\mathrm{v}\bar{\mathrm{I}}_\mathrm{h}+\mathrm{d_v}\bar{\mathrm{S}}_\mathrm{v}\\
\beta_\mathrm{v}\bar{\mathrm{S}}_\mathrm{v}\bar{\mathrm{I}}_\mathrm{h} &= \mathrm{d_v}\bar{\mathrm{I}}_\mathrm{v}
\end{aligned}$$

Let's now consider a Lyapunov function candidate

$\mathrm{V}(\mathrm{S_h},\mathrm{I_h},\mathrm{R_h},\mathrm{S_v},\mathrm{I_v}):\quad \boldsymbol{R}^5 \longrightarrow \boldsymbol{R}^+$ defined as

$$\frac{1}{2}(\mathrm{S_h}-\bar{\mathrm{S}}_\mathrm{h})^2+\frac{1}{2}(\mathrm{I_h}-\bar{\mathrm{I}}_\mathrm{h})^2+\frac{1}{2}(\mathrm{R_h}-\bar{\mathrm{R}}_\mathrm{h})^2+\frac{1}{2}(\mathrm{S_v}-\bar{\mathrm{S}}_\mathrm{v})^2+\frac{1}{2}(\mathrm{I_v}-\bar{\mathrm{I}}_\mathrm{v})^2.$$

Differentiating the Lyapunov function, V gives

$$\dot{\mathrm{V}}=(\mathrm{S_h}-\bar{\mathrm{S}}_\mathrm{h})\dot{\mathrm{S}}_\mathrm{h}+\mathrm{I_h}\dot{\mathrm{I}}_\mathrm{h}+(\mathrm{R_h}-\bar{\mathrm{R}}_\mathrm{h})\dot{\mathrm{R}}_\mathrm{h}+(\mathrm{S_v}-\bar{\mathrm{S}}_\mathrm{v})\dot{\mathrm{S}}_\mathrm{v}+\mathrm{I_v}\dot{\mathrm{I}}_\mathrm{v}+(\mathrm{N_h}-\bar{\mathrm{N}}_\mathrm{h})\dot{\mathrm{N}}_\mathrm{h}.$$

Imposing the conditions on $\dot{V}$, gives the following equation.

$$\begin{aligned}
\dot{\mathrm{V}} &= (\mathrm{S_h}-\bar{\mathrm{S}}_\mathrm{h})[\beta_\mathrm{h}\bar{\mathrm{S}}_\mathrm{h}\bar{\mathrm{I}}_\mathrm{v}-\mathrm{d_h}\bar{\mathrm{S}}_\mathrm{h}+\omega\bar{\mathrm{R}}_\mathrm{h}-\alpha\bar{\mathrm{S}}_\mathrm{h}\\
&\quad -(\beta_\mathrm{h}\mathrm{S_h}\mathrm{I_v}-\mathrm{d_h}\mathrm{S_h}+\omega\mathrm{R_h}-\alpha\mathrm{S_h})]\\
&\quad +\mathrm{I_h}[(\mathrm{d_h}+\rho_\mathrm{h}+\delta_\mathrm{h})\bar{\mathrm{I}}_\mathrm{h}-(\mathrm{d_h}+\rho_\mathrm{h}+\delta_\mathrm{h})\mathrm{I_h}]\\
&\quad +(\mathrm{R_h}-\bar{\mathrm{R}}_\mathrm{h})[(\mathrm{d_h}+\omega)\mathrm{R_h}-(\mathrm{d_h}+\omega)\bar{\mathrm{R}}_\mathrm{h}]\\
&\quad +(\mathrm{N_h}-\bar{\mathrm{N}}_\mathrm{h})[\mathrm{d_h}\bar{\mathrm{N}}_\mathrm{h}-\mathrm{d_h}\mathrm{N_h}]\\
&\quad +(\mathrm{S_v}-\bar{\mathrm{S}}_\mathrm{v})[\beta_\mathrm{v}\bar{\mathrm{S}}_\mathrm{v}\bar{\mathrm{I}}_\mathrm{h}-\mathrm{d_v}\bar{\mathrm{S}}_\mathrm{v}-(\beta_\mathrm{v}\mathrm{S_v}\mathrm{I_h}-\mathrm{d_v}\mathrm{S_v})]\\
&\quad +\mathrm{I_v}(\mathrm{d_v}\bar{\mathrm{I}}_\mathrm{v}-\mathrm{d_v}\mathrm{I_v})
\end{aligned}$$

Finally,

$$\begin{aligned}
\dot{\mathrm{V}} &= \bar{\mathrm{S}}_\mathrm{h}(\beta_\mathrm{h}\bar{\mathrm{I}}_\mathrm{v}+\mathrm{d_h}+\alpha)-\mathrm{S_h}(\beta_\mathrm{h}\mathrm{I_v}+\mathrm{d_h}+\alpha)\\
&\quad -\mathrm{I_h}(\mathrm{I_h}-\bar{\mathrm{I}}_\mathrm{h})(\mathrm{d_h}+\rho_\mathrm{h}+\delta_\mathrm{h})\\
&\quad -(\mathrm{R_h}-\bar{\mathrm{R}}_\mathrm{h})^2(\mathrm{d_h}+\omega)\\
&\quad -(\mathrm{N_h}-\bar{\mathrm{N}}_\mathrm{h})^2\mathrm{d_h}\\
&\quad -(\mathrm{S_v}-\bar{\mathrm{S}}_\mathrm{v})[\mathrm{S_v}(\beta_\mathrm{v}\mathrm{I_h}+\mathrm{d_v})-\mathrm{barS_v}(\beta_\mathrm{v}\bar{\mathrm{I}}_\mathrm{h}+\mathrm{d_v})]\\
&\quad -\mathrm{I_v}(\mathrm{d_v}\mathrm{I_v}-\mathrm{d_v}\bar{\mathrm{I}}_\mathrm{v})
\end{aligned}$$

The following assumptions are made for the Lyapunov function, $\dot{V}$ above.

- $\bar{S}_h(\beta_h \bar{I}_v + d_h + \alpha) - S_h(\beta_h I_v + d_h + \alpha)$ is negative provided $I_v > \bar{I}_v$. This condition also makes $-I_v(d_v I_v - d_v \bar{I}_v)$ negative.

- $-I_h(I_h - \bar{I}_h)(d_h + \rho_h + \delta_h)$ is negative if $I_h > \bar{I}_h$. This condition when applied to $-(S_v - \bar{S}_v)[S_v(\beta_v I_h + d_v) - \bar{S}_v(\beta_v \bar{I}_h + d_v)]$ makes it negative.

- It is also assumed that $R_h = \bar{R}_h$.

Note that the quantities $\bar{S}_h$, $\bar{I}_h$, $\bar{R}_h$, $\bar{S}_v$, and $\bar{I}_v$ are the disease-free equilibrium states.
Thus, we have shown that $\dot{V} \leq 0$ provided $S_h > \bar{S}_h$, $I_h > \bar{I}_h$, $I_v > \bar{I}_v$ and $S_v > \bar{S}_v$.

It is important to note that, $\dot{V} = 0$ only at the disease-free equilibrium point E_0.

Numerical Simulations

The two main strategies that will be consider for controlling the infectious disease, malaria are:

- a reduction in the number of infected humans and

- a reduction in the number of susceptibles humans through a program of preventative measures.

Our simulations examine the effect of different combinations of treatment and preventative measures on the transmission of the disease.

Clinical Treatment with Control

In this section, we analyse the model formulated in terms of proportions. We determine the effect of treatment on the infected populations. The

diagram below, analyses the effect on increasing the treatment rate at some level of "inoculation".

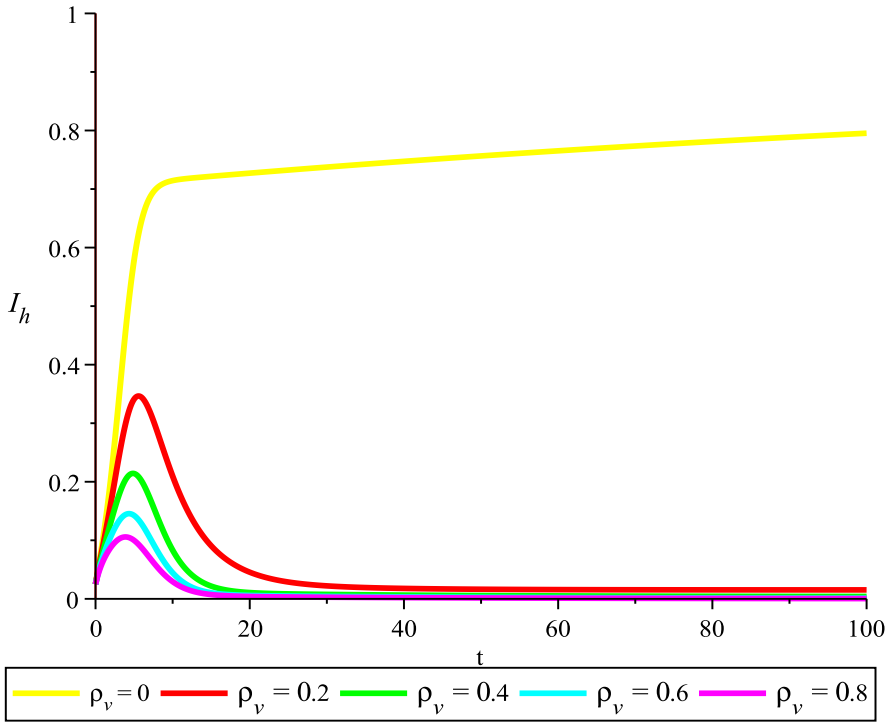

Figure 34: Effects of different rate of treatment on I_h

From Figure 34, it can be observed that, holding the "inoculation" rate constant at 10% and increasing treatment rate from 20% through to 80% decreases the number of infected humans, from 0.7 to 0.175 through 0.375, 0.275, and 0.2 respectively. Let's now consider the impact of treatment on the infected vector.

Impact of Clinical Treatment on the Infected Mosquito

The effect of different treatment rate on the infected vector can be seen in Figure 1.

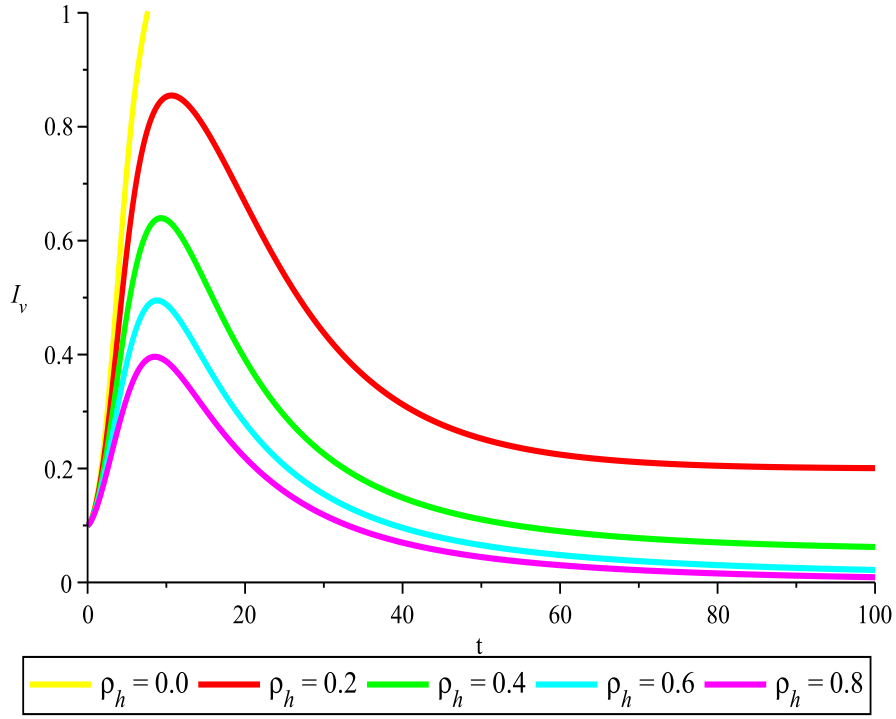

Figure 35: Effects of different rate of treatment on I_v.

In Figure 35, we examine the effect of increasing the treatment rate of the infected human, on the infected mosquito, I_v . It can be observed that, holding the "inoculation" rate constant at 10% and increasing treatment rate from 20% through to 80% decreases the number of infectives, from 0.7 to 0.175 through 0.375, 0.275, and 0.2. The implication is that the susceptible mosquitoes find it difficult to find an infected human to bite. The cycle continues, thereby decreasing their population in the long run. The end result is a malaria-free society.

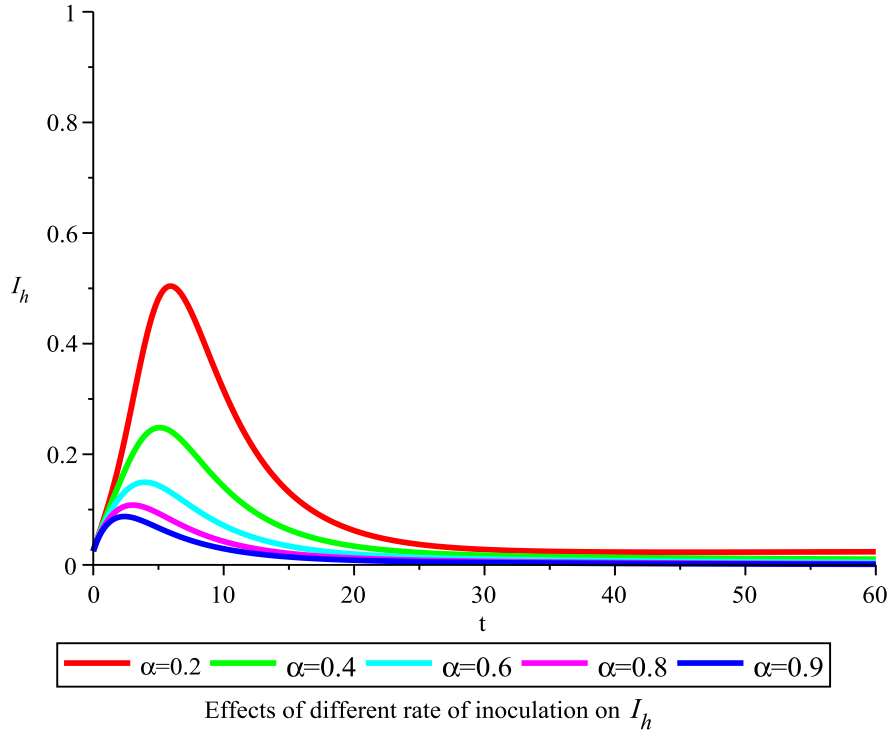

Figure 36: Effects of different rate of "inoculation" α on I_h.

The figure above, shows the effect of "inoculation" on the infected human populatio. Holding treatment rate 10%, the "inoculation" from 0.2 to 0.4, the infected humans population dropped from 0.5 o 0.25. Consequently after successfully reducing the "inoculation" to 0.8, reduces the number of infected humand to just 0.1. Another observation is that increasing the rate of "inoculation" decreases the infected human population at an increasing.

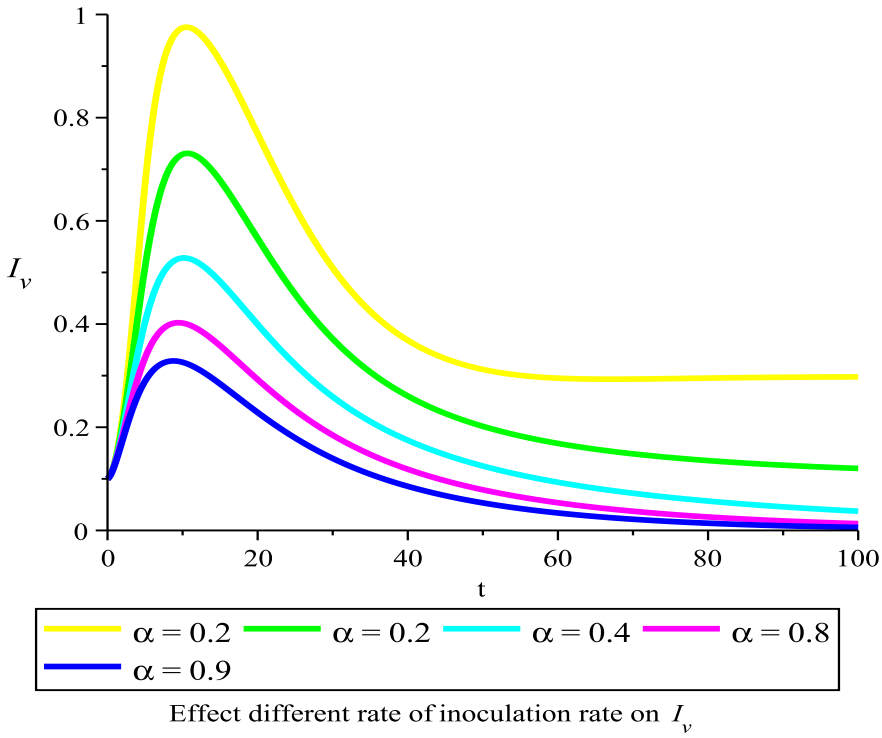

Figure 37: Effects of different rate of "inoculation" on I_v.

In Figure 37, we display the effect of various rates of "inoculation" on the infected mosquito population. The Figure shows that increasing the rate of human "inoculation" decreases the infected mosquito population. With an "inoculation" rate of 0.2, the number of infected mosquitoes drop to 0.975. Additionally, increasing the "inoculation" rate to 0.4 yields a significant drop in the proportion of infected mosquitoes. This means that there will be less infected mosquitoes and less susceptible humans to propagate the disease.

On the other hand, if "inoculation" is carried out to cover at least 50%, and treatment rate held at 20%, malaria cases in this country will be brought to the barest minimum. This will mean that less infectious humans will be available for susceptible mosquitoes to become infectious. Thus, the existence of mosquitoes will not necessarily increase the rate of malaria infection. There are many places in the world where mosquitoes abound but has not yet recorded malaria cases. Such places include Cape

Town in South Africa and Maryland in USA.

CHAPTER SIX

SUMMARY, DISCUSSION, AND CONCLUSION

In this section, we put forward the summary, discussion and conclusion

Summary

Mathematically, we modeled malaria as a 5−dimensional system of ordinary differential equations that depicted an epidemic model. We proved the existence of two equilibria points : Disease-free (E_0) and Endemic equilibrium (E_e) points.

We calculated the basic reproductive number for malaria, using the Next Generation Method . We defined the reproductive number to be $\mathcal{R}_0$, and is epidemiologically accurate in that it provides the expected number of new infections in humans from one infectious individual over the duration of the infectious period given that all other members of the population are susceptible. We showed that, assuming $\mathcal{R}_0 < 1$, then the disease-free equilibrium point, is locally asymptotically stable; and if $\mathcal{R}_0 > 1$ then DFE point is unstable. On the other hand the endemic equilibrium is stable if $\mathcal{R}_0 > 1$ and unstable otherwise. When the value of $\mathcal{R}_0$ gets larger it becomes more difficult to control the infection of the population.

Discussion

We derived and analyzed a mathematical model for the transmission and spread of malaria. We have shown that the model has both a disease-free and endemic equilibria. The disease-free equilibrium is locally and globally
asymptotically stable, if $R_0 \leq 1$, and that the endemic equilibrium exist provided $R_0 > 1$.
Simulation of the model clearly shows that, with a proper combination of treatment and a concerted effort aimed at prevention, malaria can be eliminated.

In chapter three, we looked at the effect of "inoculation" on the susceptible human class of a generic SIR model. It was observed that, gradually increasing the "inoculation" rate, decreases the number of infectives at an increasing. It was concluded that increasing "inoculation" alone will wipe out the disease from the community.

In chapter five, we constructed an SIR host and SI vector model for malaria disease which is different from the SIR model in chapter three. For this model, inoculating the S class alone may not be necessary to wipe the disease. In fact, an effective treatment offered to about 50% of the infected population, together with about 50% prevention rate is all that is required to eliminate the disease.

Among the parameters that we can control, the most sensitive parameter is α and ρ_h. The parameter α was the "inoculation" rate. Here, the aim was to reduce the total number of susceptible individuals by way of "inoculation". The effect was that a proportion of the susceptible population was "removed" through "inoculation" against the possible re-infection of the susceptible population. From the analysis, a 50% "inoculation" coupled with 50% treatment rate of the population

reduced the incidence of malaria to the barest minimum.

Conclusions and Suggestions

In this dissertation, we have analyzed the qualitative relationship between the control strategies and the parameters. A future goal is to quantitatively relate the control strategies to the parameters and to include the cost of the control strategies to directly relate the reduction in disease prevalence and transmission to the cost involved. Other future goals include improving the model to capture important features of malaria and transmission that our model does not include. We list some of these below.

- Seasonal effects: Seasonally varying environmental effects, such as rainfall, temperature, and humidity, affect many of the important factors in malaria transmission. These environment-dependent parameters include the mosquito birth rate, μ_v, mosquito death rates, different from birth rate. In this model we assumed the birth and death rate to be equivalent. We can model these seasonal effects by making some of these parameters periodic functions of time. Analyzing this periodically-forced model, including changes in the reproductive number and endemic states, would provide a more accurate picture of malaria transmission than is currently obtained from models using parameter values that are averaged over the seasons.

- Interactions between mosquitoes and humans: Currently it assumed that the number of bites per mosquito is fixed, while the number of bites per human changes depending on the number of mosquitoes. For a more accurate description of mosquito-human interaction, the

total number of bites between mosquitoes and humans would need to depend on the densities of both populations.

- Super-infection: Similar to other infections caused by macroparasites, malaria displays some properties of superinfection where reinfection when one is already infected can worsen the effects of the disease. We can include this in our model by making the recovery rate, γ, a function of the "inoculation" rate, α.

- Age structure: Age structure is important in the dynamics of malaria, as most deaths occur in infants and the average parasitemia levels of infected individuals decreases with age. Immune response also changes with age. Adding age structure also allows us to study the effects of the various control strategies on the age strata of disease prevalence. We can model age structure, either through discrete age groups or continuously through converting the system of equations to partial differential equations.

- Finally, it should be possible to validate this model by applying it to a smaller population, and then to a larger portion of the country, Ghana. This will allow us to make informed decisions about the level of intervention strategies ,"inoculation", that provide the most effective way of minimizing the incidence of malaria.