OPTIMAL CONTROL and QUALITATIVE ANALYSIS USING EPIDEMIOLOGICAL MODEL for LUMPY SKIN DISEASE (LSD)

Thesis

Submitted to
The College of Natural and Computational Sciences
Addis Ababa University

In Partial Fulfillment of the Requirements for
The Degree of
Master of Science in Computational Science

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October 15, 2017

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Abstract

Lumpy skin disease (LSD) is an infectious, eruptive, now and then mortal disease of cattle. Generally it is skin disease which is caused by a virus of the family Poxviridae. LSD disease damages cattle's hides, because of this it has economically importance. As a result of seriously affected animals by the disease there exist losses of weight, as a result of inflammation temporary or permanent reduction of milk production, as a consequence of orchitis temporary or permanent infertility or even sterility in bulls, and abortion in approximately 10 % of infected pregnant [10],(Birhanu,H. and Gezahign,A.,[5].

The study was undertaken to investigate outbreaks of lumpy skin disease (LSD), based on the research that had been taken by researchers on this area and model for controlling optimally. We used epidemiological model and Optimal control for the analysis of transmission of disease and the cost of control (vaccination). Mainly this thesis focus on the process for analyzing and computationally illustrate for optimally controlling of disease, and its factors.

Key Words:- LSD, Optimal Control, Vaccine efficacy, Lumpy skin; Viral infection; Epidemiology, Risk Factors, Epidemic, SIR, SEIR, SIS, Autonomous, Eigenvalues

Acknowledgment

First of all, I would like to praise the almighty God. His goodness and mercy make me alive. The completion of this work is not the result of my own effort only. It is the result of assistance of my lord, Jesus and the help of Saint Mary.
Second, I would like to express my sincere thanks to my advisor,Prof. Okey Oseloka Onyejekwe, who has dedicated his all effort in guiding and given his supportive and constructive comments with direction to write my study from the beginning to he end.
I would also like to express my gratitude to my families, colleagues, friends and all who had contributed for the realization of this thesis. May God bless you all!

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Chapter One

1 Introduction

Lumpy Skin Disease (LSD) is a viral high economic loss disease due to acute debility in affected animals, reduce milk production, poor growth, infertility, abortion, and sometimes death. The clinical syndrome of LSD was first described in Zambia in 1929, more cases also occur between 1943 and 1945 in Botswana, Zimbabwe and the republic of South Africa, (Hawsar,Y.A., et al., [1] and Birhanu, H., et al., [4]). The disease transmitted through biting flies. The occurrence of LSD is high during wet seasons,(RGBE,H., [2]. According to (RGBE,H.,) Thesis, Lumpy skin disease is a pox disease of cattle characterized by fever, nodules on the skin, mucous membranes and internal organs, emaciation, enlarged lymph nodes, odema of the skin, and sometimes death (Alaa, et al., [3]). In Ethiopia lumpy skin disease was first observed in the northwestern part of the country (southwest of lake Tana) in 1983.

1.1 Motivation

According to researchers, ([1],[2],[3]), LSD occurs in all agro-climatic conditions and has the potential to extend its boundaries. It is transmitted by insect vectors among the cattle sharing similar grazing and watering areas and those congregate in the same area. Good understanding of epidemiology, economic significance and control mechanisms of the disease enabled to design suitable control measures. LSD could be diagnosed using appropriate medical science. Mass vaccination is one of major effective controlling technique of the disease; separation and get rid of infected animals are optional methods. Optimal control theory is another area of mathematics that is used extensively in controlling the spread of infectious diseases at the lowest economic cost to obtain the optimal vaccination strategy. For such reasons it is important to formulate a transmission dynamics of LSD using epidemiological model with optimal control policy to eradicate the LSD and minimize the cost associated for vaccination strategy.

1.2 Statement of the Problems

Most studies of epidemic control of LSD focus on increasing the protection coverage in a population to control the disease, but they do not consider how this parameter affects the strategy over a period of time. Though some of these studies have considered vaccination strategy at different level of immunization approach none of them has studied optimal vaccination strategy by considering LSD disease models for our countries Ethiopia.

1.3 Objective of the Thesis

The general objective of this study is to model optimal control strategies, to make the number of infectious individuals as small as possible and to keep the vaccination ratio of LSD as low as possible during a certain vaccination period and implement epidemiological Modeling of LSD Disease with Optimal Control.

1.4 Specific Objective of the Thesis

- Formulate a non linear ordinary differential equation based the model of SEIRS for LSD disease.
- Show the effect of vaccination on LSD disease.
- Compare uncontrolled and controlled strategies on the dynamics of LSD disease.
- Analyze the result with Computational way of study.

1.5 Scope and limitation

We work on qualitative analysis of Lumpy Skin disease, using epidemiological model of SEIRS, and in addition we work an optimal control (one controlling mechanism which is (vaccination)), we made analysis to show the impact of control with disease to that of uncontrolled one. We utilized different mathematical models, and MATLAB programming codes for quantitative and qualitative analysis (like Runge-kutta 4th order and ODe45, Pplane and dfield MATLAB tools). The limitation of this thesis is, most of the data that we use, are estimation, and we did not classify with age group, sex group as well, in addition we did not mention the geographical locations. So that this thesis used for further study by classifying age group or sex group or in different geographical location with optimal control and qualitative analysis.

1.6 Significance of the Thesis

The following are the significances of this study:

- It will be a useful reference for any future study for monitoring and controlling strategy for LSD.
- In general, it will help for policy makers to have an understanding of how the disease can be controlled through vaccination in order to reduce the incidence rate.
- To give information for policy makers by considering appropriate parameters, know about the costs of eradication, control period and its alternatives resource allocation.
- Having Epidemiological Modeling of LSD Disease with Optimal Control of Vaccination Strategy

1.7 Study Methodology

We employ an optimal control problem with extended SEIRS compartmental model as constraints and minimize an objective (cost) function. Vaccination which is one of the most effective strategies in preventing incidence and mortality associated with LSD diseases is included in this model. We choose an optimal strategy

to minimize the total number of infectious individuals. We derive the optimality system and solve it numerically for our optimal control problem. We analyze qualitatively nonlinear system of equations by linearizion approach. We tested our theoretical findings by simulating LSD vaccination strategies and by using epidemiological parameter values. For all numerical solutions presented we use a forward-backward sweep method and the result is executed using MATLAB code.

Chapter Two

2 Review Literature

2.1 Introduction

2.1.1 What is LSD?

Lumpy skin disease (LSD) is an acute infectious disease of cattle endemic in most Sub-Saharan African countries. As a result of significant milk product loss, infertility, abortion and death, it is economically destructive viral diseases which cause several financial problems in livestock industries.
The disease is defined by fever, enlarged lymph nodes, firm, and circumscribed nodules in the skin and ulcerative lesions particularly in the mucous membrane of the mouth. Good understanding of epidemiology, economic significance and control mechanisms of the disease enabled to design suitable control measures. LSD could be diagnosed using appropriate serological and molecular techniques. Effective control measure of the disease is achieved through mass vaccination though separation and culling of infected animals are optional methods.
The virus is present in nasal, lachrymal and pharyngeal secretions, semen, milk and blood and it may remain in saliva for up to 11 days and in semen for 22 days (Barnard et al., [6]). It can also persist for up to 33 days in necrotic tissue remaining at the site of a skin lesion. (LSD virus may persist for 6 months on fomites, including clothing and equipment but there is no evidence that virus can survive more than four days in insect vectors. (Birhanu,H., et al ,)[4].
Incubation period of LSD can vary under field condition and experimental conditions vary from 5 days in experimentally inoculated animals and 24 weeks in naturally infected animals, gives a maximum incubation period, for regulatory purposes, of 28 days (Barnard, et al., [6]; OIE, [16]) .
Generally LSD

- is a viral disease of cattle's and is typically characterized by nodes of lumps on the skin.
- usually occurs during the wet summer and autumn months, when flies are in abundance.
- occurs throughout Africa.

2.1.2 Why LSD so Important?

Economic losses due to LSD depend on the magnitude of production losses due to morbidity and mortality. Milk yield fall more that 50 % in affected herds. (Rgbe,H.,[2]).

- It is a notifiable disease, which means the state veterinarian must be informed because there are specific control schemes for this disease.
- Up to 45 % of herd can get infected and the morality (death) rate may reach 10%.

- The disease causes loss of body condition because of unwillingness to eat.
- temporarily or permanently loss of milk production,
- lowered or complete loss of fertility in bulls and cows, abortion as well as permanent damage to hides (skin),(Lindsay,T.,[4]).

Figure 2.1: Vaccination

2.1.3 What type of Animals can be Affected?

- Cattle of all ages can be infected.
- Cattle which are vaccinated annually are protected and therefore less likely to infected.
- Cattle which have had the disease and survived cannot be infected again (also immune).
- Calves under 6 months of age are protected again the disease if their mother were vaccinated or had the disease previously, Lindsay,T.,[4]).

2.1.4 How do cattle become infected?

- It is transmitted by insect vectors among the cattle sharing similar grazing and watering areas and those congregate in the same barn.
- Biting flies play the most important role in spreading the virus.
- Infections increase during the wet summer and autumn months when there are more flies.

Figure 2.2: Calf Infected by Lumpy Skin Disease

- calves can infected by drinking milk from a cow which has the disease.
- the disease can also spread through the saliva of infected animals when use the same drinking though,(Lindsay,T.[4]).

2.1.5 What are the sign of Lumpy-Skin Disease in cattle?

- skin nodules and ulcers:
  - can vary from a few to hundreds
  - the size ranges from 0.5 - 5 cm
  - they occur any where on the skin, including the nose, mammary gland and vulva in cows, the scrotum in bulls, as well as in the mouth (the gums)
- Legs which become swollen and develop sores
- Enlarged lymph nodes
- Pneumonia /coughing - as a result of infection of the respiratory tract(the windpipe) and lungs.
- Nasal discharge - thick, watery to pussy fluid from the nose

2.2 Epidemiology and pattern of the disease

Based on (Birhanu,H., et al., [4] paper), Lumpy skin disease is an important, economically devastating, notifiable disease which brought production loss in cattle due to generalized malaises and chronic debility (Tuppurainen, et al. [18]). Good understanding of epidemiological aspects LSD related to pathogen, host and environment might aid for prevention mechanisms. Particular emphasis was given to exposure of hosts and pathogen in suitable environment that was facilitating transmission and distribution of the disease. The frequency of morbidity and mortality of the disease, its geographic distribution and mode of transmission in large herds of cattle were observed to cause severe economic losses (Salib and Osman [19];Tuppurainen,et al.,[18]).
The virus is present in nasal, lachrymal and pharyngeal secretions, semen, milk

and blood and it may remain in saliva for up to 11 days and in semen for 22 days (Barnard et al., [6]). It can also persist for up to 33 days in necrotic tissue remaining at the site of a skin lesion. Material from skin lesions also contains infective virus when shed (Barnard et al.,[6]).There is no evidence of the virus persisting in meat of infected animals, but it might be isolated from milk in early stages of fever (Davies,[20]).
From the paper Birhanu,H.,et al.,[4]. Stated that, Though all breeds and age group are susceptible, Bostaurusare particularly more susceptible to clinical disease than zebu cattle. Among Bostaurus, fine-skinned Channel Island breeds develop more severe disease (OIE, [16]). Lactating cows appearing to be severely affected and result in a sharp drop in milk production because of high fever caused by viral infection itself and secondary bacterial mastitis (Tuppurainen and Oura,[25]). Young animals are severely affected and clinical symptoms are rapid to appear.
Currently it is widely accepted that LSD is transmitted mainly by arthropod vectors. This vector-related transmission is apparently mechanical, rather than biological. This distinction is important because infectious organisms do not generally survive in vectors for long periods for multiplication or over-wintering in these insects. Study by Chihota, et al., [27], indicated that the virus can survive 2-6 days post feeding from infected cattle and transfers this to susceptible cattle by female mosquito,Aedesegypti during experimental infectious. The virus can survive only for about average four days and this cant permit for recurrence of disease in the coming season. It was thought that infected vectors can transmit the disease some distance kilometers from the foci of infection as the occurrence of outbreak in 1989 in Israel following aerial movement of infected insect vectors from Egypt, (Birhanu,H., et al,. [4]). Outbreaks of LSD are highly associated with seasonal peak of mechanical vectors in wet and warm weather conditions in Ethiopia (Getachewet al.,[14]). According to Birhanu,H.,et al,[4] paper, the virus could be transmitted through transstadial and transovarian in Boophilus.decoloratus and mechanical transmission by Repicephalus appendiculatus and Ambylomahebraeum. Transmission of LSD is also possible by sharing of the same feeding and watering troughs which may be contaminated by the viruses in the saliva of the infected animals or ingestion of the already contaminated food or by teratogenic agents and suckling calves may be infected through infected milk (Thomas,[26]). The incubation period of LSD is 6 to 10 days in experimentally infected animals (Babiuk et al., [8]) but is thought to be 2 to 4 weeks in naturally-infected animals (Barnard et al., [6]). The World Organization for animal health (OIE) Code gives the maximum incubation period of 28 days for regulatory purposes.

2.2.1 How can LSD be Diagnosed?

A basic diagnosis can be made by the presence of the typical lesions on the skin and in the mouth. In long haired animals you should feel for the noddles on the skin, or you can wet the hair so that you can see the nodules more easily a definite diagnosis can only be confirmed by a veterinarian by taking sample of the skin to a laboratory where they can identify the virus (this has to be done because there are other disease which cause similar signs in cattle and therefore require different methods of control and treatment. If you suspect LSD in your herd, you must inform the state veterinarian. so that the disease can be confirmed and he/she

will help you to control the disease (Lindsay,T., [4]).

2.2.2 How is LSD treated?

Nonspecific treatment (antibiotics, anti-inflammatory drugs and vitamin injections) is usually directed at treating the secondary bacterial infections, inflammation and fever, and improving the appetite of the animal(Lindsay,T.,[4]).

2.2.3 How can prevent LSD from herd

Prevention is the cheapest and best method of control of the disease. If the animals are protected, not suffer any production or financial losses as a result of the ill effects of the disease.

Vaccination (the best controlling mechanism)

The attenuated Neethling strain vaccine is a product that contains a weakened LSD virus. When this vaccine is administered the animal will develop protective antibodies (made by white blood cells). These antibodies then resist the actual virus that is transmitted by biting flies or milk and saliva of infected animals. The animal is therefore protected or immune. The Onderstepoort Veterinary Institute or the local veterinarian can supply vaccines (Lindsay,T. [4]).
All cattle should be vaccinated annually (once a year), and preferably before the summer rains to ensure good protection. Animals that had the disease and recovered, are immune and therefore do not have to be vaccinated. Calves which are under 6 months old and were born to cows which have been vaccinated or had the disease, do not need to be vaccinated. However, as soon as they are 6 months old, they have to be vaccinated annually. There may be a swelling at the site where the vaccine is given, and a temporary drop in milk production, but the swelling will disappear after a few weeks with a return to normal milk production. It is important to read the instructions for use on the vaccine labels. If you have any questions or need assistance with vaccination, contact your state veterinarian or animal health technician for help.

Fly control

It is unpractical and almost impossible to control all the flies in your herd. It is better to prevent flies from biting your animals. Cattle should be dipped in a product that contains an insecticide. Make sure that the dip includes insecticides effective against flies. Read and follow the instructions on the labels of the products. Fly repellents can be sprayed on cattle. Note that fly control will not prevent all cattle from being infected by LSD. The only way to ensure that all cattle are protected is by vaccination alone (Lindsay,T., [4])

2.3 LSD in Ethiopia

In Ethiopia, LSD was first observed in 1983 in the western part of the country (southwest of Lake Tana), according to (Mebratu, et al.,[23]). After its first appearance, an explosive sudden epidemic spread from the north through the central

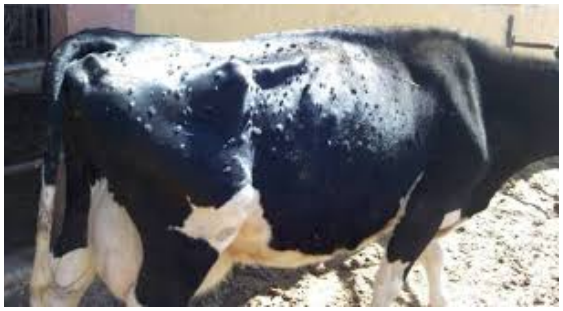

Figure 2.3: Milke Cattel Infected by LSD

to the southern part of the country. In the subsequent three to five years, it had covered the vast area of the highland and midland parts of the country.
LSD is one of reported diseases in Ethiopia which deserves outbreak notification to the National veterinary services. However, a variable degree of under-reporting of the outbreak cases could exist from different parts of the country. Based on Garis journal paper, data investigations from the national disease outbreak report database during the period 2000-2009 showed that major epidemic outbreaks of LSD occurred in 2000/2001 in the northern parts of the country in Amhara and West Oromia regions,(Gari, G.,[10]). Then it extended to the central and the southern parts of the country in 2003/04 covering large parts of Oromia and Southern Nation, Nationalities and Peoples (SNNP) regions. In 2006/07 another extensive outbreak reappeared in Tigray, Amhara and Benishangul regions in the northern and north-western parts of the country,(Gari, G.,[10]).
From 2007 up to 2009 the outbreak number progressively increased in Oromia Region situated in the central part of the country while it seemed to be gradually decreasing in the northern part of the country including Tigray, Amhara and Benishangul regions. This showed that an epidemic reoccurs after an interval of 5-6 years cycle in unvaccinated cattle population. The national disease outbreak report during these 10 years showed that LSD has spread virtually to all the regions in the country and in different agro-climatic zones,(Gari, G.,[10]).
In Ethiopia, few works have been reported in selected areas of the country on the financial impact of LSD (Gari,G.,et al.,[24]). Recently, a report on seroprevalence of disease indicated that the disease is widely distributed across the country and increases its impacts (Gari,G.,et al.,[23]). Though there were frequent outbreak reports of the disease in North Eastern part of Ethiopia, its epidemiology and financial loss were not determined. Therefore, the present study aims to provide baseline information on the epidemiological aspects, financial impacts of the diseases and financial benefits obtained from control of the diseases from livestock producers perspectives in extensive farming system, Birhanu,H.,[21].
Therefore, the use of mass vaccination applied to all breeds of cattle in the districts using an effective vaccine against LSD, such as the attenuated Neethling strain vaccine need to be considered.(Abera,Z., et al.,[17]).
According to Birhanu,H.,[21], the data that was collected for the study from Afar and Tigray region and affected cattle's as shown below:- Based on the data, more female cattle's has affected by the virus, and from those Dry cows, Lactating and Heifers orderly affected by the disease. Generally from the survey at the rate of

Table 1: Description of cattle population affected with LSD by sex and age category

No	Description	No of Population	No affected Population	Affected(%)
1	Adult Male	740	68	0.09189
2	Calves	727	50	0.06878
3	Bulls	290	29	0.100
4	Heifers	458	68	0.14847
5	Lactating cows	790	98	0.12405
6	Dry cows	437	66	0.15103

Table 2: Description of cattle population affected with LSD by sex category

No	Description	No of Population	No Affected Population	Affected (%)
1	Male Cattle	1145	129	0.011266
2	Female Cattle	2297	250	0.10884
-	Total	3442	379	0.11011

0.11011 of cattle's affected by the disease.

Chapter Three

3 Epidemiological Model

3.1 Introduction

3.1.1 Construction of basic ODE models for disease transmission

Usually most of the researchers use one ODE model of disease transmission. All ODE models of disease transmission are continuous-time compartment level models. The ODE models have variables S, I, and, if applicable, R, E. They can be interpreted as actual numbers, expected numbers, or (actual or expected) proportions of hosts in the S,I,R, and E compartments. These variables will change over time, and S(t), I(t), R(t), E(t) denote their values at a given time t. The state of the system at time t is the vector (S(t), I(t)) for SI- and SIS-models, the vector (S(t), I(t), R(t)) for SIR-models, and the vector (S(t), I(t), R(t), E(t) for SEIR-models. Let us ignore demographics, that is, births, immigration, emigration, and deaths from causes that are unrelated to the disease. Mathematically this means that at all times the equality

$$S(t) + I(t) + R(t) + E(t) = N \tag{3.1}$$

(eq(3.1) mathematicians calls as conservation law) holds, where N is a constant that represents the size of the host population. If the variables are interpreted as proportions, then we need to choose N = 1. It says that the value of some quantity, total population size in this case, remains constant. Conservation laws allow us to reduce the number of variables by expressing one of them in terms of the others and the conserved constant. This is often a useful trick. We will use it later for analyzing our models, but for constructing them it is usually easier to work with a full set of variables. ODE models are based on derivatives of the variables with respect to time.

For this to make sense, the variables should be able to take any value in some

Table 3: Description of variables

.

No	Variable	Description	
1	S	Susceptible population, that will be affected by disease	
2	E	Exposed population at for latent period	
3	I	Infected population	
4	R	Recovered population	

interval of the real line. This is strictly speaking impossible for the interpretation of the variables as actual sizes of the compartments. For large N, we can alleviate the problem to some extent by assuming that the variables count hosts in batches of thousands or even millions. One can think of them as useful approximations for very, very large populations. But for small populations their predictions may be misleading,(Winfried,[28]).

A. SI models

Let us begin with the easiest case of an SI model. Here we have only two variables: S and I. A host can only move from the S-compartment to the I-compartment as the result of an effective contact with an infectious host. If this happens, I(t) will increase, and S(t) will decrease. Since new infections are the only process that occurs in this model, the rate $\frac{dI}{dt}$ at which I(t) changes will be the rate at which hosts move from S compartment to the I-compartment. In other words, $\frac{dI}{dt}$ will be equal to the rate at which effective contacts between infectious and susceptible hosts occur,(Winfried, [28]).
In order to derive a formula for this rate, recall that compartment-based models are based on the uniform mixing assumption. This means that for all possible pairs (s,i) of an infectious host i and a susceptible host s the rate at which these particular hosts come into effective contact is the same. Thus the total rate of effective contacts between infectious and susceptible hosts will be times the product of S and I, which represents the number of all such pairs (s,i).

$$\frac{dI}{dt} = \beta SI \tag{3.2}$$

Since the only process that we are considering in this model are new infections, the rate at which I increases must be the same as the rate at which S decreases. In other words, $\frac{ds}{dt}$=$-\frac{dI}{dt}$ This gives the following system:

$$\begin{aligned} \frac{ds}{dt} &= -\beta SI \\ and \quad \frac{dI}{dt} &= \beta SI \end{aligned} \tag{3.3}$$

$\frac{ds}{dt}$=-βSI and $\frac{dI}{dt}$ = βSI We have built our first ODE model. Note that:-

$$\frac{dS}{dt} + \frac{dI}{dt} = -\beta SI + \beta SI \tag{3.4}$$

This is exactly as it should be. In an SI-model we have R(t) = E(t) = 0 at all times t, and now we have S(t) + I(t) = N is a constant. We can now substitute S = N I and rewrite (3.3) in a single variable I as follows:

$$\begin{aligned} \frac{dI}{dt} &= \beta(SI) \\ \Rightarrow \frac{dI}{dt} &= \beta(N - I)I \end{aligned} \tag{3.5}$$

The ODE (3.5) has two fixed points or equilibria, $I_1 = 0$ and I_2= N , where $\frac{dI}{dt} = 0$ and the state of the system does not change. As long as 0 < I < N the derivative $\frac{dI}{dt}$ is positive, and Infectious population (I) will increase. Thus in all solutions that start with an initial condition I(0) > 0 the number of infectious individuals will keep increasing towards the value I = N,(Winfried, [28]) . *Technically, this means that the equilibrium $I_1 = 0$ is unstable and the equilibrium $I_2 = N$ is locally asymptotically stable.*

B. SIR models

With the same procedure let us produce ODE version of the SIR model. Here we need three variables, S, I, R, and we need to consider simultaneously two processes: new infections and removal of hosts(we call it recover by some treatments or naturally). The first of these processes is the only one that affects susceptible hosts. As in the SI model, we get $\frac{dS}{dt}$=-β(SI). This process also contributes a term SI to $\frac{dI}{dt}$. Removal of hosts is the only process that affects R. It proceeds at rate $\frac{dR}{dt}$. Only hosts in I are candidates for removal, and in an SIR-model removal occurs as a result of recovery from the disease with permanent immunity or of death from the disease. In none of these (either permanent immunity or death) scenarios can hosts ever leave the R-compartment. Thus $\frac{dR}{dt}$ is proportional to the number of infectious hosts, that is, $\frac{dR}{dt} = \omega$I , where ω is the rate of removal. Since removal of hosts decreases the population of infectious (I), the process also contributes a term ωI to $\frac{dI}{dt}$ We obtain the following model:

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI \\ \frac{dI}{dt} &= \beta SI - \omega I \\ \frac{dR}{dt} &= \omega I \end{aligned} \tag{3.6}$$

This is the famous model of Kermack and McKendrick.

C. SEIR models

If we add an E-compartment to the SIR-model, we need four variables, S, E, I, R. Effective contacts with infectious hosts move susceptible hosts out of the S-compartment at rate $\frac{dS}{dt}$=-βSI and into the E-compartment at rateβSI. Hosts in the E-compartment move into the I-compartment at rate γE, and removal works exactly as in the SIR-model,(Winfried, [28]). We obtain the following ODE-version of the SEIR-model:

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI \\ \frac{dE}{dt} &= \beta SI - \gamma E \\ \frac{dI}{dt} &= \gamma E - \omega I \\ \frac{dR}{dt} &= \omega I \end{aligned} \tag{3.7}$$

D. SIS models

SIS-models, It can be derived similarly to the ODE versions of SI-, SEIR-, and SIR-models, and we have the following ODE of SIS model,(Winfried,[28]).

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI + \omega I \\ \frac{dI}{dt} &= \gamma E - \omega I \end{aligned} \tag{3.8}$$

Since S(t) + I(t) = N for all t, by letting S = N I, this model can be simplified to

$$\frac{dI}{dt} = \beta I(N - I) - \omega I = \beta I(N - I - \frac{\omega}{\beta}) \tag{3.9}$$

3.1.2 Epidemiology

Epidemiology is the study of the distribution (concerned with the frequency and pattern of health) and determinants (causes, risk factors) of health-related states or events in specified populations, and the application of this study to the control of health problems.

3.1.3 Epidemics, Pandemics, and Outbreaks

Outbreaks:- A disease outbreak happens when a disease occurs in greater numbers than expected in a community or region or during a season. An outbreak may occur in one community or even extend to several countries. It can last from days to years.
Epidemic: - occurs when an infectious disease spreads rapidly to many people. For example, in 2003, the severe acute respiratory syndrome (SARS) epidemic took the lives of nearly 800 people worldwide.
Pandemic:- is a global disease outbreak. HIV/AIDS is an example of one of the most destructive global pandemics in history, [9].
Some of the well studied epidemic models are SI, SIR,SIS,SEIR,and SEIS. This paper will focus on optimal controls of Epidemiological models SEIRS) Effective

Table 4: List of Models

No	Model Name	Propoerty	Example of Disease
1	SI	No recovery (R=0)	AIDS
2	SIR	Permanent immunity after recovery	Influenza
3	SIS	No Immunity after Recovery	H1N5
4	SEIR	is not infectious yet	Measles
5	SEIS	SIS + Latent Period	Malaria

contacts with infectious hosts move susceptible hosts out of the S-compartment to E-compartment (Exposed to be infectious) at rate Beta β and we have

$$\frac{dS}{dt} = -\beta SI \tag{3.10}$$

Hosts in the E-compartment move into I-compartment at rate γ E, and removal works exactly as in the SIR-model. We obtain the following ODE-version of the SEIR-model:

$$\boxed{\frac{dS}{dt} = -\beta(SI)} \tag{3.11}$$

$$\boxed{\frac{dE}{dt} = \beta(SI) - \gamma(E)} \tag{3.12}$$

$$\boxed{\frac{dI}{dt} = \gamma(E) - \alpha(I)} \tag{3.13}$$

$$\boxed{\frac{dR}{dt} = \alpha(I)} \tag{3.14}$$

3.1.4 Systems of Differential Equations

In general a system of first order differential equations in two unknown functions x and y has the form

$$\frac{dx}{dt} = f(t, x, y); and \frac{dy}{dt} = g(t, x, y) \tag{3.15}$$

the independent variable t denotes the time and the dependent variables x and y denote the position (x,y) in xy-plane. In this case, xy-plane is referred to as a **phase plane**. The solution of the system is a parametric function x = x(t) and y = y(t): The curve (x(t), y(t)) is called **a trajectory**.
In dynamical systems, only the solutions of linear systems may be found explicitly. The problem is that in general real life problems may only be modeled by nonlinear systems. The main idea is to approximate a nonlinear system by a linear one (around the equilibrium point). Of course, we do hope that the behavior of the solutions of the linear system will be the same as the nonlinear one. But this is not always true,(Canan,C.,[31]).

Definition 3.1 Autonomous Equations*:* - A system of two equations, which is written of the form $\frac{dx}{dt}$ =f(x,y) and $\frac{dy}{dt}$ =g(x,y) that is the variable t does not appear on the right side called **autonomous or homogeneous**.(*Autonomous means self governing*)
Note that :- Slope doesn't change from left to right.

Definition 3.2:- Equilibrium point:- The point $\widehat{x} \in \Re^n$ is an equilibrium point for the differential equation, $\frac{dx}{dt}$ = f(t,x), if f(t,$\widehat{x}$)=0 for all t.
Suppose $\overline{x}$ is an equilibrium point (with the input$\overline{u}$). Consider the initial condition x(0) = $\overline{x}$, and applying the input u(t) = $\overline{u}$ for all t $\geq t_0$, then resulting solution x(t) satisfies

$$x(t) = \overline{x}, \quad for \quad all \quad t \geq t_0 \tag{3.16}$$

it is called an ***equilibrium point*** **or solution**,(Canan,C.,[31]).

The equilibrium values provide the insight in the long-term behavior of the system and demonstrate if the system has periodic behavior or not, if the numerical solutions are sensitive on the initial conditions or not and how sensitive is the system to the changes of parameters in the model. Equilibrium, or fixed point, is a state of a system which does not change. In ODE, we can calculate equilibria by setting all derivatives to zero because nothing is changing with respect to time.

Definition 3.3 Stable equilibrium:- a system return to its equilibrium and remain there after disturbances.

Definition 3.4 Unstable equilibrium:- a system moves away from the equilibrium after disturbances.

3.2 SEIRS Model and Equation Formulation

The first mathematical model that could be used to describe an influenza epidemic was developed early in the 20^{th} century by **Kermack and McKendrick** [**?**]. This model is known as the Susceptible-Infectious-Recovered (SIR) model. All ODE models of disease transmission are continuous-time compartment-level models. The basic elements for the description of infectious diseases have been considered by epidemiological classes:

- S: measures the susceptible portion of population,
- E: Exposed population (during Latent time)
- I: Infected population, and
- R: Recovered population.

Kermack and McKendrick describe the simplest SIR model which computes the theoretical number of people infected with a contagious illness in a closed population over time. Transmission of a disease is a dynamical process driven by the interaction between susceptible and infective. The behavior of the SIR models are greatly affected by the way in which transmission between infected and susceptible individuals are modeled.
In the population (N) disease spreads and to be infected (I) the susceptible populations S, by the interaction of S and I at the rate of let say β. Here the total number of population is increased at the rate of let say α. So that the total population injected to susceptible group is in two ways. One from birth and second one from recovered group, which means the recovered population those getting their immunity, have a possibility to lose thiere immunity and be susceptible again. N=S+E+I+R.

3.2.1 Equation for Susceptible Compartment

Here natural birth and those recovered populations loss their immunity and return back to the susceptible group this increases the total population that has to be susceptible. The natural death and to be infected and within the latent time they grouped to exposed decrease the susceptible population. From this we have the following first derivative equation with respect to time eq (1). The second group is exposed compartment (E), that population the disease is in their body, but not infected, it hides in the body the time called latent time. In from the susceptible compartment and out with two sides from the natural death and to infected compartment.

$$\frac{dS}{dt} = \alpha N - \frac{\beta SI}{N} + \theta R - \phi S \tag{3.17}$$

3.2.2 Equation for Exposed Compartment

The Second compartment is Exposed, it has one in and two out population form the compartment, population at the rate of gamma γ for this paper, moves to infected I-compartment, the other one is natural death ϕ rate.

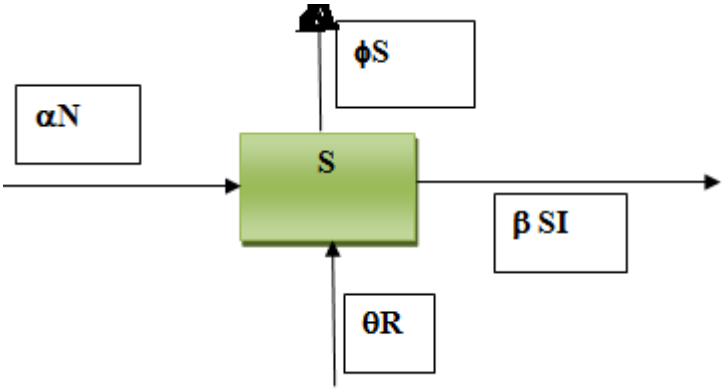

Figure 3.1: In and out of Susceptible compartment

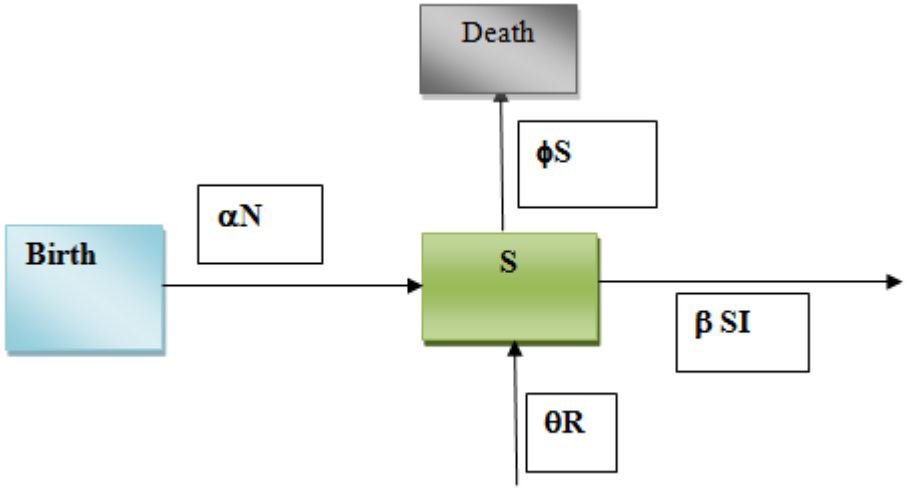

Figure 3.2: Susceptible Compartment

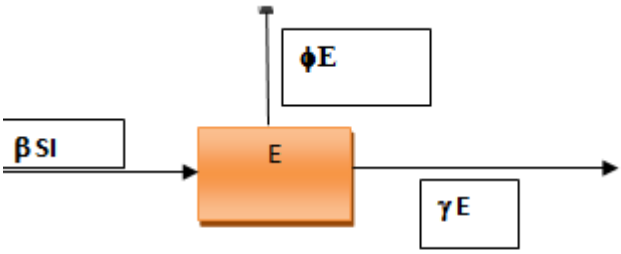

Figure 3.3: Exposed Compartment

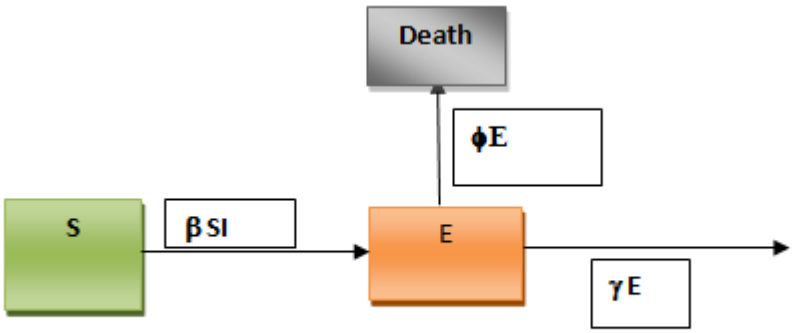

Figure 3.4: Exposed Compartment

$$\frac{dE}{dt} = \frac{\beta SI}{N} - \gamma E - \phi E \tag{3.18}$$

3.2.3 Equation for Infected Compartment

The third compartment is infected population, this group affected by the number of population that has to be infected on E compartment and move to death by natural and to recover R-compartment by treatment at the rate of ω .

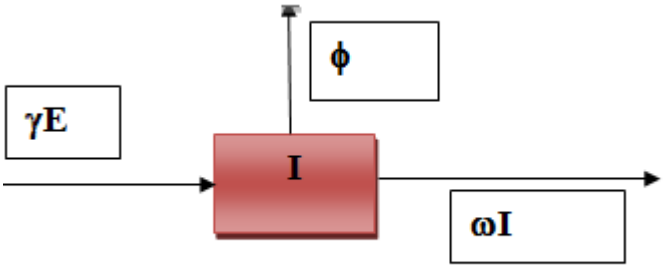

Figure 3.5: Infected Compartment

$$\frac{dI}{dt} = \gamma E - \omega I - \phi I, \frac{dI}{dt} = \gamma E - I(\omega + \phi) \tag{3.19}$$

3.2.4 Equation for Recovered Compartment

The fourth compartment is recovered population, moved infected groups to this compartment after getting their immunity based on the given treatment. After some time the population may lose their immunity and get back to susceptible compartment, so that the population size on this compartment decreases by lose immunity rate in addition to natural death.

$$\frac{dR}{dt} = \omega I - \phi I - \theta R \tag{3.20}$$

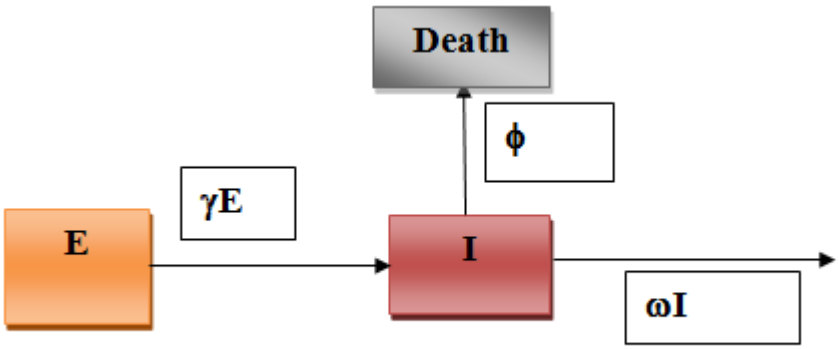

Figure 3.6: Infected Compartment

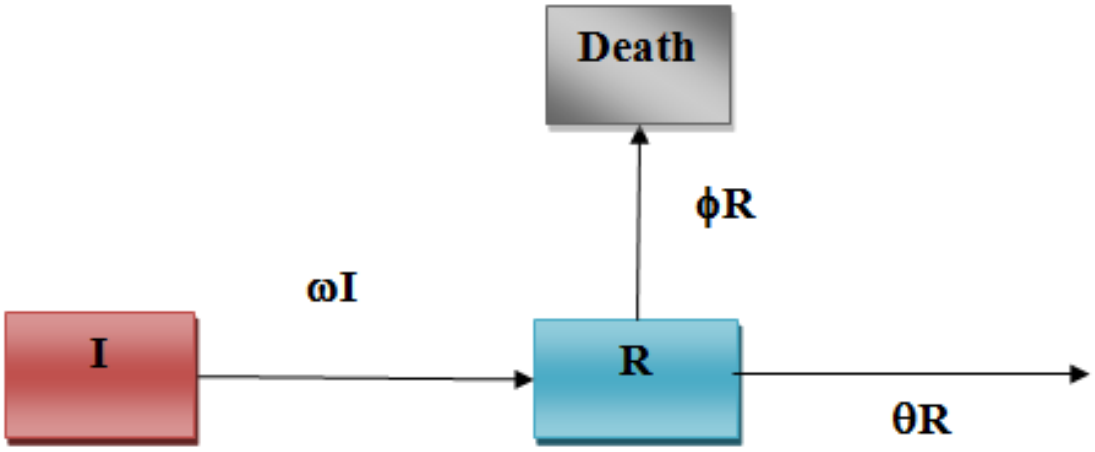

Figure 3.7: Recovered Compartment

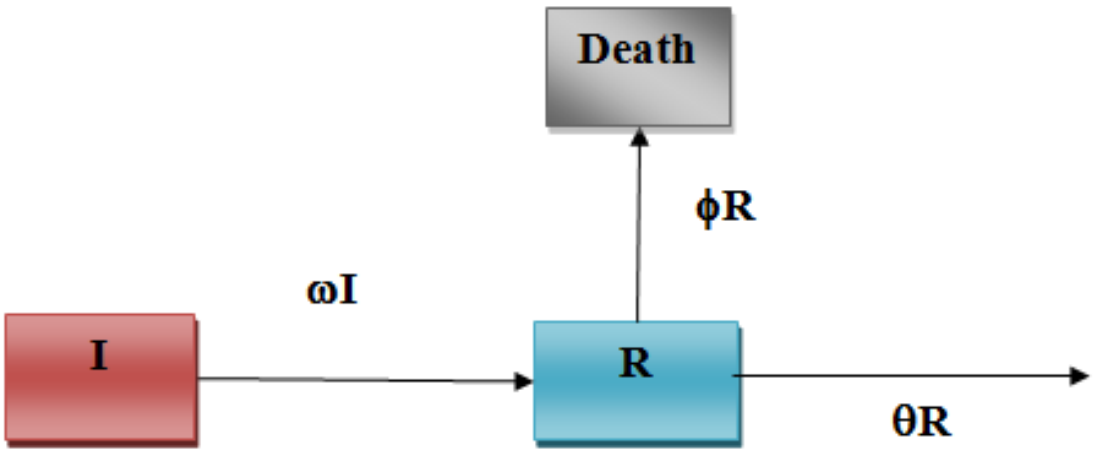

Figure 3.8: Recovered Compartment

3.3 General System of Equations for SEIRS Epidemiology

Generally we do have the following SEIRS epidemiological model, and from the equations from 1 to 4 we have the following system of first differential equations.

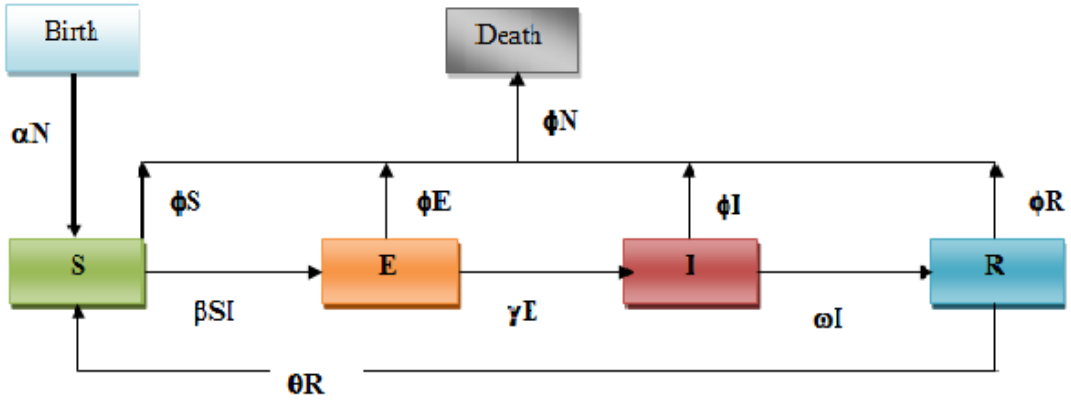

Figure 3.9: SEIRS Model with out Control

$$\frac{dS}{dt} = \alpha N - \beta SI + \theta R - \phi S \tag{3.21}$$

$$\frac{dE}{dt} = \beta SI - \gamma E - \phi E \tag{3.22}$$

$$\frac{dI}{dt} = \gamma E - I(\omega + \phi) \tag{3.23}$$

$$\frac{dR}{dt} = \omega I - \phi R - \theta R \tag{3.24}$$

Note that:- the natural death rate on each of the compartment is the same, which is

$$\phi S + \phi E + \phi I + \phi R = \phi(S + E + I + R) = \phi N \tag{3.25}$$

Where

Table 5: Descriptions for symbols

.

No	Notation	Description	Remark
1	N	Total population	
2	S	Susceptible to be exposed for infection those of who interact with the disease	
3	E	Exposed population to be infection who are infected but have not yet become infectious and can not pass the infection to other susceptible individuals.	
4	I	Infected by infectious who are capable of transmitting the infection to any susceptible individuals.	
5	R	Individuals recovered from infection who are temporarily immune from the infection	
6	α	the rate at which get birth from the total population N	
7	β	The rate that will be infectious with the interaction of the compartments of susceptible and infected population.	
8	γ	The rate which will be infected from the population of exposed	
9	ω	The rate of getting immunity after sort of treatment and move to the recovered compartment from infected compartment.	
10	Θ	The rate at which those populations may loss their immunity and moved to the susceptible compartment.	
11	ϕ	The rate of natural death	

Chapter Four

4 Numerical Analysis with out Optimal Control

4.1 Quantitative Analysis

4.1.1 Runge-Kutta 4th order Method

In numerical analysis, the RungeKutta methods are a family of implicit and explicit iterative methods, which includes the well-known routine called the ***Euler Method***, used in temporal discretization for the approximate solutions of ordinary differential equations. The most widely known member of the RungeKutta family is generally referred to as "RK4", "classical RungeKutta method" or simply as "the RungeKutta method".

Definition 4.1:-
An initial value problem be specified as follows: $\dot{y} = f(t, y), \quad y(t_0) = y_0$.
Here y is an unknown function (scalar or vector) of time t, which we would like to approximate; we called that $\dot{y}$, the rate at which y changes, is a function of t and of y itself. At the initial time t_0 the corresponding y value is y_0. The function f and the data t_0, y_0 are given.
Now pick a step-size h > 0 and define

$$\begin{aligned} y_{n+1} &= y_n + \tfrac{h}{6}\left(k_1 + 2k_2 + 2k_3 + k_4\right), \\ t_{n+1} &= t_n + h \end{aligned}$$

for n = 0, 1, 2, 3, ...,

$$\begin{aligned} k_1 &= f(t_n, y_n), \\ k_2 &= f\left(t_n + \frac{h}{2}, y_n + \frac{h}{2}k_1\right), \\ k_3 &= f\left(t_n + \frac{h}{2}, y_n + \frac{h}{2}k_2\right), \\ k_4 &= f\left(t_n + h, y_n + hk_3\right). \end{aligned}$$

Here y_{n+1} is the RK4 approximation of $y(t_{n+1})$, and the next value (y_{n+1}) is determined by the present value (y_n) plus the weighted average of four increments, where each increment is the product of the size of the interval, h, and an estimated slope specified by function f on the right-hand side of the differential equation.

- k_1 is the increment based on the slope at the beginning of the interval, using y (Euler's method);
- k_2 is the increment based on the slope at the midpoint of the interval, using $y + \frac{h}{2}k_1$;
- k_3 is again the increment based on the slope at the midpoint, but now using $y + \frac{h}{2}k_2$;

- $k_4$is the increment based on the slope at the end of the interval, using $y + hk_3$.

In averaging the four increments, greater weight is given to the increments at the midpoint. If f is independent of y, so that the differential equation is equivalent to a simple integral, then RK4 is Simpson's rule.
The RK4 method is a fourth-order method, meaning that the local truncation error is on the order of $O(h^5)$, while the total accumulated error is on the order of $O(h^4)$. For the model, SEIRS, we have four equations, for solving this differential equations and to find the numerical solutions, we write MATLAB code for solving Runke-Kutta 4th order methods. Details of equation and Runge-kutta 4th order method has done with the following MATLAB code

4.1.2 RK4-Matlab Code for Numerical solution

Matlab code for solving system of equations using Runge-Kutta 4th order method, and we have got a solution, that shows, on figure 4.1.

```
%% ------------------------------------------------------------------
    k1=(alfa*N-beta*S(i)*I(i)+theta*R(i)-fay*S(i)-u(i)*S(i));  % equation S
    l1=(beta*S(i)*I(i)-(gama*E(i))-fay*E(i));                  % equation E
    m1=(gama*E(i)-(omega+fay)*I(i));                           % equation I
    n1=(omega*I(i)-(fay+theta)*R(i)+u(i)*S(i));                % equation R
%% ------------------------------------------------------------------
```

this show the development of the matlab code for solving system of equaiton using RK4

```
%-------------------------------------------------------------------
%   The next code discribes the changes in S,E,I,R are made
%% ------------------------------------------------------------------
    S(i+1) = S(i) + (h/6)*(k1 + 2*k2 + 2*k3 + k4);
    E(i+1) = E(i) + (h/6)*(l1 + 2*l2 + 2*l3 + l4);
    I(i+1) = I(i) + (h/6)*(m1 + 2*m2 + 2*m3 + m4);
    R(i+1) = R(i) + (h/6)*(n1 + 2*n2 + 2*n3 + n4);
  end % end of the first for loop
```

```
%-------------------------------------------------------------------
%   same comments as in a3 only adjusting n values
%% ------------------------------------------------------------------
    a4=(lambda1(j)-h1*a3)*(beta*I(j-1)+fay+u(j))-(lambda2(j)-h1*b3)*...
      beta*I(j-1)-(lambda4(j)-h1*d3)*u(j);
    b4=(lambda2(j)-h1*b3)*(gama+fay)-(lambda3(j)-h1*c3)*gama;
    c4=(lambda1(j)-h1*a3)*beta*S(j-1)-(lambda2(j)-h1*b3)*beta*S(j-1)...
```

```
8          +(lambda3(j)-h1*c3)*(omega+fay)-(lambda4(j)-h1*d3)
               *(omega);
9       d4=-(lambda1(j)-h1*a1)*(theta)+(lambda4(j)-h1*d3)*drate
            ;
10 %% ------------------------------------------------------------
11 %    The following changes in lambda1,lambda2,lambda3,
       lambda4,u are made
12 %%
    ------------------------------------------------------------
13      lambda1(j-1) = lambda1(j) - (h/6)*(a1 + 2*a2 + 2*a3 +
            a4);
14      lambda2(j-1) = lambda2(j) - (h/6)*(b1 + 2*b2 + 2*b3 +
            b4);
15      lambda3(j-1) = lambda3(j) - (h/6)*(c1 + 2*c2 + 2*c3 +
            c4);
16      lambda4(j-1) = lambda4(j) - (h/6)*(d1 + 2*d2 + 2*d3 +
            d4);
```

4.1.3 ODE45 - Sample Matlab Code for Numerical solution

Here We develop a MATLAB program for solving system of equations quantitatively *Sample Matlab code for solving system of equations using ODE45 built-in function.*

After we developed the code we plot graphs that shows the number of populations on S,E,I and R compartment with time (t), that depend on the rate of infections β, rate of transmitted from E to I (γ) and the rate of the recover which the populations move from I to R (ω). For this graph we take values for β=0.02, which is the factor of affecting or transmitting the disease is to high, in other words, the number of the population on S-compartment is decreased and transfer to E-compartment with short period of time. Look at the diagrams as follow

```
1  g=@(t,y)[(alfa*N-((beta*y(1)*y(3))/N)+theta*y(4)-fay*y(1))
       ;
2                  ((beta*y(1)*y(3))/N-(gama*y(2))-fay*y(2));
3                  (gama*y(2)-(omega+fay)*y(3));
4                  %(N-y(1)-y(2)-y(3));];
5                  (omega*y(3)-fay*y(4)-theta*y(4));];
```

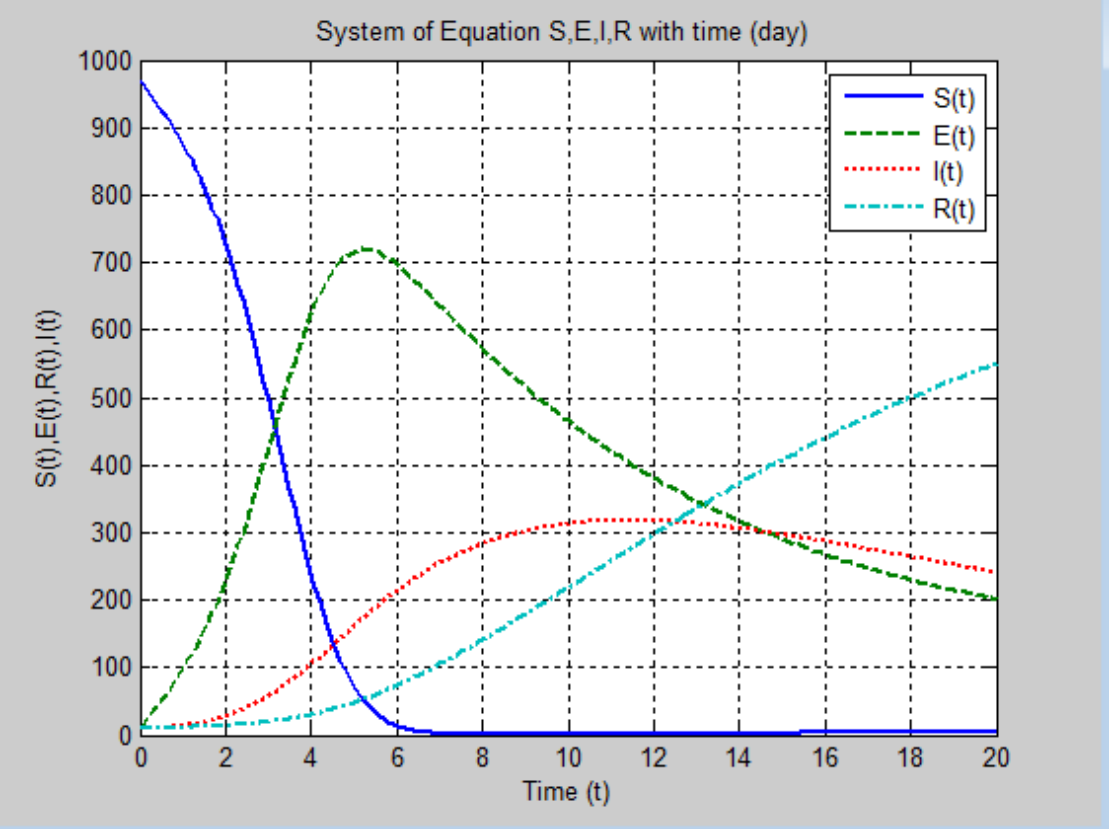

Figure 4.1: SEIRS graph with time (t)

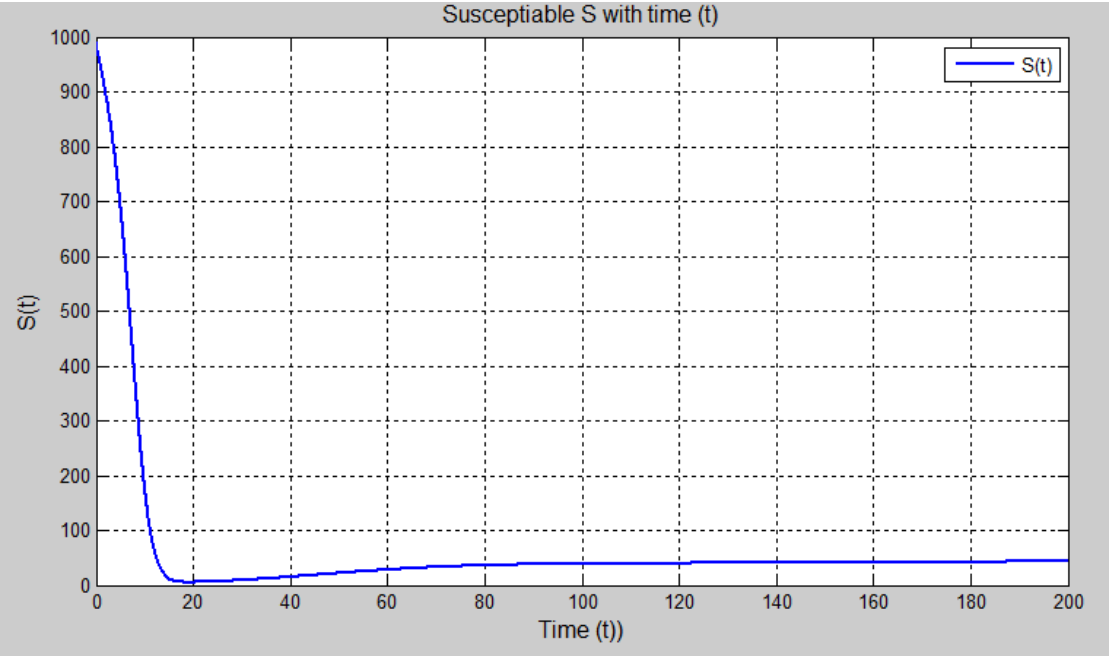

Figure 4.2: S graph with time (t)

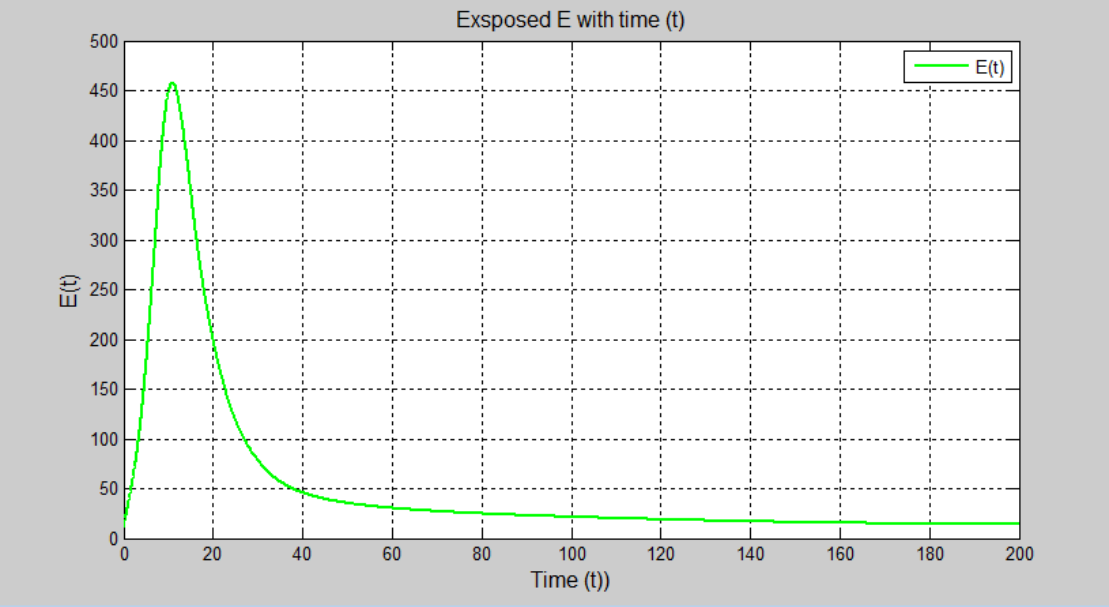

Figure 4.3: E-Graph with time (t)

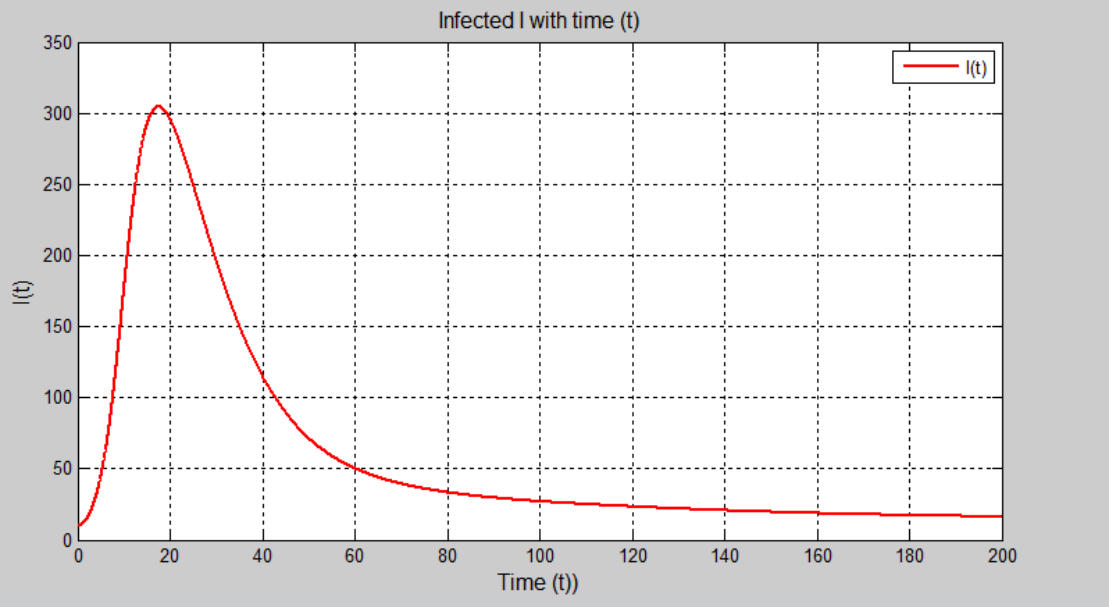

Figure 4.4: I-Graph with time (t)

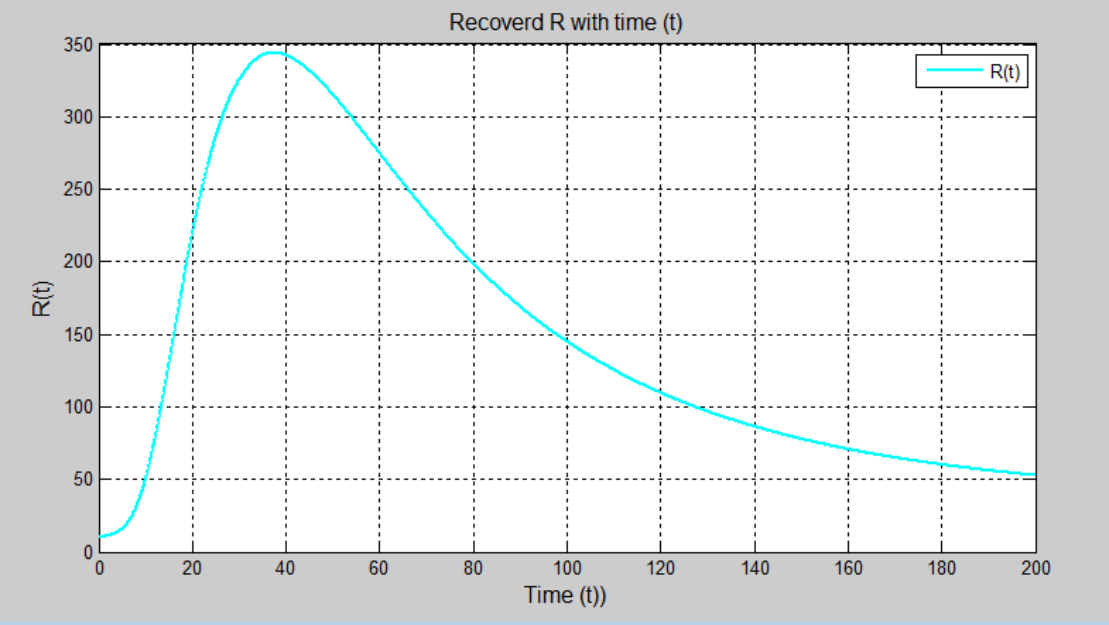

Figure 4.5: R-Graph with time (t)

For the following graph we take values for β=5.02, which is the factor of affecting or transmitting the disease is to high, in other words, the number of the population on S-compartment is decreased and transfer to E-compartment with short period of time. Look at the diagrams as follow

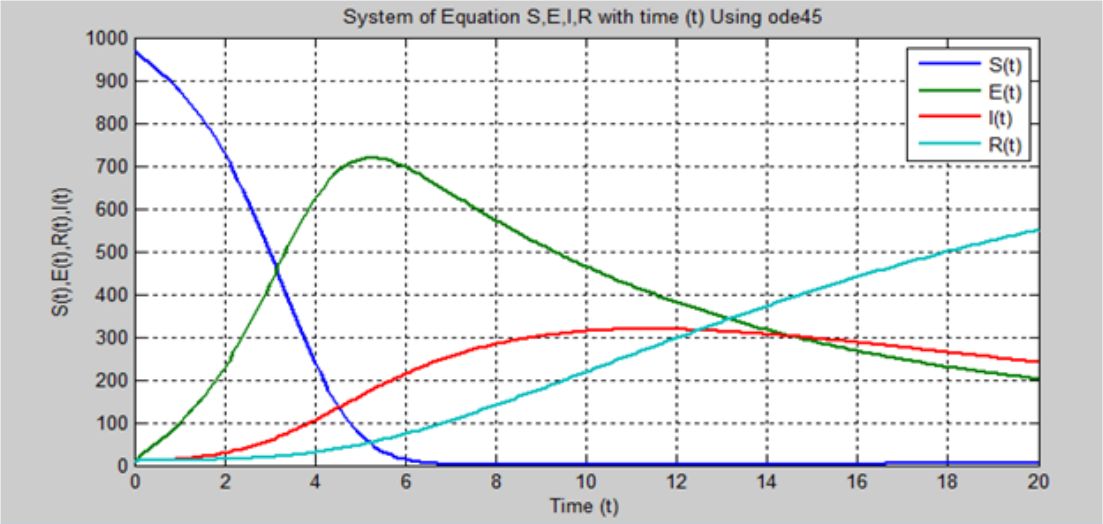

Figure 4.6: SEIR-Graph with time (t), and β=5.02

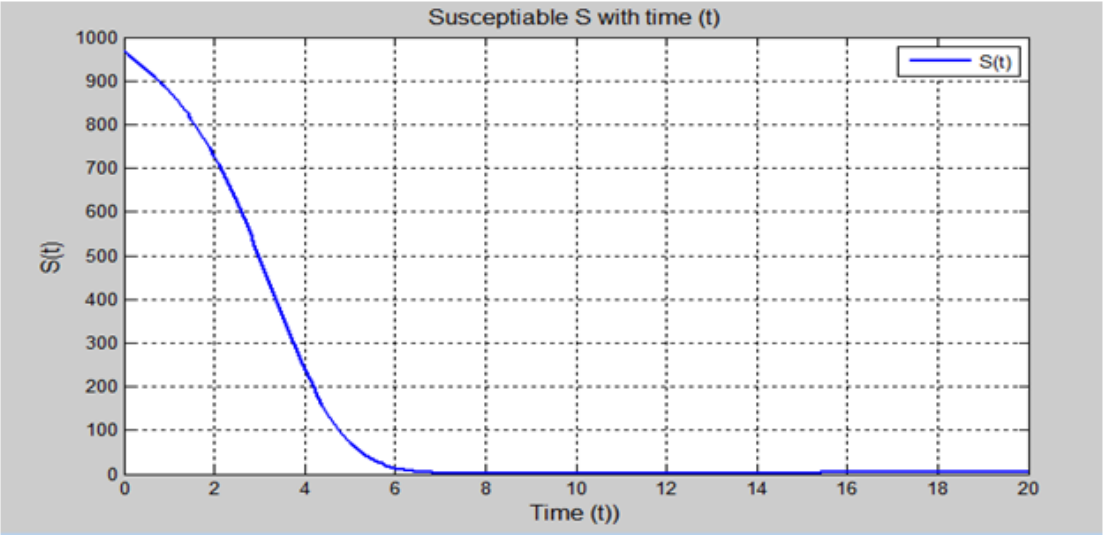

Figure 4.7: S-Graph with time (t),for β=5.02

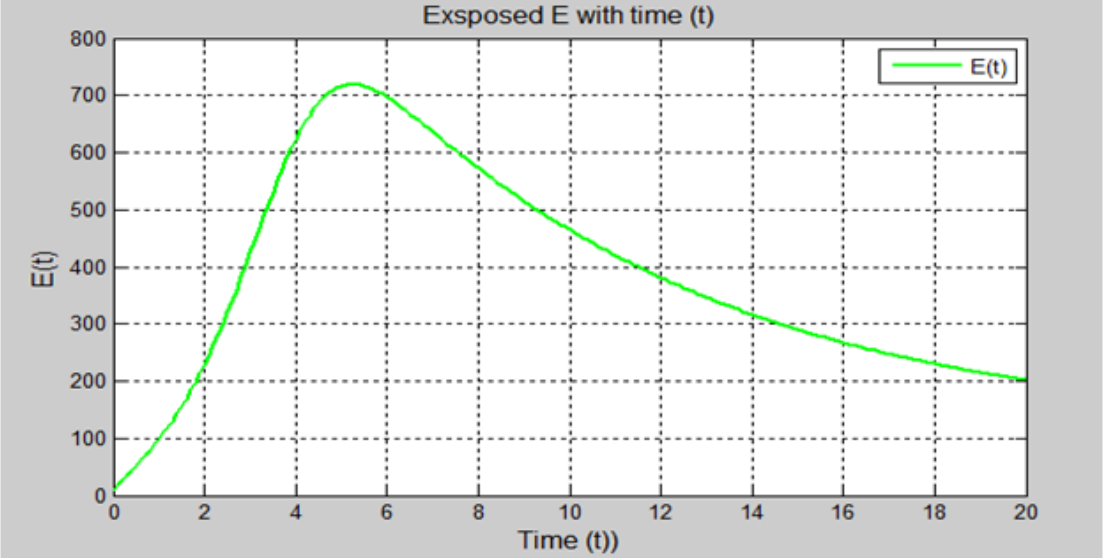

Figure 4.8: E-Graph with time (t),for β=5.02

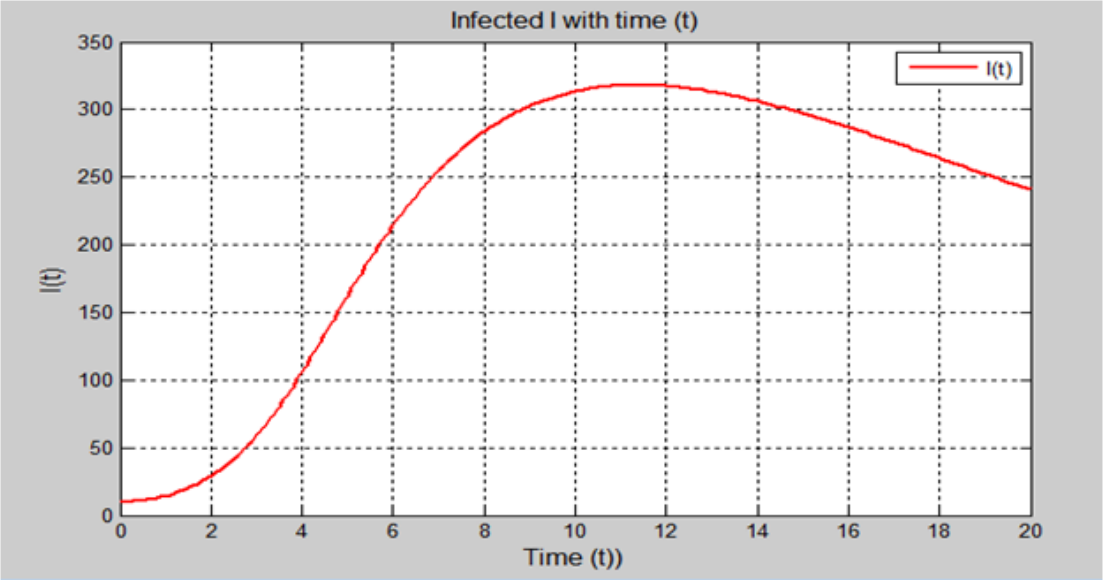

Figure 4.9: I-Graph with time (t),for β=5.02

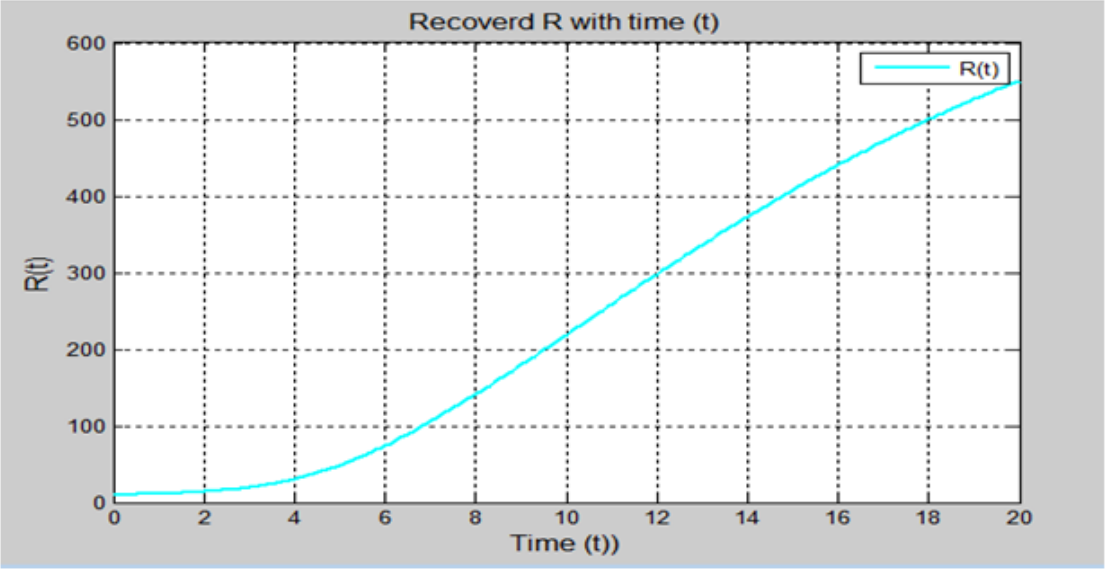

Figure 4.10: R-Graph with time (t),for β=5.02

4.1.4 Comment

Based on plots (4.1 to 4.5), using Runge-kutta 4th order and ODE45 built in function, the rate of infections from S to E, that infected population contact with s-population is β=0.02, so that the transmission factor is less. When comparing to figure (4.6 to 4.10), where in the later case the value of β is 5.02, which is to high.
The number of population in Susceptible compartment is decreased with in short period of time (t) f relatively to that of β=0.02. The question is how can reduce this rate of interaction infected with susceptible populations.

in both case the graph moves towards some constant levels with the highest population of recover, that is it is stable, but in the study of this thesis, the recovered population may loss their immunity and get back to susceptible compartment, and the issue return back and the disease is endemic.

4.2 Qualitative Analysis

4.2.1 Stability Analysis

we define about fixed point (equilibrium point),stability and unstability (definition 3.1 to 3.4) Stability is important: for

- Everything should be stable to be observable
- Crucial for understanding complex systems

The eigenvalues of a system linearized around an equilibrium can determine the stability behavior of a system around the fixed point.
Definitions 4.2 :-
4.2.1. Eigenvector:- A vector that maintains its direction after undergoing a linear transformation. Also called characteristic vectors.

4.2.2 Eigenvalue: The scalar value that the eigenvector was multiplied by during the linear transformation. Also called characteristic values.

Steps for Eigenvalue stability method

- Step 1: Determining the equilibria
- Step 2: Determine the eigenvalue of the equilibria
- Step 3: Determine the stability based on the sign of the eigenvalue

Linear stability analysis

Linear stability of dynamical equations can be analyzed in two parts: one for scalar equations and the other for two dimensional systems;

Linear stability analysis for scalar equations:-To analyze the ODE x′=f(x) locally about the equilibrium point x =$\overline{x}$, we expand the function f (x) in a Taylor series about the equilibrium point $\overline{x}$. To emphasize that we are doing a local analysis, it is customary to make a change of variables from the dependent variable x to a local variable. Let

$$x(t) = \overline{x} + u(t). \tag{4.1}$$

where it is assumed that u(t)$\ll$ 1, so that we can justify dropping all terms of order two and higher in the expansion. Substituting x(t)=$\overline{x}$+u(t). into the RHS of the ODE yields;

$$f(x(t)) = f((\overline{x}) + u(t)) \tag{4.2}$$

by using Taylors series, and dropping higher order terms, we have

$$f(x) \approx f'(\overline{x})u(t). \tag{4.3}$$

Note that dropping these higher order terms is valid since u(t) $\ll$1. Now substituting x(t) = $\overline{x}$+ u(t) into the LHS of the ODE,

$$u' = f'(\overline{x})u(t) \tag{4.4}$$

The goal is to determine if we have growing or decaying solutions. If the solutions grows, then the equilibrium point is unstable. If the solution decays, then the fixed point is stable. To determine whether or not the solution is stable or unstable we simply solve the ODE and get the solution as

$$u(t) = u_0 exp(f'(\overline{x})t) \tag{4.5}$$

where u_0 is a constant. Hence, the solution is growing if f′($\overline{x}$) > 0,we call the equilibrium point is stable and decaying if f′ ($\overline{x}$) < 0, we call the equilibrium point is unstable.

Theorem 4.1 : Suppose for scalar differential equation

$$x' = f(x) \tag{4.6}$$

the derivative function f′ is continuous on an open interval I where the equilibrium point $\overline{x}$ ∈ I, Then the equilibrium point $\overline{x}$ is locally stable if f′($\overline{x}$) < 0 and it is unstable if f′($\overline{x}$) > 0. If the equilibrium point is stable and in addition

$$\lim_{t \to \text{inf}} x(t) = \overline{x} \tag{4.7}$$

then it is called asymptotically stable equilibrium point.

Linear stability analysis for systems:- Consider the two dimensional nonlinear system. To make analysis for none-linear system of equation by linearizion and make discussion by looking at the behavior of th system we need to find stability of the system. To elaborate about the idea of stability and discussion qualitatively let us Consider the following two-dimensional system:

$$\overline{x} = f(x, y), \tag{4.8}$$
$$\overline{y} = g(x, y) \tag{4.9}$$

and suppose that ($\overline{x}$,$\overline{y}$) is a steady state, that is, f($\overline{x}$,$\overline{y}$) =0 and g($\overline{x}$,$\overline{y}$) =0. Note that a steady state is a point where an equilibrium of the system exist, which is the first derivative of the equation (the slop) becomes zero. Here our interest is to identify whether the steady state is stable or unstable. Lets discus with example, consider a small perturbation from the steady state by letting

$$\begin{aligned} x &= \overline{x} + u, \\ y &= \overline{y} + v, \end{aligned} \tag{4.10}$$

where both u and v are too small values.

If u and v *grow* then x and y move away from the steady state (equilibrium point), In this case, we say that the steady state is unstable, or

If u and v *decay to zero* then x and y move towards the steady state, in this case, we say that the steady state is stable. To see whether the perturbation grows or decays, we need to derive differential equations for u and v. We do so as follows:

$$\begin{aligned} u^{\cdot} = x^{\cdot} = f(x,y) \quad definition \\ = f(\overline{x}+u, \overline{y}+v) \quad substitution \\ = f(\overline{x},\overline{y}) + \frac{\partial f}{\partial x}(\overline{x},\overline{y})u + \frac{\partial f}{\partial x}(\overline{x},\overline{y})v + ... \\ (Taylor \quad series \quad expansion) \\ = \frac{\partial f}{\partial x}(\overline{x},\overline{y})u + \frac{\partial f}{\partial x}(\overline{x},\overline{y})v + ... \\ we \quad know \quad that f(\overline{x},\overline{y}) = 0, at \quad steady \quad point \end{aligned}$$

similarly we can have for v as

$$\frac{\partial f}{\partial x}(\overline{x},\overline{y})u + \frac{\partial f}{\partial x}(\overline{x},\overline{y})v + ... \tag{4.11}$$

Note that The . . . denote higher order terms, involving u^2 , v^2 , uv, etc. Since u and v are assumed to be small, these higher order terms are extremely very small. So we can neglect the higher order terms, we obtain the following linear system of equations :

$$\begin{bmatrix} u^{\cdot} \\ v^{\cdot} \end{bmatrix} = \begin{bmatrix} \frac{\partial f}{\partial x}(\overline{x},\overline{y}) & \frac{\partial f}{\partial y}(\overline{x},\overline{y}) \\ \frac{\partial g}{\partial x}(\overline{x},\overline{y}) & \frac{\partial g}{\partial y}(\overline{x},\overline{y}) \end{bmatrix} \begin{bmatrix} u \\ v \end{bmatrix} \tag{4.12}$$

, we call this matrix as the Jacobian matrix of the original system at the steady state ($\overline{x}$,$\overline{y}$) or (J($\overline{x}$,$\overline{y}$). The above linear system for u and v has the trivial steady state (u, v) = (0, 0), and the stability of this trivial steady state is determined by the eigenvalues of the matrix: The eigenvalues of the matrix determined by, by making characteristics equation (J($\overline{x}$,$\overline{y}$) -λ I)=0, where I is identity matrix. By finding the determinant from the characteristics of equation, and find the eigenvalues. The stability of the system of equation determined by based on obtained eigenvalue

- If the eigenvalues of the Jacobian matrix all have real parts less than zero, then the steady state is stable.
- If at least one of the eigenvalues of the Jacobian matrix has real part greater than zero, then the steady state is unstable.
- Otherwise there is no conclusion (then we have a borderline case between stability and instability).

Theorem 4.2 :- An equilibrium point ($\overline{x}$,$\overline{y}$) of the differential equation is stable if all the eigenvalues of J, the Jacobian evaluated at ($\overline{x}$,$\overline{y}$) have negative real parts. The equilibrium point is unstable if at least one of the eigenvalues has a positive real part.

Definitions 4.3 :
4.3.1. Asymptotically stable :- A critical point is asymptotically stable if all eigenvalues of the jacobian matrix J are negative, or have negative real parts.

4.3.2. Unstable: - A critical point is unstable if at least one eigenvalue of the jacobian matrix J is positive, or has positive real part.

4.3.3. Stable (or neutrally stable) :- Each trajectory move about the critical point within a finite range of distance.

4.3.4. Hyperbolic point:- The equilibrium is said to be hyperbolic if all eigenvalues of the Jacobian matrix have non-zero real parts.

4.3.5. Hyperbolic equilibria:- are robust(i.e., the system is structurally stable): Small perturbations of order do not change qualitatively the phase portrait near the equilibria. Moreover, local phase portrait of a hyperbolic equilibrium of a nonlinear system is equivalent to that of its linearization. This statement has a mathematically precise form known as the Hartman-Grobman. This theorem guarantees that the stability of the steady state ($\overline{x}$,$\overline{y}$) of the nonlinear system is the same as the stability of the trivial steady state (0, 0) of the linearized system.

4.3.6.Non-Hyperbolic point: - If at least one eigenvalue of the Jacobian matrix is zero or has a zero real part, then the equilibrium is said to be non-hyperbolic. Non-hyperbolic equilibria are not robust (i.e., the system is not structurally stable). Small perturbations can result in a local bifurcation of a non-hyperbolic equilibrium, (i.e), it can change stability, disappear, or split into many equilibria. Some refer to such an equilibrium by the name of the bifurcation,(Canan,C., [31]). Thus, the procedure to determine stability of ($\overline{x}$,$\overline{y}$) is as follows:

1. Compute all partial derivatives of the right-hand-side of the original system of differential equations, and construct the Jacobian matrix.
2. Evaluate the Jacobian matrix at the steady state.
3. Compute eigenvalues.
4. Conclude stability or instability based on the real parts of the eigenvalues.

Note: The theorem and procedure apply to N -dimensional systems.
Stability test for 2 by 2 matrices
let us we have a matrix A= $\begin{bmatrix} a & b \\ c & d \end{bmatrix}$ and let T = a+ d and D= ad - bc (determinant of the matrix). the matrix A is stable if T< 0 and D >0 either spiral sink or nodal sink. Generally we can have the following note's
Note that:- for graphical representation of stability analysis using

Table 6: Eigenvalue stability methods

.

No	Eigenvalue type	Stability	Oscillatory Behavior	Notation
1	All real and +	Unstable	None	Nodal source
2	All real and -	Stable	None	Nodal sink
3	Mixed Real	Unstable	None	Saddle point
4	+a +bi	Unstable	Undamped	Spiral source
5	-a+bi	Stable	Damped	Spiral Sink
6	0+bi	Unstable	undamped	Center

Table 7: Stability test for 2 by 2 matrices

.

No	Stability type	matrix test Condition	stability
1	Source	T>0, D >0, $T^2 \geq 4D$	Unstable
2	Sink	T<0, D >0, $T^2 \geq 4D$	Stable
3	Saddle	D <0, $T^2 \geq 4D$	Unstable
4	Spiral source	T>0, D >0, $T^2 < 4D$	Unstable
5	Spiral sink	T<0, D >0, $T^2 < 4D$	Stable
6	Center	T=0, D >0, $T^2 < 4D$	Neural

pplane see Appendix C

4.2.2 Construction of Next Generation Matrix

The basic reproduction number R_0 is arguably the most important quantity in infectious disease epidemiology. It is among the quantities most urgently estimated for emerging infectious diseases in outbreak situations, and its value provides insight when designing control interventions for established infections. From a theoretical point of view R_0 plays a vital role in the analysis of, and consequent insight from, infectious disease models,(Diekmann,O., et al, [29]).
There is hardly a paper on dynamic epidemiological models in the literature where R_0 does not play a role. R_0 is defined as the average number of new cases of an infection caused by one typical infected individual, in a population consisting of susceptible only. It has been shown that R_0 is mathematically characterized by regarding infection transmission as a demographic process, where producing offspring is not seen as giving birth in the demographic sense, but as causing a new infection through transmission (we will refer to this as an epidemiological birth). In a natural way this leads to viewing the infection process in terms of consecutive generations of infected individuals, in complete analogy to demographic generations. Subsequent generations growing in size then indicate a growing population (i.e. an epidemic), and the growth factor per generation indicates the potential for growth. In a natural way this growth factor is then the mathematical characterization of R_0 (Diekmann,O. et al, [29]). The next generation matrix is

$$K = FV^{-1} \tag{4.13}$$

where F and V are transmission and transition matrices, respectively, as presented in [29]. The basic reproduction number is the eigenvalue of largest magnitude, or spectral radius of the next generation matrix, that is, the number of all new infectious host types in the next generation.

$$R_0 = \rho(k) = \rho(FV^{-1}) \tag{4.14}$$

where ρ denotes the spectral radius (dominant eigenvalue) of the matrix FV. Let$\overline{X}$(t) be the vector of disease states. The vector of disease states from the equation (3.11 to 3.14) is the exposed and infectious compartement, $\overline{X}$=(E,I)^T The states can be written as

$$\frac{dE}{dt} = \beta SI - \gamma E - \phi E \tag{4.15}$$

$$\frac{dI}{dt} = \gamma E - I(\omega + \phi) \tag{4.16}$$

Note that equation (4.8 and 4.9) are made of two compartments E and I which are disease transmission and transmission. These are used for the determination of R_0. The we have matrixes F= $\begin{bmatrix} BSI \\ 0 \end{bmatrix}$ V= $\begin{bmatrix} (\gamma+\phi)E \\ (\omega+\phi)I - \gamma E \end{bmatrix}$ Next we differentiate both matrices F and V with respect to I and E to get F and V respectively. Then we can find the Jacobian for each matrix F and V at no disease (I*=0) equation (3.11). The equilibrium at no disease for equation (3.11 to 3.14) is

$$(S^*, E^*, I^*, R^*) = (\frac{N}{\phi}, 0, 0, \frac{N}{\phi})$$

Linearization using the Jacobian matrix for equation (4.15 and 4.16) yields

$$\frac{\overline{X}(t)}{dt} = J\overline{X}(t) \tag{4.17}$$

Thus the basic reproduction number for SEIRS model is

$$R^0 = \frac{\beta\gamma}{(\gamma+\phi)(\omega+\phi)} \tag{4.18}$$

4.2.3 Bifurcations

Dynamical systems that involve differential equations contain parameters. A slight variation in a parameter can have significant impact on the solution. How to continue equilibria and periodic orbits of dynamical systems with respect to a parameter? How to compute stability boundaries of equilibria and limit cycles in the parameter space? How to predict qualitative changes in systems behavior (bifurcations) occurring at these equilibrium points? on this we will also see the classification of bifurcations in terms of equilibria and periodic orbits. Especially it will present the specific bifurcation called Hopf bifurcation which refers to the development of periodic orbits from stable equilibrium point, as a bifurcation parameter crosses a critical value. Since the theory of bifurcation from equilibria based on center manifold reduction and Poincar-Normal forms, the direction of

bifurcations for the mathematical models will also be explained using this theory. Finally, by introducing several software packages and numerical methods this chapter will also cover the techniques to determine and continue in some control parameters all local bifurcations of periodic orbits of dynamical systems and relevant normal form computations combined with the center manifold theorem, including periodic normal forms for periodic orbits.
In general, in a dynamical system, a parameter is allowed to vary, then the differential system may change. An equilibrium can become unstable and a periodic solution may appear or a new stable equilibrium may appear making the previous equilibrium unstable. The value of parameter at which these changes occur is known as bifurcation value and the parameter that is varied is known as the bifurcation parameter, (Govaerts,W., et al,[30]).
Scalar autonomous differential equations can not have periodic solutions. Hopf bifurcation occurs in systems of differential equations consisting of two or more equations. This type is also referred to as a Poincare-Andronov-Hopf bifurcation. Let us define Equation (1) to be structurally stable in the case there are no qualitative changes occurring. However, the ODE (Ordinary Differential Equation) might change qualitatively. At that point, bifurcations will have occurred. Many of the basic principles for one dimensional systems apply also for two-dimensional systems. Let us define a two-dimensional system,(Canan,C., [31]).

Basic concepts of bifurcation analysis

In dynamical systems, a bifurcation occurs when a small smooth change made to the parameter values (the bifurcation parameters) of a system causes a sudden qualitative" or topological change in its behavior. Generally, at a bifurcation, the local stability properties of equilibria, periodic orbits or other invariant sets changes. It has two types;

Local bifurcations:- which can be analyzed entirely through changes in the local stability properties of equilibria, periodic orbits or other invariant sets as parameters cross through critical thresholds;and

Global bifurcations:- which often occur when larger invariant sets of the system collide with each other, or with equilibria of the system. They cannot be detected purely by a stability analysis of the equilibria ,(Canan,C., [31]).

$$\begin{aligned} x\prime &= f(x, y, t) \\ y\prime &= g(x, y, t) \end{aligned} \tag{4.19}$$

Equilibria can be found by taking the equations equal to zero, i.e.,

$$\begin{aligned} f(x, y, t) &= 0 \\ g(x, y, t) &= 0 \end{aligned} \tag{4.20}$$

We have three possibilities for the stability of an equilibrium, stable equilibrium, unstable equilibrium, and saddle equilibrium. A two-dimensional stable equilibrium is attracting in two directions, while a two-dimensional unstable equilibrium

is repelling in two directions. A saddle point is attracting in one direction and repelling in the other direction. In the less formal literature saddles are often considered just unstable equilibria. A second remark is that also the dynamics of the system around the equilibria can differ. The attracting or repelling can occur via straight orbits (a node) or via spiralling orbits (a spiral or focus). Note that, it is not possible to have a saddle focus in two dimensions. It is possible though in three of higher dimensional systems.

Bifurcation analysis

Even though the Bifurcation analysis has for one dimension, for this paper We focus Bifurcation analysis on two dimensional system of equation,by considering our system equations.

Hopf bifurcation

Definition 4.4 : A Hopf or Poincare-Andronov-Hopf bifurcation is a local bifurcation in which a fixed point of a dynamical system loses stability as a pair of complex conjugate eigenvalues of linearization around the fixed point cross the imaginary axis of the complex plane.

Consider the two dimensional system

$$\begin{aligned} \frac{dx}{dt} &= f(x, y, \tau), \\ \frac{dy}{dt} &= g(x, y, \tau) \end{aligned} \tag{4.21}$$

where τ is the parameter and suppose that $(\overline{x}(\tau)\ ,\overline{y}(\tau))$ is the equilibrium point and let $\alpha(\tau) \pm \mathrm{i}\beta(\tau)$ are the eigenvalues of the Jacobian matrix which is evaluated at the equilibrium point. In addition lets assume that the change in the stability of the equilibrium point occurs at $\tau = \tau^*$ where $\alpha(\tau^*)=0$.
First the system is transformed so that the equilibrium is at the origin and the parameter τ at $\tau^* = 0$ gives purely imaginary eigenvalues. The System of equation (4.21) is rewritten as follows;

$$\begin{aligned} \frac{dx}{dt} &= a_{11}(\tau)x + a_{12}(\tau)y + f_1(x, y, \tau), \\ \frac{dy}{dt} &= a_{21}(\tau)x + a_{22}(\tau)y + g_1(x, y, \tau). \end{aligned} \tag{4.22}$$

The linearization of the system (4.21) about the origin is given by $\frac{dX}{dt} = \mathrm{J}(\tau)\mathrm{X}$, where $\mathrm{X} = \begin{bmatrix} x \\ y \end{bmatrix}$ and $\mathrm{J}(\tau) = \begin{bmatrix} a_{11}(\tau) & a_{12}(\tau) \\ a_{21}(\tau) & a_{22}(\tau) \end{bmatrix}$ is the Jacobian matrix evaluated at origin.

Theorem 4.3. (Hopf bifurcation theorem)
Let f_1 and g_1 , in system (4.22) have continuous third order partial derivatives in x and y. Suppose that the origin is an equilibrium point of (4.22) and that the Jacobian matrix $\mathrm{J}(\tau)$ as above, is valid for all sufficiently small $|\tau|$. Moreover,

assume that the eigenvalues of matrix J(τ) are $\alpha(\tau) \pm$ i $\beta(\tau)$, where $\alpha(0) = 0$, $\beta(0) \neq 0$ such that the eigenvalues cross the imaginary axis with nonzero speed, i.e., $\frac{d\alpha}{d\tau} |_{\tau=0} \neq 0$.
Then in any open set $\cup$ containing the origin in $\Re^2$ and for any $\tau_0 > 0$, there exists a value $\overline{\tau}$,—$\overline{\tau}$— $< \tau_0$, such that the system of differential equations (4.21) has a periodic solution for $\tau = \overline{\tau}$ in $\cup$. (Allen, L.J.S). Note: The Hopf bifurcation requires at least a two dimensional differential equation system to appear.

Definition 4.5: **-**The bifurcation stated in the Hopf bifurcation theorem is called supercritical if the equilibrium point (0, 0) is asymptotically stable when $\tau = 0$ (at the bifurcation point) and it is called subcritical if the equilibrium point (0, 0) is negatively asymptotically stable (as t) when $\tau = 0$.

4.2.4 Routh Hurwitz stability

In control system theory, the RouthHurwitz stability criterion is a mathematical test that is a necessary and sufficient condition for the stability of a linear time invariant (LTI) control system. The Routh test is an efficient recursive algorithm that English mathematician Edward John Routh proposed in 1876 to determine whether all the roots of the characteristic polynomial of a linear system have negative real parts. German mathematician Adolf Hurwitz independently proposed in 1895 to arrange the coefficients of the polynomial into a square matrix, called the Hurwitz matrix, and showed that the polynomial is stable if and only if the sequence of determinants of its principal sub-matrices are all positive. The two procedures are equivalent, with the Routh test providing a more efficient way to compute the Hurwitz determinants than computing them directly. A polynomial satisfying the RouthHurwitz criterion is called a Hurwitz polynomial (Wikipedia [**?**]. The importance of the criterion is that the roots p of the characteristic equation of a linear system with negative real parts represent solutions ept of the system that are stable (bounded). Thus the criterion provides a way to determine if the equations of motion of a linear system have only stable solutions, without solving the system directly. The Routh test can be derived through the use of the Euclidean algorithm and Sturm's theorem in evaluating Cauchy indices. Hurwitz derived his conditions differently.
RouthHurwitz criterion for second, third, and fourth-degree polynomials
Definition 4.1 :- Routh Hurwitz stability criterion
For a second-degree polynomial:- $\boxed{P(s) = s^2 + a_1 s + a_0}$, all the roots are in the left half plane (and the system with characteristic equation $P(s) = 0$ is stable) if and only if both coefficients satisfy $a_i > 0$.
For a third-order polynomial : - $\boxed{P(s) = s^3 + a_2 s^2 + a_1 s + a_0}$, the conditions are that a_2 and a_0 must be positive, and $a_2 a_1 > a_0$. In general, ***the Routh stability criterion states that*** *all first-column elements of the Routh array are* **to be of the same sign**. *Systems meeting the above criteria are said to be open-loop stable; otherwise, they are unstable because there are sign changes in the first-column elements.*

4.2.5 Finding Local Stability for our Epidemiological model SEIRS

From equation eq(3.20 -3.23) above we can have the following formulations

$$S(t) + E(t) + R(t) + I(t) = N(t) \tag{4.23}$$

$$S' + E' + I' + R' = \frac{dN}{dt} \tag{4.24}$$

$$\Rightarrow \frac{dN}{dt} = \alpha N - \phi N = N(\alpha - \phi) \tag{4.25}$$

$$\Rightarrow \alpha = (\frac{1}{N})\frac{dN}{dt} + \phi \tag{4.26}$$

from equation 4.4

$$\alpha = (\frac{1}{N})\frac{dN}{dt} + \phi$$
$$\Rightarrow \frac{1}{N}dN = (\alpha - \phi)dt$$
$$\Rightarrow \int \frac{1}{N}dN = \int (\alpha - \phi)dt$$

Thus we have

$$N = \exp^{(\alpha-\phi)*t} \tag{4.27}$$

We have S + E + I + R=N which implies R=N-S - E- I - R and rewrite system of equations shown above on eq(12- 15) , and we have instead of finding from the known variable N, lets transform into

$$s = \frac{S}{N}, e = \frac{E}{N}, i = \frac{I}{N}, r = \frac{R}{N}$$
$$s + e + i + r = 1$$
$$\Rightarrow r = 1 - s - e - i \Rightarrow r = 1 - [s + e + i] \tag{4.28}$$
$$s' + e' + i' + r' = 0 \tag{4.29}$$

Now we have the following system of equations
1)..... $\frac{ds}{dt}$

$$\frac{dS}{dt} = \frac{d(sN)}{dt} = \frac{ds}{dt} * N + s * \frac{dN}{dt}$$
$$\Rightarrow \frac{ds}{dt} = \frac{1}{N} * [\frac{dS}{dt} - s * \frac{dN}{dt}]$$
$$\Rightarrow \frac{ds}{dt} = \frac{1}{N} * [\alpha * N - \beta * sN * iN + \theta * rN - \phi * sN - s * \frac{dN}{dt}]$$
$$\Rightarrow \frac{ds}{dt} = \alpha - \beta * si + \theta * r - \phi * s - s * \frac{1}{N} * \frac{dN}{dt}$$
$$\Rightarrow \frac{ds}{dt} = \alpha - \beta * si + \theta * r - s * (\phi + \frac{1}{N}\frac{dN}{dt})$$

$$\Rightarrow \frac{ds}{dt} = \alpha - \beta * si + \theta * r - s\alpha \tag{4.30}$$

2).....$\frac{de}{dt}$

$$\frac{dE}{dt} = \frac{deN}{dt} = \frac{de}{dt} * N + e * \frac{dN}{dt}$$
$$\Rightarrow \frac{de}{dt} = \frac{1}{N} * [\frac{dE}{dt} - e * \frac{dN}{dt}]$$
$$\Rightarrow \frac{de}{dt} = \frac{1}{N} * [\beta * sN * iN - \gamma * eN - \phi * eN - e * \frac{dN}{dt}]$$
$$\Rightarrow \frac{de}{dt} = \beta * si - \gamma * e - \phi * e - e * \frac{1}{N} * \frac{dN}{dt}$$
$$\Rightarrow \frac{de}{dt} = \beta * si - \gamma * e - e * (\frac{1}{N}\frac{dN}{dt} + \phi)$$

$$\Rightarrow \frac{de}{dt} = \beta * si - \gamma * e - e\alpha \tag{4.31}$$

3).....$\frac{di}{dt}$

$$\frac{dI}{dt} = \frac{diN}{dt} = \frac{di}{dt} * N + i * \frac{dN}{dt}$$
$$\Rightarrow \frac{di}{dt} = \frac{1}{N} * [\frac{dI}{dt} - e * \frac{dN}{dt}]$$
$$\Rightarrow \frac{di}{dt} = \frac{1}{N} * [\gamma * eN - \omega * iN - \phi * iN - i * \frac{dN}{dt}]$$
$$\Rightarrow \frac{di}{dt} = \gamma * e - \omega * i - \phi * i - i * \frac{1}{N} * \frac{dN}{dt}$$
$$\Rightarrow \frac{di}{dt} = \gamma * e - \omega * i - i * (\frac{1}{N}\frac{dN}{dt} + \phi)$$

$$\Rightarrow \frac{di}{dt} = \gamma * e - \omega * i - i\alpha \tag{4.32}$$

4).....$\frac{dr}{dt}$

$$\frac{dR}{dt} = \frac{drN}{dt} = \frac{dr}{dt} * N + r * \frac{dN}{dt}$$
$$\Rightarrow \frac{dr}{dt} = \frac{1}{N} * [\frac{dR}{dt} - r * \frac{dN}{dt}]$$
$$\Rightarrow \frac{dr}{dt} = \frac{1}{N} * [\omega * iN - \theta * rN - \phi * rN - r * \frac{dN}{dt}]$$
$$\Rightarrow \frac{dr}{dt} = \omega * i - \theta * r - \phi * r - r * \frac{1}{N} * \frac{dN}{dt}$$
$$\Rightarrow \frac{dr}{dt} = \omega * i - \theta * r - r * (\frac{1}{N}\frac{dN}{dt} + \phi)$$

$$\Rightarrow \frac{dr}{dt} = \omega * i - \theta * r - r\alpha \tag{4.33}$$

Now, from equation (22) e have r=1-[s+e+i] , and lets substitute in to each of equations (24,25, and 26), and then we have the following system of equations.

$$\frac{ds}{dt} = A - e\theta - i\theta - As - \beta(si) \tag{4.34}$$

$$\frac{de}{dt} = \beta(si) - eC \tag{4.35}$$

$$\frac{di}{dt} = \gamma e - i(D) \tag{4.36}$$

$$where - A = \alpha + \theta \tag{4.37}$$

$$C = \gamma + \alpha \tag{4.38}$$

$$D = \omega + \alpha \tag{4.39}$$

$$\tag{4.40}$$

From equation (23), we ahve

$$\frac{dr}{dt} = -(\frac{ds}{dt} + \frac{de}{dt} + \frac{di}{dt}) \tag{4.41}$$

Thuse

$$\frac{dr}{dt} = -[A - e\theta - i\theta - As - \beta(si) + \beta(si) - eC + \gamma e - i(D)] \tag{4.42}$$

From the transformed subsystem in (4.12, 4.13 and 4.14), the local stability is analyzed to determine the disease-free equilibrium (DFE):

$$\overline{X}_{DFE} = (s, e, i) = (s^*, 0, 0) \tag{4.43}$$

and endemic equilibrium (EE):

$$\overline{X}_{EE} = (s, e, i) = (s^*, 0, 0) \tag{4.44}$$

Specifically, the equilibrium points are computed by setting $\frac{ds}{dt}$=0, $\frac{de}{dt}$=0, and $\frac{di}{dt}$=0 and solving for s, e, and i in (4.12,4.13 and 4.14) to compute the two equilibrium points. From the equilibrium points, the Jacobian matrix J is calculated. The equilibrium point by definition (1.2) $\frac{ds}{dt}$ =0 , $\frac{de}{dt}$=0 and $\frac{di}{dt}$=0, so that let as find the equilibrium point for DFE.

4.2.6 The Jacobian matrix

Take the partial derivatives with respect to s in the first column ,respect to e in second column and respect to i in the third column.
Evaluate the Jacobi at the steady states of s,e and i

$$J(X) = J_{(s,e,i)} = \begin{bmatrix} \frac{ds}{dt} \\ \frac{de}{dt} \\ \frac{di}{dt} \end{bmatrix} = \begin{bmatrix} A - e\theta - i\theta - As - \beta(si) \\ \beta(si) - eC \\ \gamma(e) - Di \end{bmatrix} = \begin{bmatrix} F \\ G \\ H \end{bmatrix} \tag{4.45}$$

from the Jacobian matrix evaluate the equilibrium point to decide on the local stability, which is directly determined from the eigenvalues λ of:

$$|J(X) - \lambda I| = 0 \tag{4.46}$$

Based on the eigenvalues λ of (4.24), the linearized system will either be stable (all the eigenvalues of the Jacobian evaluated at the equilibrium point contain negative real parts) or unstable (at least one of the eigenvalues of the Jacobian evaluated at the equilibrium point has positive real part) for the transformed subsystem, this leads as to a theorem

Theorem 1. :- An equilibrium point X^* of the differential equation X^*=f(x) is stable if all the eigenvalues of J (The Jacobian Matrix) , the Jacobian evaluated at x , have negative real parts. The equilibrium point is unstable if at least one of the eigenvalues has a positive real part, (Marc, 2005, [38]). theorem

4.2.7 Disease-Free Equilibrium

$$J(s,e,i) = J(s,0,0) = \begin{bmatrix} \frac{\partial F}{\partial s}, & \frac{\partial F}{\partial e}, & \frac{\partial F}{\partial i} \\ \frac{\partial G}{\partial s}, & \frac{\partial G}{\partial e}, & \frac{\partial G}{\partial i} \\ \frac{\partial H}{\partial s}, & \frac{\partial H}{\partial e}, & \frac{\partial H}{\partial i} \end{bmatrix} \tag{4.47}$$

$$= \begin{bmatrix} -A-\beta(i) & -\theta & -\theta-\beta(s) \\ \beta(i) & -C & \beta(s) \\ 0 & \gamma & -D \end{bmatrix} \tag{4.48}$$

Now let us find the eigenvalue of the Jacobi at the steady point (s,0,0)

$$\left|J_{(s,e,i)} - \lambda(I)\right| = 0 \tag{4.49}$$

$$\Rightarrow \left| \begin{bmatrix} -A-\beta(i) & -\theta & -\theta-\beta(s) \\ \beta(i) & -C & \beta(s) \\ 0 & \gamma & -D \end{bmatrix} - \lambda(I) \right| = 0 \tag{4.50}$$

$$\Rightarrow J_{(s,0,0)} = \left| \begin{bmatrix} -A-\beta(i)-\lambda & -\theta & -\theta-\beta(s) \\ \beta(i) & -C-\lambda & \beta(s) \\ 0 & \gamma & -D-\lambda \end{bmatrix} \right| = 0 \tag{4.51}$$

$$\Rightarrow J_{(s,0,0)} = \left| \begin{bmatrix} -A-\lambda & -\theta & -\theta-\beta(s) \\ 0 & -C-\lambda & \beta(s) \\ 0 & \gamma & -D-\lambda \end{bmatrix} \right| = 0 \tag{4.52}$$

In disease free equilibrium, e=i=0, and

$$\frac{ds}{dt} = 0 \Rightarrow A - \theta(e) - \theta(i) - A(s) - \beta(si) = 0$$
$$\Rightarrow A - A(s) = 0; \Leftrightarrow s = 1 \tag{4.53}$$

Expand the above formulation and we have;

$$(-A-\lambda)\begin{bmatrix}-C-\lambda & \beta \\ \gamma & -D-\lambda\end{bmatrix}=0 \tag{4.54}$$

By evaluating the determinants in (4.32), the eigenvalues are determined from the cubic polynomial: Note that the other result becomes zero, and we have

$$\begin{aligned}\Rightarrow P(\lambda)=(-A-\lambda)\left[CD+\lambda(D)+\lambda(C)+\lambda^2-\beta\gamma\right]=0\\ \Rightarrow -CDA-\lambda(DA)-\lambda(AC)-\lambda^2(A)+\beta\gamma(A)-\lambda(CD)_-\\ -\lambda^2(D)-\lambda^2(C)-\lambda^3+\beta\gamma\lambda=0\\ \Rightarrow P(\lambda)=\lambda^3+\lambda^2[A+C+D]+\lambda[AD+AC+CD_-\\ -\beta\gamma]+CDA-\beta\gamma A=0\end{aligned} \tag{4.55}$$

where the three eigenvalues λ are dependent on the parameters γ and β and constants A, C, and D. Unfortunately, the eigenvalues are difficult to compute for the cubic polynomial in (4.33) without any specific values for the parameters γ and β and constants A, C, and D. In order to determine the parameter and constant independent local stability of the DFE $\overline{X}_{(DFE)}$ in (4.21), the Routh Hurwitz criteria is applied to the cubic polynomial in (4.33) with the coefficients: Let :-

$$\begin{aligned}a_1&=A+C+D\\ a_2&=AD+AC+CD-\beta\gamma\\ \Rightarrow a_2&=A(D+C)+CD-\beta\gamma\\ a_3&=CDA-\beta\gamma A\end{aligned}$$

from equation (4.15,4.16 and 4.17)

$$a_1=3\alpha+\theta+\gamma+\omega \tag{4.56}$$

$$a_2=(\alpha+\theta)(\gamma+2\alpha+\omega)+(\gamma+\alpha)(\alpha+\omega)-\beta\gamma \tag{4.57}$$

$$a_3=(\gamma+\alpha)(\omega+\alpha)(\alpha+\theta)-\beta\gamma(\alpha+\theta) \tag{4.58}$$

Based on the Routh-Hurwitz criteria for a cubic polynomial P(λ), the three conditions:

$$a_1>0 \tag{4.59}$$

$$a_3>0 \tag{4.60}$$

$$and, a_1*a_2>a_3 \tag{4.61}$$

must satisfied for the DFE X_{DFE} in (4.21) to be locally stable. For the first condition (4.37):

$$a_1=A+C+D>0 \tag{4.62}$$

since the constants A>0, C>0 and D>0 in (4.15,4.16 and 4.17) , with the second condition (4.22)

$$a_3=CDA-\beta\gamma A>0 \tag{4.63}$$

if :

$$\frac{CDA}{\beta\gamma A} > 0 \tag{4.64}$$

From the third condition (4.23)

$$a_1 * a_2 = (A + C + D)(AD + AC + CD - \beta\gamma) \tag{4.65}$$

by cancellation of ACD and -$\beta\gamma$A in (4.41) and (4.43) is simplified as :

$$\begin{aligned} A^2(D+C) + C^2(A+D) + D^2(A+C) + 3ACD - \beta\gamma(A+C+D) > 0 \\ \frac{A}{C} + \frac{A}{D} + \frac{C}{D} + \frac{C}{A} + \frac{D}{C} + \frac{D}{A} + 2 > \frac{C\beta\gamma}{ACD} + \frac{D\beta\gamma}{ACD} \\ (\frac{A^2}{C} + \frac{A^2}{D} + \frac{AC}{D} + \frac{AD}{C} + 2) + (C+D) > \frac{A\beta\gamma}{ACD}(C+D) \end{aligned} \tag{4.66}$$

where :

$$\frac{A\beta\gamma}{ACD} \leq 1 \tag{4.67}$$

As a result of the Routh-Hurwitz criteria, all the eigenvalues λ in the cubic polynomial P(λ) in (4.33) have negative real parts to conclude that the DFE $\overline{X}_{(DFE)}$ in (4.21) is locally stable with (4.42).

4.2.8 Endemic Equilibrium Point

An Endemic Equilibrium the steady state where the disease becomes endemic, which means (s,e,i,r greater than zero),From the transformed subsystem in (4.34 to 4.36), the EE $\overline{x}_{EE}$ in (4.44) is computed by developing a relationship between i and e through $\frac{di}{dt}$=0 as :

$$\frac{di}{dt} = 0 = \gamma e - Di \tag{4.68}$$

Or:

$$i = \frac{\gamma}{D}e \tag{4.69}$$

Where:

$$\frac{e}{i} = \frac{D}{\gamma} \tag{4.70}$$

And by examining $\frac{de}{dt}$=0, we have

$$\frac{de}{dt} = 0 = \beta si - Ce \tag{4.71}$$

Or: - we have

$$s = \frac{C}{\beta}\frac{e}{i} \tag{4.72}$$

Then by substituting eq(4.70) in to (4.72) to get the first coordinate of EE $\overline{X}_{EE}$ as :

$$s = \frac{CD}{\beta\gamma} \tag{4.73}$$

And with $\frac{ds}{dt}$=0 we have :

$$\frac{ds}{dt} = 0 = A - \theta e - \theta i - As - \beta si \tag{4.74}$$

Or we have :

$$s(A + \beta i) = A - \theta e - \theta i \tag{4.75}$$

Then now eq(4.73 inserted into eq(4.75) with the value of s, and we have :

$$\frac{CD}{\beta\gamma}(A + \beta i) = A - \theta e - \theta i \tag{4.76}$$

After distribuiting and arranging terms in eq(4.76) we have:

$$i(\frac{CD}{\gamma} + \theta) = A - \theta e - \frac{ACD}{\beta\gamma} \tag{4.77}$$

from eq(4.69) $\Rightarrow$

$$(\frac{\gamma}{D}e)(\frac{CD}{\gamma} + \theta) = A - \theta e - \frac{ACD}{\beta\gamma} \tag{4.78}$$

Or by rearranging eq(4.78) we have

$$e[(\frac{\gamma}{D})(\frac{CD}{\gamma} + \theta) + \theta] = A - \frac{ACD}{\beta\gamma} \tag{4.79}$$

by simplifing eq(4.79) we have got

$$e[(C + \frac{\theta\gamma}{D} + \theta] = A - \frac{ACD}{\beta\gamma} \tag{4.80}$$

Or

$$e[\frac{CD + \theta\gamma + \theta D}{D}] = \frac{\beta\gamma A - ACD}{\beta\gamma} \tag{4.81}$$

To get the second coordinate of EE $\overline{X}_{EE}$ as :

$$e = (\frac{D}{CD + \theta\gamma + \theta D})(\frac{\beta\gamma A - ACD}{\beta\gamma}) \tag{4.82}$$

Then through substitution of eq(4.82) to eq(4.69), the third coordinate of the EE $\overline{X}_{EE}$ is given as follow:

$$i = (\frac{\gamma}{D})(\frac{D}{CD + \theta\gamma + \theta D})(\frac{\beta\gamma A - ACD}{\beta\gamma}) \tag{4.83}$$

$$i = (\frac{\beta\gamma A - ACD}{\beta(CD + \theta\gamma + \theta D)}) \tag{4.84}$$

Thus from eq(4.73), eq(4.82) and eq(4.84), the EE $\overleftarrow{X}_{EE}$ in eq(4.44) is given by:

$$\overline{X}_E E = (s, e, i) = (s^*, e^*, i^*)$$
$$= (\frac{CD}{\beta\gamma}, (\frac{D}{CD + \theta\gamma + \theta D})(\frac{\beta\gamma A - ACD}{\beta\gamma}), (\frac{\beta\gamma A - ACD}{\beta(CD + \theta\gamma + \theta D)}) \tag{4.85}$$

From given equation (4.85) it makes sense only if :

$$\beta\gamma A - ACD > 0 \tag{4.86}$$

Since all the constants A, B, C, and D and parameters θ, γ, and β in (4.85) are positive values. By manipulating the inequality in (4.86), the epidemic condition reproduction number R_0 is given as:

$$R_0 = \frac{\beta\gamma A}{ACD} > 1 \tag{4.87}$$

The epidemic condition R_0 in (4.87) is the basic reproduction value and is the most important quantity to consider for analyzing any epidemiological model. In particular, R_0 determines whether an epidemic occurs for infectious diseases since R_0 is the average number of secondary infections produced by one infected individual during the mean period of infection in a fully susceptible population.
If $R_0 \leq 1$, then, on average, the number of new infections produced by one infected individual over the mean course of the infectious disease is less than unity, which implies the infectious disease dies out eventually.
Conversely, if $R_0 > 1$, then, on average, the number of new infections produced by one infected individual is greater than unity, which leads to the persistence of the infectious disease as an epidemic.
At the EE $\overline{X}_{EE}$ in (4.85),and from equation (4.34 to 4.36),the Jacobian matrix J(X) is given by: $J(\overline{X}_{EE}) = \begin{bmatrix} -\beta i^* - A & -\theta & -\theta - \beta s^* \\ \beta i^* & -C & \beta s^* \\ 0 & \gamma & -D \end{bmatrix}$ with the characteristics equation having eigenvalue λ

$$|J(\overline{X}_{EE} - \lambda I| = 0 \tag{4.88}$$

OR this is eauivalently written as $\begin{bmatrix} -\beta i^* - A - \lambda & -\theta & -\theta - \beta s^* \\ \beta i^* & -C - \lambda & \beta s^* \\ 0 & \gamma & -D - \lambda \end{bmatrix} = 0$

Which is expanded as:

$$(-\beta i^* - A - \lambda)\begin{vmatrix} -C - \lambda & \beta s^* \\ \gamma & -D - \lambda \end{vmatrix} + (\theta)\begin{vmatrix} -\beta i^* & \beta s^* \\ 0 & -D - \lambda \end{vmatrix} + \text{-}$$
$$(-\theta - \beta s^*)\begin{vmatrix} \beta i^* & -C - \lambda \\ 0 & \gamma \end{vmatrix} = 0 \tag{4.89}$$

Through evaluation of the determinants in (4.89), the eigenvalues λ are computed from the cubic polynomial:

$$\begin{aligned} p(\lambda) = \lambda^3 + \lambda^2(A + C + D + \beta i^*) + \\ \lambda(\beta C i^* + \beta D i^* + AC + AD + CD + \beta\theta i^*) - \\ (\beta CD i^* + \beta^2\gamma s^* i^* + ACD - \beta\theta D i^* + \beta\theta i^*) = 0 \end{aligned} \tag{4.90}$$

by substituting s,e,i from equation (4.73,4.82 and 4.84) we have

$$p(\lambda) = \lambda^3 + \lambda^2(A + C + D - \beta(\frac{\beta\gamma A - ACD}{\beta(CD + \theta\gamma + \theta D)})) - \lambda(\beta C(\frac{\beta\gamma A - ACD}{\beta(CD + \theta\gamma + \theta D)}) + \beta D(\frac{\beta\gamma A - ACD}{\beta(CD + \theta\gamma + \theta D)}) + AC + AD + CD + \beta\theta(\frac{\beta\gamma A - ACD}{\beta(CD + \theta\gamma + \theta D)})) - (\beta CD(\frac{\beta\gamma A - ACD}{\beta(CD + \theta\gamma + \theta D)}) + \beta^2\gamma(\frac{CD}{\beta\gamma})(\frac{\beta\gamma A - ACD}{\beta(CD + \theta\gamma + \theta D)})) + ACD - \beta\theta D(\frac{\beta\gamma A - ACD}{\beta(CD + \theta\gamma + \theta D)}) + \beta\theta\gamma(\frac{\beta\gamma A - ACD}{\beta(CD + \theta\gamma + \theta D)})) = 0 \quad (4.91)$$

where the three eigenvalues are dependent on the parameters and , constants A, C, and D, and first and third coordinates of EE $\overline{X}_{EE}$, namely s* andi* in (4.85). In a similar manner to the eigenvalues for the cubic polynomial in (4.55), the eigenvalues for the cubic polynomial in (4.91) are even more difficult to compute without any specific values for the parameters γ, β and θ constants A, C, and D. The Routh-Hurwitz criteria with conditions is again applied to now the cubic polynomial in (4.91) to determine the parameter and constant independent local stability of the EE $\overline{X}_{EE}$ with the coefficients:

$$a_1 = (A + C + D + \beta(\frac{\beta\gamma A - ACD}{\beta(CD + \theta\gamma + \theta D)})) \quad (4.92)$$

$$a_2 = (\beta C(\frac{\beta\gamma A - ACD}{\beta(CD + \theta\gamma + \theta D)}) + \beta D(\frac{\beta\gamma A - ACD}{\beta(CD + \theta\gamma + \theta D)}) + AC + AD + CD + \beta\theta(\frac{\beta\gamma A - ACD}{\beta(CD + \theta\gamma + \theta D)})) \quad (4.93)$$

$$a_3 = (\beta CD(\frac{\beta\gamma A - ACD}{\beta(CD + \theta\gamma + \theta D)}) + \beta^2\gamma(\frac{CD}{\beta\gamma})(\frac{\beta\gamma A - ACD}{\beta(CD + \theta\gamma + \theta D)}) + ACD - \beta\theta D(\frac{\beta\gamma A - ACD}{\beta(CD + \theta\gamma + \theta D)}) + \beta\theta\gamma(\frac{\beta\gamma A - ACD}{\beta(CD + \theta\gamma + \theta D)})) \quad (4.94)$$

Rearranging the equation, and since the constants A > 0, C > 0, and D > 0 and parameters $\theta > 0$, $\beta > 0$, $\gamma > 0$ First condition a_1 >0, and with the second condition a_3 >0, which is , after simplifying a_3, we have

$$a_3 = \beta\gamma A - ACD > 0 \quad (4.95)$$

From this for third condition and after simplifying equation (4.92 to 4.94) and the product a_1 and a_2, we have $a_1\ a_2 > a_3$ As a consequence of the Routh-Hurwitz criteria, all the eigenvalues λ in the cubic polynomial P(λ) in (4.91) have negative real parts to conclude that the DFE $\overline{X}_{EE}$ in (4.85) is locally stable with (4.87).

4.2.9 Using Phase-Plane diagram

PPLANE8,(8 stands for the version, we can use as 6,7, or 8), plots vector fields for planar autonomous systems. It allows the user to plot solution curves in the phase plane. It also enables the user to plot these solutions in a variety of plots versus the independent variable. There are a number of advanced features, such as finding equilibrium points, displaying linearizations, and plotting. For analyzing qualitatively, we have used pplane,by observing the graph on the pplane, we can generalize the behavior of the system of equations, for detail explanations of the dfiled and pplane, about the implementations, and utilizations,*(refer Appendex A,B and C).*

In figure (4.11) we can see, the arrows sink towards one of equilibrium point

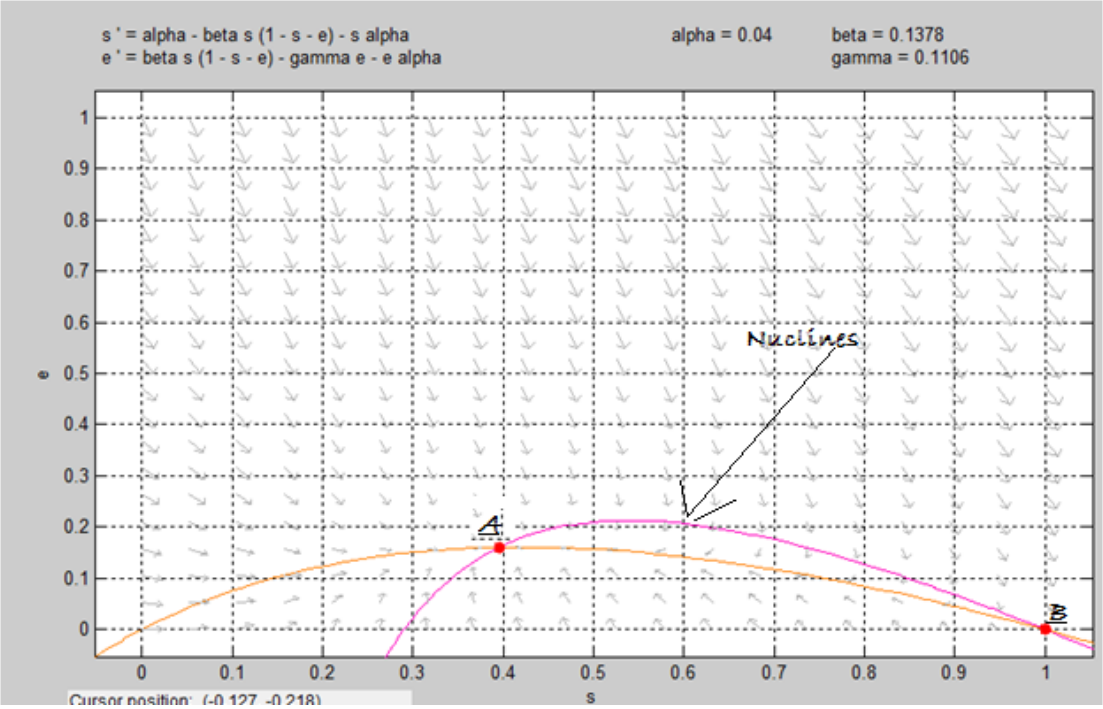

Figure 4.11: The nucline of ds/dt=0 and de/dt=0, and intersects at equilibrium points A and B. This shows the system of equations becomes zero at their intersection points. These points are called steady point.

A(0.39526,0.16062), and its respected eigenvalues λ_1=-0.04445 and λ_2=-0.20735), both are negative, see figure (4.12), pplane show the result of the Jacobi, Eigenvalues and Eigenvectors; on the other hand at equilibrium point B(1,0), the arrow towards to the point to one side of the nucline and outward from the point on the other side of the nuclline, this equilibrium point is called Saddle point and its Eigenvalues are λ_1=0.0978 and λ_2= -0.1378, one negative and one positive, see figure (4.13)Now qualitatively we can concluded about the behavior of the equations. That stable at the equilibrium point A, which is all the arrows sinks to the equilibrium and on the other equilibrium point B it is Unstable.

Again lets consider β=5.02, and look at the following figures

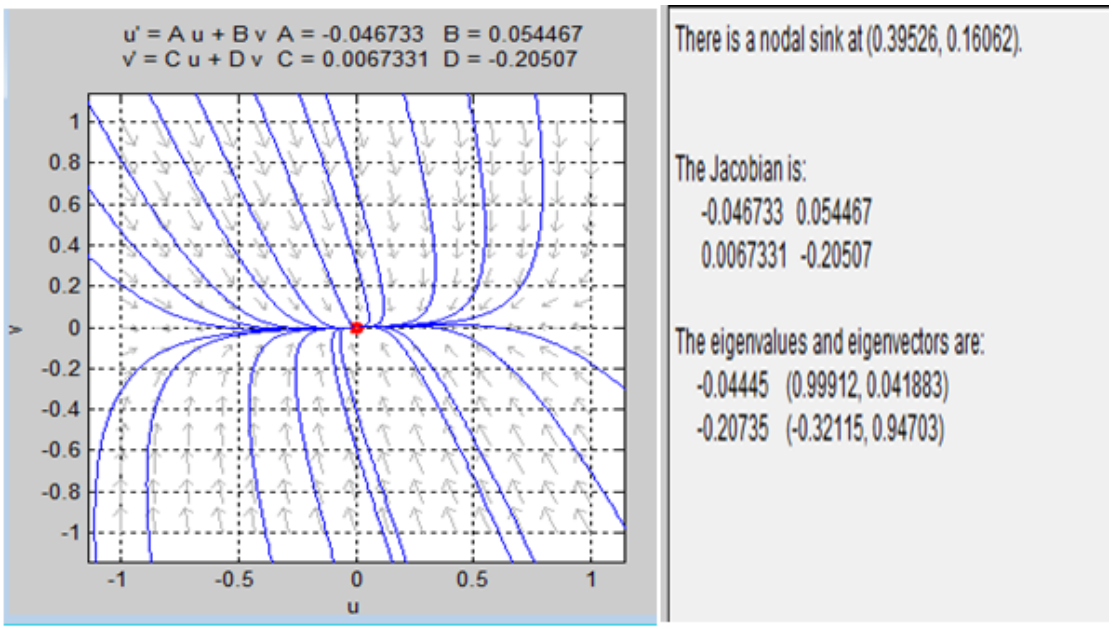

Figure 4.12: Linearaization at equilibrium point (0.39526,0.16062), it is nodal sink, at this point, the diseased reduce and die out), here we have also the Jacobi, lamda (eigenvalue and eigenvectors), here the eigenvalues both are negative which is, at this point the system is stable.

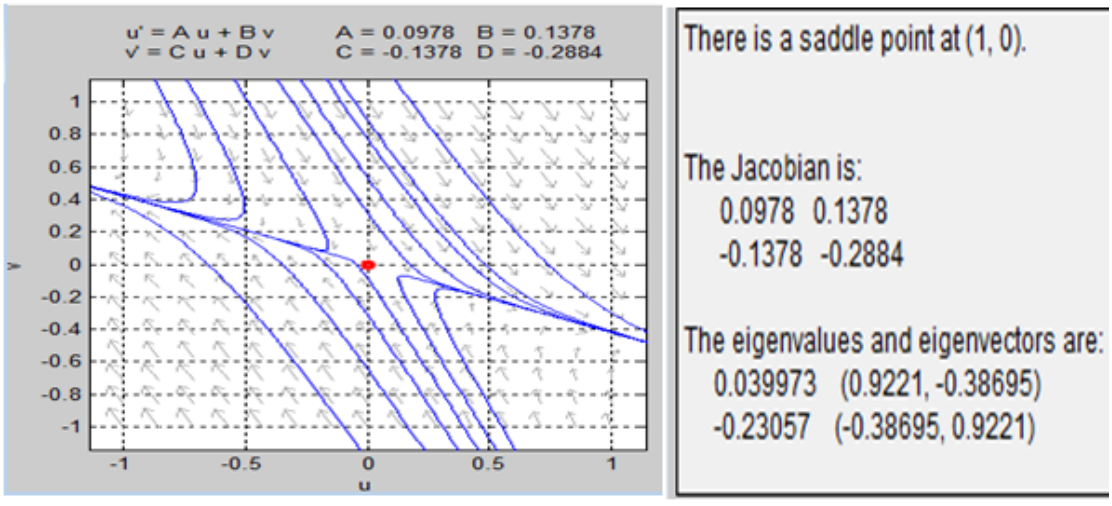

Figure 4.13: Linearization on other equilibrium point (1,0) is is saddle point, and the eigen values are not the same sign, which is the system of equation at this point is unstable.

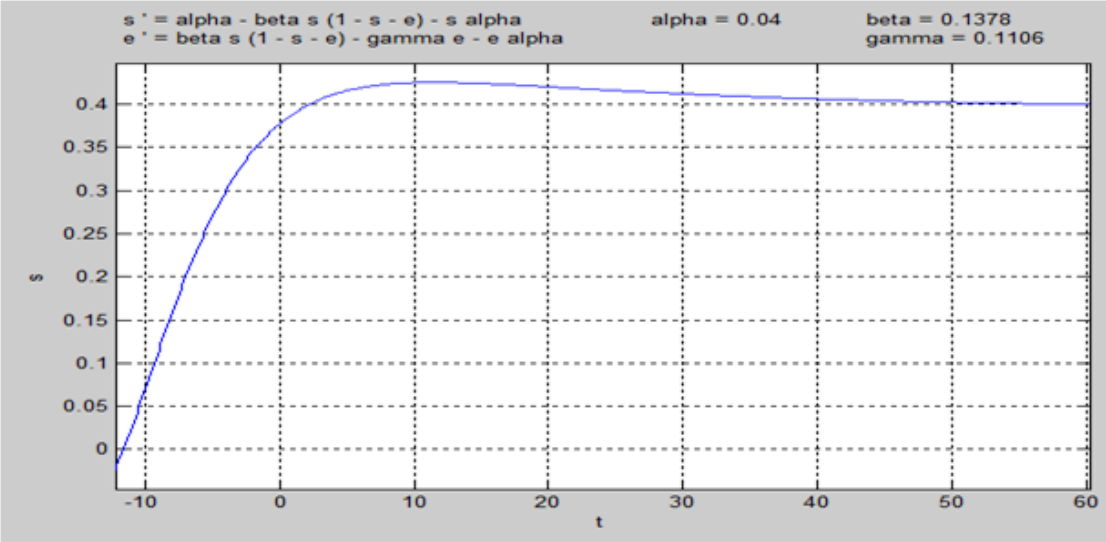

Figure 4.14: The behavior of S diagram using pplane, it increases from the initial point, and after it goes down and it looks like constant, that is stablility comes.

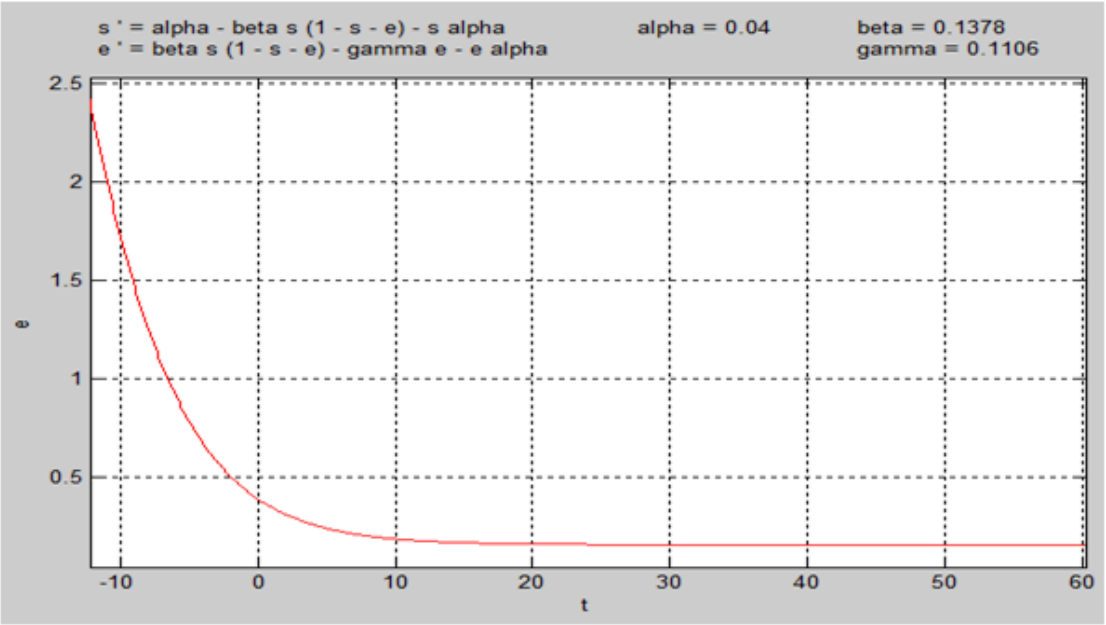

Figure 4.15: The behavior of e diagram using pplane, it decrease down and it becomes constant

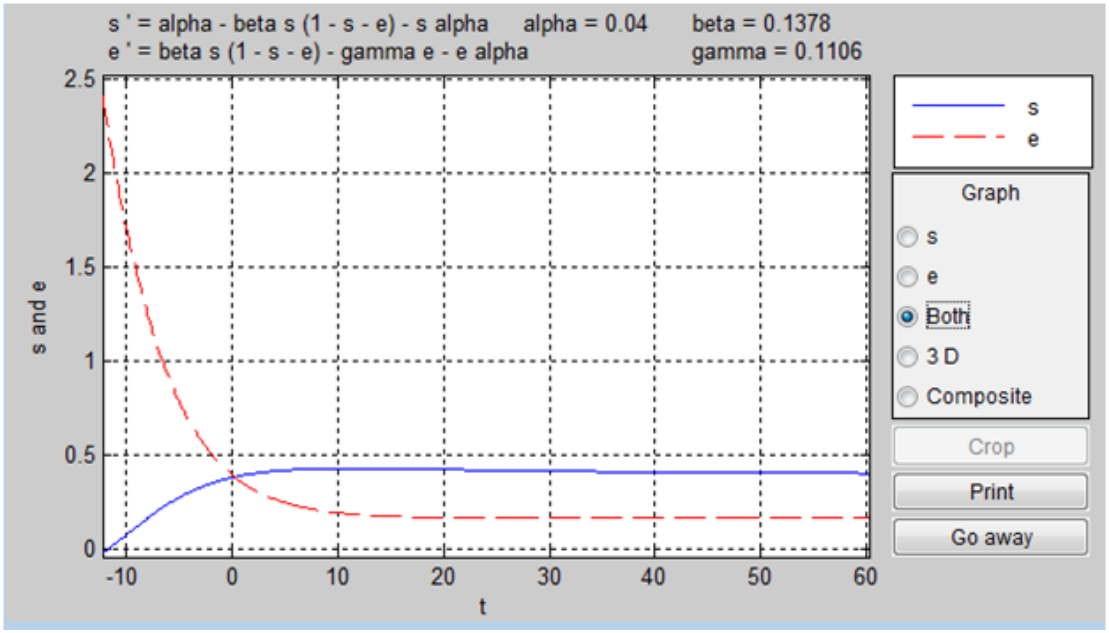

Figure 4.16: The position of s and e diagram using pplane, at alpha=0.04

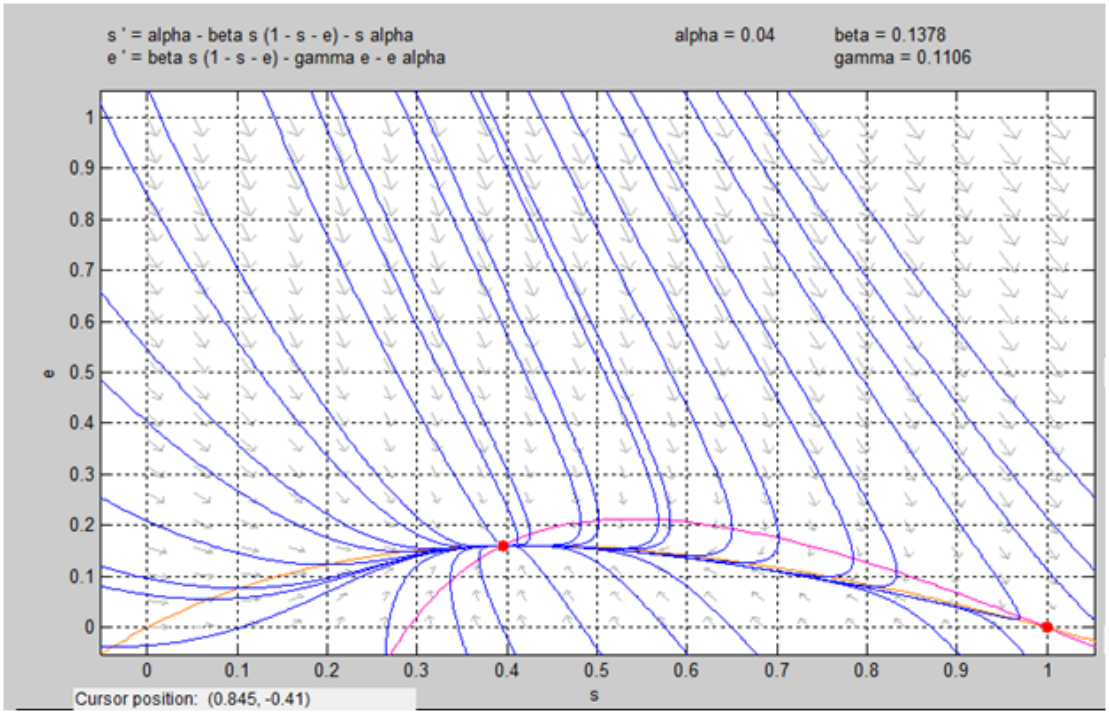

Figure 4.17: Phase Plane diagram, at apha=0.04

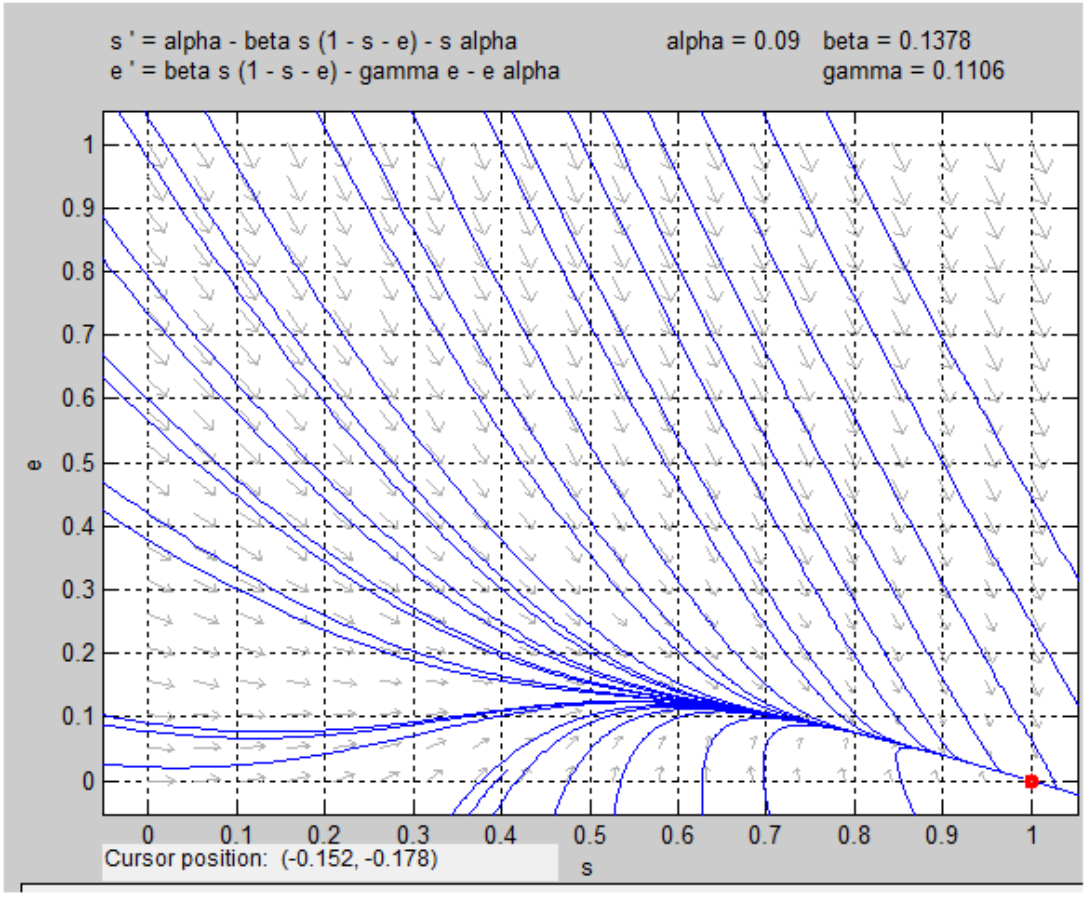

Figure 4.18: Phase Plane diagram, at alpha=0.09

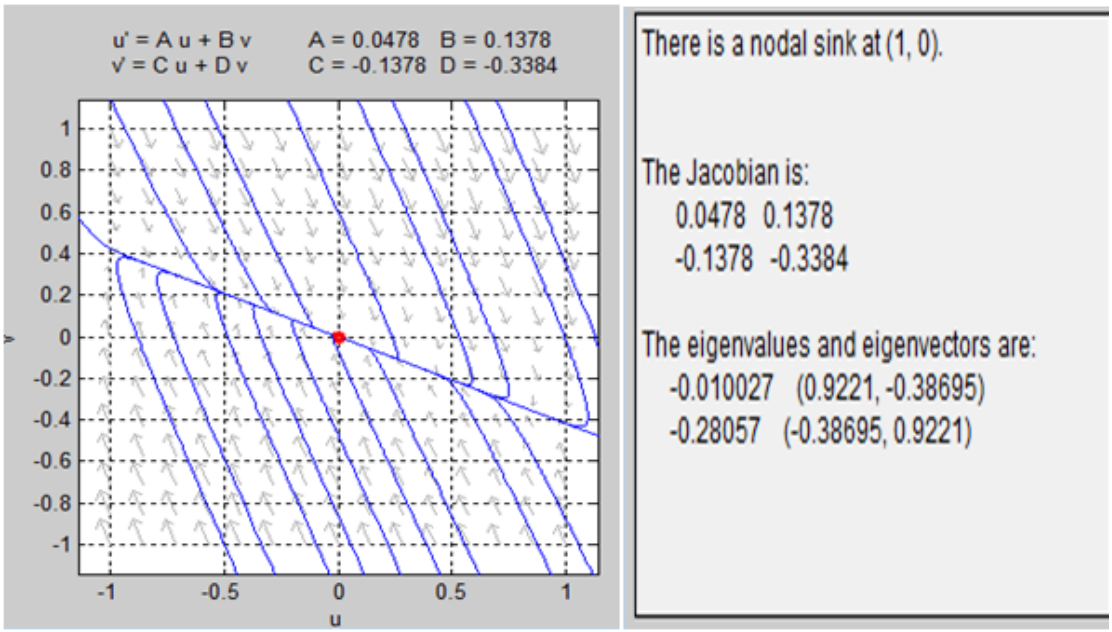

Figure 4.19: Linearization at equilibrium point, at alpha=0.04

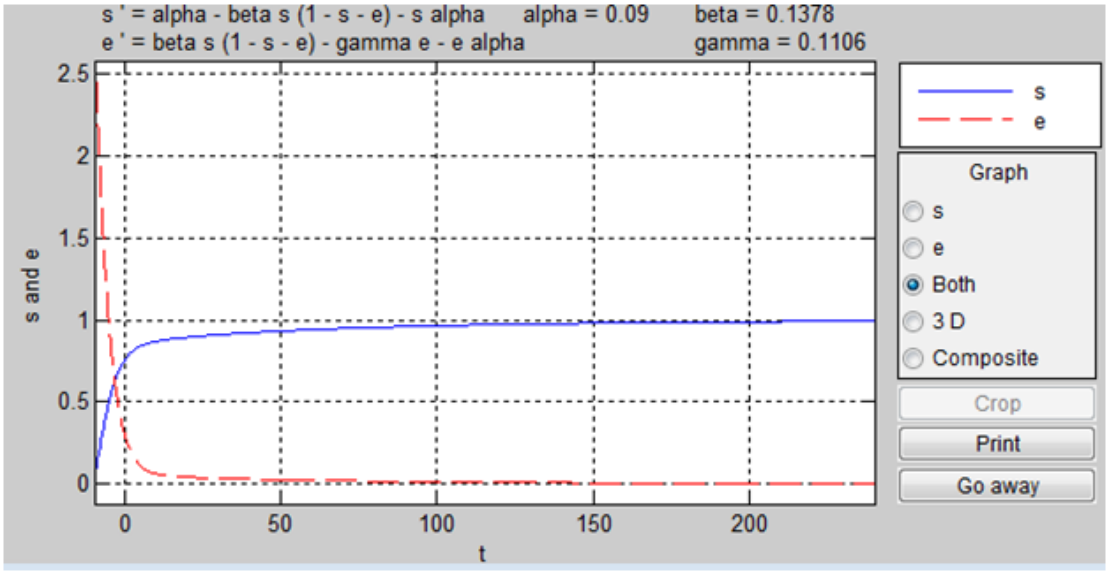

Figure 4.20: s-e diagram, at alpha=0.09

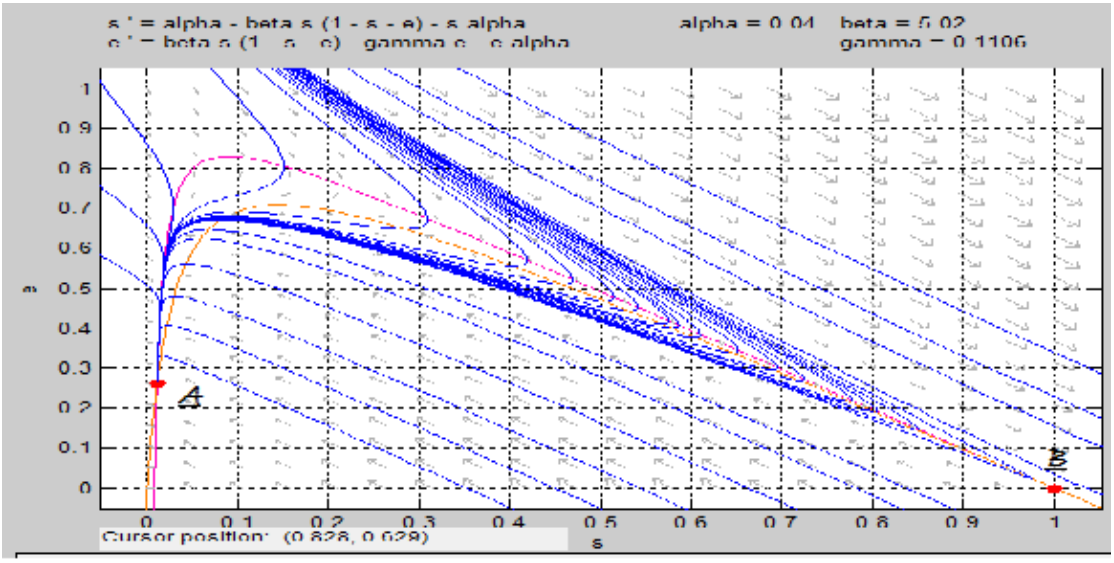

Figure 4.21: s-e diagram, at beta=5.02, the equilibrium point A and B, at A is nodal sink and saddle at B, stable and unstable respectively

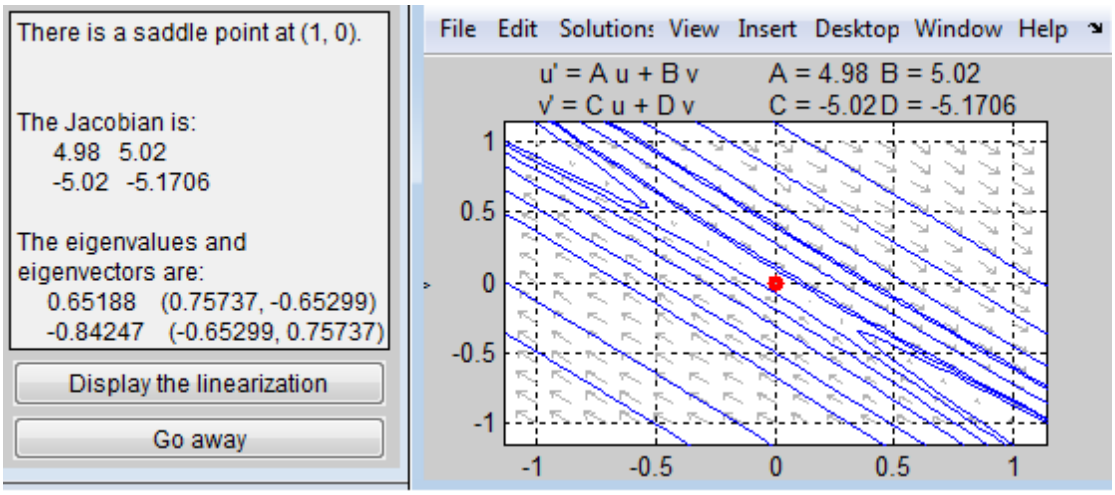

Figure 4.22: Jacobi, Eigenvalues and linearizion for the equilibrium point B at the figure(4.21), at beta=5.02, and at equilibrium point, it is saddle point

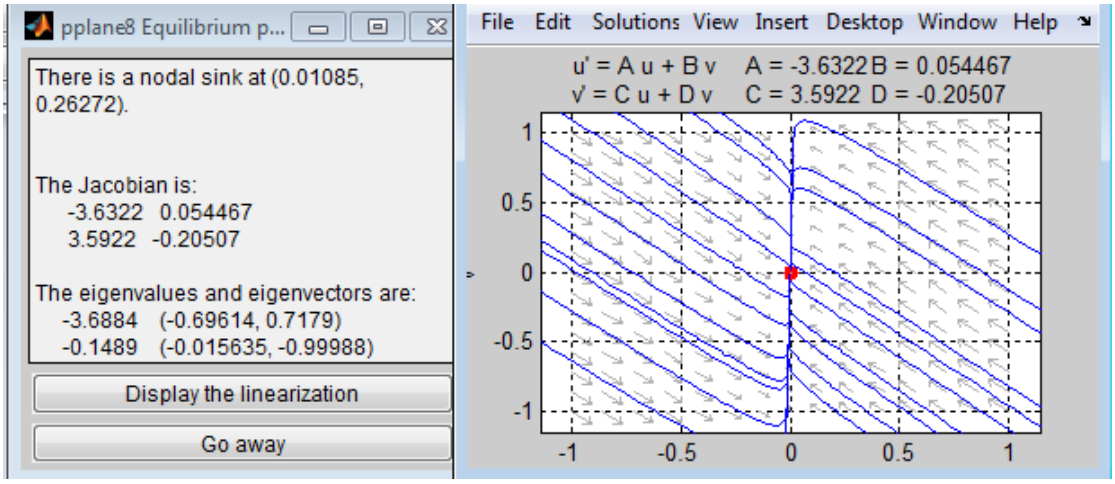

Figure 4.23: Jacobi,Eigenvalues and linearizion, at beta=5.02, and at equilibrium point in figure (4.21) A(0.01085,0.26272), it is nodal sink at this point

4.3 Comment on qualitative analysis

For figure (4.11 to 4.20) we took β=0.1378, α =0.04, at the equilibrium point A in figure (4.11) both the eigenvalues are negative, so that all the solutions at this point is sink and it is stable. That means the spread of the disease from susceptible to exposed, infected to recovery and from recovery to susceptible transition is stable, almost the rate is not changed, and it may die out. Where as at the equilibrium point B in figure 4.11, the eigenvalues has different sign, and we call it the point is saddle point, and the solution is not stable, which is the disease may spread or it may have outbreak, we know that it is not controlled, if the disease spread time arrives at the point B, in figure 4.11.

Chapter Five

5 Theory of Optimal Control

5.1 Introduction

Optimal control deals with the problem of finding a control law for a given system such that a certain optimality criterion is achieved. A control problem includes a sot functions that is a function of state and control variable. N optimal control is a set of differential equations describing the paths of the control variables that minimize the cost function. The control can be derived using Pontryagins maximum principles (a necessary condition also known as Pontryagins minimum principle or simply Pontryagins Principle), or by solving the Hamilton-Jacobi-Bellman Equations (a sufficient condition). Numerical methods for optimal control problems are generally nonlinear and therefore, generally do not have analytic solutions. As a result, it is necessary to employ numerical methods to solve optimal control problems. In the early years of optimal control (C. 1950s to 1980s) the favored approach for solving optimal control problems was that of indirect methods. An indirect method, the calculus of variations is employed to obtain the first-order optimality conditions. These conditions result in a two-point boundary-value problem. This boundary-value problem actually has a special structure because it arises from taking the derivative of a Hamiltonian. Thus, the resulting dynamical system is a Hamiltonian system of the form

$$\boxed{\dot{x} = \frac{\partial H}{\partial \lambda}} \tag{5.1}$$

$$\boxed{\dot{\lambda} = \frac{-\partial H}{\partial x}} \tag{5.2}$$

where

$$\boxed{H = L + \lambda^T a - \mu^T b} \tag{5.3}$$

,(Suzanne,L. and John,T., [36]), is the augmented Hamiltonian and in an indirect method, the boundary-value problem is solved (using appropriate boundary or transversality conditions). The beauty of using an indirect method is that the state and adjoint (i.e) are solved for and the resulting solution is ready verified to be an extremal trajectory. In a direct method, the state and/or control are approximated using an appropriate function approximation. Simultaneously, the cost functional is approximated as a cost function. Then the coefficient of the function approximations are treated as optimization variables and the problem is transcribed to a nonlinear optimization problem of the form: Minimize F(z) Subject to the algebraic constraint $g(z) = 0h(z) \leq 0$ Multi-objective Optimal Control Suppose,$x(t) \in X \subset \Re^n$ represents the state variables of a system and u(t) $\in \cup \subset \Re^n$, represents the control variables at time t, with $t_0 \leq t \leq t_f$. An optimal control problem consists of finding a piecewise continuous control u(t) and the associate state x(t) that optimizes a cost functional J[x(t), u(t)]. The majority of mathematical models that uses the optimal control theory rely on the Pontryagins Maximum Principle, which is a first-order condition for finding the

optimal solution. This is reproduced for convinces.(pontrygins Maximum Principle Lenhart and Workman (2007)) If $\dot{u}$ and $\dot{x}$ are optimal for the problem considering optimal control is state equation, u(t) is the control, t is the independent variable, t_0 is the initial time, it is the terminal time. In eq(5.3) it is free which is the state can grow over time unconditionally. Global Extreme where D is the domain Local Extreme a maximum or minimum a small interval, where I is the domain Existence of an optimal control,(.

5.2 Numerical Solutions of optimal Control Problems

Consider the optimal control problem

$$max_U \int_{t_0}^{t_1} f(t, x(t), u(t))dt \tag{5.4}$$

$$subjectto : x' = g(t, x(t), u(t)) \tag{5.5}$$

$$x(t_0) = x_0, \quad x(t_1) \quad free \tag{5.6}$$

To find a piecewise continuous function u(t) which is maximize the integral, total-enumeration methods or linear programming techniques can be employed. Any solution to the above optimal control problem must also satisfy

$$x'(t) = g(t, x(t), u(t)), x(t_0) = x_0, \tag{5.7}$$

$$\lambda(t) = -\frac{\partial H}{\partial x} = -(f_x(t, x, u) + \lambda(t)g_x(t, x, u)), \lambda(t_1) = 0, \tag{5.8}$$

$$0 = \frac{\partial H}{\partial x} = -(f(t, x, u) + \lambda(t)g_u(t, x, u)), atu^* \tag{5.9}$$

defined in eq . eqref e2 Equation 8 the optimal condition, can usually be manipulated to find a representation of u* in terms of t, x, and . Here we can form ODE for x and , then the first two equations form a two-point boundary value problem, and now we can use numerical methods to solve ordinary differential equations like (Runge-Kutta).
To do this first we are given an initial condition for ***the state x*** but a finale time condition for adjoint .
Second g is function of t, x, and u only. Since the values for are not needed to solve x using a standard ODE solver. Many problems require bounds on the control to achieve a realistic solution. Suppose, for instance, that our control is the amount of vaccination or chemicals used in a system. Then, clearly we require this amount to be nonnegative, i.e u $\geq$ 0.Often; the control must be bounded above. Perhaps there are physical limitations on the amount of chemicals or environmental regulations which prohibit a certain level of use. We could also have a problem where the control is the percentage of some strength or use.
Optimal control with bounded control: An optimal control with bounded control can be written in the form

$$max_u J(x(t), (u)) = \int_{t_0}^{t_f} f(t, x(t), u(t))dt \tag{5.10}$$

Subject to

$$x' = g(t(x,(t),u(t)) \tag{5.11}$$
$$x(t_0) < x_0 \tag{5.12}$$
$$a \leq u(t) \leq b \tag{5.13}$$

where a,b are fixed real constants and a < b. It is necessary to develop alternative necessary for solving the optima problems conditions. Proposition (Necessary conditions): If u * (t) and x*(t) are optimal for problem (5.38,5.39 ,5.40), then there exists a piecewise differentiable adjoint variable λ (t) such that

$$\boxed{H(t,x^*(t),u(t),\lambda(t)) \leq H(t,x(t),u^*(t),\lambda(t))} \tag{5.14}$$

,(Suzanne,L.,et al, [35]). for all controls u at each time t, where H is the Hamiltonian previously defined and

$$\lambda'(t) = -\frac{\partial H(x^*(t),u^*(t),\lambda(t)}{\partial x} \quad (adjoint \quad condition) \tag{5.15}$$
$$\lambda(t_f) = 0 \quad (Transversality \quad condtion) \tag{5.16}$$

By an adaptation of the Pontryagin's Maximum Principle(PMP), the OC must satisfy (optimality condition):
u*=

$$\begin{cases} a & if \quad \frac{\partial H}{\partial u} < 0, \quad a < \frac{\partial H}{\partial u} < b \quad if \quad \frac{\partial H}{\partial u} = 0, \quad b < \frac{\partial H}{\partial u} < b \quad if \quad \frac{\partial H}{\partial u} > 0 \end{cases} \tag{5.17}$$

if we have a minimization problem, then u* is chosen to minimize H point wise. This has effect of reversing < and >. If $\frac{\partial^2 H}{\partial u^2} < 0$ at u* then $u*$ is the maximization of the problem, while $\frac{\partial^2 H}{\partial u^2} < 0$ goes with minimization. We can write in a compact way the optimal $\frac{\partial H}{\partial u} = 0$ control obtained without truncation, bounded by a and b,(Esayas,Z. [12]).

$$\boxed{u^*(t) = min\left\{a, max\left\{b, \frac{\partial H}{\partial u}\right\}\right\}} \tag{5.18}$$

5.3 Forward-Backward Sweep algorithm

The technical definition of an optimal control problem is the process of determining control and state trajectory for a dynamic system over a period of time to minimize a performance index. The set of variables (functions) used to describe the mathematical state of the system. Forward-Backward Sweep method.
Algorithm for Forward-Backward Sweep methods

1. Making an initial guess for u over the interval. Store the initial guess as u
2. Using he initial condition x(t0) =x0 and stored values for u, solve x forward in time according to its differential equation in the optimality system.
3. Using the transversality condition (t1) = 0 and the stored values for u and x, solve backward in time according to its differential equation in the optimal system.

4. Update the control by entering the new x and values into the characterizing of u.

5. Check convergence. If values of the variables in this iteration and the last iteration are negligibly small, output he current values as solutions. If values are not small, return to second step.

When making the initial guess, u=0 is almost always sufficient. However if certain problems exist that needs division by zero, in this case we need to adjust our initial guess, if the algorithm has problems converging.
For tis thesis I used a Runge-Kutta 4 routine. Specifically, if x'(t)=f(t,x(t)) and x(t) are known, the the approximation of x(t+h) is given by

$$x(t+h) = x(t) + \frac{h}{6}(k_1 + 2k_2 + 2k_3 + 2k_4) \tag{5.19}$$

where

$$k_1 = f(t, x(t)) \tag{5.20}$$
$$k_2 = f(t + \frac{1}{2}h, x(t) + \frac{1}{2}k_1) \tag{5.21}$$
$$k_3 = f(t + \frac{1}{2}h, x(t) + \frac{1}{2}k_2) \tag{5.22}$$
$$k_4 = f(t + h, x(t) + k_3) \tag{5.23}$$
$$\tag{5.24}$$

On the stability and accuracy to this Runge-Kutta routines, it is sufficient to require $\sum_i = 1^n$ | u(i) - u $_{old}(i)$ to be small, where u(i) is the vector of estimated values of the control during the current iteration, and $u_{old}(i)$ is the vector of estimated values from the previous iteration. Both these vectors are of length n, which is the number of time steps. After the number of time steps, we took strict convergence test, we will require the percentage error to be negligibly small, i.e.,

$$\frac{\mid u - u_{old} \mid}{\mid u \mid} \leq \delta \tag{5.25}$$

where δ is the accepted tolerance. The control (or Control function) is an operation that controls the recording, process transmission of data. For standard problem the solution of basic optimal control problem, a set of what is called ***necessary condition must be satisfied.*** The state variable (function)
Consider the optimal control problem

$$_{max} \int_0^1 Ax(t) - Bu^2(t)dt \tag{5.26}$$

Subject to:-

$$x'(t) = -\frac{1}{2}x^2(t) + Cu(t) \tag{5.27}$$

$$x(0) = x_0 \quad fixedx(1)free$$

We require B > 0, so that this is a maximization problem. Note that the Hamiltonian given by

$$H = Ax - Bu^2 - \frac{1}{2} + C\lambda u. \tag{5.28}$$

Using optimal condition

$$0 = \frac{\partial H}{\partial u} = -2Bu + C\lambda \Rightarrow u^* = \frac{C\lambda}{2B} \tag{5.29}$$

by calculating , we can find that

$$x'(t) = -\frac{1}{2}x^2 + Cu, x(0) = x_0 \tag{5.30}$$

$$\lambda'(t) = -A + x\lambda, \lambda(1) = 0 \tag{5.31}$$

Now based on **Runge-Kutta forward sweep**, we can solve x in time. Where k_1 is the first differential equations, and then k_2, k_3, and k_4 is solving by x is replaced by x+ $\frac{h}{2k_1}$ and so on... and we are also adjust the time variable t by replacing it with t + $\frac{h}{2}$. There is no explicit dependence on t in the differential equation, but u is a function of t. So that we should replace u(i) with u(i +$\frac{h}{2}$).

The next one is solving λ, again the **Runge-Kutta backward sweep** solving λ time. to find k_1 it comes directly from the differential equation, and then for next k_2, λ is replace by λ - $\frac{h}{2k_1}$, and son on. we are moving backward in time, so the time increment is actually -$\frac{1}{N}$. Generally$\lambda(2)$ is used to find $\lambda(1)$.
The new u^* is calculated as let say ;

$$u1 = C * \frac{\lambda}{2 * B} \tag{5.32}$$

$$u = 0.5 * (u1 + oldu) \tag{5.33}$$

which means, the control u is set as the average of the last iteration of u name d oldu, and the new representation. This is the convex combination. Next the convergence test parameter of each of variables (x,u, λ), should be calculated, by taking the initial guess value of δ let say 0.0001.

$$contest1 = \delta * \sum(|\ (u)\ |) - \sum(|\ odlu - u\ |); \tag{5.34}$$

$$contest2 = \delta * \sum(|\ (x)\ |) - \sum(|\ (odlx - x)\ |); \tag{5.35}$$

$$contest3 = \delta * \sum(|\ (\lambda)\ |) - \sum(|\ (odl\lambda - \lambda)\ |); \tag{5.36}$$

$$contest = min(contest1, min(contest2, contest3)); \tag{5.37}$$

Finally find as y_1 =t; y_2=x; y_3 = λ and y_4 =u; This is well illustrated with the MATLAB program.

5.3.1 Steps for formulating optimal systems

In our optimal control problem having two unknowns, u * and x * , at the start. We have introduced an adjoint variable λ , which is similar to a Lagrangian multiplier. It attaches the differential equation information onto the maximization of the objective functional. Outline of how this theory can be applied to the simplest problems.

- Formulate the Hamiltonian for the problem

$$H(t, x, u, \lambda) = f(t, x, u) + \lambda g(t, x, u) \tag{5.38}$$

- Write the adjoint differential equation, transversality boundary condition and optimality condition. Now there are three unknown, u^* , x^* and λ

$$\lambda' = -\frac{\partial H}{\partial x} \Rightarrow \lambda' = -(f_x + \lambda g_x) \quad (Adjointcondition) \tag{5.39}$$

$$\lambda(t_f) = 0(trnsversalitycondition) \tag{5.40}$$

$$\frac{\partial H}{\partial u} = 0 \Rightarrow f_u(t, x, u) + \lambda g_u) = 0(optimalcondition \tag{5.41}$$

- solve for u^* in terms of x^* and λ
- After finding the optimal states and adjoint, solve for the optimal control.

5.4 Solutions with one Optimal Control (Vaccination)

Based on the researches that has shown above vaccination is the most effective controlling mechanism for LSD. Now on this paper, I described here using Epidemiological model for computing how effective the vaccination as one of the control mechanism and finding the optimality of the case. First let as define each of the compartments and their respective Ordinary Differential equations. A typical optimal control problem requires a performance index or cost function (J[x(t),u(t)]), a set of state variables (x(t) $\in$ X) and a set of control variables (u(t) $\in$ U) in a time t, $t_0 \leq t \leq t_f$. The main goal consists in finding a piecewise continuous control u (t) and the associated state variable x (t) to minimize a given objective functional. Basic optimal control Problem in Lagrange formulation: An optimal control problem is in the form (5.4 and 5.5).

5.4.1 OC Equations in Susceptible Compartment

The first compartment is Susceptible compartment, on this compartment new born cattle's not vaccinated are added and vaccinated populations after a year if not vaccinated again it can be included on this group. vaccinated and exposed ones are out of this compartment. The equation of the model is given by

$$\boxed{\frac{dS}{dt} = \alpha(1 - v_1)N - \beta SI - v_2 S + \theta R - \phi S} \tag{5.42}$$

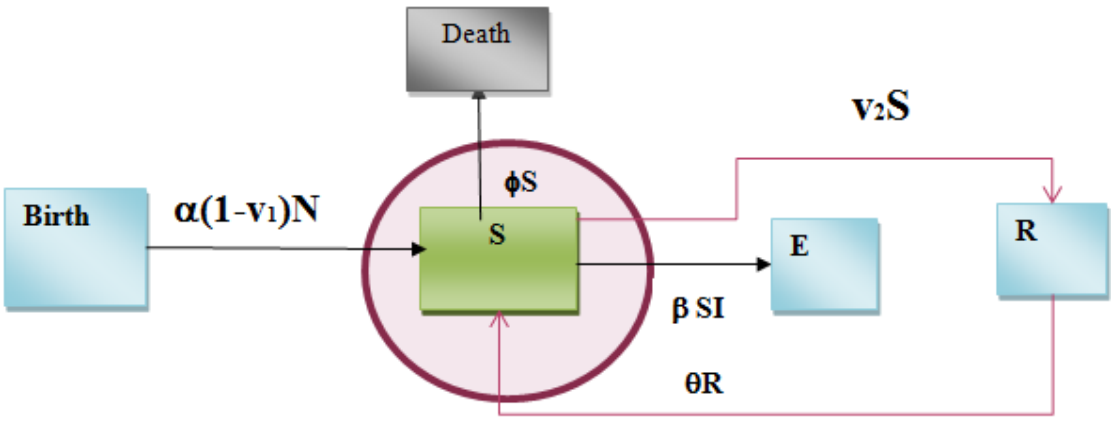

Figure 5.1: OC with Vaccination S-Compartment

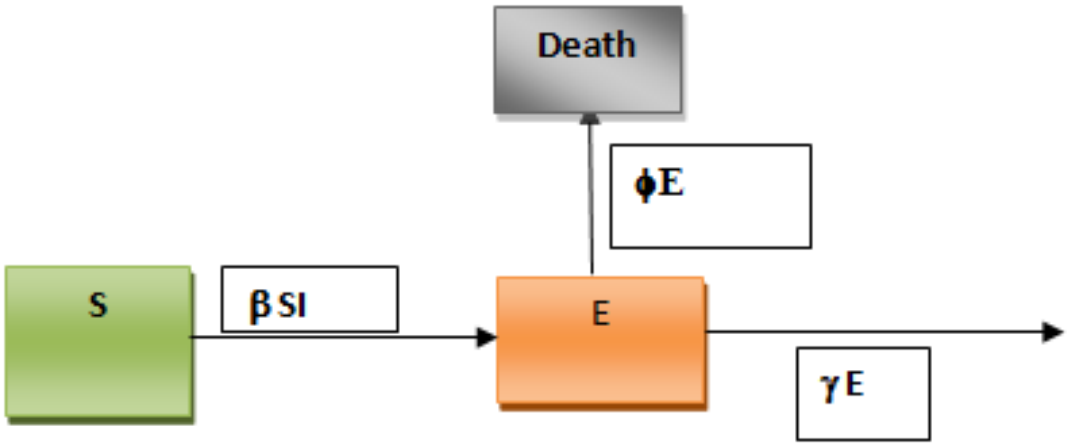

Figure 5.2: OC with Vaccination E-Compartment

5.4.2 OC Equations in Exposed Compartment

The next compartment is Exposed on which means,

$$\boxed{\frac{dE}{dt} = \beta SI - \phi E - \gamma E} \tag{5.43}$$

5.4.3 OC Equations in Infected Compartment

In I compartment, already infected with in latent time (t) at the rate of gamma, will move to infected compartment, at this stage the populations are infectious, if the populations interact with the susceptible group it will transmit the disease, but also if this groups has treatment like vaccination, it will move to recover group.

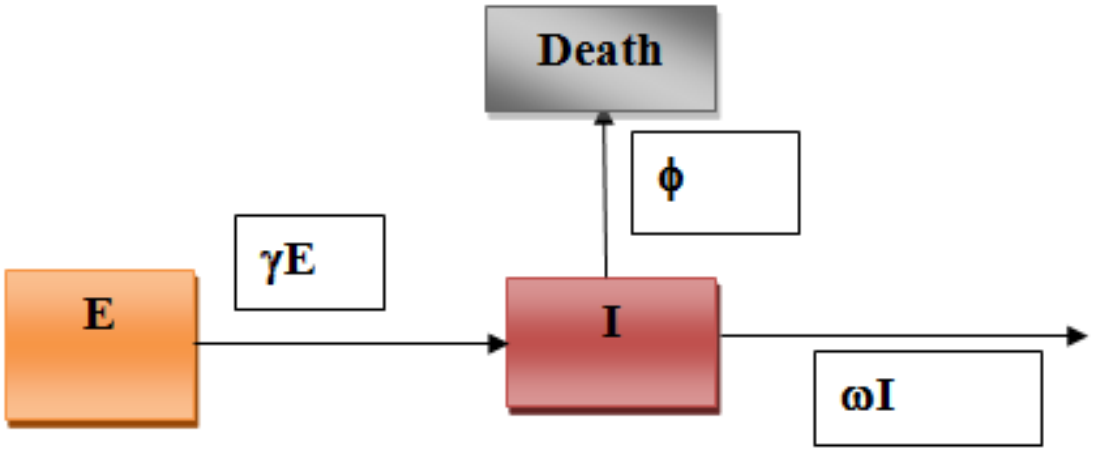

Figure 5.3: OC with Vaccination I-Compartment

$$\boxed{\frac{dI}{dt} = \gamma E - \phi I - \omega I} \tag{5.44}$$

5.4.4 OC Equations in Recovered Compartment

here we need to write about R compartment

$$\boxed{\frac{dR}{dt} = \alpha v_1 N + v_2 S + \omega I - \phi R - \theta R} \tag{5.45}$$

5.4.5 OC General Equations

Here I have to write about I compartment

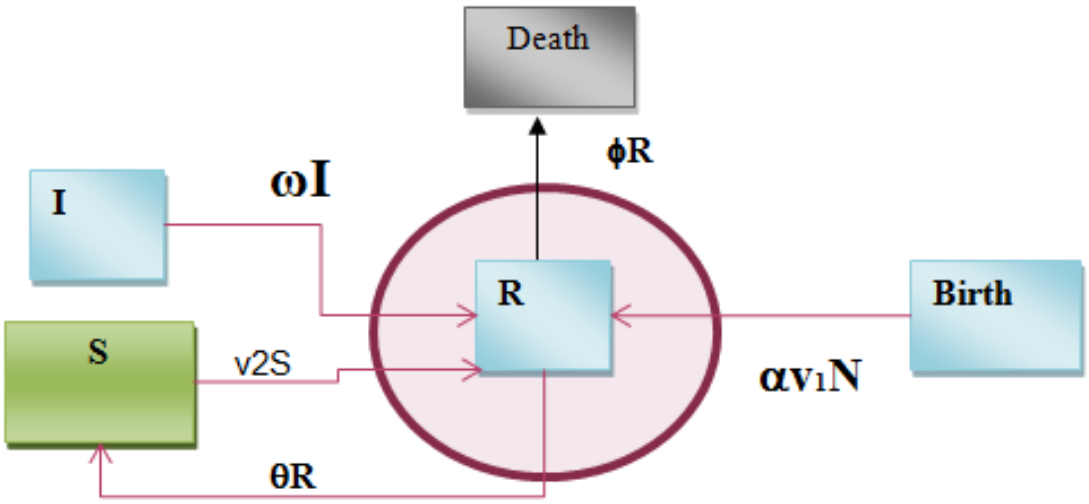

Figure 5.4: OC with Vaccination R-Compartment

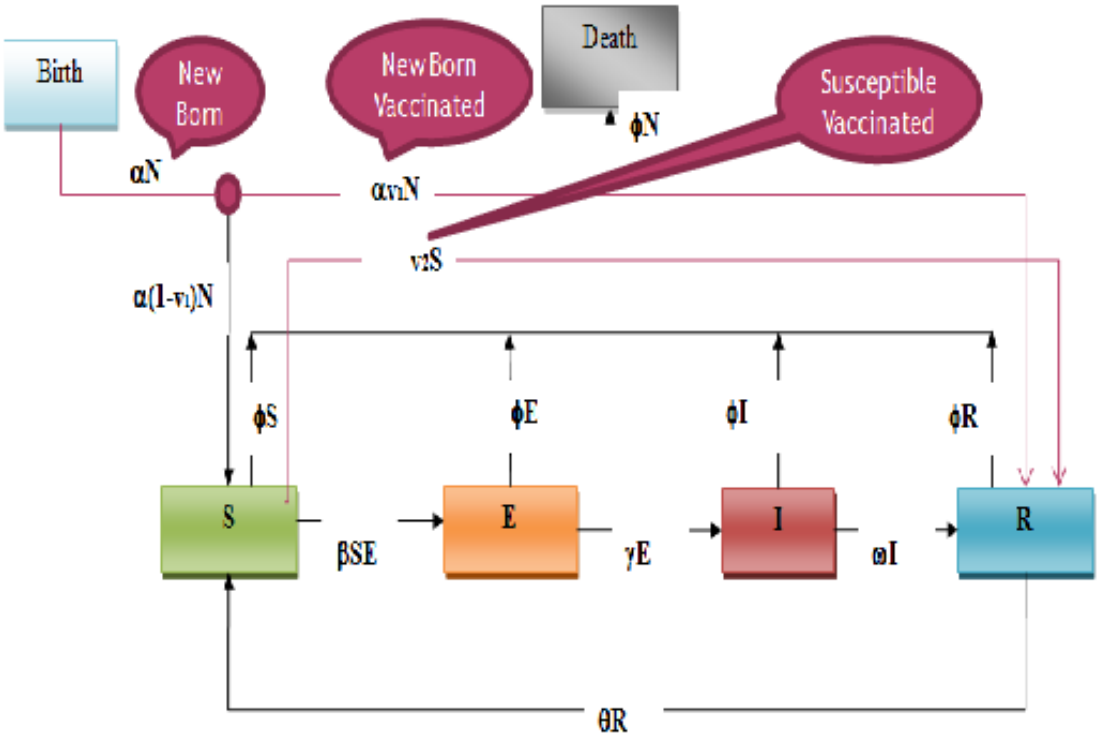

Figure 5.5: OC with Vaccination

$$\frac{dS}{dt} = \alpha(1 - v_1)N - \beta SI - v_2 S + \theta R - \phi S \tag{5.46}$$

$$\frac{dE}{dt} = \beta SI - \phi E - \gamma E \tag{5.47}$$

$$\frac{dI}{dt} = \gamma E - \phi I - \omega I \tag{5.48}$$

$$\frac{dR}{dt} = \alpha v_1 N + v_2 S + \omega I - \phi R - \theta R \tag{5.49}$$

Note that on the above system of equations (5.46,5.47,5.48 and 5.49) we have two stages of vaccination. The first one is just during getting birth the next one is those who are not taking vaccination and are in susceptible compartment. Now let's start from vaccination given only for susceptible compartment, there is no vaccination during getting birth. So that our system ordinary differential equation rewrite as the following.

$$\frac{dS}{dt} = \alpha N - \beta SI - uS + \theta R - \phi S \tag{5.50}$$

$$\frac{dE}{dt} = \beta SI - \phi E - \gamma E \tag{5.51}$$

$$\frac{dI}{dt} = \gamma E - \phi I - \omega I \tag{5.52}$$

$$\frac{dR}{dt} = uS + \omega I - \phi R - \theta R \tag{5.53}$$

with initial conditions,

$$S(0) = S_0 \geq 0, E(0) = E_0 \geq 0$$
$$I(0) = I_0 \geq 0, R(0) = R_0 \geq 0,$$

The optimal problem and the main objectives of this thesis is to minimize the objective (cost) functional J considering the costs of vaccination of susceptible population let's given by:

$$J(u) = \int_0^t (AI + \frac{1}{2}Bu^2)dt \tag{5.54}$$

* T represents the vaccination period (LSD vaccination has taken annually)
* The parameter A are balancing cost factors due to the size of infective and
* B represents the weight attached on the cost of vaccination or A and B are weight parameter describing the comparative importance of the two terms (disease burden and cost) in the functional respectively.

A high value of A means that it is more important to reduce the disease burden than to reduce the vaccination costs or a less value of B means that it is more important to reduce the vaccination costs than to reduce the disease burden. It assumed that the cost of the vaccination is nonlinear and take a quadratic form. The control u is the percentage of the susceptible that is vaccinated per unit time. Thus, u lies between 0 and 1 while u max will depend on the amount of resources available to implement each of the control measures.
If u = 0 , then no vaccination is done which model (5.50,5.51,5.52 and 5.53) is uncontrolled and u = 1 indicates that all susceptible population is vaccinated. The rate of vaccination is assumed to take values in [0, 0.9] instead of [0,1] to eliminate the case where the entire susceptible population is vaccinated [39], [40], [41]. The vaccination cost could include the cost of the vaccine, cost of syringes, cost of safety boxes, the vaccine storage cost, other related overheads.
Our target is to minimize the objective functional defined above by decreasing the

number of infected individuals and increasing the number of recovered individuals. This is achieved using possible minimal control variables, u or minimizing the cost of the vaccination at each time unit within the implementation period. The Optimal Control Problem of nonlinear dynamics of SEIRS LSD epidemic model given by;

$$min_u J(u) = min \int_0^t (AI + \frac{1}{2}Bu^2)dt \tag{5.55}$$

Subject to:

$$\begin{aligned} \frac{dS}{dt} &= \alpha N - \beta SI - uS + \theta R - \phi S \\ \frac{dE}{dt} &= \beta SI - \phi E - \gamma E \\ \frac{dI}{dt} &= \gamma E - \phi I - \omega I \\ \frac{dR}{dt} &= uS + \omega I - \phi R - \theta R \end{aligned}$$

with initial conditions,

$$S(0) = S_0 \geq 0, E(0) = E_0 \geq 0 I(0) = I_0 \geq 0, R(0) = R_0 \geq 0,$$

Control set defined as,

$$U = u(t) | 0 \leq u \leq u_{max} < 1, \quad t \in [0, t]$$

Based on Pontryagin's Maximum Principle (PMP) and From the definition of Hamiltonian which stated in equation (5.38), for the optimal control problem considered in (5.55), the control u , state variables S ,E ,I , R and S with corresponding adjoint functions to be determined suitably $\lambda 1$, $\lambda 2$, λ 3 and λ 4 . We have the Hamiltonian function:

$$\begin{aligned} & H(t, S, E, I, R, u, v, \lambda 1, \lambda 2, \lambda 3, \lambda 4) \\ &= f(t, S, E, I, R, u, v) + \sum_{i=1}^{4} \lambda_i g_i(t, S, E, I, R, u, v) \\ &\Rightarrow f(t, S, E, I, R, u, v) + \lambda_1 \frac{dS}{dt} + \lambda_2 \frac{dE}{dt} + \lambda_3 \frac{dI}{dt} + \lambda_4 \frac{dR}{dt} \end{aligned} \tag{5.56}$$

Then by Substituting each of the derivatives in equation (5.55) into equation (5.56) and by applying PMP to the Hamiltonian, we have:

$$\begin{aligned} H = (AI + \frac{1}{2}Bu^2) + \{ & \lambda_1(\alpha N - \beta SI - uS + \theta R - \phi S) + \\ & \lambda_2(\beta SI - \phi E - \gamma E) + \\ & \lambda_3(\gamma E - \phi I - \omega I) + \\ & \lambda_4(uS + \omega I - \phi R - \theta R)\} \end{aligned} \tag{5.57}$$

i Adjoint function with respect to S

$$\lambda_1^* = -\frac{\partial H}{\partial S}$$
$$\Rightarrow \lambda_1^* = -[\lambda_1(\beta I - u - \phi) + \lambda_2(\beta I) + \lambda_4 u]$$
$$\boxed{\lambda_1^* = \lambda_1(-\beta I + u + \phi) - \lambda_2 \beta I - \lambda_4 u} \tag{5.58}$$

ii Adjoint function with respect to E

$$\lambda_2^* = -\frac{\partial H}{\partial E}$$
$$\Rightarrow \lambda_2^* = -[\lambda_2(-\phi - \gamma) + \lambda_3(\gamma)] \tag{5.59}$$
$$\boxed{\lambda_2^* = \lambda_2(\phi + \gamma) - \lambda_3(\gamma)} \tag{5.60}$$

iii Adjoint function with respect to I

$$\lambda_3^* = -\frac{\partial H}{\partial I}$$
$$\Rightarrow \lambda_3^* = -[A + \lambda_1(-\beta S) + \lambda_2(\beta S) + \lambda_3(-\phi - \omega) + \lambda_4(\omega)] \tag{5.61}$$
$$\boxed{\lambda_3^* = -A + \lambda_1(\beta S) - \lambda_2(\beta S) + \lambda_3(\phi + \omega) - \lambda_4(\omega)} \tag{5.62}$$

iv Adjoint function with respect to R

$$\lambda_4^* = -\frac{\partial H}{\partial R}$$
$$\Rightarrow \lambda_4^* = -[\lambda_1(\theta) + \lambda_4(-\theta - \phi)] \tag{5.63}$$
$$\boxed{\lambda_4^* = -\lambda_1(\theta) + \lambda_4(\theta + \phi)} \tag{5.64}$$

From equations (5.58 to 5.61) the adjoint functions are

$$\begin{aligned} \lambda_1^* &= \lambda_1(-\beta I + u + \phi) - \lambda_2 \beta I - \lambda_4 u \\ \lambda_2^* &= \lambda_2(\phi + \gamma) - \lambda_3(\gamma) \\ \lambda_3^* &= -A + \lambda_1(\beta S) - \lambda_2(\beta S) + \lambda_3(\phi + \omega) - \lambda_4(\omega) \\ \lambda_4^* &= -\lambda_1(\theta) + \lambda_4(\theta + \phi) \end{aligned} \tag{5.65}$$

With transversality conditions we have

$$\lambda_i(T) = 0, \quad i = 1, 2, 3, 4 \tag{5.66}$$

Next let as consider optimal condition for determining the characterization of the optimal control u*. The optimal condition by differentiating the Hamiltonian H with respect to u based on the equation (5.41) for each control u^*. We have the following optimality system: $\frac{\partial H}{\partial u}$=0 at u=u* $\Rightarrow$ Bu + $\lambda_1(-S)$, at u=u*, then we have

$$\boxed{u^*(t) = (\lambda_1)\frac{S}{B}} \tag{5.67}$$

taking into account the bound on u* and its characterization obtain;
u*=

$$\begin{cases} 0 & if \quad \frac{\partial H}{\partial u} < 0, \quad (\lambda_1)\frac{S}{B} \quad if \quad \frac{\partial H}{\partial u} = 0, \quad 0.9 \quad if \quad \frac{\partial H}{\partial u} > 0 \end{cases} \tag{5.68}$$

So that the optimal control u* can be put as in a compact form :

$$u^* = max\left(min\left((\lambda_1)\frac{S}{B}, 0.9\right), 0\right) \tag{5.69}$$

Hence, using the characterization of the optimal control, we have the following optimality system:

$$\begin{aligned} S' &= \alpha N - \beta SI - uS + \theta R - \phi S \\ E' &= \beta SI - \phi E - \gamma E \\ I' &= \gamma E - \phi I - \omega I \\ R' &= uS + \omega I - \phi R - \theta R \end{aligned}$$

$$S(0) = S_0 \geq 0, E(0) = E_0 \geq 0 I(0) = I_0 \geq 0, R(0) = R_0 \geq 0,$$

$$\begin{aligned} \lambda_1^* &= \lambda_1(-\beta I + u + \phi) - \lambda_2\beta I - \lambda_4 u \\ \lambda_2^* &= \lambda_2(\phi + \gamma) - \lambda_3(\gamma) \\ \lambda_3^* &= -A + \lambda_1(\beta S) - \lambda_2(\beta S) + \lambda_3(\phi + \omega) - \lambda_4(\omega) \\ \lambda_4^* &= -\lambda_1(\theta) + \lambda_4(\theta + \phi) \end{aligned} \tag{5.70}$$

The next step is using A Runge-Kutta method is a multiple-step method, where the solution at time t_{k+1} is obtained from a defined set of previous values $t_j k$,. . . , t_k and j is the number of steps, use equation (5.19 to 5.24)

5.4.6 Numerical Simulation

we solve numerically the optimality system (5.70) using the forward-backward sweep method developed by Suzanne,L. and John,T.W, [36]. In this formulation, there exist initial conditions for the state variables and terminal conditions for the adjoint variables. That is, the optimality system is a two-point boundary value problem, with separated boundary conditions at times t_0 and t_f [51, 52]. Those ordinary differential equations in (5.70) comprising the optimality system are numerically solved together with the control characterization which is used to simulate the LSD vaccination strategies. The processes begin with an initial guess on the control variable. Then, the state equations are solved simultaneously forward in time, and next the adjoint equations are simultaneously solved backward in time. The control is updated by inserting the new values of states and adjoint into its characterization, and the process is repeated until convergence occurs, this is done by MATLAB program.

5.4.7 RK4 backward Forward Sweep Matlab Program

We write MATLAB Code for solving OC using RK4 backward forward, based on the data given, uisng optimal control we have the following graphs.

Based on the table (8) data, we have the following figures.

Table 8: Parameters for Numerical simulations

No	Parameters	Description	Value	Reference
1	S_0	Initial Susceptible population	0.9	Estimation
2	E_0	Initial Exposed population	0.1	Estimation
3	I_0	Initial Infected population	0.1	Estimation
4	R_0	Initial Recovered population	0.1	Estimation
5	α	Natural birth rate	0.09	Estimation
6	ϕ	Natural death rate	0.02	Estimation
7	β	Contact rate with infected	0.1378	Rgbe[2]
8	γ	Latent rate (E to I)	0.1106	Rgbe[2]
9	ω	Recovery rate (I to R)	0.076	Estimation
10	θ	loss immunity rate (R to S)	0.0091	Estimation
11	A	Weight parameter	1 to 1000	Estimation
12	B	Weight parameter	0.01 to 50	Estimation
13	[0,t]	Vaccination period	[0,24 months]	Estimation
14	[0,u]	Vaccination ratio	[0,0.9]	Estimation

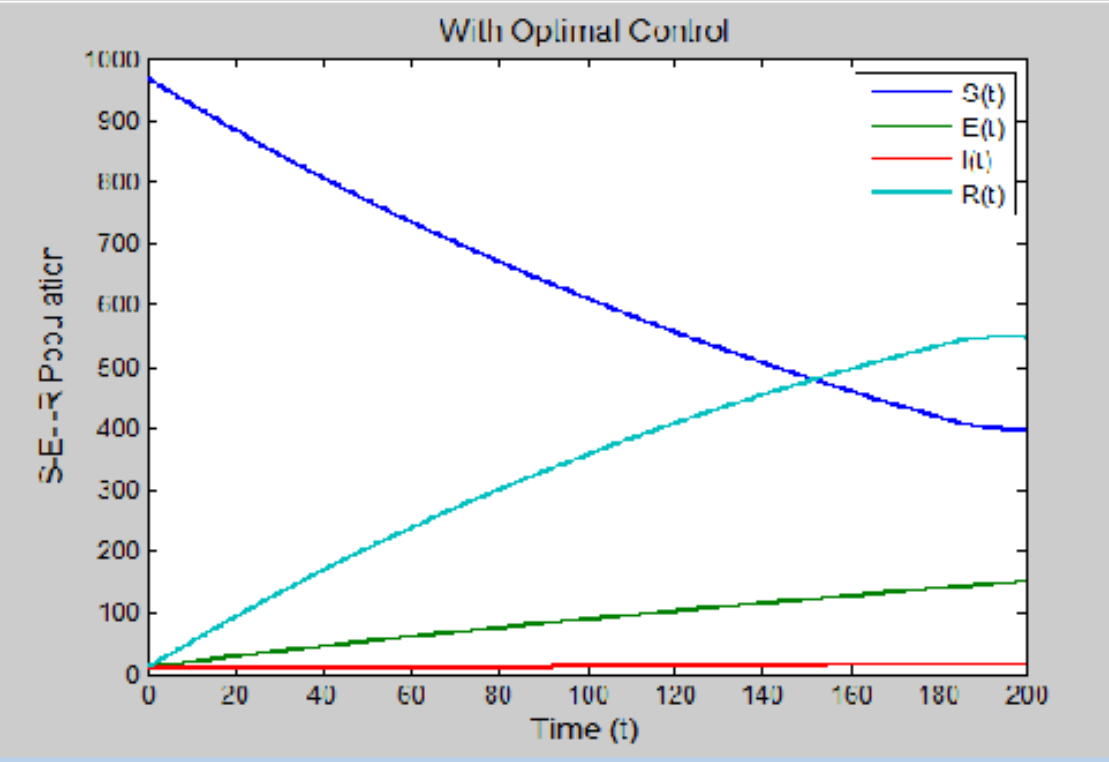

Figure 5.6: S-E-I-R, with beta=0.2, A=100 and B=0.04, the populations in S-compartment is increase and increase in R-compartment with time (t). E and I compartment population increase at very low rate and it goes constant, from the figure shows that after some time (t) the system becomes stable.

Next we change the rate of infectious β=5.02, whihc means Infected populaiton

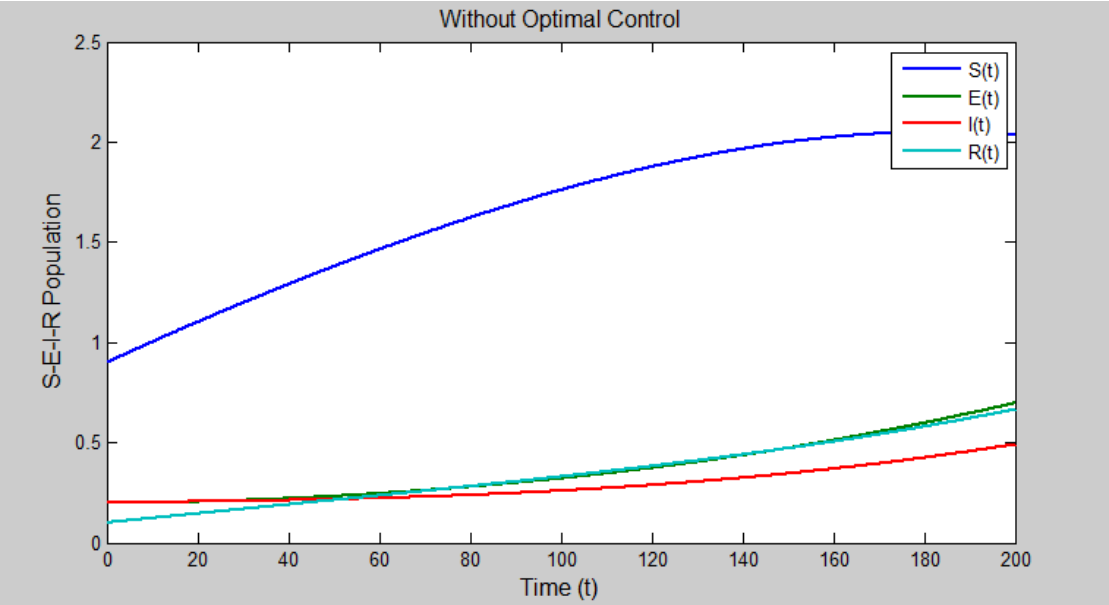

Figure 5.7: S-E-I-R With Out Optimal Control

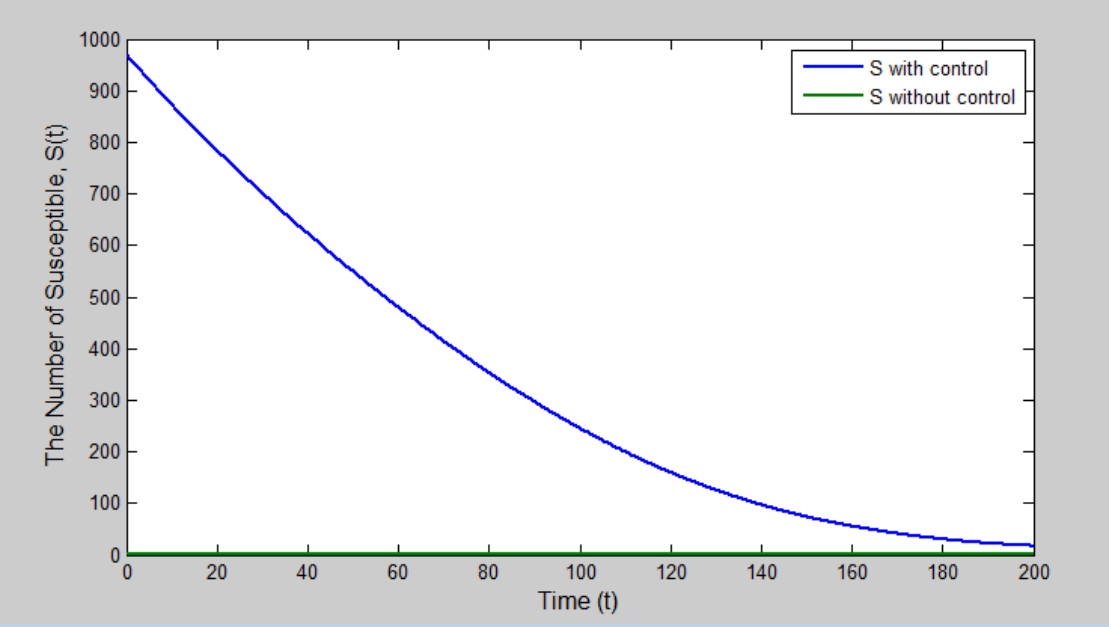

Figure 5.8: S-With and with out Optimal Control

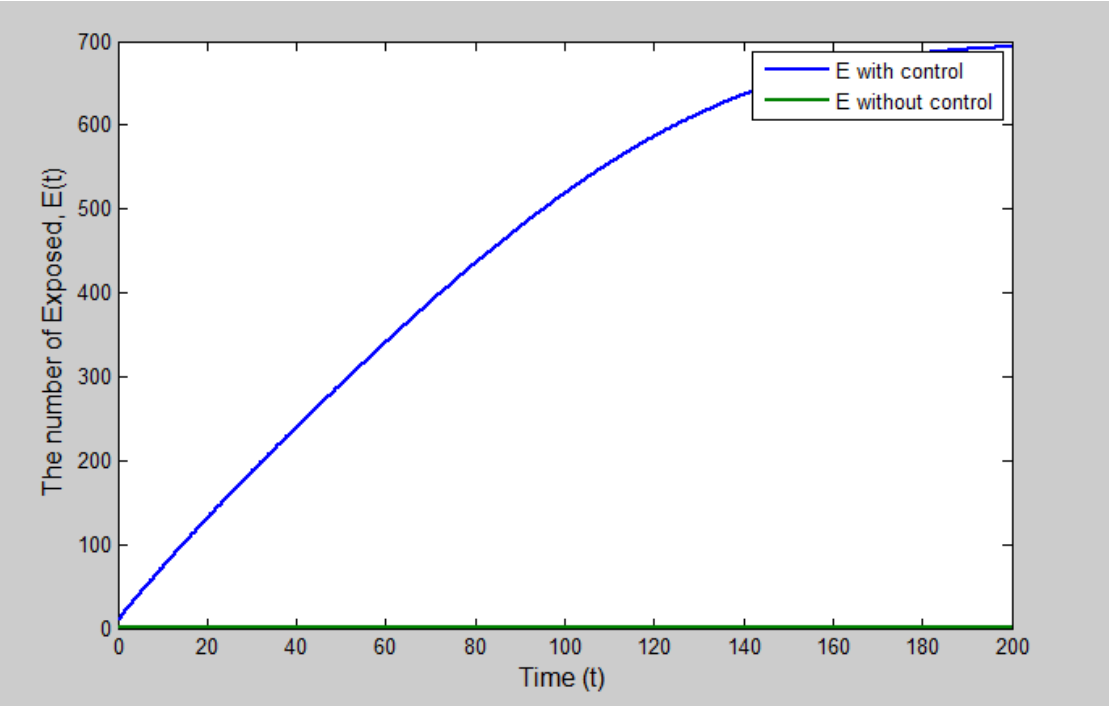

Figure 5.9: E-With and with out Optimal Control

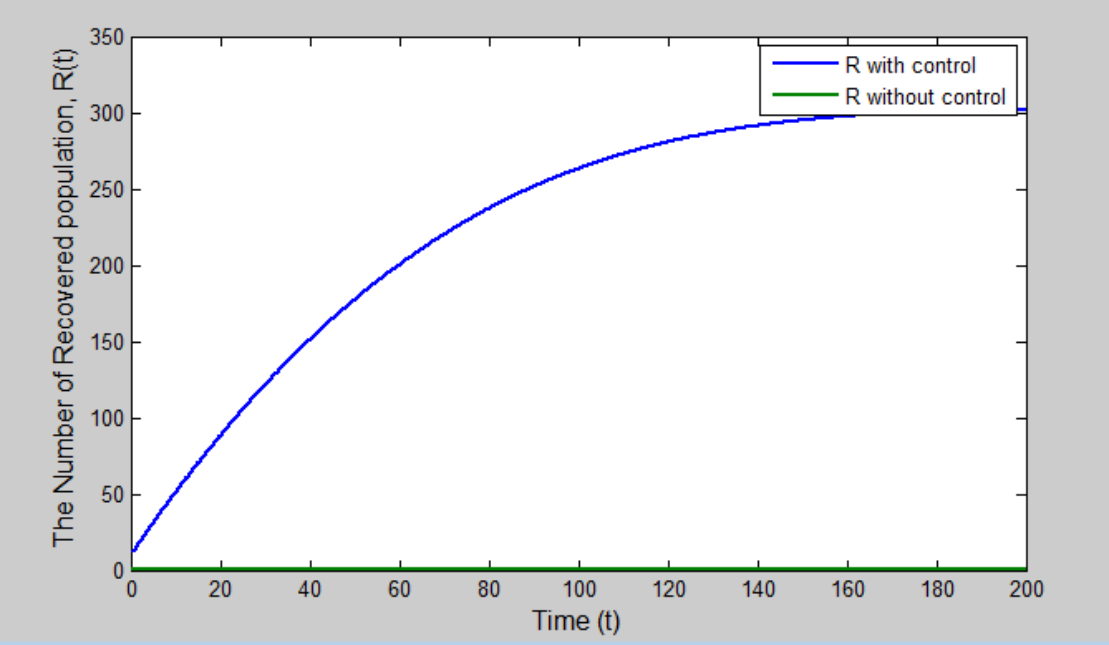

Figure 5.10: R-With and with out Optimal Control

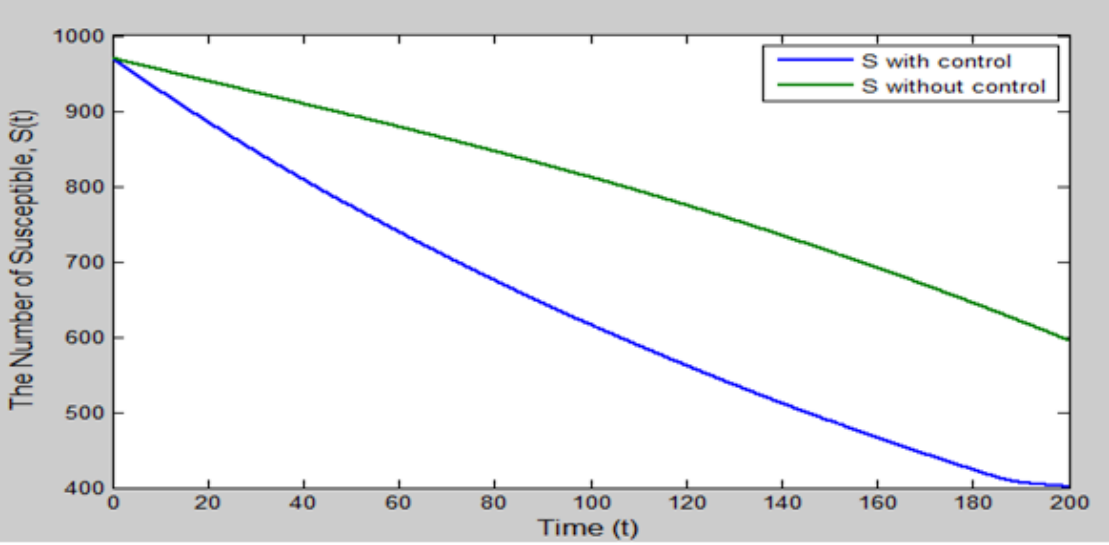

Figure 5.11: S-With and with out Optimal Control, β=0.02, the rate at which the number of populaiton decresing is high if there is control, it moves directly to the R-compartment.

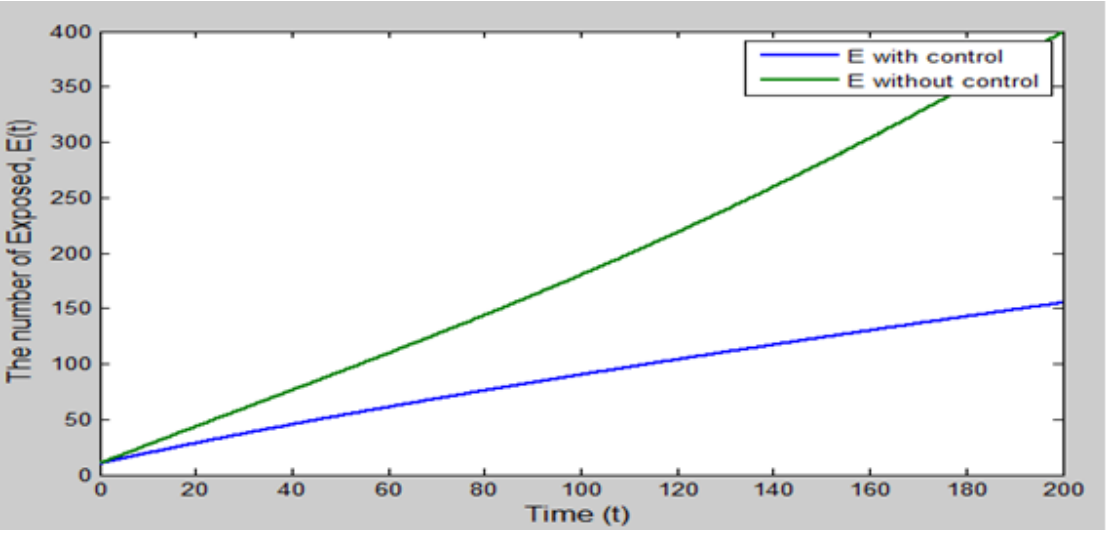

Figure 5.12: E-With and with out Optimal Control,β=0.02, populaiton in E-compartment decrease when there is control

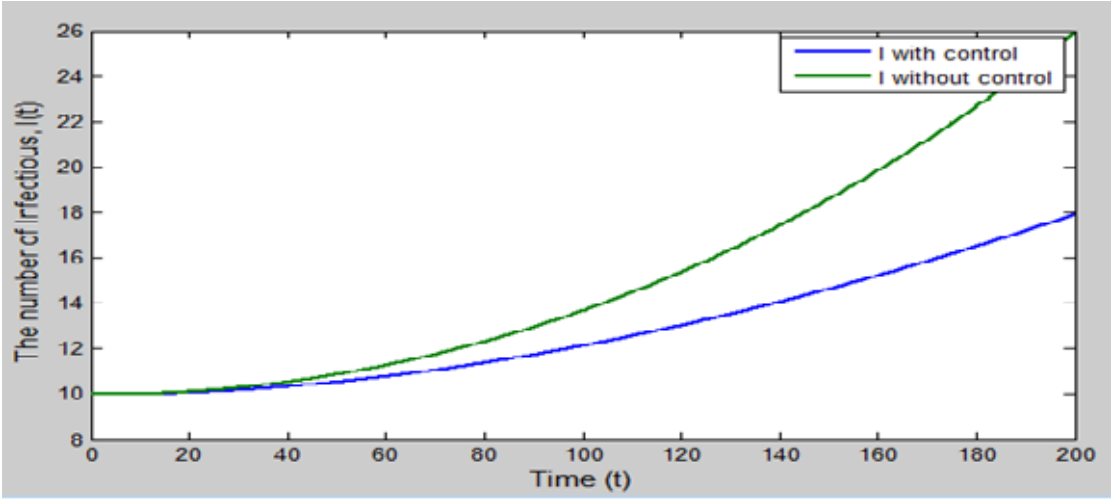

Figure 5.13: I-With and with out Optimal Control, β=0.02, population in I-compartment increase if there is not control, than if it has control

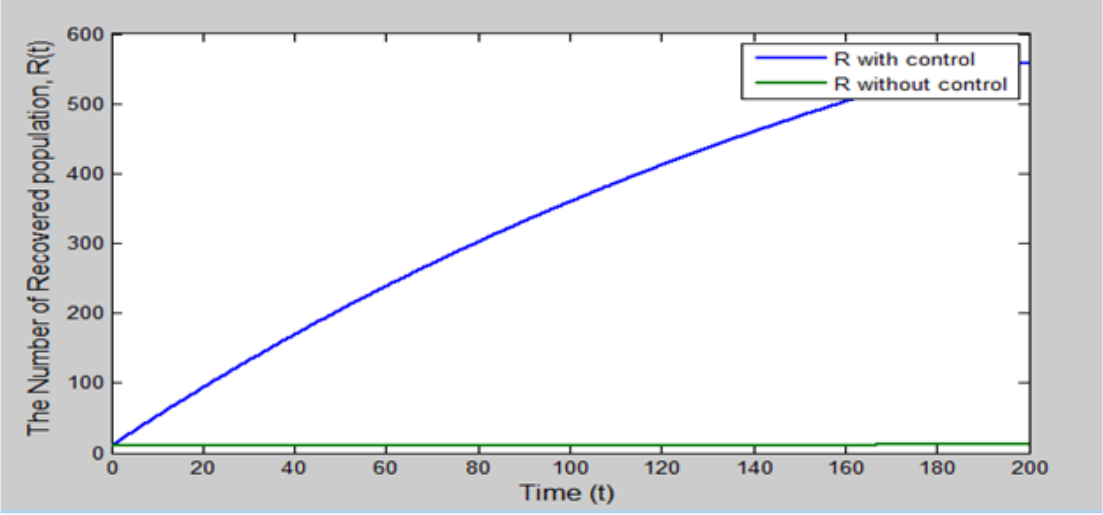

Figure 5.14: R-With and with out Optimal Control,β=0.02, R-with control is increases.

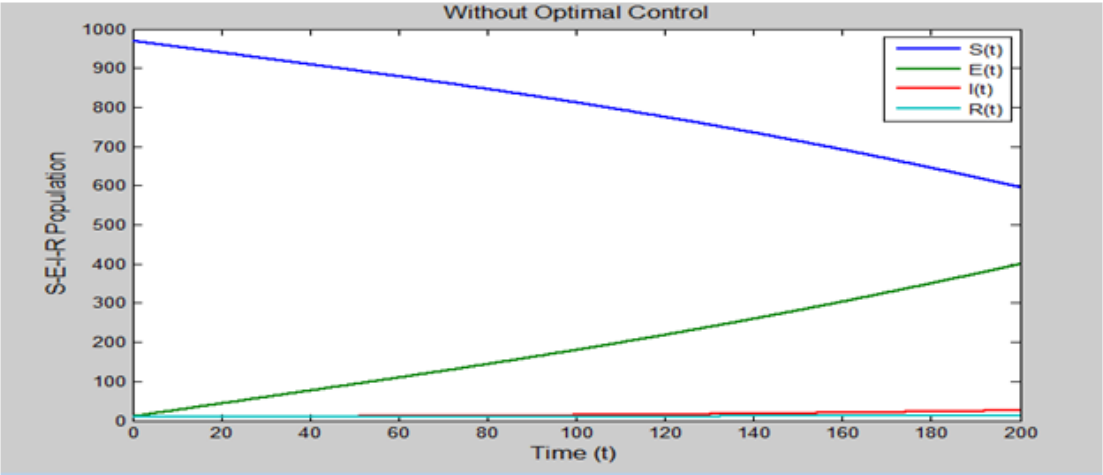

Figure 5.15: S-E-I-R with out Optimal Control, β=0.02, since there is no optimal control the number of populaiton in S-compartment decrease and E-compartment increase, where as I also

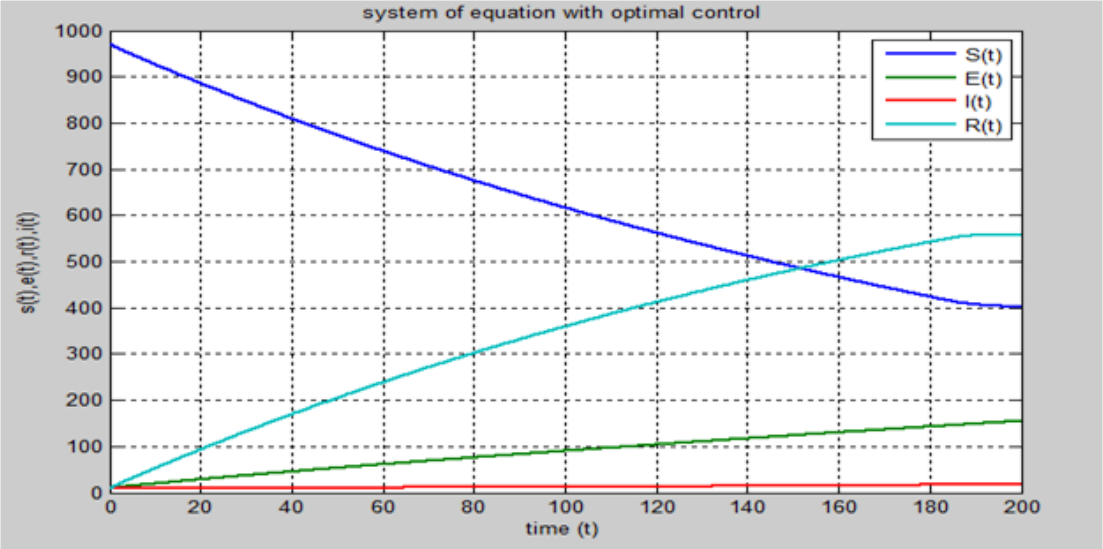

Figure 5.16: S-E-I-R with Optimal Control,β=0.02, here most of population in S-compartment decrease and the population in R-compartment is increase after control

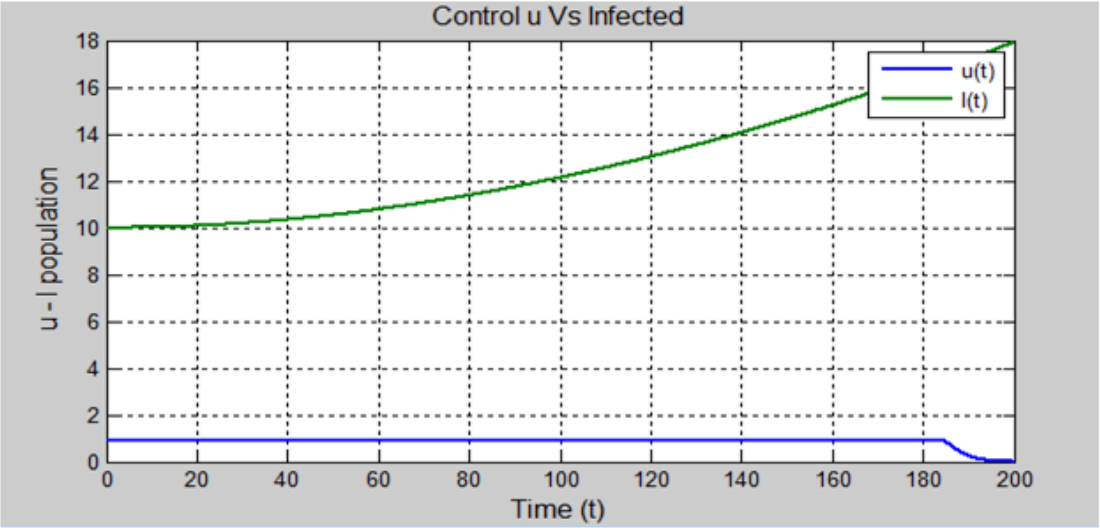

Figure 5.17: u and l, β=0.02, here infected is increase if there is no control, where as it decrease if it has control u

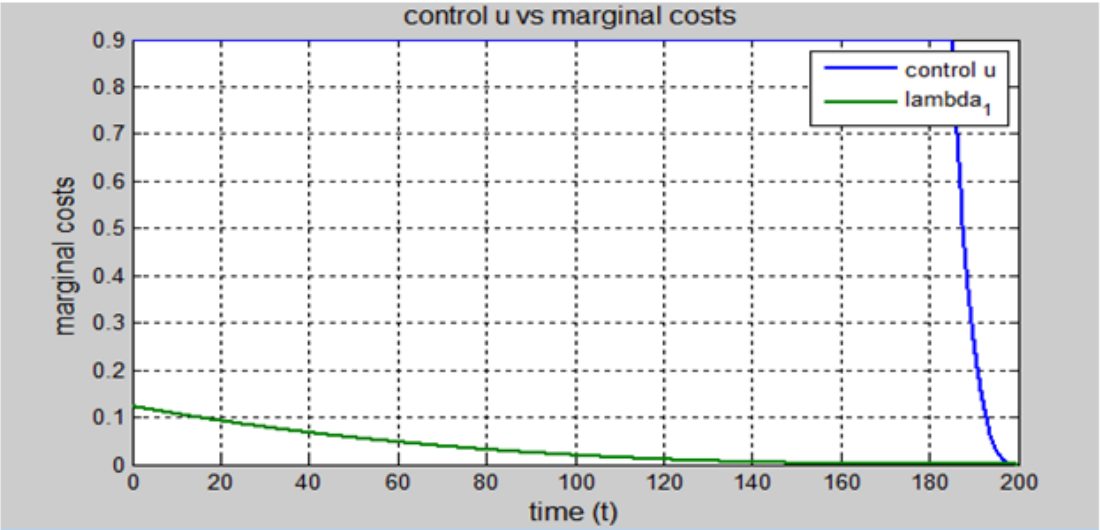

Figure 5.18: U and Lamda1, at β=0.02, the control u is starting decrease after it goes constantly, and the cost at the begining was a little high and after controlling it decrease.

Table 9: Parameters for Numerical simulations

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No	Parameters	Description	Value	Reference
1	S_0	Initial Susceptible population	970	Estimation
2	E_0	Initial Exposed population	10	Estimation
3	I_0	Initial Infected population	10	Estimation
4	R_0	Initial Recovered population	10	Estimation
5	α	Natural birth rate	0.04	Estimation
6	ϕ	Natural death rate	0.00002	Estimation
7	β	Contact rate with infected	0.02	Guess
8	γ	Latent rate (E to I)	0.1106	Guess
9	ω	Recovery rate (I to R)	0.1406	Estimation
10	θ	loss immunity rate (R to S)	0.0191	Estimation
11	A	Weight parameter	100	Estimation
12	B	Weight parameter	0.04	Estimation
13	[0,t]	Vaccination period	[0,24 months]	Estimation
14	[0,u]	Vaccination ratio	[0,0.9]	Estimation

the rate of interaction with susceptible is increase, there is highly contaminated and the disease spreads to fast, with the same rate that transfer from E to I, and the graph is

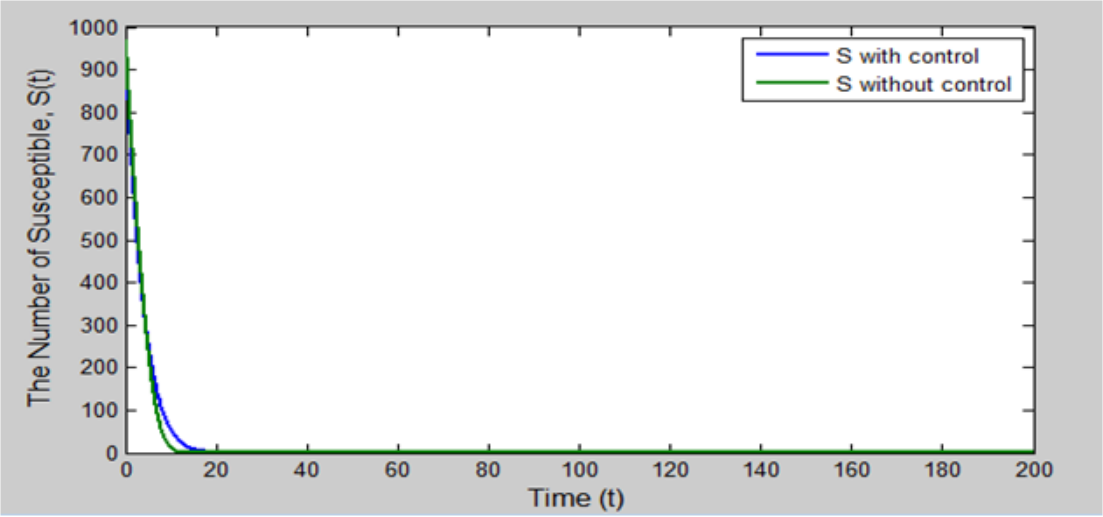


Figure 5.19: S-With and with out Optimal Control,β=5.02

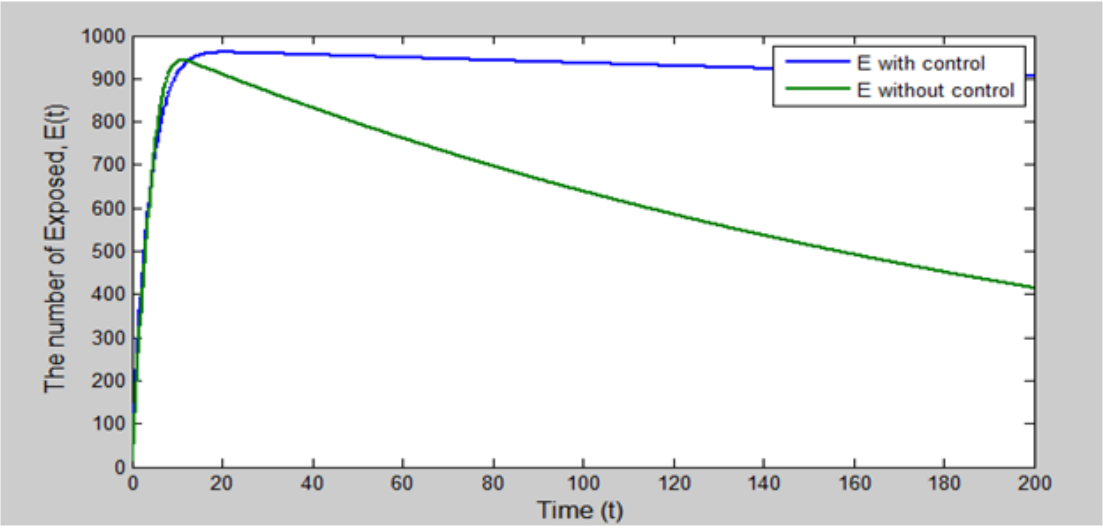


Figure 5.20: E-With and with out Optimal Control,β=5.02

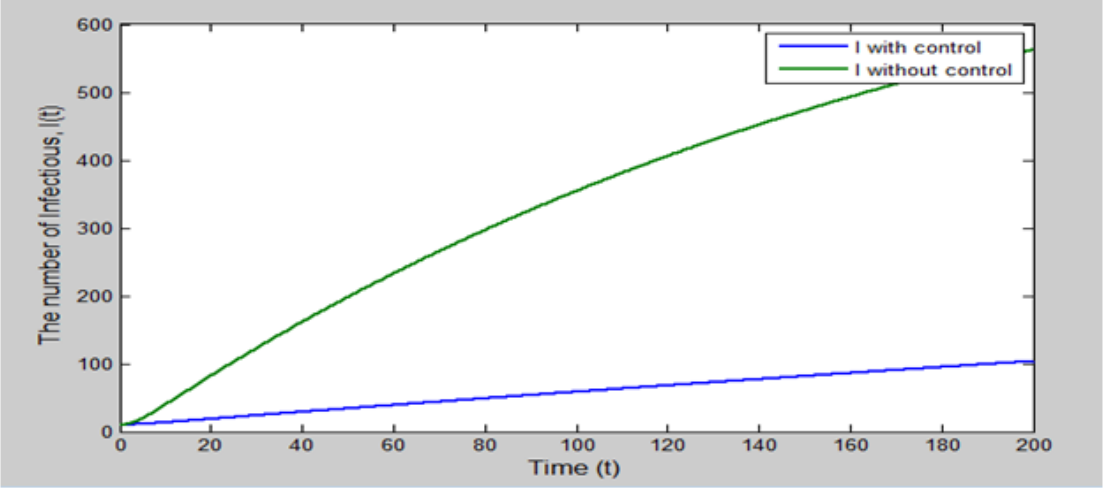


Figure 5.21: I-With and with out Optimal Control,β=5.02

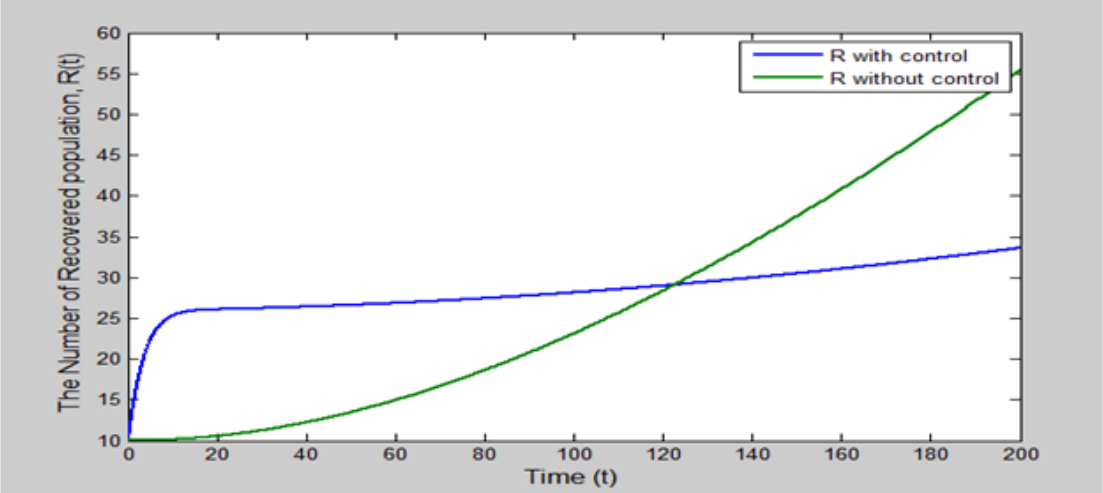


Figure 5.22: R-With and with out Optimal Control,β=5.02

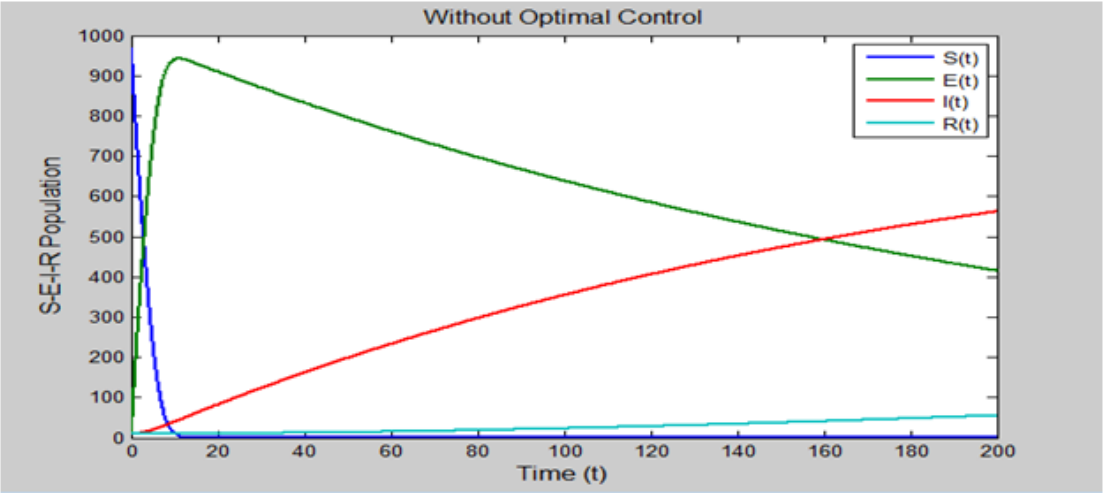


Figure 5.23: S-E-I-R with out Optimal Control,β=5.02

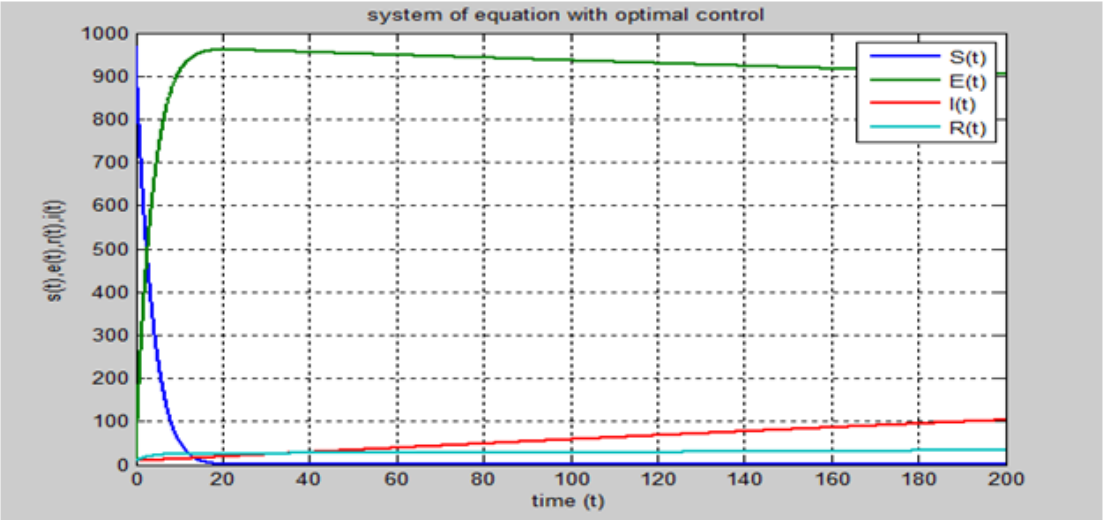


Figure 5.24: S-E-I-R with Optimal Control,β=5.02

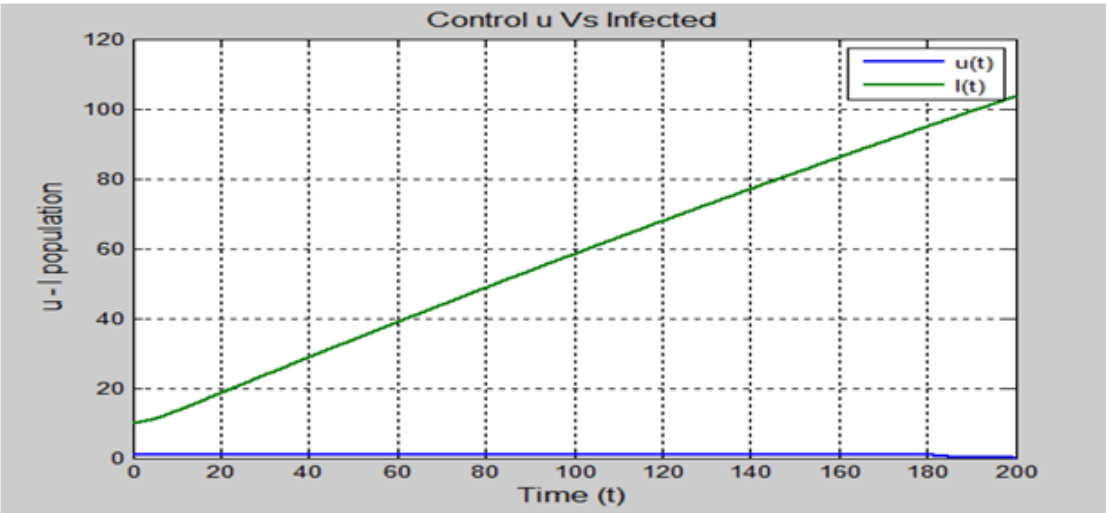


Figure 5.25: u and l with control,β=5.02

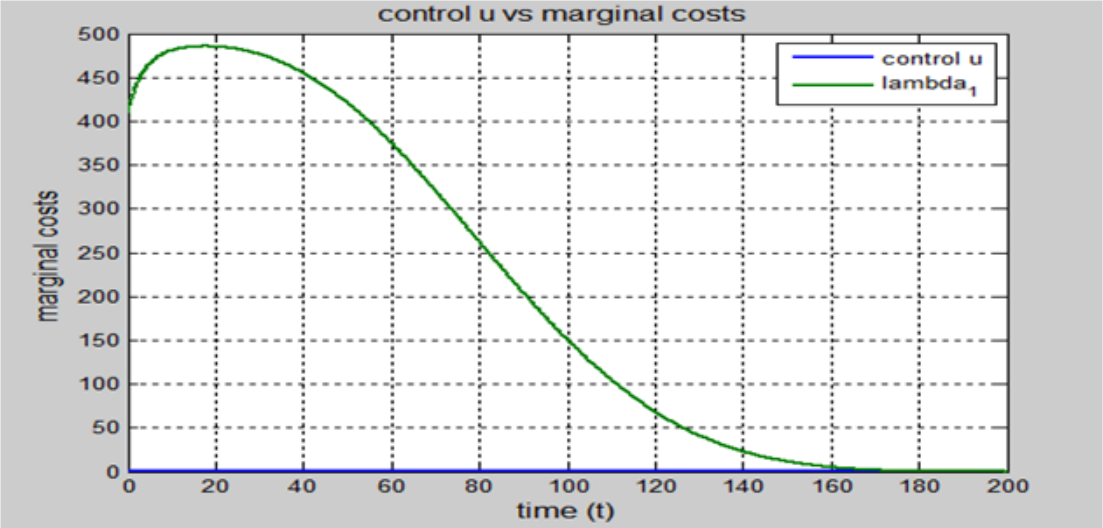
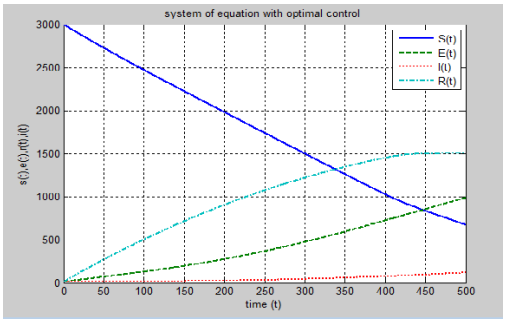
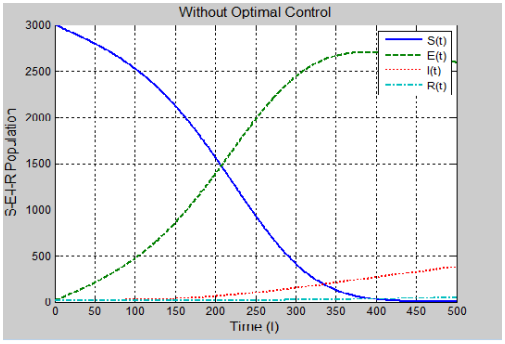


Figure 5.26: U and Lamda1,β=5.02

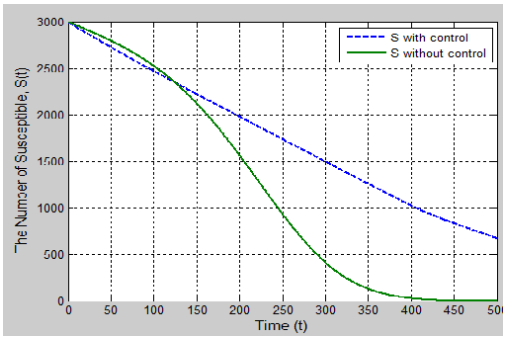


(a) SEIRS with optimal control;the number of S populations is decreased and the number of Recovered population increase in with time (t). The number of population in E-compartment is also increase at low rate. Since here we used control, after some time the total population will be included in recovered group. But our model is possibility the population loss their immunity, the number of populations in Exposed also increases, and in the long run the disease is become more of endemic and it is also stable.

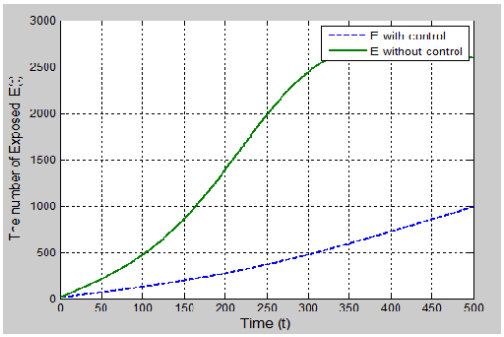


(b) SEIRS without optimal control;the number of S populations is decreased and the number of Exposed populations is increase in with time (t), with reciprocal ratio. Since the factor of the population contamination with the disease too high, and our model there is loss of immunity, almost all th population moves to E-compartment. Almost the recovered populations is near to zero and infected populations is increase at low rate.

Figure 5.27: (a) is SEIRS, with optimal control, and Figure 4.2: (b) is SEIRS without optimal control, Where β=0.02, α=0.0004,γ=0.29,ω=0.3,θ=0.00002,ϕ=0.00002, A=1000 and B=200,S_0=3000, E_0=I_0=R_0 = 10. The rate of transmitting disease is less than the rate of infectious and recovering

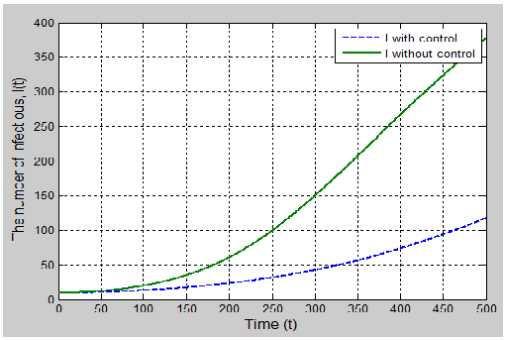


(a) Population S with and without optimal control;In both cases with and without control , the population size is decreased, but the rate of decreasing has difference,in controlling case the rate is low.

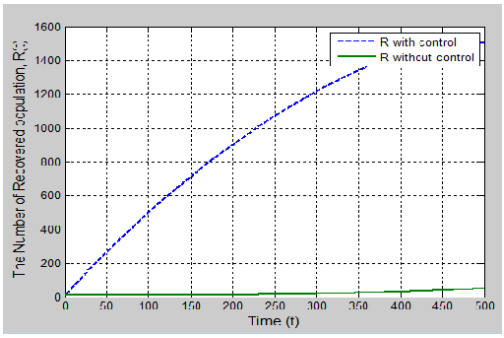


(b) Population E with and without optimal control;In both cases with and without control , the population size is increases, but the rate of increasing has difference,in controlling case the rate is low.

Figure 5.28: (a) is S, with and without optimal control, and Figure 4.3: (b) is E with and without optimal control, Where β=0.02, α=0.0004,γ=0.29,ω=0.3,θ=0.00002,ϕ=0.00002, A=1000 and B=200,S_0=3000, E_0=I_0=R_0 = 10.

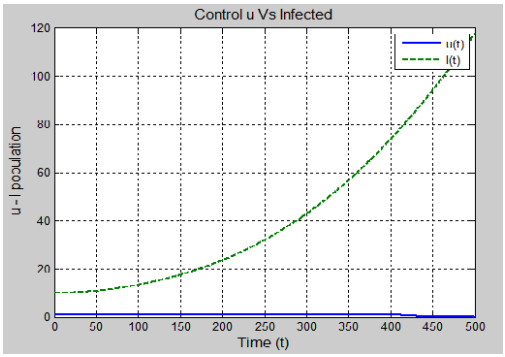


(a) Population I with and without optimal control;In both cases with and without control, the population size is increases, but the rate of increasing has difference,in controlling case the rate is low.

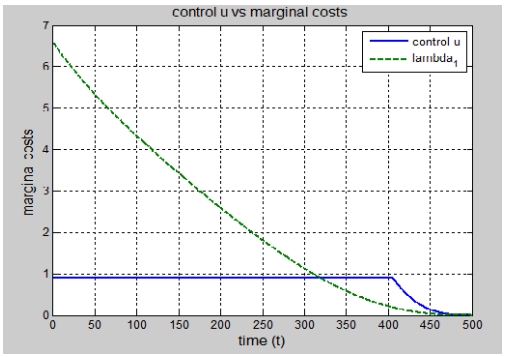


(b) Population R with and without optimal control;In both cases with and without control, the population size is increases, but the rate of increasing has difference,in controlling case the rate is very high.

Figure 5.29: (a) is SEIRS, with optimal control, and Figure 4.4: (b) is SEIRS with out optimal control, Where β=0.02, α=0.0004,γ=0.29,ω=0.3,θ=0.00002,ϕ=0.00002, A=1000 and B=200,S_0=3000, E_0=I_0=R_0 = 10.

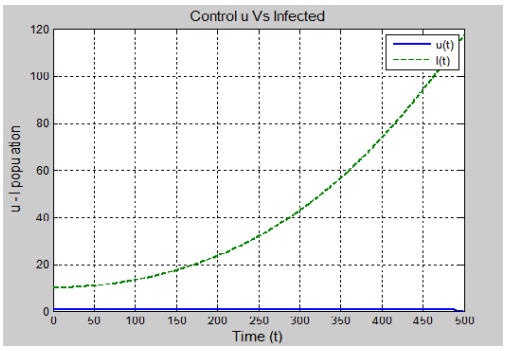


(a) Control U and infection I with time (t);infection rate is to high, where as the rate of controlling is to low. Since the rate of exposing the disease is to high, the cost is to high for controlling.

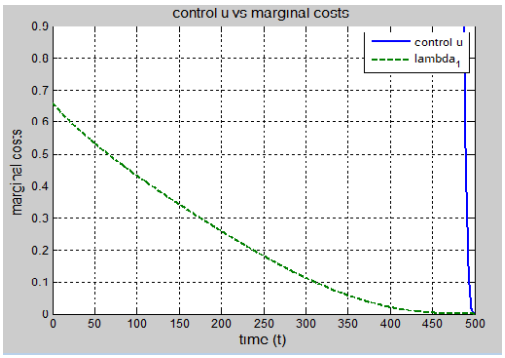


(b) Control U and lambda λ (adjoint) with time (t);the rate of decreasing lambda is to high, where as the rate of controlling (u) is at upper bound (0.9), and then after some time it decreases.

Figure 5.30: (a) Control u and infected I, with optimal control, and Figure 4.5: (b) Control u and the adjoint function λ, Where β=0.02, α=0.0004,γ=0.29,ω=0.3,θ=0.00002,ϕ=0.00002, A=1000 and B=200,S_0=3000, E_0=I_0=R_0 = 10.

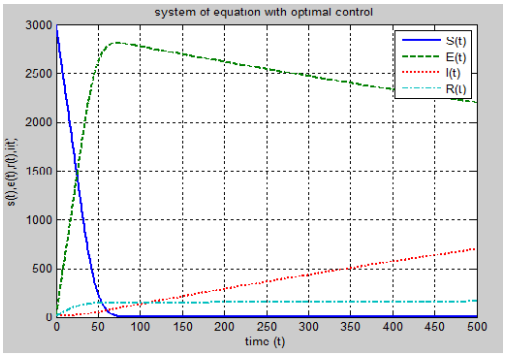


(a) Control U and infection I with time (t);infection rate is to high, where as the rate of controlling is to low, here the value of B is very very low, B=0.04.

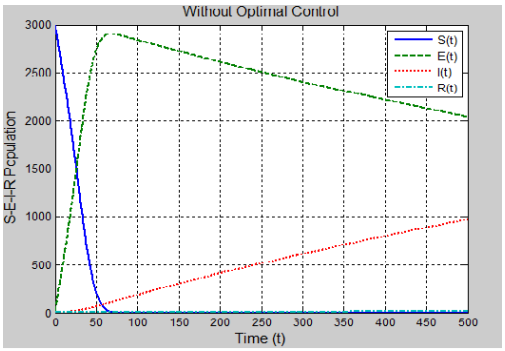


(b) Control U and lambda λ (adjoint) with time (t);the rate of decreasing lambda is to high, where as the rate of controlling (u) is at upper bound (0.9), and then after some time it decreases very fastly

Figure 5.31: (a) is Control (u) and lamda and Figure 4.6: (b) is SEIRS with out optimal control, Where β=0.02, α=0.0004,γ=0.29,ω=0.3,θ=0.00002,ϕ=0.00002, A=100 and B=0.04,S_0=3000, E_0=I_0=R_0 = 10.

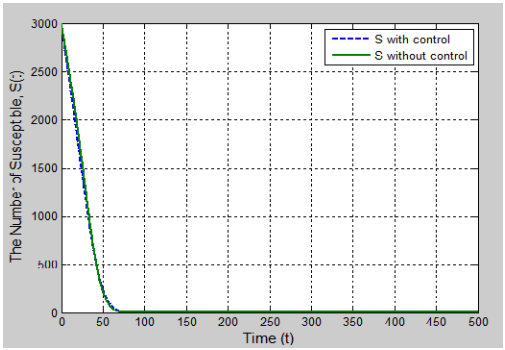


(a) SEIRS with optimal control;the number of S populations is decreased, the number of Exposed population increase in with time (t). The number of population in R-compartment is also increase at very very low rate.

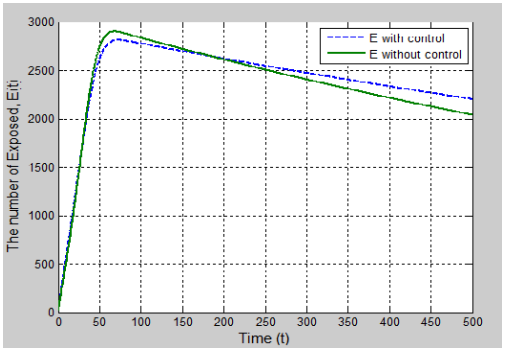


(b) SEIRS without optimal control;the number of S populations is decreased and the number of Exposed population increase in with time (t). The number of population in I-compartment is increase.

Figure 5.32: (a) is SEIRS, with optimal control, and Figure 4.7: (b) is SEIRS without optimal control, Where β=1.02, α=0.0004,γ=0.29,ω=0.3,θ=0.00002,ϕ=0.00002, A=1000 and B=200,S_0=3000, E_0=I_0=R_0 = 10.

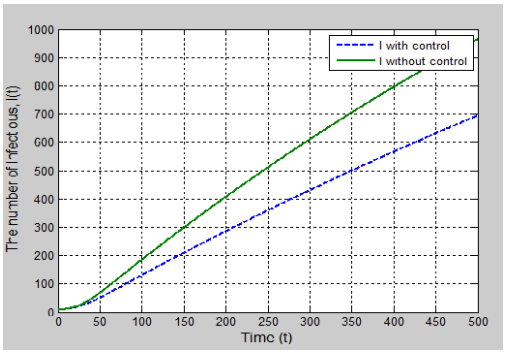


(a) Population S with and without optimal control;In both cases with and without control , the population size is decreased, almost at equal rate, since the rate of exposing is too high.

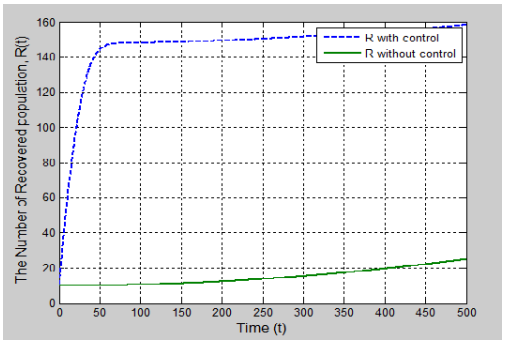


(b) Population E with and without optimal control;In both cases with and without control is the population size is increases for some time and decrease and then it becomes at sable, which means in controlling case more of the population is in E-Compartment.

Figure 5.33: (a) is S with and without optimal control, and Figure 4.8: (b) is E with and without optimal control, Where β=1.02, α=0.0004,γ=0.29,ω=0.3,θ=0.00002,ϕ=0.00002, A=1000 and B=200,S_0=3000, E_0=I_0=R_0 = 10.

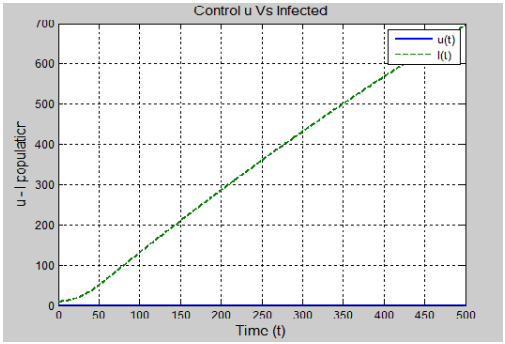


(a) Population I with and without optimal control;In both cases with and without control , the population size is increases, but the rate of increasing has difference,in controlling case the rate is low.

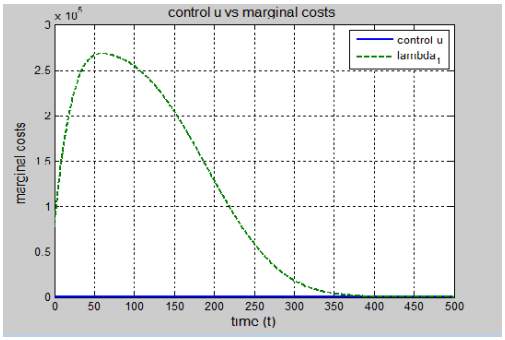


(b) Population R with and without optimal control;In both cases with and without control, the population size is increases, but the rate of increasing has difference,in controlling case the rate is very high.

Figure 5.34: (a) is I with and without optimal control, and Figure 4.9: (b) is R with and without optimal control, Where β=1.02, α=0.0004,γ=0.29,ω=0.3,θ=0.00002,ϕ=0.00002, A=1000 and B=200,S_0=3000, E_0=I_0=R_0 = 10.

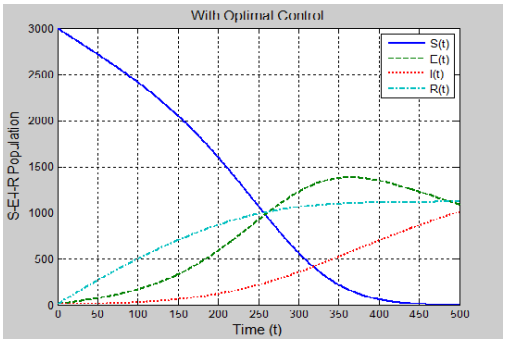


(a) Control U and infection I with time (t);infection rate is to high, where as the rate of controlling is to low. Since the rate of exposing the disease is to high, the cost is to high for controlling.

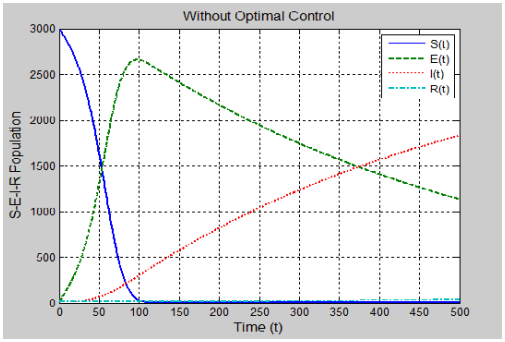


(b) Control U and lambda λ (adjoint) with time (t);lambda is increase for some time (t) and then decreased, where as the rate of controlling (u) is at lower bound (0.1). This means the disease is not under controlling.

Figure 5.35: (a) is u-I, with optimal control, and Figure 4.10: (b) is u-lambda with optimal control, Where β=1.02, α=0.0004,γ=0.29,ω=0.3,θ=0.00002,ϕ=0.00002, A=1000 and B=200,S_0=3000, E_0=I_0=R_0 = 10.

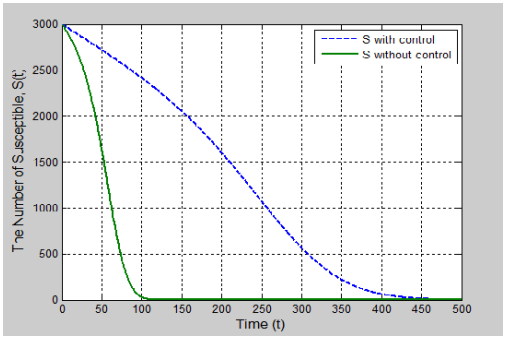


(a) SEIRS with optimal control;the number of S populations is decreased and the number of Exposed population increase in with time (t) and then decrease after some time. The number of population in R-compartment is also increase at low rate. Since the rate of exposed is less than infected rate, from the graph shown that the population of exposed, infected and recovered are at equal level.

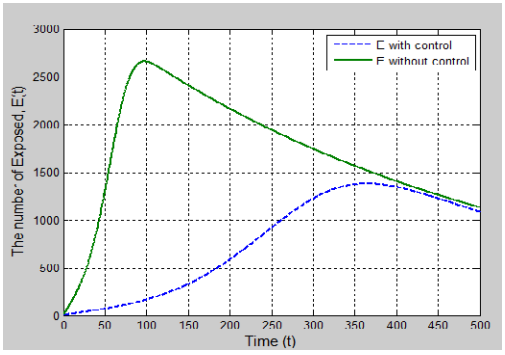


(b) SEIRS without optimal control;the number of S populations is decreased and the number of Exposed population increase in with time (t) and then decrease after some time, which means the rate of infected is higher and the infected population increased. Since here there no controlling, the disease becomes outbreak.

Figure 5.36: (a) is SEIRS, with optimal control, and Figure 4.11: (b) is SEIRS with out optimal control, Where β=0.02, α=0.0004,γ=1.29,ω=0.3,θ=0.00002,ϕ=0.00002, A=1000 and B=200,S_0=3000, E_0=I_0=R_0 = 10.

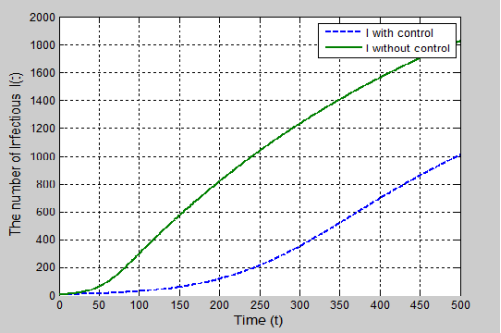


(a) Population S with and without optimal control;In both cases with and without control, the population size is decreased, but the rate of decreasing has difference,in controlling case the rate is low.

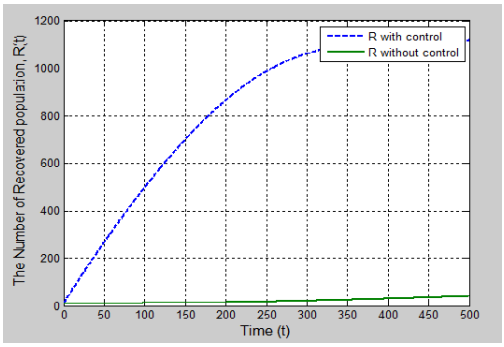


(b) population E with and without optimal control;the population of E with controlling increase at very high rate and decrease, which shows that the disease is not fully controlled.

Figure 5.37: (a) is S, with optimal control, and Figure 4.12: (b) is E with out optimal control, Where β=0.02, α=0.0004,γ=1.29,ω=0.3,θ=0.00002,ϕ=0.00002, A=1000 and B=200,S_0=3000, E_0=I_0=R_0 = 10.

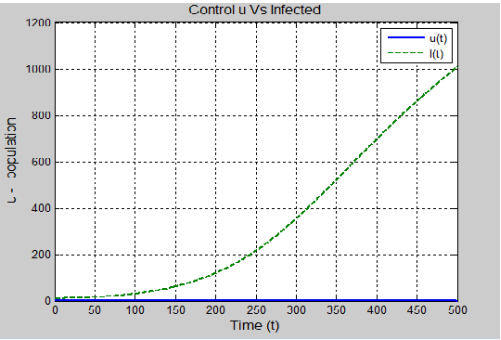


(a) Population I with and without optimal control;In both cases with and without control, the population size is increases, but the rate of increasing has difference,in controlling case the rate is low..

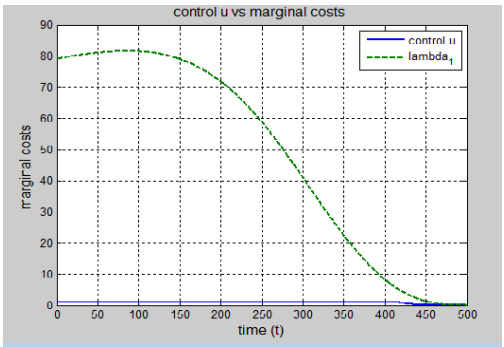


(b) Population R with and without optimal control;In both cases with and without control, the population size is increases, but the rate of increasing has difference,in controlling case the rate is very high.

Figure 5.38: (a) is I with and without optimal control, and Figure 4.13: (b) is R with and without optimal control, Where β=0.02, α=0.0004,γ=1.29,ω=0.3,θ=0.00002,ϕ=0.00002, A=1000 and B=200,S_0=3000, E_0=I_0=R_0 = 10.



(a) Control u and infection I with time (t);infection rate is to high, where as the rate of controlling is to low, at lower bound (0.1), the disease could not be controlled. Since the rate of infected is too high.



(b) Control u and lambda λ (adjoint) with time (t);the rate of decreasing lambda is to high, where as the rate of controlling (u) is at lower bound (0.1).

Figure 5.39: (a) is u and I , with optimal control, and Figure 4.14: (b) is U and Lambda with out optimal control, Where β=0.02, α=0.0004,γ=1.29,ω=0.3,θ=0.00002,ϕ=0.00002, A=1000 and B=200,S_0=3000, E_0=I_0=R_0 = 10.

5.4.8 Comment on Optimal Control Analysis

The figure (5.6) shows that SEIRs with optimal control, where the number of susceptible populations decrease, where as the number of recovered populations increase with the time t , this is also shown in figure (5.8) S with control and S without control. Exposed is also increase. In the case of control the number of susceptible is increase in (figure 5.7). Figure (5.10) shows that the number of recovered population is increase when we use control, and almost zero when there is no control. Ion figure 5.17 when there is no control (vaccination),the number of infected is higher than the number of population when we use optimal control, that is the number of population that infected is very low with time (t). In figure 5.18, the control (u) is decreased after some time (t) and the cost (lamda1) is decrease when we compare to the initial cost to vaccinate the populations.

Chapter Six

6 Conclusions and Recommendation

6.1 Conclusions

In this thesis we have discuses about optimal control of LSD disease subordinate to SEIRS epidemiological model. Even though for lumpy skin disease there are other controlling mechanism, here we used to demonstrate the optimal control analysis is vaccination control strategy; We established and discussed the conditions for the stability of the model equilibria.
Basically we focus on modeling ordinary differential equations, for solving and studying the behavior of the model qualitatively, we used different mathematical methods, in addition to MATLAB graphical technique, we discussed and demonstrate stability, equilibria, based on their eigenvalues.
Develop an optimal control problem for dynamics of LSD model and study the effect of optimal vaccination strategy for driving LSD diseases with vaccine towards eradication within a specified period.
We wanted to determine optimal control strategies that would minimize not only the infected cattle's but also the cost of implementation of the control as well. We used Pontryagins maximum principle to characterize the controls and derive the optimality system.
we presented graphically for uncontrolled and controlled mathematical models. The optimal control problem we presented has an efficient method based on identifying the best intervention; optimal vaccination schedule and control strategies of LSD. In numerical simulation, we propose an algorithm based on the forward-backward sweep method. The state equations are solved simultaneously forward in time, and next the adjoint equations are simultaneously solved backward in time. control measures and low cost is clear and expected.

6.2 Findings and General conclusions

The resulting optimality system showed that; a system with optimal control as well as without control dynamics has a very desirable effect upon the population for reducing the number of infected individuals during the control period in properly managed. As the control period increases the number of population saved from LSD gradually disease increased. Epidemiological Modeling of LSD Disease with Optimal Control of Vaccination Strategy. Based on our LSD model and parameters the result of optimal vaccination strategy at different vaccination ratio (u) shown, LSD extinction will be possible if the vaccination ratio of susceptible population is greater than or equal to 0.5, which implies that as the vaccination ratio increases further, then the cases of LSD infection will reduce gradually. But if the vaccination ratio is less than this value, LSD outbreak may exist in the long run.

6.3 Limitations and Recommendations

In this thesis, for simplicity we are not considering the some aspects of the disease. Study on this area shows that,the disease has seasonal behavior, usually the disease highly spreads on wet season ().In addition if the cow is vaccinated then the probability of calf infected with the diseases is very low, and if cattle's have vaccination annually totally could not be infected. All the type (sex and age difference) has impact to catch with the disease. For this thesis we consider the probability infected with the disease is equal, we did not consider the air conditions and geographical locations.

So that we recommended that based on this thesis further studying will be applying for LSD in optimal control and qualitative analysis using epidemiological models. In this thesis most of the methods and models are included, tools and guides that helps for conclusions and decision is here. The researcher can use the material as a tool for demonstration and making analysis by changing the parameters that will collect data from the location where the diseases is forthcoming.

Appendix

A Note on Matlab dfield and pplane

dfield (direction field) and pplane (phase plane) are software programs for the interactive analysis of ordinary differential equations (ODE).Several textbooks on differential equations refer to and use dfield and pplane. Among them are Differential Equations and Differential Equations with Boundary Value Problems by John Polking, Albert Boggess, and David Arnold [42].
For making clear and easy our discussion let as consider the following second order differential equations.

$$y'' - 3y' - 2y = 0 \tag{A.1}$$

, Since ppalne or dfield works on first ODE, we need to convert the equation into first order.
Now let,

$$y' = x \tag{A.2}$$
$$\Rightarrow y'' = y' \tag{A.3}$$
$$thuse \quad the \quad equationy'' - 3y' - 2y = 0 \Rightarrow x' - 3x - 2y = 0 \tag{A.4}$$

we have none linear first order equation.

$$\Rightarrow x' = 3x + 2y \tag{A.5}$$

So that from equation (A.5 and A.2) we have couple of ODE

$$\begin{aligned} x' &= 3x + 2y \\ y' &= x \end{aligned} \tag{A.6}$$

We are reducing the higher order differential equations in to first order differential equations, and then this equations can be directly qualitatively analyze by pplane. Note that, If we have more that two non-linear system of equations we need to reduce in to two equations, to apply on pplane.

B Direction field (dfield)

DFIELD8,(note that suffix number is the version number (6,7 or 8), is to use routine which takes a user defined first order differential equation, and plots its direction field. It also allows the user to plot solution curves.
Step-1- Download Software-

1. Open your any one of Internet browser
2. Write the following link on the Internet address bar
   http://math.rice.edu/ dfield/
3. Click dfield8 and pplan8 on the list of download links (for version 8)
4. We have download files "dfield8.m and pplane8.m

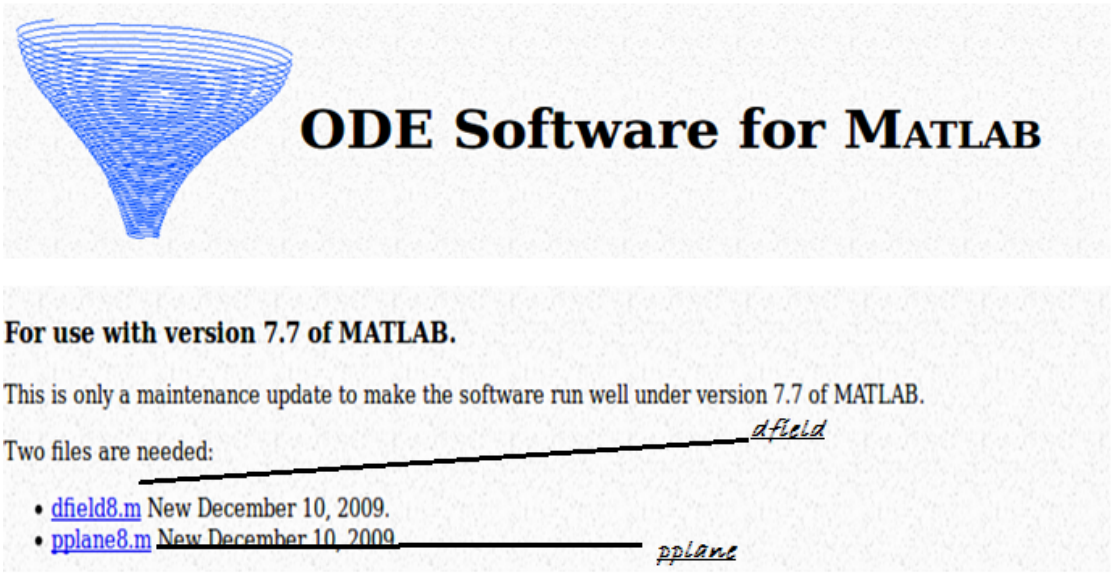


Figure B.1: website that downloads the file dfiled8.m and pplan8.m

Step-2- Install and Running the Software into MATLAB program-

1. Copy the file (dfiled8.m and pplane8.m) and paste into the path where MATLAB program is running. (or to we can put it any where which is convenient for our work, but to run the file on the MATLAB program first we need to change the path of MATLAB where the file is located, (see figure B.2). Figure B.2 arrow 1 shows the path of MATLAB program running, and 2 shows the file is located on the same path.

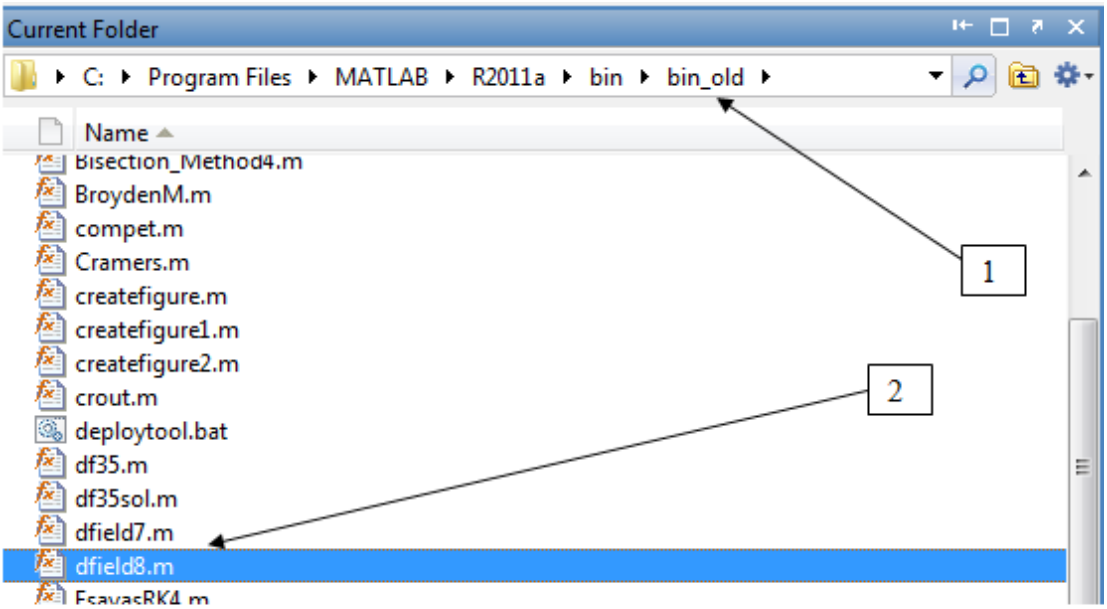


Figure B.2: dfiled and pplane is in the path of running MATLAB program

2. In command windows of MATLAB program write dfiled8 or pplane8 (as we want which program need to run), and press enter key,(see figure B.3) , then

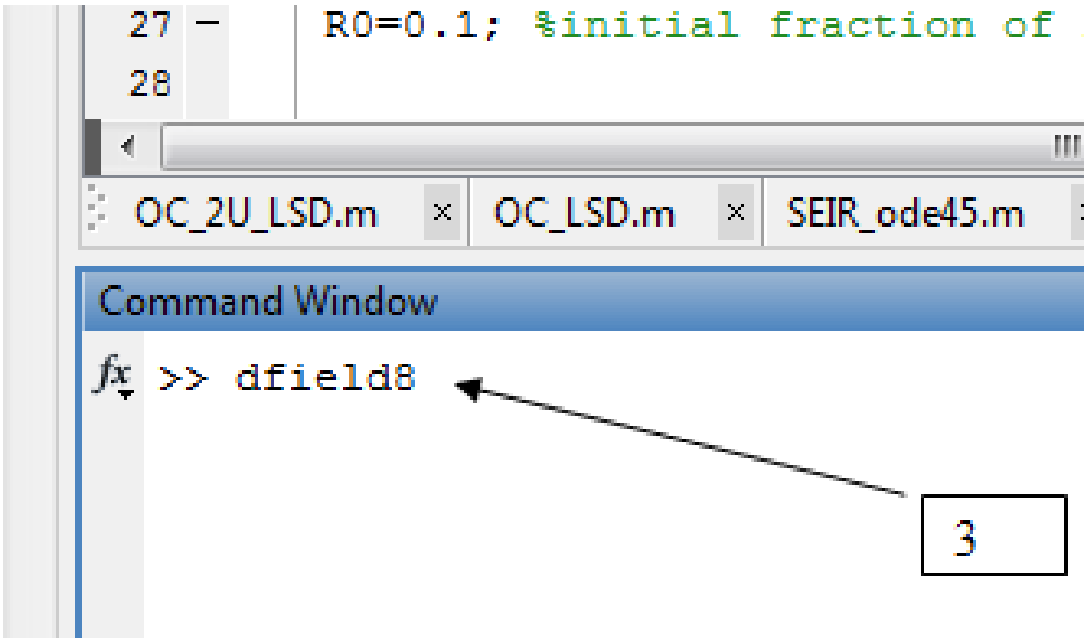


Figure B.3: dfiled and pplane move to the path of MATLAB

we have default display window, (see figure B.4).

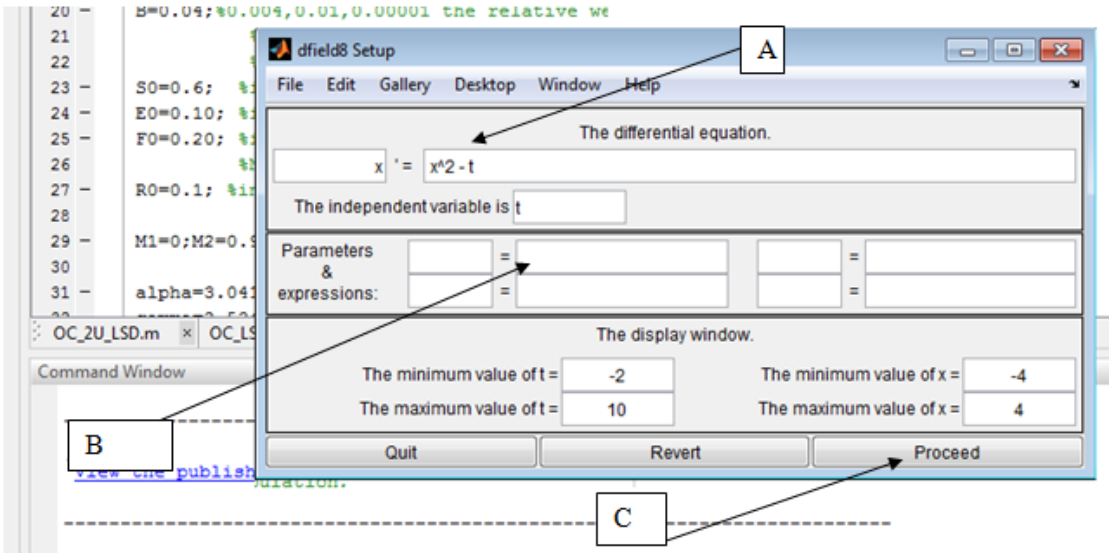


Figure B.4: dfiled page setup

Step-3- Using dfiled

1. Write our differential equations on the equation bar (see figure B.4 arrow A), equation that appears on the bar is default equation.

2. If we want to change the value of the parameter, write the parameter and its respective value (see figure B.4 arrow B and figure B.5 arrow D)

3. After we made change the value of the parameter, minimum maximum value of the independent variable, then press the button Proceed), (see figure B.4 arrow C)

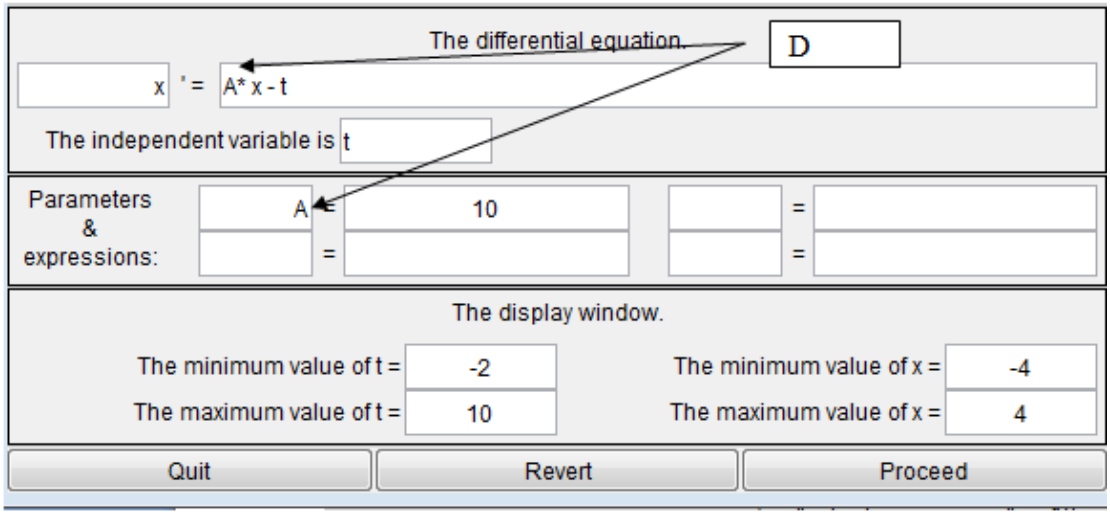


Figure B.5: Equations by changing the parameter value A

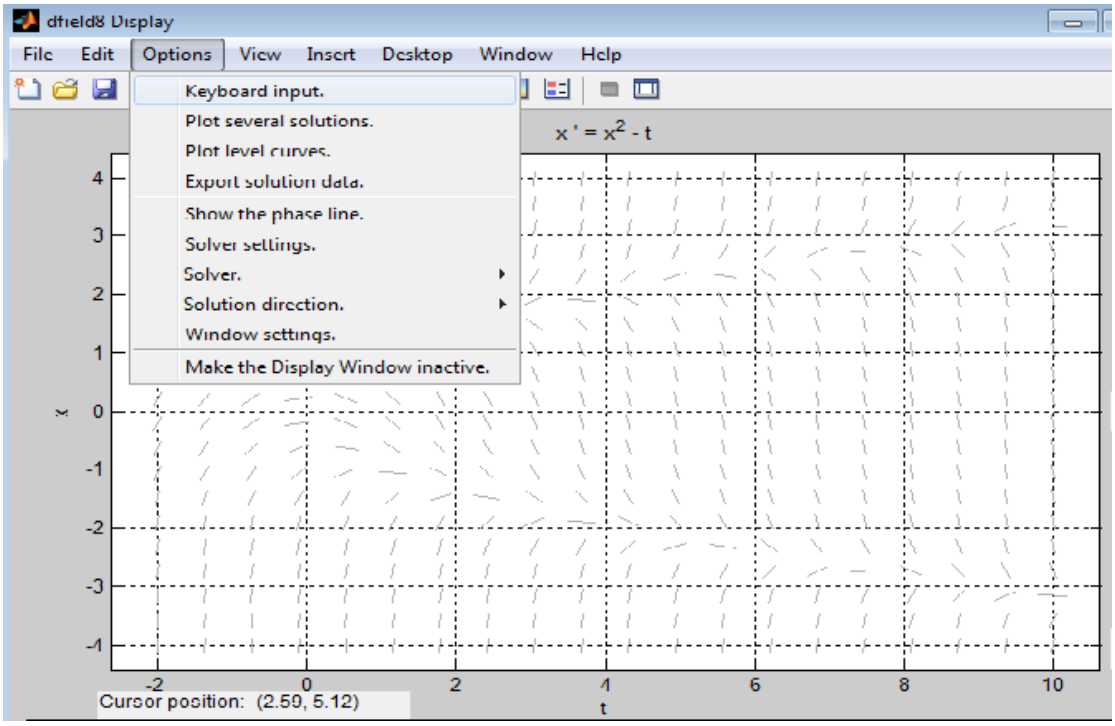


Figure B.6: dfiled with out graph, it has directed arrows

4. Now we have dfield display windows (see figure B.6)
5. To see the direction of the graph we have two options, one on menu bar click option then click keyboard input menu (see figure B.6),
6. We have got figure B.7 the small boxed figure having (dfield keyboard input).
7. Enter the initial value for independent and dependent variable, then enter Compute button, then we have got the line on the figure B.7.
8. Or we can click on the body of the displayed windows and we have figure B.8)

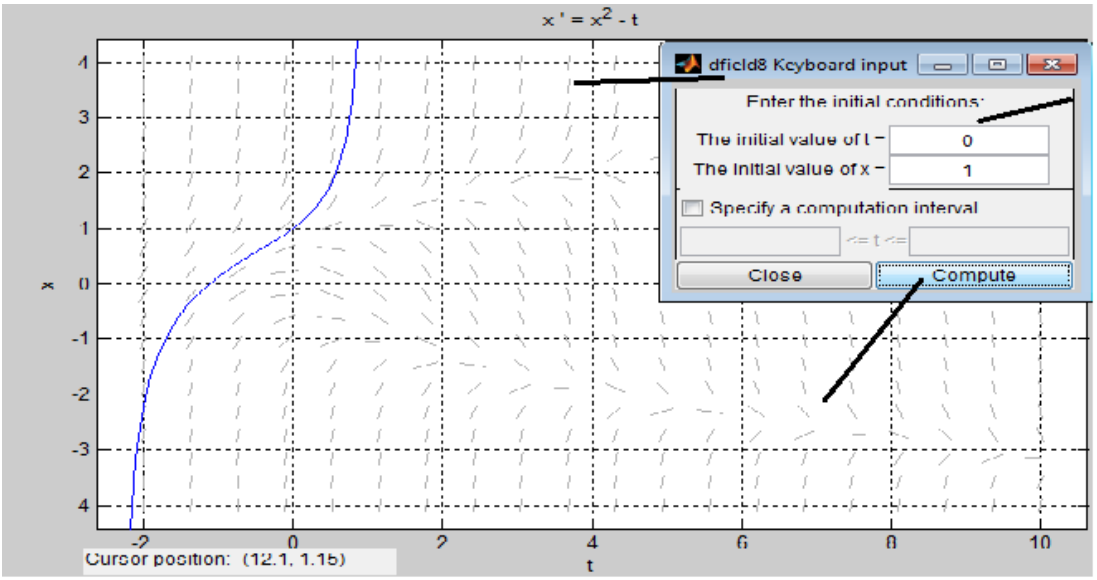


Figure B.7: dfiled with keyboard input

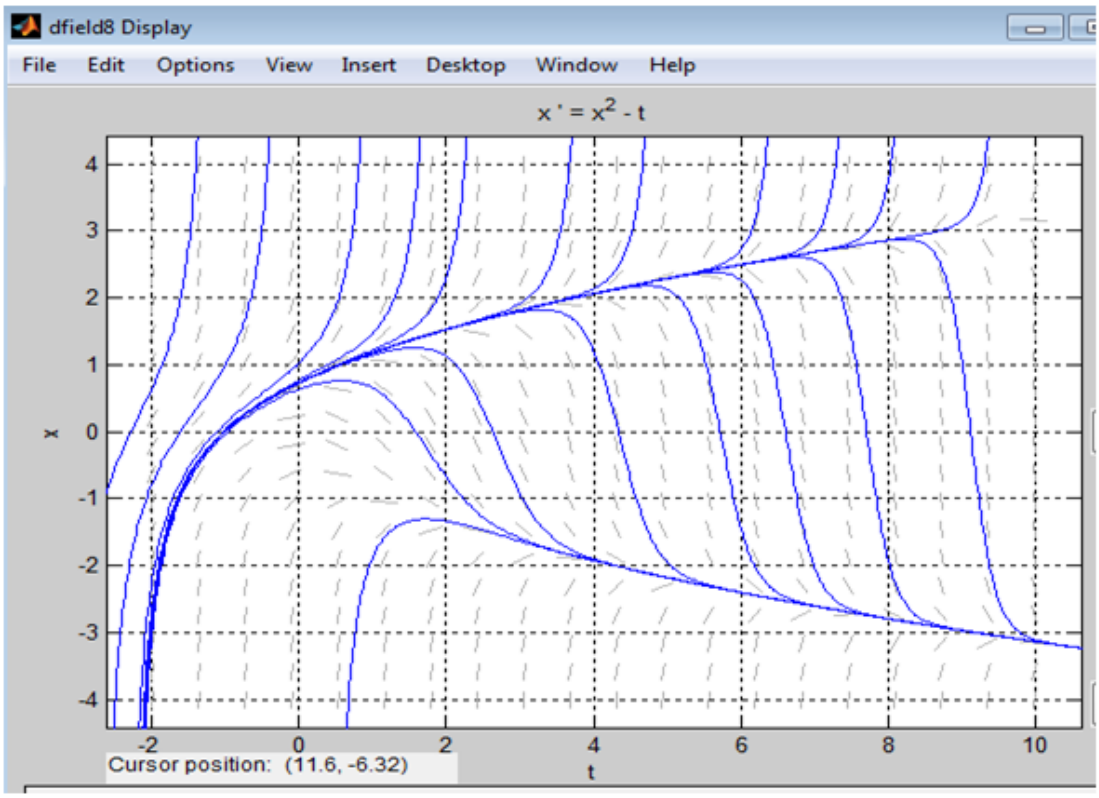


Figure B.8: dfiled having several solutions

C Phase Plane (PPlane)

PPLANE8 plots vector fields for planar autonomous systems. It allows the user to plot solution curves in the phase plane. It also enables the user to plot these solutions in a variety of plots versus the independent variable. There are a number of advanced features, such as finding equilibrium points, displaying linearizations, and plotting figures.

C.1 pplane setup

As shown in dfiled case appendix B. On the MATLAB command window write pplane8 and press Enter key, then we have pplane8 setup windows, (see figure C.1)

- Write system of first order differential equation on the equation bar, (see figure C.1 arrow E.
- If we need to change the parameter of the variables, put the variable values on the space (parameter or expression).
- Set the minimum and maximum value of the two independent variables (here independent variables are x and y. Note that x and y are dependent,(see figure C.1 arrow F)
- Then press proceed button, then we have pplan8 display windows, (see figure C.2)

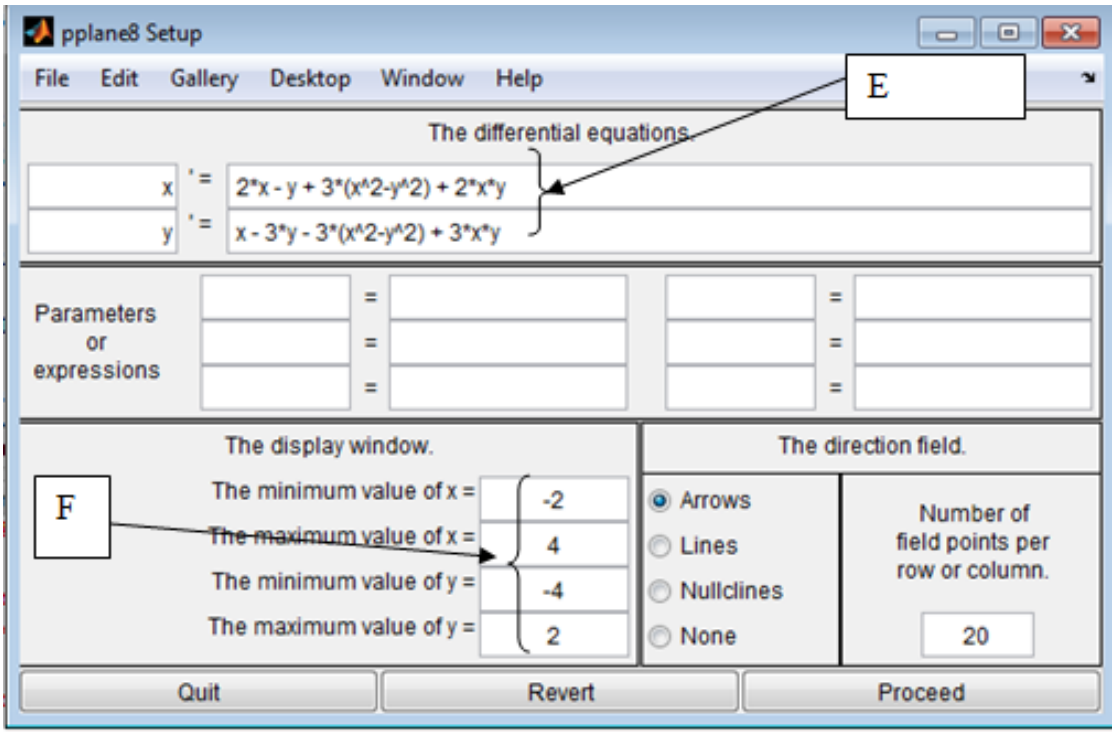


Figure C.1: pplane page setup

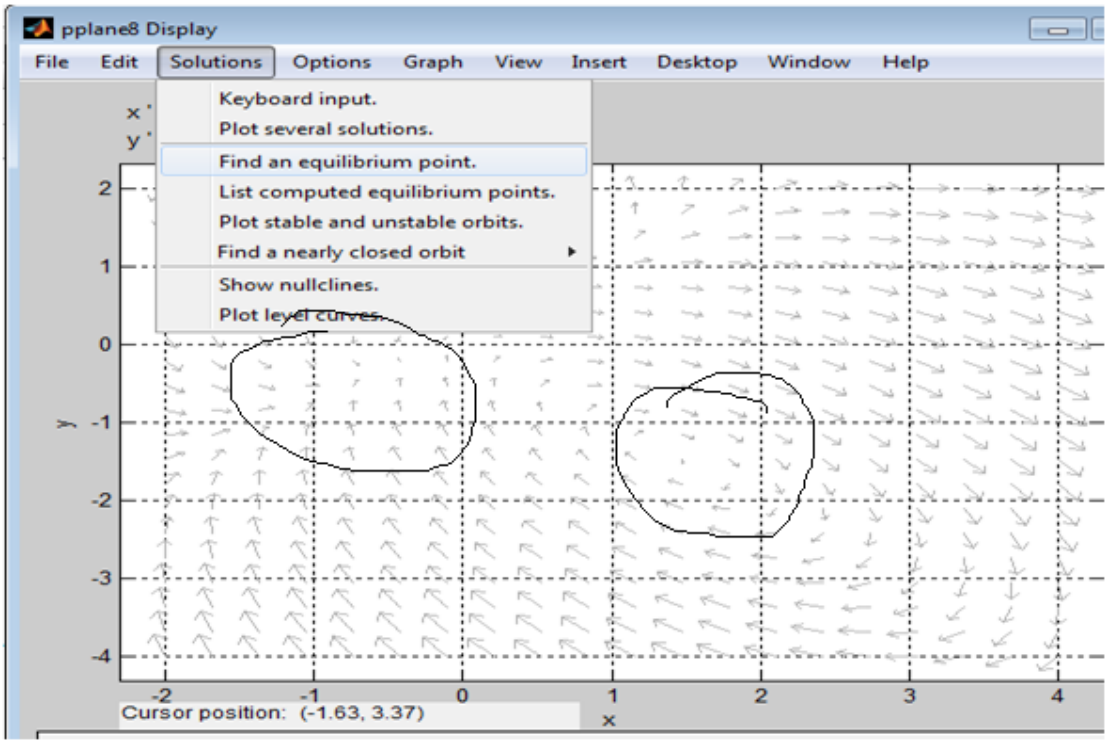


Figure C.2: pplane display window

- To enter initial value for x and y, on top menu bar click on Solutions → Click Key board input.

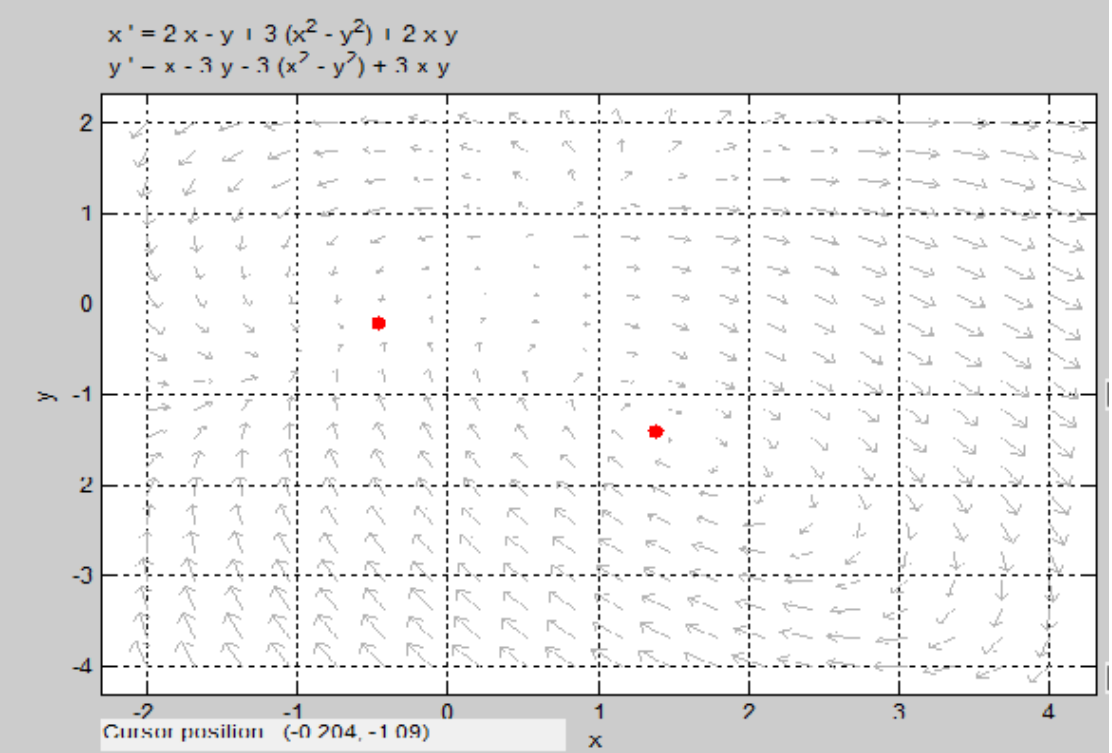


Figure C.3: Equilibrium points

- To find the equilibrium point on top menu bar click on Solutions → Click Find an equilibrium point, then on the display window, look at the position of the arrows and click where the arrows are sink or sources, or spiral, (see figure C.2 and C.3)
- To show nullclines, on top menu bar click on Solutions → Click Show nullclines, then we have nullclines on the pplane display windows, (see figure C.4)
- If we want to find the Jacobi, Eigenvalue, Eigenvectors, and stability, click on the equilibrium point and we have new windows,(See figure C.5). On figure C.5
  - Arrow G shows , system of equations that is entered on the setup windwos.
  - Arrow K shows, the equilibrium point, when click at the equilbirum point we have the small window ("pplane8 Equilibrium point data").
  - Arrow I shows, the value of the Jacobi matrix
  - Arrow L the eigenvalues of the system of equation, (0.070398+8.0001i, 0.070398-8.0001i),positive Real Positive complex and positive real negative complex eigenvalues.
  - Arrow H shows, the value of equilibrium pint (1.387, -1.4177), and the behavior of the system of equations (it is Spiral source).

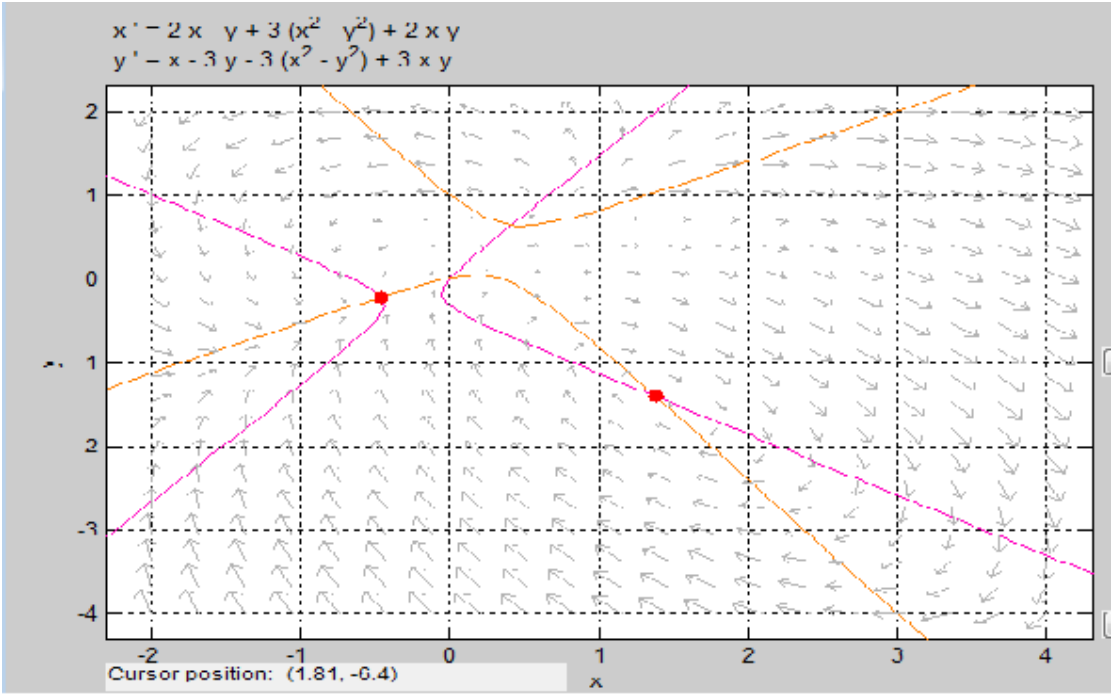


Figure C.4: Equilibrium points

- By clicking on the display window we have different figures, see figure C.5).
- To display separately the independent on top menu bar click on Solutions → Click Graph, then on we have new windows, t-plot, (see figure C.6 and C.7).
- by Changing teh Graph option, we can have x vs t, y vs t or both x-y vs t, graph, even we can have 3D graphs, (see figure C.8).

Those above shown figures are on one of the equilibrium point that has complex eigenvalue, figure C.9 is with equilibrium point (-0.46612,-0.22089), having eigenvalues (-1.7127,-5.2495) both are negative and real, this is sink nodal, which is stable at this equilibrium point, (see figure C.9).

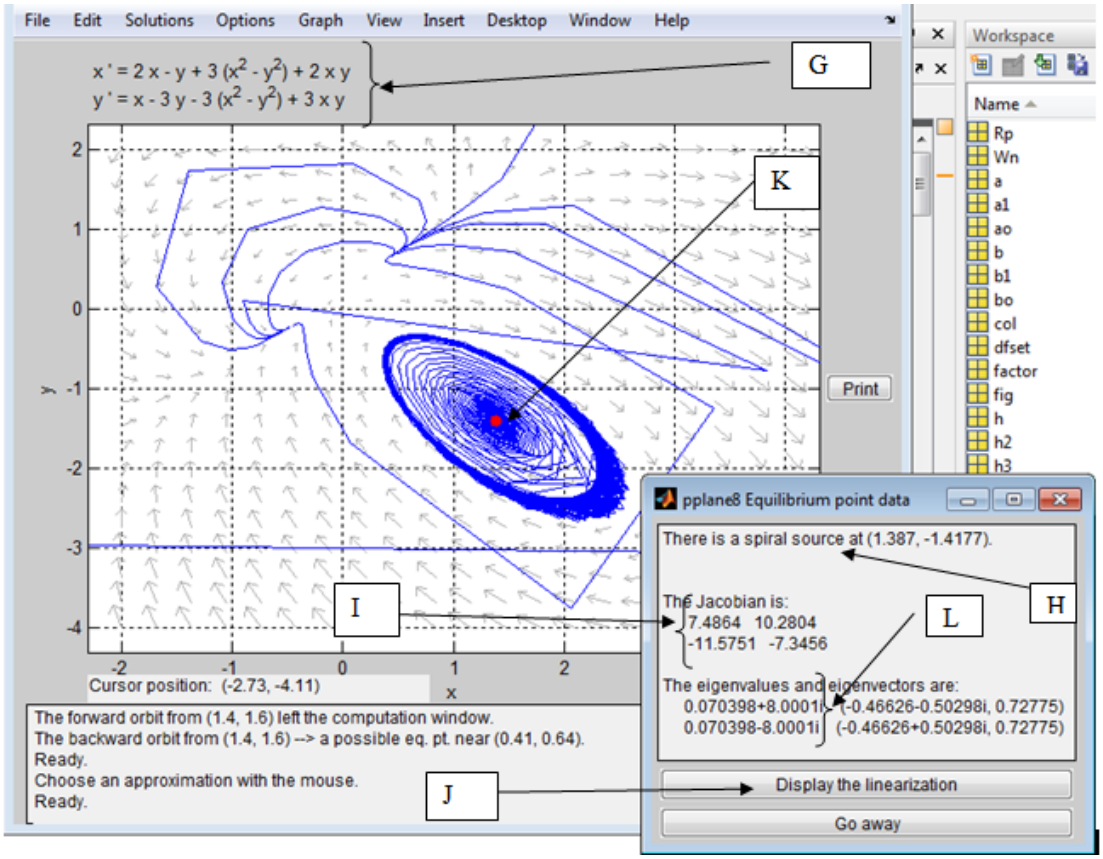


Figure C.5: pplane diagram and its Jacobi, eigenvalue and eigenvector

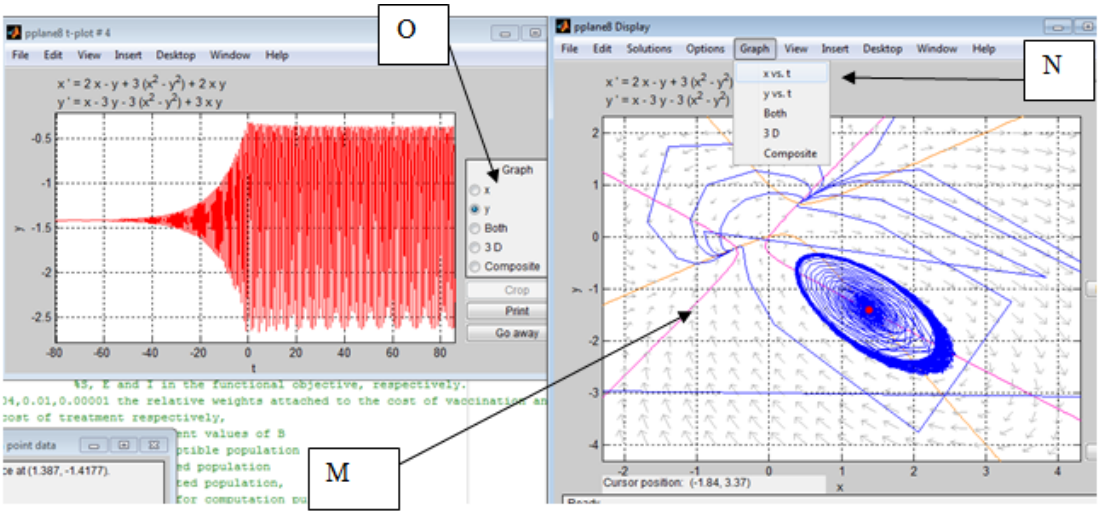


Figure C.6: pplane nullcline and graph of each variables

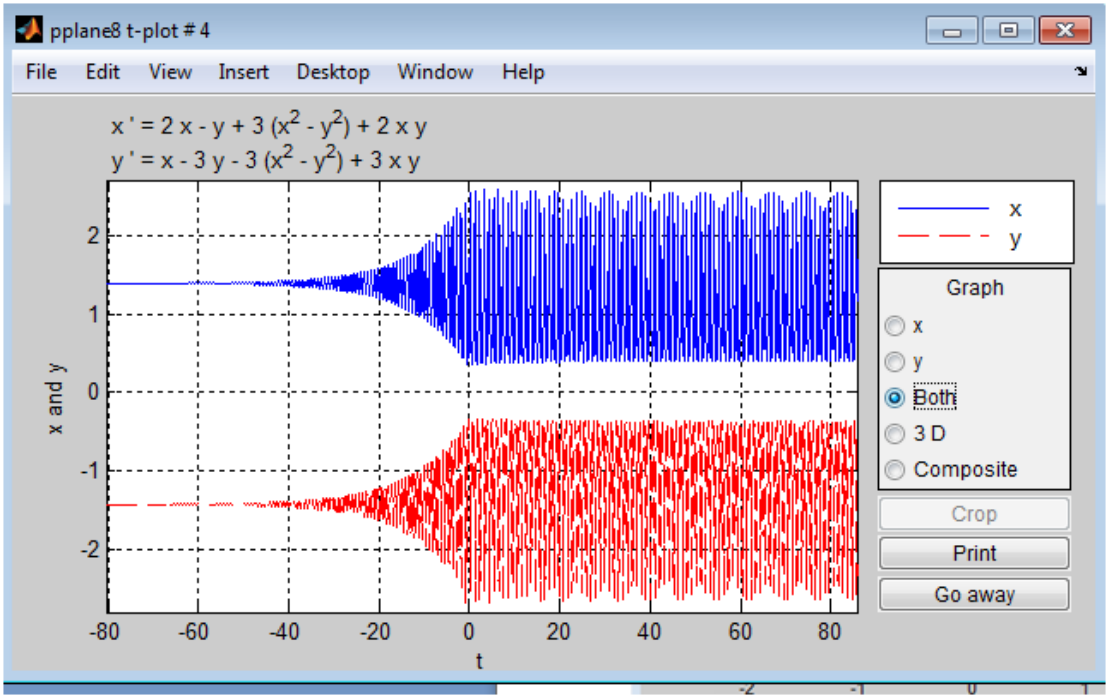


Figure C.7: Graph of each system of equations with respect to time (t)

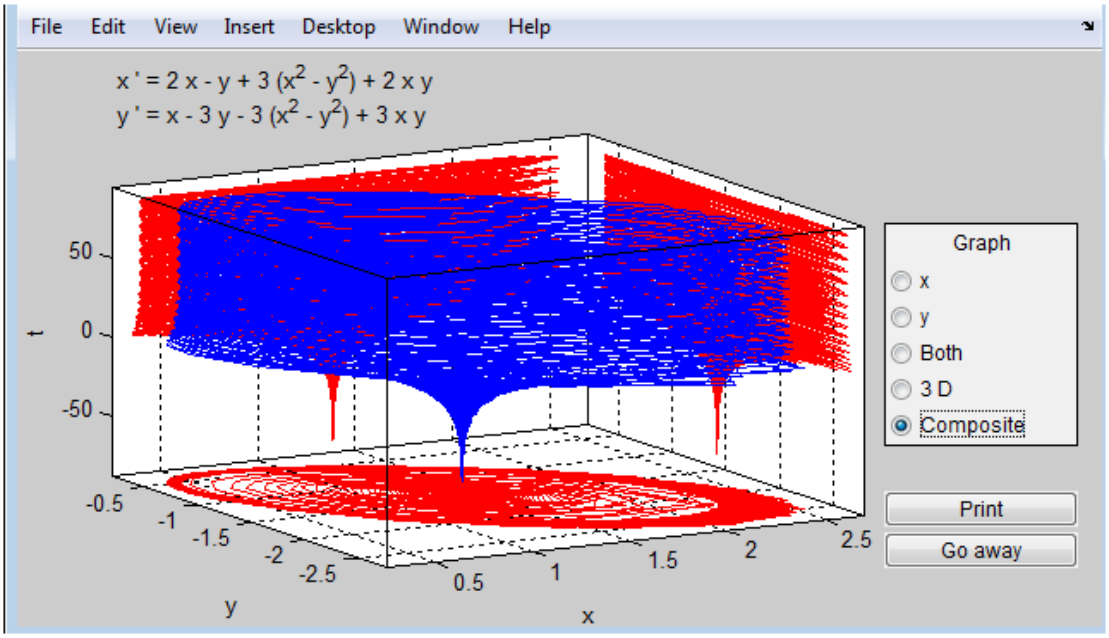


Figure C.8: Graph of the system of equation in 3D view

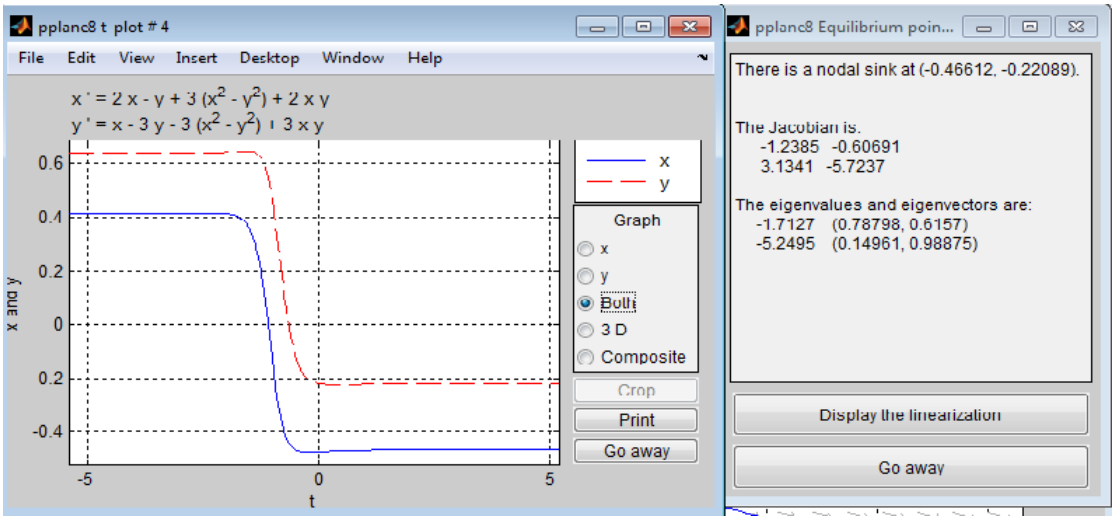


Figure C.9: x-y vs t graph at equilibrium point (-0.46612,-0.22089)

C.2 Discussion with example

To make it more clear again about stability nodal sink, spiral sink, sours, spiral, let as consider, second order equation that we reduced as first order coupled equation, see equations (A.1 and A.6).

x′=3x+2y and y′=x. Using pplan8 lets determining the behavior of the equation,(see figure C.10), we put the equations on pplan8 setup. We have equilibrium point at (0,0). When we see the graph arrow, some of the arrows away from the nullcline with one side of the nullcline and into the nullcline with the other side, (see figure C.11). If we have such directed graph, The equilibrium point,we call it, saddle point.

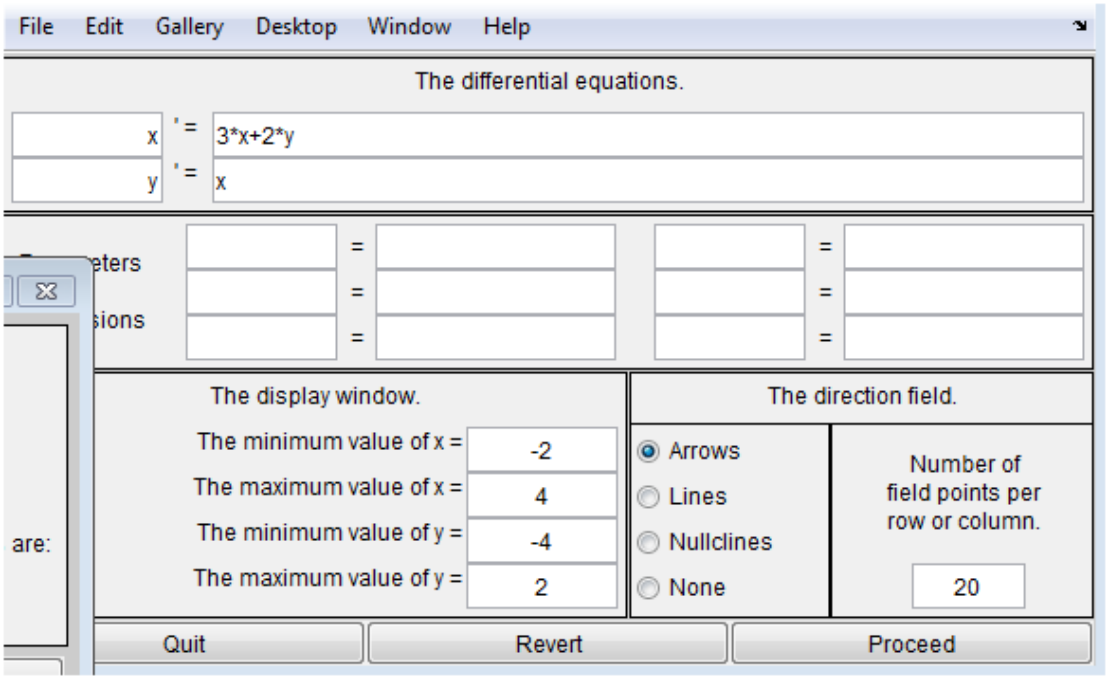


Figure C.10: pplane for determining the behavior of the system

Moreover, when we look at the Jacobi, Eigenvalue, there are one positive and one

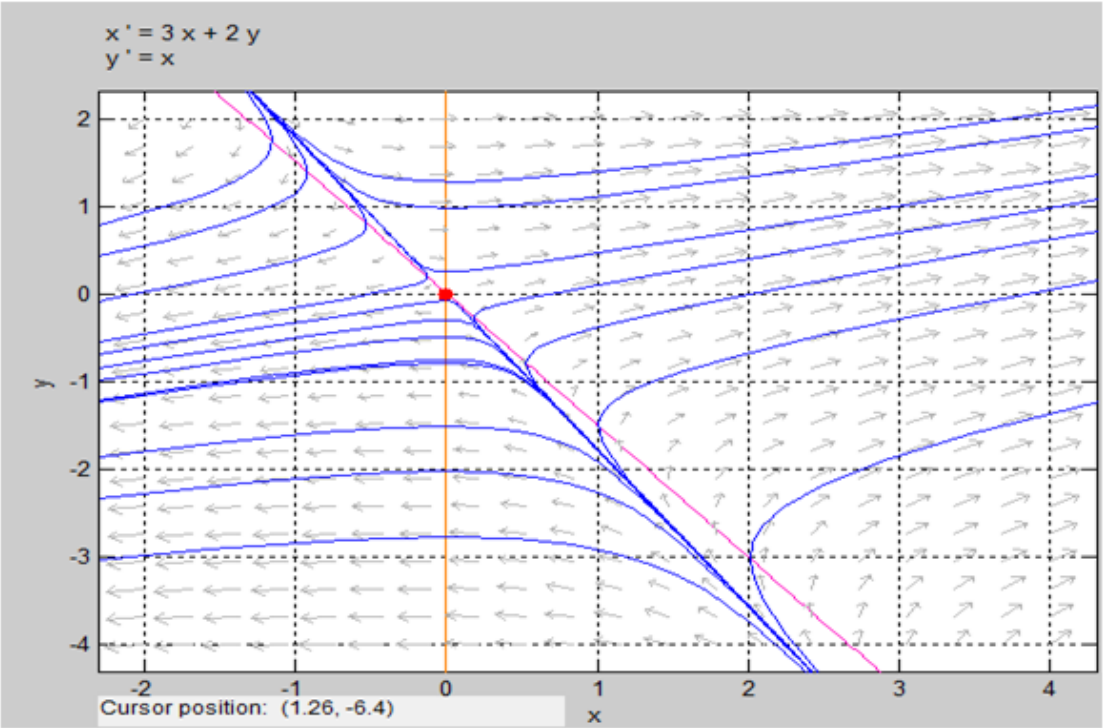


Figure C.11: saddle point at fixed point (unstable)

negative eigenvalues, so that, by our definition we call it again it is saddle point, (see figure C.12). Now Let us the change the equation as x′=3x-2y, in this case, we have equilibrium point (0,0) and all the arrows are out of the equilibrium,(see figure C.13), we call it nodal source,by simple guess, and from our definition with out finding the eigenvalues, we can deduce that both eigenvalue have the same sign which is positive, (see figure C.14), the Eigenvalues are (2 and 1), and the point (0,0) is nodal source, the system of equations at that point is unstable. Unstable means, for the case of disease it grownup, may occur outbreak.

Again Let us the change the equation as x′=-3x-2y, in this case, we have also equilibrium point (0,0) and all the arrows are into the equilibrium,(see figure C.15), we call it nodal sink,by simple guess, and from our definition with out finding the eigenvalues, we can deduce that both eigenvalue have the same sign which is negative, (see figure C.16), the Eigenvalues are (-2 and -1), and the point (0,0) is nodal sink, the system of equations at that point is stable. stable means, for the case of disease it decays, may eradicate the disease after some time t.

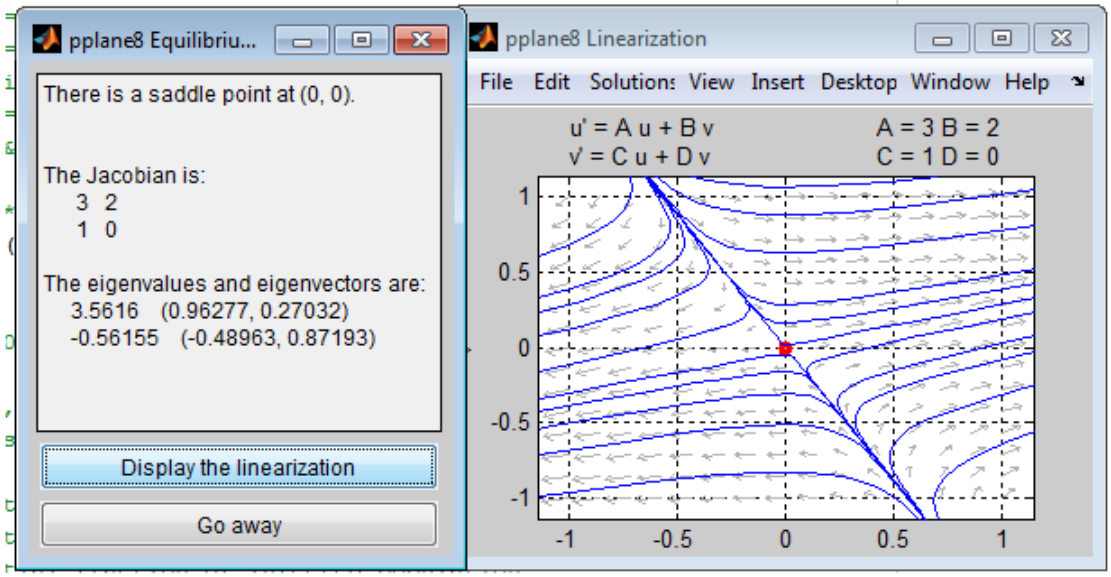


Figure C.12: The Jacobi, eigenvalue and linearization

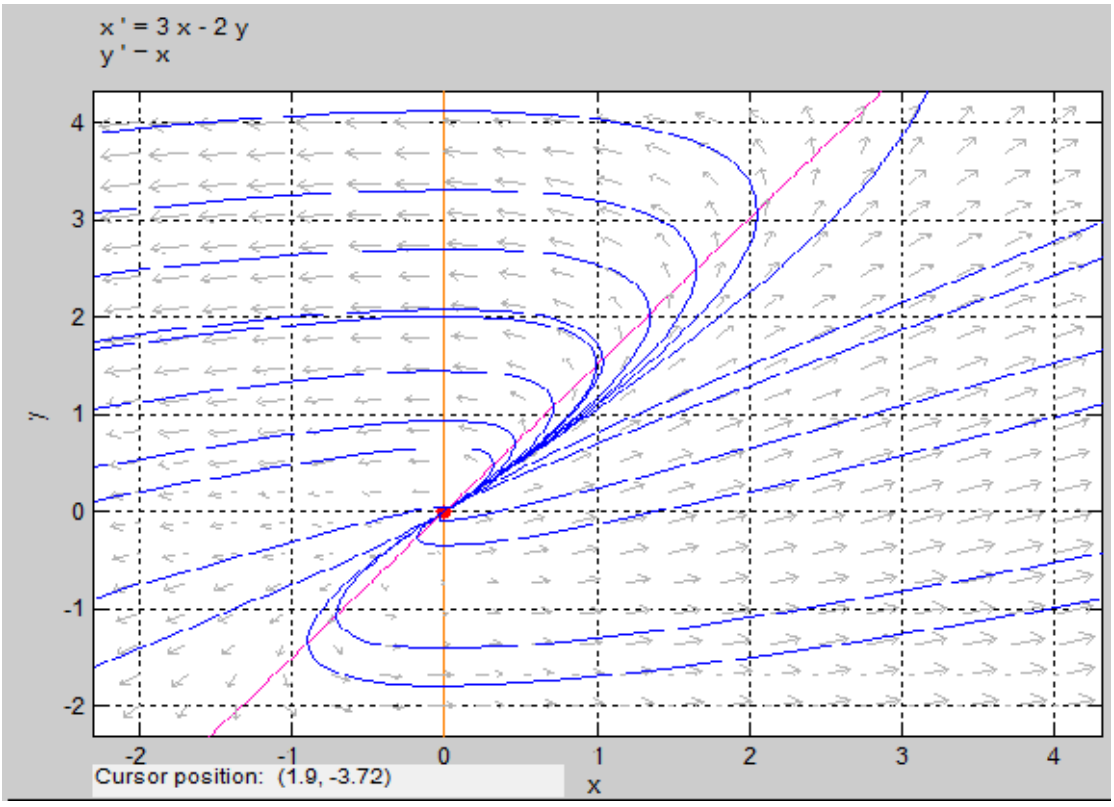


Figure C.13: pplane with nuclines and equilibrium point, the arrows are out from the point.

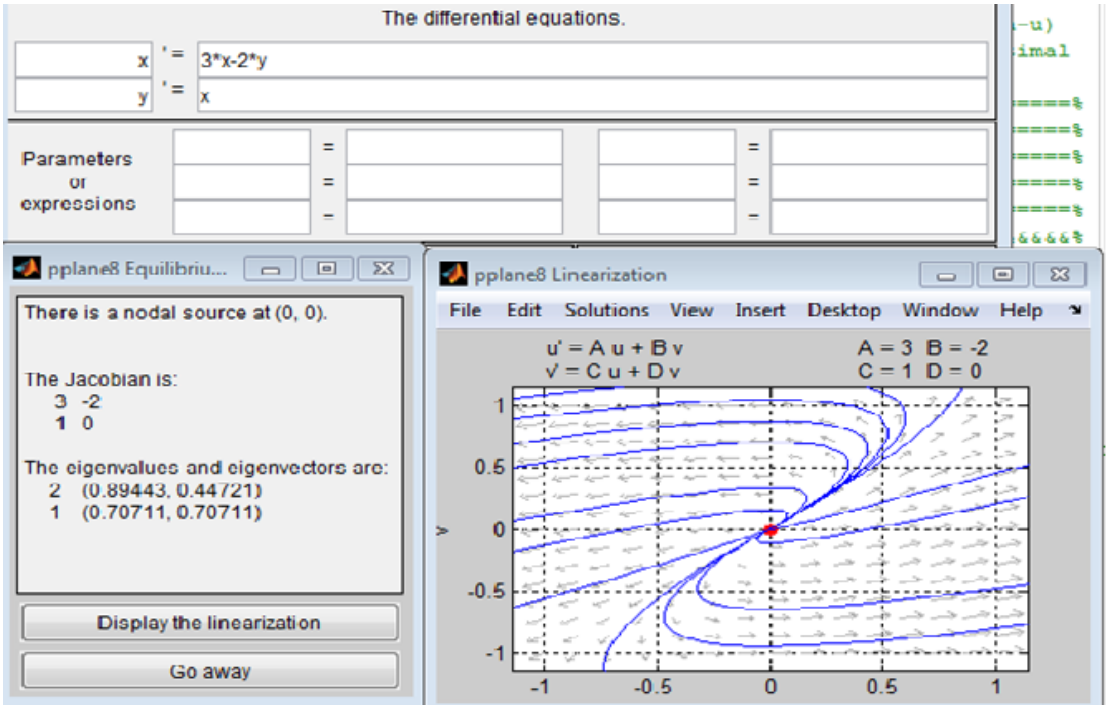


Figure C.14: Changing equation, positive eigenvalues, nodal source at the fixed point

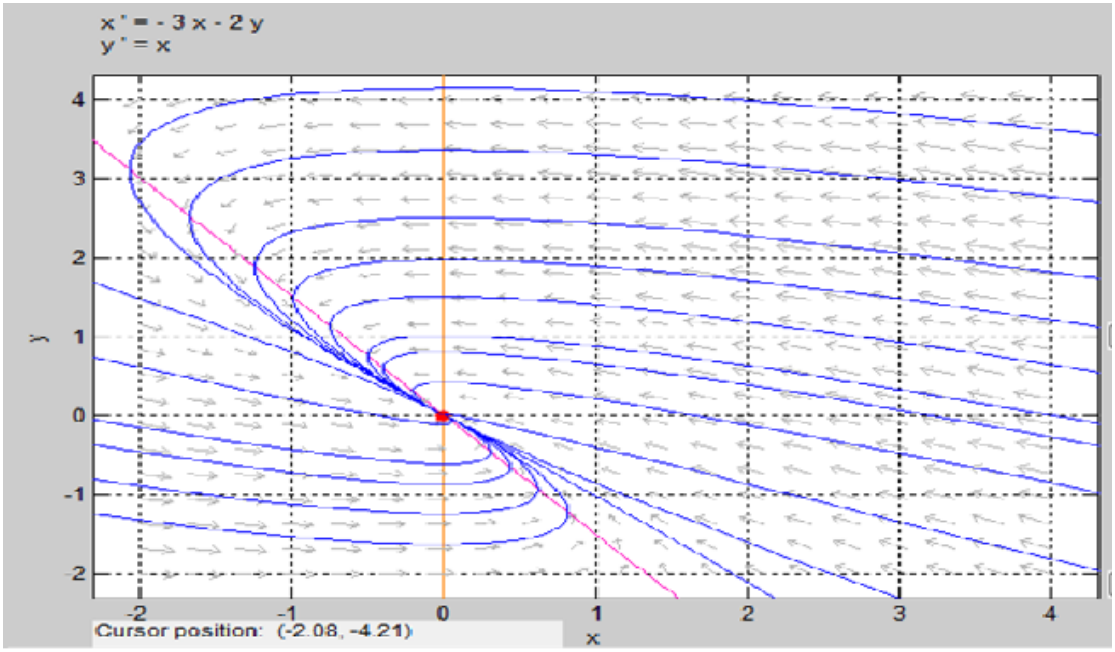


Figure C.15: pplane diagram, with nullcline and equilibrium, nodal sink, all inwards to the fixed point

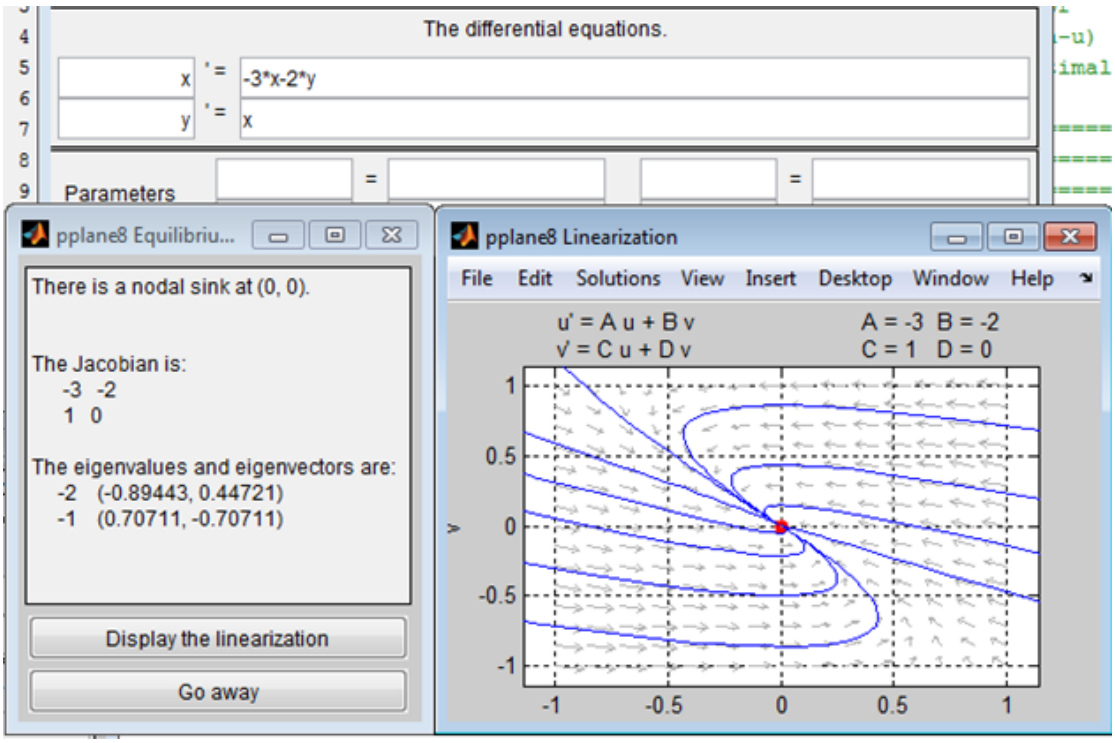


Figure C.16: the jacobi, eigenvalue and linearization, with nodal sink

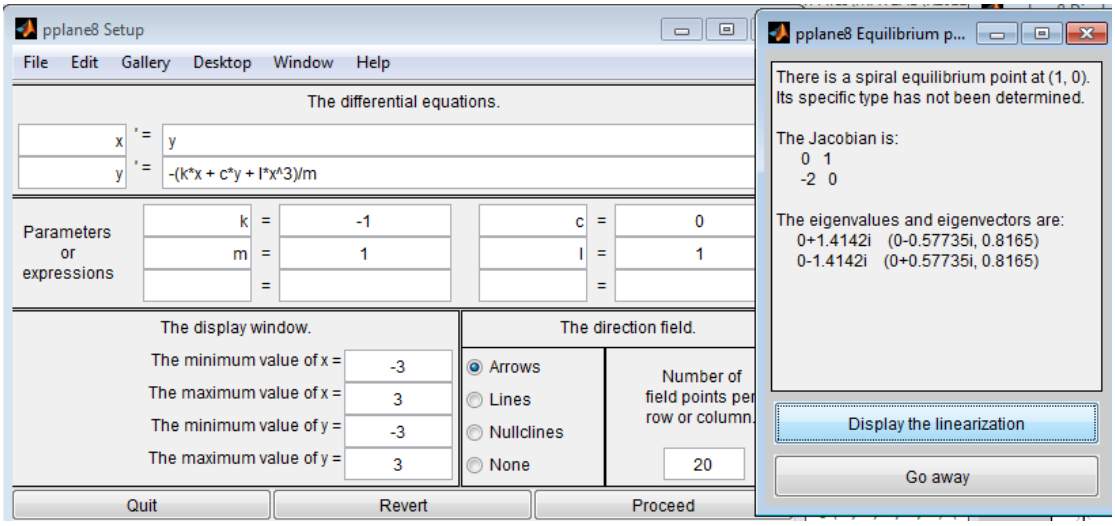


Figure C.17: Duffing's Equation, with complex eigenvalue, Eginevalue and Jacobi

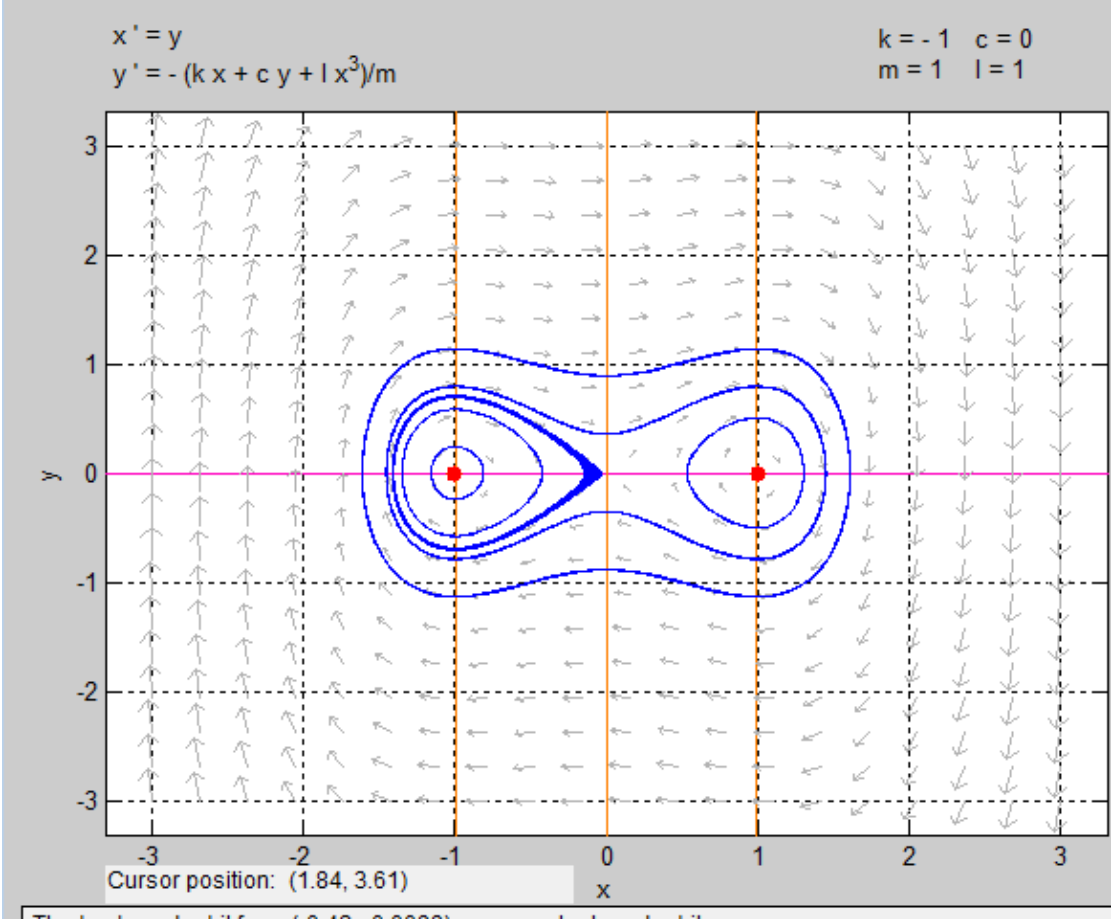


Figure C.18: Duffing's Equation, with complex eigenvalue

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