Mathematical modelling of the HIV/AIDS epidemic and the effect of public health education.

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Keywords

disease-free equilibrium

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local and global stability

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almost sure exponential stability

Abstract

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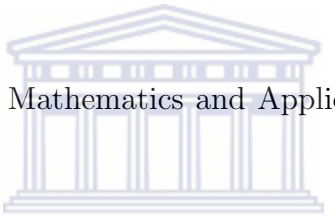
MSc Dissertation, Department of Mathematics and Applied Mathematics, University of the Western Cape.



HIV/AIDS is nowadays considered as the greatest public health disaster of modern time. Its progression has challenged the global population for decades. Through mathematical modelling, researchers have studied different interventions on the HIV pandemic, such as treatment, education, condom use, etc. Our research focuses on different compartmental models with emphasis on the effect of public health education. From the point of view of statistics, it is well known how the public health educational programs contribute towards the reduction of the spread of HIV/AIDS epidemic. Many models have been studied towards understanding the dynamics of the HIV/AIDS epidemic. The impact of ARV treatment have been observed and analysed by many researchers. Our research studies and investigates a compartmental model of HIV with treatment and education campaign. We study the existence of equilibrium points and their stability. Original contributions of this dissertation are the modifications on the model of Cai et al. [1], which enables us to use optimal control theory to identify optimal roll-out of strategies to control the HIV/AIDS. Furthermore, we introduce randomness into the model and we study

the almost sure exponential stability of the disease free equilibrium. The randomness is regarded as environmental perturbations in the system. Another contribution is the global stability analysis on the model of Nyabadza et al. in [3]. The stability thresholds are compared for the HIV/AIDS in the absence of any intervention to assess the possible community benefit of public health educational campaigns. We illustrate the results by way simulation

The following papers form the basis of much of the content of this dissertation,

[1] L. Cai, Xuezhi Li, Mini Ghosh, Boazhu Guo. Stability analysis of an HIV/AIDS epidemic model with treatment, **229** (2009) 313-323.

[2] C.P. Bhunu, S. Mushayabasa, H. Kojouharov, J.M. Tchuenche. Mathematical Analysis of an HIV/AIDS Model: Impact of Educational Programs and Abstinence in Sub-Saharan Africa. *J Math Model Algor* **10** (2011),31-55.

[3] F. Nyabadza, C. Chiyaka, Z. Mukandavire, S.D. Hove-Musekwa. Analysis of an HIV/AIDS model with public-health information campaigns and individual withdrawal. *Journal of Biological Systems,* **18, 2** (2010) 357-375.

Through this dissertation the author has contributed to two manuscripts [4] and [5], which are currently under review towards publication in journals,

[4] G. Abiodun, S. Maku Vyambwera, N. Marcus, K. Okosun, P. Witbooi. Control and sensitivity of an HIV model with public health education (under submission).

[5] P.Witbooi, M. Nsuami, S. Maku Vyambwera. Stability of a stochastic model of HIV population dynamics (under submission).

Declaration

I declare that this is my own work, that it has not been submitted for any degree or examination in any other university, and that all the sources I have used or quoted have been indicated and acknowledged by complete references.

Sibaliwe Maku Vyambwera

Signed: .....

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First of all, I would like to thank the almighty God who gave me strength during hard times beyond what I expect from myself. I would like to thank my supervisor, Prof. Peter Witbooi, for his tremendous support, help and guidance throughout my dissertation. Many thanks to all the UWC lecturers who taught me and the staff of the department. I would also like to thank the University of Western Cape for their financial support through the Mellon Fellowship.

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Contents

List of Acronyms

a.s, almost surely

SDE, Stochastic Differential Equation

HAART, Highly Active Antiretroviral Therapy

List of Notations

σ, perturbation parameter

Q, a martingale measure equivalent to the market measure

$\mathbb{P}$, a probability measure, usually the market measure

$(\Omega, \mathcal{F}, \mathbb{P})$, Probability triple

$\{\mathcal{F}_n\}_{n\geq 0}, \{\mathcal{F}_t\}_{t\geq 0}$, Filtration

W, Brownian motion or Wiener process

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Chapter 1

General Introduction

1.1 Intoduction to HIV/AIDS

Acquired immune deficiency syndrome or acquired immunodeficiency syndrome (AIDS) is a disease of the human immune system caused by human immunodeficiency virus (HIV). For more information refer to Sepkowitz [46]. AIDS has developed into a global pandemic (which is an epidemic of infectious disease that spreads through human population across a large region, continent or worldwide) since the first patients were identified in 1982. However, the early history of HIV in South Africa was contained, like in the early phase of the epidemic elsewhere, among gay men. In 1982, two homosexual men were diagnosed with HIV. Out of 250 blood specimen taken from homosexual men in Johannesburg, South Africa's largest city, 32 were infected. Half the sample had more than 20 different sexual partners in 12 months. The initial concentration of HIV within the gay community led to the belief that AIDS was a homosexual disease, with the wider population largely ignoring the risk, and the apartheid government excusing itself from acting. It is currently reported that 34 million people currently living with with HIV, 2.5 million are being newly infected and 1.7 million AIDS death occurred in 2011, [57]. It was reported that South Africa's national AIDS plan was to focus on the rapid scale-up of HIV treatment and almost 2 million people are now on ARV as compared to fewer than

1 million in 2009, [57].

1.1.1 HIV Transmission

Many people still misunderstand the process of transmission of HIV from one person to another, see [56] of Kim for instance. Knowing the basics helps you avoid getting the virus if you are HIV-negative, and avoid giving it to someone else if you are HIV-positive. HIV is transmitted through direct contact of a mucous membrane or the bloodstream with a bodily fluid containing HIV such as blood, semen, vaginal fluid and breast milk. The disease can be passed during unprotected sex with an HIV-infected person. HIV is not spread through body fluids such as sweat, tears or saliva (spit). The spread of HIV can be prevented. There are ways to avoid, or at least reduce, contact with body fluids that spread HIV.

1.1.2 Methods of Transmission

In the past, HIV was spread accidentally by transfusion with blood products, such as whole blood or the factor used by hemophiliacs. Many people were infected this way. The blood supply is now much more strictly tested and controlled. The odds of being infected from receiving blood or blood factor in SA are very low. One cannot get HIV from donating blood if a new sterile (clean) needle is used for each donation, see [56].

An HIV-infected mother can transmit HIV to her infant during pregnancy, delivery or while breastfeeding. Medical care and HIV drugs given during pregnancy can almost eliminate the risk of a baby getting HIV from its mother. HIV-positive mothers should not breastfeed their babies. People can also become infected with HIV when using injection drugs through sharing needles and other equipment. This risk may be reduced by cleaning needles with a bleach solution before re-using them. However, some experts question how effective this method really is in reducing transmission. It is best to use

fresh needles each time to eliminate any risk of infection. Many cities offer free needle exchange programs. Tattoos or body piercings should always be done by a licensed professional whose equipment is autoclaved, not just sterilized with alcohol.

Every sexual act (oral, anal, or vaginal) that involves sexual fluids of some kind has at least some risk. Barriers, such as condoms (male and female), dental dams (thin squares of latex), and latex gloves help reduce risk substantially. Unsafe sex (sex without condoms or barriers) puts you and your partner at risk for HIV or other sexually transmitted diseases (STDs). Safer sex (sex using condoms or other barriers correctly and consistently) protects you and your partner.

1.1.3 How HIV is not Transmitted

HIV cannot be transmitted except when certain body fluids are exchanged. One can greatly reduce the risk of transmission by:

- Avoiding contact with sexual fluids by always practicing safer sex.
- Abstaining from sex unless you and your partner are both HIV-negative and in a long-term, monogamous relationship.
- Not injecting drugs, or if you do, always using new or clean needles.
- Finding out your HIV status if you are planning to get pregnant and working with a knowledgeable health care provider and obstetrician if you are HIV-positive.

If you protect yourself in these ways, you do not need to be afraid of getting or passing HIV by casual contact. HIV is not transmitted by hugs, dancing, sharing food or drinks, using a shower, bath, or bed used by an HIV-positive person, kissing (between people with no significant dental problems), sharing exercise equipment, bug bites, see [56].

Over time, infection with HIV can weaken the immune system to the point that the system has difficulty fighting off certain infections. These types of infections are known as opportunistic infections. These infections are usually controlled by a healthy immune system, but they can cause problems or even be life-threatening in someone with AIDS. The immune system of a person with AIDS has weakened to the point that medical intervention may be necessary to prevent or treat serious illness.

1.2 Immunology of HIV/AIDS

The Human immunodeficiency virus, HIV, infects cells in the immune system and the central nervous system. The T-helper lymphocytes are the main types of cell that HIV infects. The role of these cells in the immune system is to coordinate the actions of other immune system cells. A large reduction in the number of these cells results in weakening the immune system. HIV infects the T-helper cells because it has the protein called $CD4^+$ on its surface, which HIV uses to attach itself to the cells before entering to them. For more information see the book of Ronald [45] and Brauer [9]. That is why the T-helper cell is referred to as $CD4^+$T lymphocyte. Once it attaches itself into a cell, HIV produces new copies which are capable of infecting other cells. When the age of infection increases, HIV infection leads to a severe reduction in the number of T-helper cells which are responsible to help fight diseases.

1.2.1 Stages of HIV/AIDS

The evolution of the virus in the human body, and the response of the body typically takes several years. According to WHO (World Health Organization) clinical staging of HIV/AIDS, HIV infection has four distinct stages: primary infection stage, asymptomatic stage, symptomatic stage, and advanced AIDS stage, we refer the reader to [44]. Knowing what stage of HIV infection an individual is in can help physicians design treatment plans. In order to diagnose an individual as being in a specific stage of HIV, the World Health Organization (WHO) developed a set of criteria that can be used worldwide. The

criteria rely on symptoms, instead of CD4 and viral load test, since many developing countries do not have the facilities to perform these complicated tests. This staging system helps clinicians to decide whether the patient is eligible for treatment or not, especially in resource-constrained setting where $CD4^+$ count measurement or other diagnostic methods are not yet developed.

Stage 1: Primary HIV infection

The first stage of HIV infection is called primary infection. Primary infection begins shortly after an individual first becomes infected with HIV. This stage lasts for a few weeks. During this period, individuals experience symptoms similar to the flu. Very few individuals seek treatment during this time, and those who do are usually misdiagnosed with a viral infection. Often, if an HIV test is performed, it will come back negative, since antibodies are not yet being produced by the individual's immune system. Since antibodies have not yet developed, HIV continues to replicate and results in very high levels of the virus, see Ejigu [18]. In the first few weeks after being infected, infected individuals are highly infectious. At this stage there is a large amount of HIV in the peripheral blood (the blood in the circulating system not in the lymphatic system, bone marrow, liver or speen), around 10^6 copies of virus per μl of blood. Antibodies and cytotoxic lymphocytes start being produced as a response to the virus which is known as sero-conversion. At this stage about 20 percent of people who are HIV positive show symptoms which are not mild. However, the diagnosis of HIV infection is missed at this stage. Those who believe they have been exposed to HIV should repeat the test after six months.

Stage 2: Asymptomatic HIV

In the second stage, individuals are free from any symptoms of HIV although there may be swollen glands. Levels of HIV in the blood are very low, but are detectable. If an HIV test is performed, it will come back positive. While the individual is asymptomatic, the HIV in their blood is reproducing constantly. This stage lasts about ten years, but can be much longer or shorter depending on the individual and is characterized by a CD^4+

count around 500 cells per μl.

Stage 3: Symptomatic HIV

In the third stage, the immune system has become so damaged by HIV that symptoms begin to appear. As a results, it leads to greater $CD4^+$ cell destruction and the immune system is not able to keep up with replacing the $CD4^+$ cells that are lost. As the immune system fails, symptoms start to develop, the reader is referred to Robertson [44]. Symptoms are typically mild at first, and then slowly become more severe. Opportunistic infections, infections that take advantage of the immune system's vulnerable state, begin to occur. These infections affect almost all the systems of the body and include both infections and cancers. Some common opportunistic infections include tuberculosis, cytomegalovirus, and shingles. In this stage HIV infection is often characterized by by multi-system disease and infections in almost all body systems. Treatment for a specific infection or cancer is often carried out, however the main cause is the action of HIV as it attacks the immune system. Unless HIV itself can be reduced, immune suppression will continue to be weaker.

Stage 4: Acquired Immune Deficiency Syndrome

In the fourth and final stage, a person is diagnosed as having AIDS. The progression to AIDS can be characterized by having a $CD4^+$ count of 200 per ml or below, while the normal situation is around 1000 per ml. At this stage, the infected individual is likely to develop opportunistic infections in their respiratory system, gastro-intestinal system, central nervous system and on the skin as well. Once a person is diagnosed with AIDS, the AIDS status is permanent. For more information we refer you to Robertson [44].

A blood test can determine if a person is infected with HIV, but if a person tests positive for HIV, it does not necessarily mean that the person has AIDS. A diagnosis of AIDS is made by a physician according to the CDC AIDS Case Definition. A person infected with HIV may receive an AIDS diagnosis after developing one of the CDC-defined AIDS

indicator illnesses. A person with HIV can also receive an AIDS diagnosis on the basis of certain blood tests (CD4 counts) and may not have experienced any serious illnesses.

1.3 Treatment.

There is currently no publicly available vaccine or cure for HIV or AIDS. However, a vaccine that is a combination of two previously unsuccessful vaccine candidates was reported in September 2009 to have resulted in a 30 percent reduction in infections in a trial conducted in Thailand, [56], [44], [57]. Additionally, a course of antiretroviral treatment administered immediately after exposure, referred to as post-exposure prophylaxis, is believed to reduce the risk of infection if begun as quickly as possible. In July 2010, a vaginal gel containing tenofovir, a reverse trancriptase inhabitor, was shown to reduce HIV infection rates by 39 percent in a trial conducted in South Africa.

However, due to the incomplete protection provided by the vaccine and/or post-exposure prophylaxis, the avoidance of exposure to the virus is expected to remain the only reliable way to escape infection for some time yet. Current treatment for HIV infection consists of highly active antiretroviral therapy or HAART. This has been highly beneficial to many HIV-infected individuals since its introduction in 1996, when the protease inhibitor-based HAART initially became available. Current HAART options are combinations (or cocktails) consisting of at least three drugs belonging to at least two types, or classes, of antiretroviral agents. Typically, these classes are two nucleoside analogue reverse trancriptase inhibitors (NARTIs or NRTIs) plus either a protease inhibitor or a non-nucleoside reverse transcriptase inhibitor (NNRTI) [56].

There is no empirical evidence for withholding treatment at any stage of HIV infection, and death rates are almost twice as high when therapy is deferred (until the CD4 count falls below 500) compared to starting therapy when the CD4 count is above 500. How-

ever, the timing for starting HIV treatment is still subject to debate. The United States Panel on Antiretroviral Guidelines for Adults and Adolescents in 2009 recommended that antiretroviral therapy should be initiated in all patients with a CD4 count less than 350, with treatment also recommended for patients with CD4 counts between 350 and 500. However for patients with CD4 counts over 500, the expert Panel was evenly divided, with 50 percent in favor of starting antiretroviral therapy at this stage of HIV disease, and 50 percent viewing initiating therapy at this stage as optional. They noted that, patients initiating antiretroviral therapy should be willing and able to commit to lifelong treatment and should understand the benefits and risks of therapy and the importance of adherence [21].

New classes of drugs such as entry inhibitor provide treatment options for patients who are infected with viruses already resistant to common therapies, although they are not widely available and not typically accessible in resource-limited settings. Because AIDS progression in children is more rapid and less predictable than in adults, particularly in young infants, more aggressive treatment is recommended for children than adults. In developed countries where HAART is available, doctors assess their patients thoroughly: measuring the viral load, how fast CD4 declines, and patient readiness. They then decide when to recommend starting treatment [55], [57].

HAART neither cures the patient nor does it uniformly remove all symptoms. High levels of HIV-1, often HAART resistant, return if treatment is stopped. Moreover, it would take more than a lifetime for HIV infection to be cleared using HAART. Despite this, many HIV-infected individuals have experienced remarkable improvements in their general health and quality of life, which has led to a large reduction in HIV-associated morbidity and mortality in the developed world. One study suggests the average life expectancy of an HIV infected individual is 32 years from the time of infection if treatment is started when the CD4 count is 350/μL [56]. Life expectancy is further enhanced if antiretroviral therapy is initiated before the CD4 count falls below 500/μL.

In the absence of HAART, progression from HIV infection to AIDS has been observed to occur at a median of between nine to ten years and the median survival time after developing AIDS is only 9.2 months. However, HAART sometimes achieves far less than optimal results, in some circumstances being effective in less than fifty percent of patients. This is due to a variety of reasons such as medication intolerance or side effects, prior ineffective antiretroviral therapy and infection with a drug-resistant strain of HIV. However, non-adherence and non-persistence with antiretroviral therapy is the major reason most individuals fail to benefit from HAART.

The reasons for non-adherence and non-persistence with HAART are varied and overlapping. Major psychosocial issues, such as poor access to medical care, inadequate social supports, psychiatric disease and drug abuse contribute to non-adherence. The complexity of these HAART regimens, whether due to pill number, dosing frequency, meal restrictions or other issues along with side effects that create intentional non-adherence also contribute to this problem. The side effects include lipodystrophy, dyslipidemia, insulin resistance, an increase in cardiovascular risks, and birth defects.

Anti-retroviral drugs are expensive, and the majority of the world's infected individuals do not have access to medications and treatments for HIV and AIDS. Unfortunately, for now the vaccine is considered to be able to halt the pandemic [56]. This is because a vaccine would cost less, thus being affordable for developing countries, and would not require daily treatment. However, after over 20 years of research, HIV-1 remains a difficult target for a vaccine For more information we refer the reader to [44], [46], [57], [55].

1.4 HIV and AIDS public health education programs

The expansion and improvement of HIV and AIDS education around the world is critical to preventing the spread of HIV. Effective HIV and AIDS education can help prevent new

infections by providing people with information about HIV and how it is passed on, and in doing so equip individuals with the knowledge to protect themselves from becoming infected with the virus. HIV and AIDS education can take place in many different environments, from classes at school to families and friends sharing knowledge at home. It is important that this education is provided in a variety of settings to ensure that the most vulnerable and marginalized groups in society are reached, and that accurate information about HIV and AIDS is reinforced from different sources.

The most common place for people to learn about HIV and AIDS is at school. Due to their capacity and universality, schools are a crucial setting for educating young people about AIDS. As young people are at a high risk of becoming infected with HIV, it is vital that they are educated about HIV transmission before they are exposed to situations that put them at risk of HIV infection (for example, before they are sexually active). Schools play a major role in shaping the attitudes, opinions and behavior of young people and so are ideal environments for teaching the social as well as the biological aspects of HIV and AIDS. Members of the wider community can also increase their knowledge about HIV and AIDS through the school environment. Teachers who expand their understanding of the subject while planning lessons and receiving teacher training can pass this information on to adults as well as pupils, and the same can be said for children themselves; once informed about AIDS, they can tell their parents or their friends what they have learned.

Educating people at work is an important way of providing people with vital prevention information, and can reach people who have previously missed out on HIV and AIDS education. Furthermore, it is estimated that nine out of ten people living with HIV are working [44]. Providing education in the workplace is important for protecting those at work living with HIV, and for helping them to live healthily and stay in work [55].

There are a great variety of methods and materials that can be used to educate people about HIV and AIDS, including radio and television, booklets, billboards, comic strips,

street theatre, AIDS fundraising events and many more. The form in which HIV and AIDS education should be delivered depends on those who are being educated. In order to reach the target group, it needs to be considered which environments they will be most receptive in, and what media is most relevant to them. How HIV and AIDS education should be delivered also depends on the principal aims of the education programme. Sometimes education on HIV and AIDS is about giving people information which they will remember on a long term basis, about how to protect themselves, the difference between HIV and AIDS, and helping to reduce discrimination. Other education strategies are intended to have more immediate effects, and may target people when they are most likely to take part in risky behavior i.e. in nightclubs or holiday resorts.

Mathematical models have become important tools in analyzing the spread and control of infections diseases. For more details see Hethcote [22]. The model formulation process clarifies assumptions, variables, and parameters. Moreover models provide conceptual results such as thresholds, basic reproduction numbers, contact numbers and replacement numbers. Understanding the transmission characteristics of infections diseases in communities, regions and countries can lead to better approaches to decreasing the transmission of these diseases. Mathematical models are used in comparing, planning, implementing, evaluating and optimizing various detection, prevention, therapy and control programs [22].

The purpose of the dissertation is to find ways to stabilize HIV/AIDS. We have read that the model of Cai et al. [12] allows some infected individuals to move from the symptomatic phase to the asymptomatic phase by all sorts of treatment methods. In Chapter 3, we reviewed a model taken from Nyabadza et al. [38]. The model of HIV/AIDS inspects the decline in infection by supporting sexual behaviour change through public health information campaigns and also by withdrawal of individual with AIDS from sexual behaviour. We have investigated the basic reproduction number R_0 (using the next generation matrix) as a threshold parameter that determines whether a disease can invade a population

and the equilibrium solution(i.e. the disease free equilibrium and the endemic equilibrium). We further introduce the global stability of a disease free equilibrium, followed by simulations.

In chapter 4, we introduce a model taken from Bhunu et al. [7]. We formulate the basic reproduction number, followed by some simulations. We examine how counseling and testing coupled with a decrease in sexual activities could affect the HIV epidemic in resource limited communities. In chapter 5 we introduce our main model with the basic reproduction number. We present the global stability of a disease free equilibrium and the local stability of the endemic equilibrium. We further present the sensitivity analysis of R_0 and simulation. The optimal control has been formulated in Chapter 6 with simulations. We finally introduce the stochastic HIV model using the paper of Cai et al. [12], followed with simulations.

In these three models, we will investigate the role of public health campaigns by looking at different behavior of the population. We use these three different approaches so that we can see which model is more useful in regards to the stability of HIV/AIDS. In chapter 3 we will look at HIV/AIDS with education, followed by chapter 4, where we look at the different sexual behavior of individuals with HIV/AIDS with education. Finally, In chapter 5 we will look at the behavior of HIV/AIDS with treatment and education included.

1.5 Literature Review

During the development of epidemiology modeling in the population, deterministic (compartmental) models played a central role. These are the papers where the deterministic model has been used [12], [34], [38], [24], [39], [40], [8], [54] and so on. Such models divide the population into homogeneous sub-populations. The models that are labeled by SI, SIS, $SEIS$, and $SEIR$ are mostly used where the sub-populations are Susceptible, Exposed, Infected and Recovered or Removed.

In [38], Nyabadza et al. looked at a model of HIV/AIDS that examine the diminution in infection by promoting a change in sexual behavior through public health information campaigns and individuals with AIDS to abstain from sexual activities. Both the endemic and disease free equilibrium have been investigated. Numerical simulations are presented using the fourth order of Runge-Kutta. The results from their research have shown that media campaigns had led to a reduction in the prevalence of the disease but may not be the only ultimate strategy in the fight against HIV/AIDS. It has also shown that an increase in the distribution of public health information campaigns has lead to a decrease in occurrence of a disease. In the case of the individual with AIDS abstaining from sexual activities has also reduced the effect of the disease.

The impact of educational campaigns as a control measure for the spread of HIV/AIDS has been investigated by Mukandavire et al. in [34]. The authors present a sexual transmission model with explicit incubation period. Their results suggested that educating sexually immature and sexually mature individuals concurrently is more effective in slowing down HIV/AIDS than concentrating on cohort public health educational campaign of sexually immature or sexually mature individuals only. It is shown that in their study, in situations where education is effective and with with reasonable average number of HIV infected partners, public health campaigns can slow down the epidemic.

An epidemic HIV/AIDS model with treatment has been investigated in the paper by Cai et al, see [12]. The model allows some infected individuals to move from symptomatic phase to the asymptomatic phase by all kinds of treatments. The authors introduced the time delay to the model in order to investigate the effect of the time delay on the stability of the endemically infected equilibrium. This discrete time delay has also been used to the model to describe the time from the start of the treatment in the symptomatic stage until the treatment effects becomes clear. It was found that treatment can be used to make the disease free equilibrium (E_0) stable when it would be unstable in the absence of treatment. On the other hand using the time delay can induce oscillation in the system. Biologically, this means that there is a critical value for the treatment-induced delay which determines the stability of the infected equilibrium E^*. That is, the infected equilibrium E^* is asymptotically stable when antiretroviral drugs on average show positive effects in patients within less than time delay.

The HIV/AIDS epidemic in resource limited communities has been studied by Bhunu et al. in [7]. The authors suggested in their research that effective conselling and testing will be able to control the HIV/AIDS epidemic. Therefore, it was investigated that the continuing increase of the HIV/AIDS in resource poor settings may be an indication of poor counseling. The results show that educational programs regarding HIV/AIDS have a positive impact in controlling the disease. They also suggested that giving free antiretroviral drugs to HIV positive individuals who change their sexual behavior and have withdrawn from sexual contacts may be an effective tool to control the epidemic.

A continuous model for HIV/AIDS disease progression has been formulated and physiological interpretations were provided by Ida et al. in [24]. The abstract theory was then applied to show existence of unique solutions to the continuous model describing the behavior of the HIV virus in the human body and its reaction to treatment by antiretroviral therapy. The product formula has suggested appropriate discrete models describing the dynamics of host pathogen interactions with HIV1 and is applied to perform numerical

simulations based on the model of the HIV infection process and disease progression. Finally, the results of the numerical simulations are visualized and it was observed that the results of Ida et al. [24] agreed with medical and physiological aspects.

A simple deterministic HIV/AIDS model incorporating condom use, sexual partner acquisition, behavior change and treatment as HIV/AIDS control strategies has been formulated by Nyabadza et al. in [39] using a system of ordinary differential equations with the object of applying it to the current South African situation. The authors fit the model to a data from UNAIDS/WHO on HIV/AIDS in South Africa and the epidemiological facts sheets shows the current prevalence scenario. The results compare very well with other research outcomes on the HIV/AIDS epidemic in South Africa. Projections were made to track the changes in the number of individuals who were able to be under treatment, an important group as far as public health planning is concerned.

Nyabadza and Mukandavire [40] formulated a deterministic HIV/AIDS model that incorporates condom use, screening through HIV counseling and testing(HCT). A regular testing and treatment as control strategies has been proposed with the objective of quantifying the effectiveness of HCT in preventing new infections and predicting the long-term dynamics of the epidemic. The authors fit the model to a current prevalence data in South Africa from UNAIDS/WHO reports and epidemiological fact sheet. They looked at a recently launched HTC campaign to model its possible impact on the dynamics of the disease. The model shows that HTC its self has a very little impact in reducing the prevalence of HIV unless the ability of the campaign exceed an evaluated threshold in the absence of bifurcation. The results has shown that force of infection can only be reduced through behavior change, condom use and reduction in the number of sexual partners and these form the pillars of prevention of new infection. The results has show that the presence of bifurcation has an important implications in the control of HIV/AIDS. The model in [40] has shown that it cannot be eliminated by simply reducing the value of reproduction number R_0 to below unity.

In this paper Bhunu et al. [8] has considered a more robust systematic and complete qualitative analysis of a two strain HIV/AIDS model with treatment of AIDS patients. The treatment with amelioration results in an increase in number of HIV patient and a decrease in Aids patients. Bhunu et al has advised that treatment with amelioration should always be accompanied by public health education. The authors investigated that if the drugs used for therapy are 100 percent effective and a positive change in the sexual behavior of treated individuals is achieved, treatment with amelioration will not increase the development of HIV/AIDS in societies but will help communities by lengthening the lives of the infected, thus, reducing morbidity/mortality and socio-economic costs. Further the analysis of the reproduction numbers show that the use of antiretroviral therapy to improve the quality of life of AIDS patients with antiretroviral sensitive, HIV results in an increase of antiretroviral resistant HIV cases supporting the argument that antiretroviral resistance develops as result of selective pressure on non-resistant strains due to antiretroviral use.

A non-linear mathematical model has been propose and analyzed to study the spread of HIV/AIDS with direct inflow of infective in a population with inconsistent volume structure in [41]. Naresh et al [41] has looked at a model without inflow of HIV infective including interaction with pre-AIDS individuals and Model without inflow of HIV infective and no interaction with pre-AIDS individuals. It was found that if the direct inflow of the infective has been allowed in the community the disease always persist. The endemicity is extensively reduced if direct inflow of infective is restricted and pre-Aids individuals do not take place in sexual activities. Naresh et al suggested sexual partners should be restricted and unsafe sexual iteration should be avoided with an infective in order to reduce the spread of the disease. Thus the spread of infection can be slowed down if direct inflow of infectives is restricted into the population. It was also noted that the increase in the number of sexual partners further reduces the total population by way of spreading the disease. Thus in order to reduce the spread of the disease, the number

of sexual partners should be restricted and unsafe sexual interaction should be avoided with an infective.

In the paper [54], Zurakowskia and Teel has proposed the interaction of the immune system and human immunodeficiency virus where we will introduce the possibility of using highly active anti-retroviral therapy (HAART) to stimulate the vaccine. They further present a model predictive control (MPC) based method for determining optimal treatment. Finally they analyze the simulations by using algorithms where they apply robustness measurement noise, robustness modeling error, robustness combined errors, and varying the cost function.

An SIR model with six compartments where there is an interaction between HIV and TB epidemics has been investigated in [6]. They further look at sensitivity of the steady states with respect to changes in parameter values. The authors examine that most of the control measures studied have an obvious positive impact in controlling the HIV or TB epidemics, this is the case for condom use, increased TB detection and preventive treatment. The situation for ART is more complicated. However, although the future for the prevalence of HIV is uncertain, it seems that a generalized access to ART would lead to a significant decrease of the TB notification rate. They further concluded that it is difficult to guess if the observations drawn from the model with parameters adapted to the particular South African township are still valid for less crowded areas with high HIV prevalence. finally reliable data on both HIV and TB are still rare.

In [35], Mukandavire and Garira formulated and analyzed a sex-structured model for heterosexual transmission of HIV/AIDS. The model has been further divided into two classes, consisting of individuals involved in high-risk sexual activities and individuals involved in low-risk sexual activities. The model is described as the movement of individuals from high to low sexual activity group as a result of public health education campaigns. The threshold parameter which is the basic reproduction number has been obtained and their

stability (local and global) of the disease free equilibrium. The model has been extended to incorporate sex workers, and their role in the spread of HIV/AIDS in settings with heterosexual transmission was explored. In order to assess the possible community benefits of public health educational campaigns in controlling HIV/AIDS comprehensive analytic and numerical techniques were employed. Mukandavire and Garira [35] concluded that the presence of sex workers enlarges the epidemic threshold R_0, thus fuels the epidemic among the heterosexuals, and that public health educational campaigns among the high-risk heterosexual population reduces R_0, thus can help slow or eradicate the epidemic.

The models mentioned so far are deterministic and they do not consider the stochastic disturbance of environment which exists in fact. When the environmental noise is not taken into account, an ordinary differential equation is used for AIDS transmission for instance. The introduction of stochastic modeling has provided new insights into the population dynamics of the disease. We can refer to [17, 25, 29, 32, 52, 47]. In particular, stochastic modeling of HIV/AIDS can be found by Ding et al. and Jiang et al. in [17, 25].

In the paper of Lahrouz et al. [29] they have formulated an SIRS epidemic model with saturated incidence rate and disease-inflicted mortality. In the same paper, the authors have further looked at the stochastic version. The global existence and positivity of the solution of the stochastic system has been established. Under suitable conditions on the intensity of the white noise perturbation, the global stability in probability and p^{th} moment of the system has been proved. In this regard, this dissertation refers mainly to the papers [29, 50].

Chapter 2

Mathematical tools

Epidemiology is the study of the distribution and determinants of diseases, for both infectious and non-infectious diseases. Originally the term was used to refer only to the study of epidemic infection diseases, but it is now applied more broadly to other diseases as well. Mathematical models have become important tools in analyzing the spread and control of infections diseases. The review paper [22] of Hethcote expands on this point. The model formulation clarifies assumptions, variables, and parameters. Moreover models provide conceptual results such as thresholds, basic reproduction numbers, contact numbers and replacement numbers. Understanding the transmission characteristics of infectious diseases in communities, regions and countries can lead to better approaches to decreasing the transmission of these diseases. As explained in [22], mathematical models are used in comparing, planning, implementing, evaluating and optimizing various detection, prevention, therapy and control programs [22]. We introduce the following definitions and theorems necessary to model the population dynamics of HIV/AIDS.

2.1 Epidemiological terminology

The prevalence of a disease is defined as the percentage of a particular population that is infected with a disease. The incidence of a disease is the rate at which new infections occur. Hence if the number of people infected with a particular disease at the start of

a particular year is d, out of a population of size N, and n new infections occur over the course of the year, then the prevalence rate at the start of the year is $\frac{d}{N}$ and the annual incidence rate is $\frac{n}{N-d}$. When the disease is introduced into a population, it usually expands rapidly at first, with prevalence rate rising. In some cases the prevalence drops to zero, but in many cases, prevalence stabilizes at a non-zero level that is referred to as endemic prevalence.

2.2 Basic Linear Equation

The general first-order differential equation for the function $y = y(x)$ is written as

$$\dot{y} = f(x, y),$$

where $f(x, y)$ can be any function of the independent variable x and dependent variable y. For more information, the reader may consult the book [13] of Chasnov.

2.3 Invariant Region

A set M is an *invariant set* with respect to a system of ordinary differential equations $\dot{x} = f(x)$ if

$$x(0) \in M \Rightarrow x(t) \in M, \text{for all } t \in \mathbb{R}.$$

A set M is a *positively invariant set* with respect to $\dot{x} = f(x)$ if

$$x(0) \in M \Rightarrow x(t) \in M, \text{for all } t \geq 0.$$

2.4 Equilibrium

Definition 2.1.1 Given a system of differential equations $\dot{x} = f(t)$, an equilibrium x^* of this system is a point in the state space for which $X(t) = x^*$ is a solution for $f(t) = 0$,

for all t. For more detail see Allen [31].

Definition 2.1.2. [31].

(a) An equilibrium solution x of $\dot{X}= F(X)$ is said to be *locally stable* if for each $\epsilon > 0$ there exist a $\delta > 0$ with the property that every solution $X(t)$ of $\dot{X}= F(X)$ with initial condition $X(t_0) = X_0$ and

$$\|X_0 - x\|_2 < \delta,$$

satisfies the condition that

$$\|X_t - x\|_2 < \epsilon$$

for all $t \geq t_0$. If the equilibrium is not locally stable it is said to be *unstable*.

(b) An equilibrium solution x is said to be *locally asymptotically* stable if it is locally stable and if there exist $\gamma > 0$ such that

$\|X_0 - x\|_2 < \gamma$ implies $\lim_{t\to\infty} \|X(t) - x\|_2 = 0$.

2.5 Routh-Hurwitz criteria

Consider the characteristic equation

$$\Omega^n + a_1\Omega^{n-1} + a_2\Omega^{n-2} + ... + a_{n-1}\Omega + a_n = 0$$

determining the n eigenvalues, Ω, of a real $n \times n$ square matrix A. Then the eigenvalues Ω all have negative real parts if

$$H_1 > 0, H_2 > 0, H_3 > 0, ...H_n > 0$$

where

$$H_n = \begin{vmatrix} a_1 & 1 & \cdots & 0 \\ a_3 & a_2 & \vdots & 0 \\ \vdots & \vdots & \vdots & \vdots \\ 0 & 0 & 0 & a_n \end{vmatrix}.$$

The steady state is stable (that is, Re $\Omega < 0$) for all λ if and only if $H_j \geq 0$ for all $j = 1, 2, 3, ..., n$, see Allen [31].

2.6 Linearization

Let (U^*, V^*) be a steady state of

$$\dot{U} = f(U, V), \qquad \dot{V} = g(U, V), \tag{2.1}$$

so that $f(U^*, V^*) = g(U^*, V^*) = 0$. Let $u = U - U^*$ and $v = V - V^*$. We assume that we may neglect higher order terms if u and v are sufficiently small, and we obtain the approximate (linearized) equations

$$\dot{u} = f_u(U^*, V^*)u + f_v(U^*, V^*)v, \tag{2.2}$$

$$\dot{v} = g_u(U^*, V^*)u + g_v(U^*, V^*)v, \tag{2.3}$$

or, defining the Jacobian matrix $J(U, V)$ in the usual way,

$$\dot{w} = J^* w, \tag{2.4}$$

where w is the column vector (u, v), and a star denotes the evaluation at the steady state. The behavior of the system near (U^*, V^*) depends on the eigenvalues of the matrix $J^* = J(U^*, V^*)$. It can be shown that the neglect of higher order terms is valid, and the non-linear system behaves like a linear system near the steady state, as long as neither of the eigenvalues of J^* has zero real part.

Making the definitions $\beta = \text{tr}J^*$, $\gamma = \det J^*$, $\delta = \text{disc}J^*$, the eigenvalue equation is $\lambda^2 - \beta\lambda + \gamma = 0$, and we may determine the character of the steady state from the signs

of these, see Britton[10]. We quote the theorem.

Theorem 2.4.1 *(Steady states and eigenvalues) [10],*

- *If $\gamma < 0$, the (trivial) steady state of the second order system is at (2.4) is a saddle point. Both eigenvalues are real one positive and one negative.*
- *If $\gamma > 0$, $\delta > 0$, $\beta < 0$, it is a stable node. Both eigenvalues are real and negative.*
- *If $\gamma > 0$, $\delta > 0$, $\beta > 0$, it is an unstable node. Both eigenvalues are real and positive.*
- *If $\gamma > 0$, $\delta < 0$, $\beta < 0$, it is a stable focus. The eigenvalues are complex conjugate, with negative real part.*
- *If $\gamma > 0$, $\delta < 0$, $\beta > 0$, it is an unstable focus. The eigenvalues are complex conjugates, with positive real part.*
- *If $\gamma > 0$, $\delta < 0$, $\beta = 0$, it is a center. The eigenvalues are complex conjugates, and purely imaginary.*

Theorem 2.4.2 Linearization Theorem [10]. *Let us suppose that the non-linear system*

$$\dot{y} = Y(y) \tag{2.5}$$

have a simple fixed point at $y = 0$. Then, in a neighborhood of the origin, the phase portraits of the system and its linearization are qualitatively equivalent provided the linearized system is not at center [10].

Lemma 2.4.3 [48]. *Suppose that x_0 is a disease free equilibrium of a system*

$$\dot{x}_i = f_i(x) = F_i(x) - V_i(x), i = 1, \ldots, n \text{ and } f_i(x)$$

satisfy the condition that if $x \geq 0$, then

$$F_i, V_i^+, V_i^- \geq 0 \text{ for } i = 1, \ldots, n.$$

Through the condition that if $F(x_0)$ is set to zero, then all eigenvalues of $Df(x_0)$ have negative real parts then derivatives $DF(x_0)$ and $DV(x_0)$ are partitioned as

$$DF(x_0) = \begin{pmatrix} F & 0 \\ \\ 0 & 0 \end{pmatrix}, \; DV(x_0) = \begin{pmatrix} V & 0 \\ \\ J_3 & J_4 \end{pmatrix},$$

where F and V are the $m \times m$ matrix defined by

$$F = \left(\frac{\partial F_i}{\partial x_j}(x_0) \right), \text{ and } V = \left(\frac{\partial V_i}{\partial x_j}(x_0) \right) \text{ with } 1 \leq i, j \leq m.$$

Further, F is nonnegative, then V is a nonsingular M-matrix and all eigenvalues of J_4 have positive real part.

2.7 Liapunov stability

An important technique in stability theory for differential equations is one known as the *direct method of Liapunov*. A Liapunov function is constructed to prove stability or asymptotic stability of an equilibrium in a given region.

Definition 2.2.1. A positive-definite function V in an open neighborhood of the origin is said to be a *Liapunov* function for the autonomous differential system, $\dot{x} = f(x, y)$, $\dot{y} = g(x, y)$, if $\dot{V}(x, y) \leq 0$ for all $(x, y) \in U - (0, 0)$. If $\dot{V}(x, y) < 0$ for all $(x, y) \in U - (0, 0)$, the function V is called a *strict Liapunov* function.

Theorem 2.2.2 (Liapunov's Stability Theorem [31].) *Let (0,0) be an equilibrium of the autonomous system $\dot{x} = f(x, y)$ and let V be a positive definite C^1 function in a neighbourhood U of the origin.*

1. *If $\dot{V}(x, y) \leq 0$ for all $(x, y) \in U - (0, 0)$, then $(0, 0)$ is stable.*

2. *If* $\dot{V}(x,y) < 0$ *for all* $(x,y) \in U - (0,0)$, *then* $(0,0)$ *is asymptotically stable.*

3. *If* $\dot{V}(x,y) > 0$ *for some* $(x,y) \in U - (0,0)$, *then* $(0,0)$ *is unstable.*

We note that in case 1 the function V is a Liapunov function and in case (2) V is a strict Liapunov function.

2.8 Compound matrix

Let B be an $n \times n$ matrix. For more information we refer to Wang and Song [49]. The second additive compound matrix of B, denoted by $B^{[2]}$, is an $\begin{pmatrix} n \\ 2 \end{pmatrix} \times \begin{pmatrix} n \\ 2 \end{pmatrix}$ matrix. For instance, if $B = (b_{ij})$ is a 3×3 matrix, then

$$B^{[2]} = \begin{pmatrix} b_{11} + b_{22} & b_{23} & -b_{13} \\ b_{32} & b_{11} + b_{33} & b_{12} \\ -b_{31} & b_{21} & b_{22} + b_{33} \end{pmatrix}.$$

2.9 Compartmental modelling

We explain the idea of a compartmental model by the way of a simple example. The approach for modelling the transmission of infection disease in human populations is usually to subdivide the population under consideration into subpopulations or a number of epidemiological classes called compartments and the resulting model is called a compartmental model. These compartments are defined with respect to disease status of an individual. We can consider a standard model where the population is divided into three classes such as Susceptible individuals, Infected individuals and a class of AIDS progressed individuals. The population number in each class is represented as a function of time, by $S(t)$, $I(t)$ and $A(t)$ respectively.

- Susceptible: Individuals who are not infected. They are able to catch the disease and once they have contracted it they move to the infected compartment.
- Infected: Individuals who are are infected. It is assumed that they can spread the disease to susceptible individuals.
- AIDS class: Individuals who are infected and show AIDS related symptoms.

The number of susceptible individuals can increase due to newly recruited individuals, while the number can decrease due to new infections as a results of interaction with infected individuals in class $I(t)$ and also due to natural death. Infected individuals who joined the class $I(t)$ can progress to $A(t)$ or may die due to natural death. After progression to $A(t)$, individuals are removed from this class due to natural or disease induced death.

The total sexually mature population at a given time is the sum of individuals in all classes, and is given by

$$P(t) = S(t) + I(t) + A(t).$$

We describe the parameters as follows, The term μN is the recruitment rate per unit time into the susceptible class and μ is the average death rate by natural causes. The parameter c represents the rate of sexual contacts of an infected individual with susceptible individuals per unit time. The parameter β is the probability of infecting per effective contact and α is the rate of progression of infected individuals to AIDS class per unit of time. The term ν is the disease induced death rate of individuals in AIDS class per unit of time. The following model has been taken from the paper of Ejigu [18]. Similar models can be found in papers of [53], [27], [23], [31]. We will have the following system of equations:

$$\begin{aligned} \frac{dS(t)}{dt} &= \mu N - \frac{c\beta S(t)I(t)}{N(t)} - \mu S(t), \\ \frac{dI(t)}{dt} &= \frac{c\beta S(t)I(t)}{N(t)} - (\mu + \alpha)I(t), \end{aligned} \tag{2.1}$$

$$\frac{dA(t)}{dt} = \alpha I(t) - (\mu + \nu)A(t).$$

Depending on the disease or the level of sophistication we want to reach, more classes may be introduced.

2.10 The basic reproduction number

The basic reproduction number is sometimes referred to as a ratio. It is one of the most useful threshold parameters or invariants, which characterize mathematical properties concerning infectious disease models [12], [22], and [43]. It is widely used in mathematical epidemiology models. The analysis of the model includes finding equilibrium points (steady states) of the model, finding the basic reproduction number R_0 and investigating the stability of the equilibrium points (disease-free and endemic equilibrium) which will be characterized using the invariant R_0.

Definition 2.2.1 The Basic Reproduction Number or Basic Reproduction Ratio is defined as the average number of secondary infections that are produced when one infected individual is introduced into a group of susceptible individuals. For more information see Allen [31], Van den Driessche and Watmough [48].

It is implicitly assumed that the infected outsider is in the host population for the entire infectious period and mixes with the host population in exactly the same way that a population native would mix. The basic reproduction number R_0 turns out to be the threshold quantity that determines whether a disease can invade a population. If $R_0 < 1$, then on average an infected individual produces less than one new infected individual over the course of its infectious period, and the infection cannot grow. Conversely, if $R_0 > 1$ then each infected individual produces, on average, more than one new infection, and the disease can invade the population [43].

We obtain the equilibria of the system (2.1) by setting the time derivatives in the equations to be equal to zero. The equilibrium point at $S_e = N$ and $I_e = A_e = 0$ represents a disease free equilibrium. The endemic equilibrium is as follows

$$S_e = (\mu + \alpha)\frac{N}{\beta},$$

$$I_e = \frac{\mu N}{\beta}[R_0 - 1].$$

We notice that since the model has one infected compartment, then we can obtain R_0 by following the definition, the rate of transmission multiply by the infection period. The parameter β is the rate of transmission and the infectious period is

$$\frac{1}{\mu + \alpha}.$$

Thus

$$R_0 = \beta\frac{1}{\mu + \alpha} = \frac{\beta}{\mu + \alpha}.$$

However, for more complicated models with several infected compartments the definition of R_0 is not sufficient to calculate R_0. The basic reproduction number R_0 can be determined using the method of next-generation matrix as presented in Van den Driessche and Watmough [48]. When we have more than one infected compartment we will use the next generation matrix to find the basic reproduction number.

2.11 The next generation matrix

The next generation method introduced by Van den Driessche and Watmough [48], is a general method of finding R_0 in a case where we have more than one infected compartment. Suppose we have n disease compartments and m non-disease compartments, and let $x \in \mathbb{R}^n$ and $y \in \mathbb{R}^m$ be subpopulations in each of these compartments. We denote the rate of secondary infection increase of the i^{th} disease compartment by F_i and V_i the rate disease

progression, death and recovery decrease the i^{th} compartment. Thus we have the following compartmental model:

$$\begin{aligned} \frac{dx_i}{dt} &= F_i(x,y) - V_i(x,y), \qquad i = 1,...,n, \\ \frac{dy_i}{dt} &= g_j(x,y), \qquad j = 1,...,m, \end{aligned}$$

The calculation of the basic reproduction number is based on linearization of the ordinary differential equation (ODE) model about a disease free equilibrium, while the following assumption ensure the existence of the equilibrium and well-posedness of the model.

- Assume $F_i(0,y) = 0$ and $V_i(0,y) = 0$ for all $y \geq 0$ and $i = 1,...,n$. All new infections are secondary infections arising from infected host, there is no immigration of individuals into the disease compartments.

- Assume $F_i(0,y) \geq 0$ for all non-negative x and y and $i = 1,...,n$. The function F represents new infections and can not be negative.

- Assume $V_i(0,y) \leq 0$ whenever $x_i = 0, i = 1,...,n$. Each component, V_i represents a net outflow from compartment i and must be negative (inflow only) whenever the compartment is empty.

- Assume $\sum_{i=1}^{n} V_i(x,y) \geq 0$ for all non-negative x and y. This sum represent the total outflow from all infected compartments. Terms in the model leading to increase in $\sum_{i=1}^{n} x_i$ are assumed to represent secondary infections and therefore belong in F.

- Assume the disease free system $\frac{dy}{dt} = g(0,y)$ has a unique equilibrium that is asymptotically stable. That is, all solution with initial conditions of the form $(0,y)$ approach a point $(0,y_0)$ as $t \to \infty$. This point is referred to as the disease free equilibrium.

Now assuming that F_i and V_i meet the above conditions, we can form the next generation matrix FV^{-1} from matrices of partial derivatives of F_i and V_i. Now we have

$$F = \Big[\frac{\partial F_i(x_0)}{\partial x_j}\Big]$$

and

$$V = \Big[\frac{\partial V_i(x_0)}{\partial x_j}\Big],$$

where $i,\ j = 1, ..., m$ and where x_0 is the disease free equilibrium. The entries of FV^{-1} give the rate at which infected individuals in x_j produce new infections in x_i, times the average length of time an individual spends in a single visit to compartment j. R_0 is given by the spectral radius (dominant eigenvalue) of the matrix FV^{-1}.

If the basic reproduction number is less than unity i.e., $R_0 < 1$ then the disease-free equilibrium is locally asymptotically stable, which implies that the disease will die out in the population. On the other hand, if the reproduction number is greater than unity, then the endemic equilibrium is locally asymptotically stable. The technique used to determine the stability of the equilibrium points for complex models will be shown in the following Chapters.

2.12 Staged Progression of HIV model

The staged progression model has a single uninfected compartment and infected individuals progress through several stages of the disease with changing infectivity. This model is applicable to many diseases, mainly HIV/AIDS, where transmission probabilities vary as the viral load in an infected individual changes. For more information see [48], and it has been applied in [18], [38]. Thus we have the following model:

$$\begin{aligned}
I_1^{'} &= \sum_{k=1}^{m-1} \frac{\beta_k S I_k}{N} - (\nu_1 + d_1) I_1, \\
I_i^{'} &= \nu_{i-1} I_{i-1} - (\nu_1 + d_1) I_i, \ \ i = 2, ..., m-1, \\
I_m^{'} &= \nu_{m-1} I_{m-1} - d_m I_m, \\
S^{'} &= b - bS - \sum_{k=1}^{m-1} \frac{\beta_k S I_k}{N}.
\end{aligned} \tag{2.6}$$

The model assumes standard incidence, death rate $d_i > 0$ in each infectious stage, and the final stage has a zero infectivity due to morbidity. Infected individuals spend on average, $\frac{1}{v_i}$ time units in stage i.

Thus we have the following basic reproduction number from the model (2.6):

$$\begin{aligned} R_0 &= \frac{\beta_1}{\nu_1 + d_1} + \frac{\beta_2 \nu_1}{(\nu_1 + d_1)(\nu_2 + d_2)} + \frac{\beta_3 \nu_1 \nu_2}{(\nu_1 + d_1)(\nu_2 + d_2)(\nu_3 + d_3)} \\ &\quad + ... + \frac{\beta_{m-1} \nu_1 ... \nu_{m-2}}{(\nu_1 + d_1)...(\nu_{m-1} + d_{m-1})}. \end{aligned}$$

The i'th term in R_0 represents the number of new infections produced by a typical individual during the time it spends in the i'th infectious stage. More specifically, $\frac{\nu_{i-1}}{(\nu_{i-1}+d_{i-1})}$ is the fraction of individuals reaching stage $i-1$ that progress to stage i, and $\frac{1}{\nu_i+d_i}$ is the average time an individual entering stage i spends in stage i. Hence, the i'th term in R_0 is the product of the infectivity of individuals in stage i, the fraction of initially infected individuals surviving at least to stage i, and the average infectious period of and individual in stage i.

2.13 Optimal control method

Optimal control theory has been used as a very powerful mathematical tool to make decisions involving complex biological situations and it has been derived from the calculus of variations. Optimal control techniques are of great use in developing optimal strategies to control various kinds of diseases. For more information, consult the book of Lenhart and Workman [30]. It has been used, for instance, in finding the percentage of the population that should be vaccinated as time evolves in a given epidemic model to minimize the number of infected and the cost of implementing the vaccination strategy.

The behavior of a dynamic system is described by the state variable(s). We assume that there is a way to control the state variable(s) x, by acting upon it with a suitable control. We noticed that the dynamic system (state x) depends on the control u. The goal is to adjust the control u in order to minimize or maximize a given objective functional, $J(u(t), x(t), t)$, that attains the desired goal, and the required costs to achieving it. The

optimal control is obtained when the desired goal is achieved with the least cost. The functional depends on the control and the state variables. There are a number of different methods for calculating the optimal control for a specific model. Pontryagin Maximum Principle for example allows the calculation of the optimal control for an ordinary differential equations model system with given constraints. See the book of Lenhart and Workman [30].

The following are characteristics that an optimal control problem may exhibit

- Controllability: ability to use controls to steer a system from one position to another.
- Observability: deducing system information from control input and observe output.
- Stabilization: implementing controls to force stability.

The principal technique for the optimal control problem is to solve a set of necessary conditions, that an optimal control and corresponding state must satisfy. It is important to understand the logical difference between necessary conditions and the sufficient conditions of solution sets.

Let us considering the optimal control problem of the form below.

Determine

$$\min_u \left\{ \phi(t_f, x(t_f)) + \int_0^{t_f} g_0(t, x(t), u(t))dt \right\}$$

where

$$f(x(t)) = [x_1(t), x_2(t), ..., x_{n_s}(t)]^T \in \mathbb{R}^{\mathbf{n}}$$

is the state vector and

$$u(t) = [u_1(t), u_2(t), u_3(t), ..., u_{n_c}(t)]^T \in \mathbb{R}^{\mathbf{m}}$$

is the control vector.

The state and the control variables are governed by the dynamics described by a set of first order differential equations:

$$\frac{dx}{dt} = f(t, x(t), u(t)) \qquad x_0 = x(0), 0 \leq t \leq t_f \tag{2.3}$$

The functions:

$$f(h_0) : T \times \mathbb{R}^n \times \mathbb{R}^m \to \mathbb{R}^n$$

$$f(g_0) : T \times \mathbb{R}^n \times \mathbb{R}^m \to \mathbb{R}^n$$

are continuously differentiable with respect to each component of x and u, and piecewise continuous with respect to t.

2.14 Pontryagin's Maximum Principle

The Pontryagin's Maximum Principle converts the maximization or minimization of the objective functional J, coupled with the state variable into pointwise maximizing or minimizing of the Hamiltonian with respect to the control. The Hamiltonian $H(t, x, u, \lambda)$ is a function of four variables. Time t is the underlying variable for each of x, u and λ is a function of t, called the adjoint variable.

Theorem 2.2.3. [30] If $u^*(t)$ and $x^*(t)$ are optimal for problem (2.3), then there exists a piecewise differential adjoint variable $\lambda(t)$ such that

$$H(t, x^*(t), u(t), \lambda(t)) \leq H(t, x^*(t), u^*(t), \lambda(t))$$

for all controls u at each time t, where the Hamiltonian H is

$$H = f(t, x(t), u(t)) + \lambda(t) g(t, x(t), u(t))$$

and

$$\frac{\lambda(t)}{dt} = -\frac{\partial H(t, x^*(t), u^*(t), \lambda(t))}{\partial x},$$

$$\lambda(t_f) = 0.$$

Necessary conditions: If $u^*(t)$ and $x^*(t)$ are optimal, then the following conditions hold:

$$\frac{\lambda(t)}{dt} = -\frac{\partial H(t, x^*(t), u^*(t), \lambda(t))}{\partial x},$$

$$\lambda(t_f) = 0,$$

$$\frac{\partial H(t, x^*(t), u^*(t), \lambda(t))}{\partial u} = 0.$$

Sufficient conditions: If $u^*(t)$, $x^*(t)$ and $\lambda(t_f)$ satisfy the following conditions

$$\frac{\lambda(t)}{dt} = -\frac{\partial H(t, x^*(t), u^*(t), \lambda(t))}{\partial x},$$

$$\lambda(t_f) = 0,$$

$$\frac{\partial H(t, x^*(t), u^*(t), \lambda(t))}{\partial u} = 0,$$

then $u^*(t)$ and $x^*(t)$ are optimal.

2.15 Sensitivity analysis

Sensitivity analysis is used to determine the relative importance of model parameters to disease transmission. We perform the analysis by calculating the sensitivity indices of the basic reproduction number, R_0, because it determines whether or not the infectious disease will spread in the population. Sensitivity analysis is commonly used to determine the robustness of model predictions to parameter values, since there usually errors in data

collection and pre-assumed values. It also allows for the measurement of relevant changes in a state variable when a parameter changes.

In performing the sensitivity analysis, we apply the method called normalized forward sensitivity index of a variable that has been used quite commonly, and it is defined as the ratio of relative change in the variable to the relative change in the parameter. The sensitivity may also be defined using partial derivatives when the variable is a differentiable function of the parameter.

Definition: The normalized forward sensitivity index of an invariant, J, that depends on a parameter, k, is defined as :

$$r_k^{J_0} := \frac{\partial J_0}{\partial k} \times \frac{k}{J_0}.$$

2.16 Brownian Motion

Brownian motion refers to the ceaseless, irregular random motion of small particles immersed in a liquid or gas, as observed by R. Brown in 1827. The phenomenon can be explained by the perpetual collisions of the particles with the molecules of the surrounding medium. The stochastic process associated with the Brownian motion is called the Brownian process or the Wiener process. The concept has found application in a wide range of fields. So for instance, Brownian motion has become one of the fundamental building blocks of modern quantitative finance. Indeed, the basic continuous time model for financial asset prices assumes that the log-return of a given financial asset follow a Brownian motion with drift. There are also interesting applications of Brownian motion to epidemiology. For more information the reader may consult Mao, [33].

Definition: Let $(\Omega, \mathcal{F}, P)$ be a probability space with filtration $\{\mathcal{F}_t\}_{t\geq t_0}$. A one dimensional Brownian motion is a real valued continuous $\{\mathcal{F}_t\}$ adapted process $\{B_t\}_{t\geq t_0}$ with the following properties:

(*i*) $B_0 = 0$ almost surely;

(*ii*) for $0 \leq s < t < \infty$, the increment $B_t - B_s$ is normally distributed with mean zero and variance $t - s$;

(*iii*) for $0 \leq s < t < \infty$, the increment $B_t - B_s$ is independent of $\{\mathcal{F}_s\}$;

(*vi*) B_t is continuous in $t \geq 0$.

We refer the reader to the book of Mao, [33].

2.17 The multi-dimensional Itô's formula

Let $x(t)$ be a d-dimensional *Itô's process* on $t \geq 0$ with the stochastic differential [33], i.e., a stochastic process of the form

$$dx(t) = f(t)dt + g(t)dB(t),$$

where $f \in L^1(\mathbb{R}_+; \mathbb{R}^d)$ and $g \in L^2(\mathbb{R}_+; \mathbb{R}^{d\times m})$. Then any $V(x(t), t)$ is again an Ito's process with the stochastic differential given by

$$\begin{aligned} dV(x(t),t) &= \left[V_t(x(t),t) + V_x(x(t),t)f(t) + \frac{1}{2}\text{trace}(g^T(t)V_{xx}(x(t),t)g(t))\right] \\ &+ V_x(x(t),t)g(t)dB(t). \qquad a.s. \end{aligned}$$

Note that

$$dtdt = 0, dB(t_i)dt = 0, dB_i dB_i = dt, dB_i dB_j = 0 \text{ if } i \neq j. \tag{2.7}$$

2.18 Stability in probability theory

Consider the general n-dimensional stochastic system

$$dx(t) = f(t, x(t))dt + g(t, x(t))dB(t) \tag{2.8}$$

on $t \geq 0$ with initial value $x(0) = x_0$. The solution is denoted by $x(t, x_0)$. Assume that $f(t, 0) = g(t, 0) = 0$ for all $t \geq 0$, so the origin point is an equilibrium of (2.8) The equilibrium $x = 0$ of the system (2.8) is said to be:

(i) Stable in probability if for all $\epsilon > 0$,

$$\lim_{x_0 \to 0} P\left(\sup_{t \geq 0} |x(t, x_0)| \geq \epsilon\right) = 0;$$

(iv) Almost surely exponentially stable if for all $x_0 \in \mathbb{R}^n$

$$\lim_{x_0 \to 0} \sup \frac{1}{t} \ln |x(t, x_0)| < 0 \quad a.s.;$$

We refer the reader to a paper of Lahrouz et al., [29].

2.19 Differential Operator

We define the differential operator L associated with the following equation:

$$dx(t) = f(x(t), t)dt + g(x(t), t)dB(t) \qquad t \geq t_0,$$

by

$$L = \frac{\partial f(x(t), t)}{\partial t} + \sum_{i=1}^{d} f(x, t) \frac{\partial}{\partial x_i} + \frac{1}{2} \sum_{i,j=1}^{d} \left[g(x, t) g^T(x, t)\right]_{i,j} \frac{\partial^2}{\partial x_i \partial x_j}.$$

If L acts on a function of $V \in C^{2,1}(S_h \times \mathbb{R}_+; \mathbb{R}_+)$, then

$$LV = V_t(x, t) + V_x(x, t) + \frac{1}{2} \text{trace}\left[g^T(x, t) V_{xx}(x, t) g(x, t)\right],$$

where $V_t = \frac{\partial V}{\partial t}$, $V_x = \left(\frac{\partial V}{\partial x_1}, ..., \frac{\partial V}{\partial x_d}\right)$, $V_{xx} = \left(\frac{\partial^2 V}{\partial x_i \partial x_j}\right)_{d \times d}$. For more information the reader may consult the book of Mao, [33].

Chapter 3

A 4-compartment model of HIV with Education

Public health information campaigns and withdrawal of individuals with AIDS from sexual activities has been investigated in Nyabadza et al. [38]. The model for HIV/AIDS incorporates HIV prevention using mass media campaigns and withdrawal of individuals with AIDS. The model was revisited in [1]. In the paper of [1], the focus was on control and sensitivity of an HIV model with public health education. In this Chapter we offer a discussion of the work in [38]. In particular we use a Lyapunov function to prove the global stability, an original contribution, now included in [1]. We also contributed in this model by running some simulation.

All parameters of the model are assumed to be positive. Using the model of Nyabadza [38], the recruitment rate of susceptible individuals is given by μK and μ is the per capita natural death rate of individuals in all classes. The transfer rate from the asymptomatic compartment to the symptomatic compartment is given by σ. The parameter ρ is the progression rate of infected individuals from I_2 to A and δ represent the per capita disease induced death per unit time. The parameter c is the contact rate of susceptible individuals with infected individuals and β is the probability of infection. The effectiveness of

information as it spreads in preventing HIV transmission in an environment with public health HIV/AIDS information campaigns is quantified by parameter α. Susceptible are infected with HIV following unprotected sexual contact with an infected individual at a rate $\lambda(I, A)$. The proposed contact rate is set to depend on the number of infected individuals in the population, which is of the form $\frac{c\beta g(I,A)}{\psi(I,A)}$, where $g(I, A) = I_1(t)+\eta_1 I_2(t)+\eta_2(1-q)A$ and $\psi(I, A) = 1 + \alpha g(I, A)$. We thus have the following system of equations:

$$\begin{aligned} S^{'}(t) &= \mu K - \mu S - \lambda(I, A)S, \\ I_1^{'}(t) &= \lambda(I, A)S - (\mu + \sigma)I_1, \\ I_2^{'}(t) &= \sigma I_1 - (\mu + \rho)I_2, \\ A^{'}(t) &= \rho I_2 - (\mu + \delta)A, \end{aligned} \tag{3.1}$$

where

$$\lambda(I, A) = \frac{c\beta(I_1 + \eta_1 I_2 + \eta_2(1 - q)A)}{1 + \alpha(I_1 + \eta_1 I_2 + \eta_2(1 - q)A)},$$

η_1 and η_2 measure the relative infectivity of I_2 and A, when compared to I_1 and $I = (I_1 + I_2)$. We assume that all parameters are positive and the initial conditions of the model system (1) are as follows:

$$S(0) = S_0 > 0, I_1(0) = I_{10} > 0, I_2(0) = I_{20} > 0, \text{ and } A(0) = A_0 > 0.$$

3.1 Invariant region

The system in model (3.1) describes a human population, and hence we need to be sure that the solution $S(t), I_1(t), I_2(t)$ and $A(t)$ of the model (3.1) remain non-negative all the time. In other words, solutions of model (3.1) with given non-negative initial data remain positive all the time and bounded in a region G. Thus we have the following Lemma.

Lemma 3.1. [38] *The region G defined by*

$$G = \left\{(S(t), I_1(t), I_2(t), A(t)) \in \mathbb{R}_+^4 : N \leq K\right\},$$

is positively invariant and attracting with respect to model system (3.1).

3.2 Disease free equilibrium

Now, we study equlibria of the model. We have found the disease free equilibrium $S = K, I_1 = 0, I_2 = 0$ and $A = 0$, by equating the time derivative on the LHS in system (3.1) to be equal to zero, simplifying and solving the equations simultaneously. Thus we have the following theorem.

Theorem 3.2. *The model given by the system (3.1) has a unique feasible disease free equilibrium given by*

$$E_0 = (S_0, I_1, I_2, A_0) = (K, 0, 0, 0).$$

It can be checked easily by using system (3.1).

3.3 Basic reproduction number

The analysis of the model includes finding equilibrium points of the model, finding the threshold value, basic reproduction number R_0 and investigate the stability of the equilibrium points (disease-free and endemic which will be characterized using the threshold value R_0). The basic reproduction number has already been calculated in [38], and we will just supply some details here. We will use the method used of Van den Driessche and Watmough [48], to find the basic reproduction number of the model. The basic reproduction number is defined in Chapter 2. It is important to note that R_0 is a dimensionless number and not a rate, which would have units of time^{-1}. Since we have more than one infected compartment, we will use the next generation matrix method.

Thus we have

$$F = \begin{pmatrix} c\beta K & c\beta\eta_1 K & c\beta\eta_2 K(1-q) \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

and

$$V=\begin{pmatrix} \mu+\sigma & 0 & 0 \\ -\sigma & \mu+\rho & 0 \\ 0 & -\rho & (\mu+\sigma)(\mu+\rho) \end{pmatrix}.$$

By using the adjoint method we have the following inverse:

$$V^{-1}=\frac{1}{(\mu+\sigma)(\mu+\rho)(\mu+\sigma)}\begin{pmatrix} (\mu+\rho)(\mu+\sigma) & 0 & 0 \\ \sigma(\mu+\delta) & (\mu+\sigma)(\mu+\delta) & 0 \\ \sigma\rho & 0 & (\mu+\sigma)(\mu+\rho) \end{pmatrix}.$$

The reproduction number is given by the spectral radius (dominant eigenvalue) of the matrix FV^{-1}, denoted by $\rho(FV^{-1})$. Thus,

$$\rho(FV^{-1})=\frac{c\beta K}{\mu+\sigma}\left[1+\frac{\eta_1\sigma}{\mu+\rho}+\frac{\eta_2\sigma\rho(1-q)}{(\mu+\rho)(\mu+\delta)}\right],$$

where

$$R_1=\frac{c\beta K}{\mu+\sigma}, R_2=\frac{c\beta\eta_1 K}{(\mu+\rho)(\mu+\sigma)}$$

and

$$R_3=\frac{c\beta\eta_2 K}{(\mu+\delta)(\mu+\rho)(\mu+\sigma)},$$

represents the contribution of the asymptomatic, symptomatic and AIDS individuals to the overall model reproduction number R_0 respectively.

3.4 Endemic equilibrium

Theorem 3.4. [38] *If $R_0 > 1$, the model given in (3.1) has a unique endemic equilibrium point given by*

$$E^* = (S^*, I_1^*, I_2^*, A^*),$$

given by the following:

$$\begin{aligned} S^* &= \frac{(\sigma+\mu)(\alpha\mu+\beta c\Gamma+\alpha\mu(R_0-1))}{\beta c\Gamma(\alpha\mu+\beta c\Gamma)}, \\ I_1^* &= \frac{\mu(R_0-1)}{\alpha\mu+\beta c\Gamma}, \\ I_2^* &= \frac{\sigma\mu(R_0-1)}{(\rho+\mu)(\alpha\mu+\beta c\Gamma)}, \\ A^* &= \frac{\rho\sigma\mu(R_0-1)}{(\rho+\mu)(\delta+\mu)(\alpha\mu+\beta c\Gamma)}. \end{aligned} \tag{3.1}$$

3.5 Global stability of E_0

We now establish the global stability of the disease free equilibrium. The following result forms part of the paper [1].

Theorem 3.6. *The disease-free equilibrium E_0 of the model (3.1) is globally asymptotically stable in G if $R_0 < 1$.*

Proof. Let us first fix the following constants a_1, a_2, a_3 and ξ, $a_1 = (mu+\rho)(\mu+\delta)$, $a_2 = Kc\beta[\eta_1(\mu+\delta)] + \rho\xi]$, $a_3 = \xi Kc\beta(\mu+\rho)$, where $\xi = \eta_2(1-q)$.
Now we define the following function $V = V(I_1(t), I_2(t), A(t))$, which we shall prove to be a Lyapunov function at the point $(I_1, I_2, A) = (0, 0, 0)$.

$$V = a_1 I_1 + a_2 I_2 + a_3 A.$$

Then

$$V' = a_1 I_1' + a_2 I_2' + a_3 A'.$$

Now noting that $S(t) < K$ for all t and $\lambda < c\beta(I_1 + \eta_1 I_2 + \xi A)$,
it follows that we can write:

$$\dot{V} < Q_1 I_1 + Q_2 I_2 + Q_3 A,$$

where the coefficients Q_i have the following values:

$$\begin{aligned} Q_1 &= a_1[cK\beta - (\mu + \sigma)] + a_2\sigma, \\ Q_2 &= a_1\eta_1 cK\beta - a_2(\mu + \rho) + a_3\rho, \\ Q_3 &= a_1\xi cK\beta - a_3(\mu + \delta). \end{aligned}$$

Now we notice that when substituting the values of a_1, a_2, a_3 and ξ, we obtain the following:

$$\begin{aligned} Q_2 &= a_1\eta_1 cK\beta - cK\beta[\eta_1(\mu + \delta) + \xi\rho](\mu + \rho) + a_3\rho \\ &= a_1\eta_1 cK\beta - a_1\eta_1 cK\beta - cK\beta\rho\xi(\mu\rho) + cK\beta\xi(\mu + \rho)\rho \\ &= 0 \end{aligned}$$

Likewise, for Q_3 we find:

$$\begin{aligned} Q_3 &= \xi cK\beta(mu + \rho)(\mu + \delta) - \xi cK\beta(mu + \rho)(\mu + \delta) \\ &= 0. \end{aligned}$$

Finally we turn to Q_1.

$$\begin{aligned} Q_1 &= a_1 cK\beta + a_2\sigma - a_1(\mu + \sigma) \\ &= (\mu + \sigma)\left[\frac{cK\beta}{(\mu + \sigma)} + \frac{a_2\sigma}{a_1(\mu + \sigma)} - 1\right] \\ &= (\mu + \sigma)\left[\frac{cK\beta}{(\mu + \sigma)} + \frac{cK\beta[\eta_1(\mu + \delta) + \rho\xi]\sigma}{(\mu + \rho)(\mu + \delta)(\mu + \sigma)} - 1\right] \\ &= a_1(\mu + \sigma)\left[\frac{cK\beta}{\mu + \sigma}\left\{1 + \frac{\eta_1\sigma}{\mu + \rho} + \frac{\rho\xi\sigma}{(\mu + rho)(\mu + \delta)}\right\} - 1\right] \\ &= (\mu + \rho)(\mu + \delta)(\mu + \sigma)[R_0 - 1] \\ &\leq 0, \end{aligned}$$

since $R_0 \leq 1$. It follows that V is a Lyapunov function as asserted.
This completes the proof. □

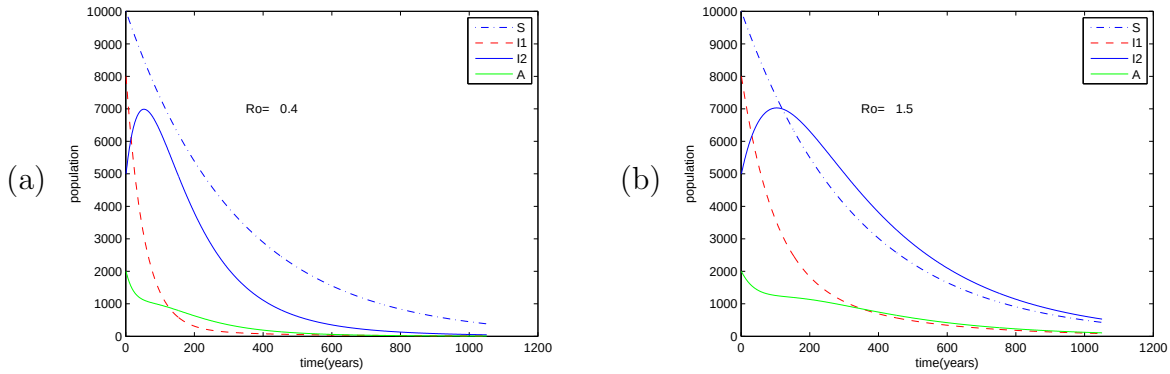


Figure 3.1: Variation of the HIV/AIDS population of the model system 3.1.

3.6 Numerical Simulation

To study the behavior of system (3.1) numerically, a forth order Runge-Kutta scheme is used. We consider a hypothetical population of one million sexually active individuals at time $t = 0$. An annual increase of 49,300 individuals was assumed in the paper of Nyabandza et al. [37]. We consider the numerical simulations that illustrates the theorem on the stability of disease free and endemic equilibrium. In Figure 3.1(a) the simulation illustrates the variation of S, I_1, I_2, and A with time whenever $R_0 < 1$. For the case of $R_0 > 1$ it is shown in figure 3.1(b). In Cai et al. [12] symptomatic individuals are assumed to have a lower rate of infection when compared to the asymptomatic individuals. In this model we however assume that symptomatic individuals have a higher viral load and are thus more infectious, since viral load affects infection rate. The higher the viral load the higher the likelihood of infection. The probability of β may vary considerably. We thus consider $1 \leq \eta_1, \eta_2 \leq 2$ in our simulations. The death rate due to the disease is chosen to be 0.33 per year. The parameter values have been taken form Nyabadza et al. [38]. Table 3.1 summarizes all the parameters used in the simulations.

Table 3.1: Model parameters and their interpretations

Parameter description	Parameter	Estimated value
Recruitment rate	μK	0.05
Proportion of withdrawals by AIDS cases	q	0.5
Rate of becoming symptomatic	σ	0.18
Natural death rate	μ	$0.02 \geq \mu \geq 0.03$
Exposure rate to media campaigns	α	1
Rate of developing AIDS	ρ	0.06
Probability of transmission	β	0.02
Partner acquisition rate	c	1.5
Enhancement factors	η_1	1.6
Enhancement factors	η_2	1.8
Disease-induced death rate	σ	0.18

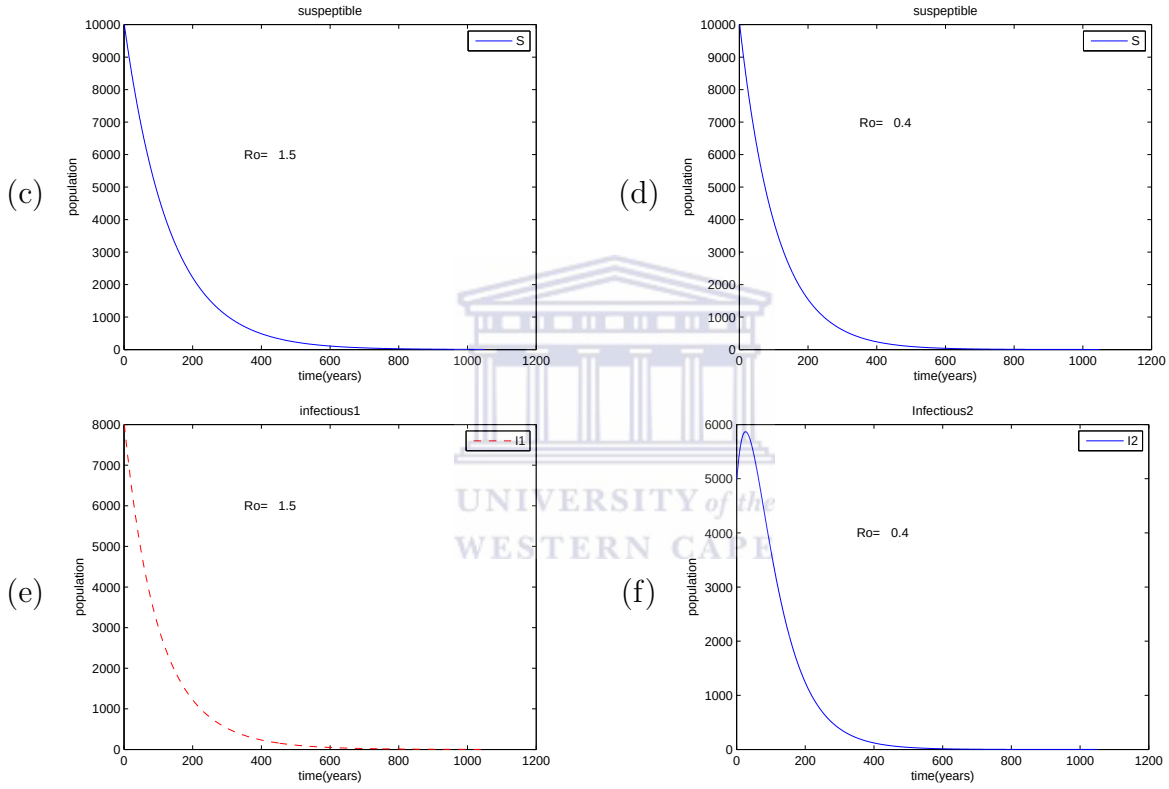


Figure 3.2: Deterministic trajectories of the HIV/AIDS population dynamics of the model system 3.1

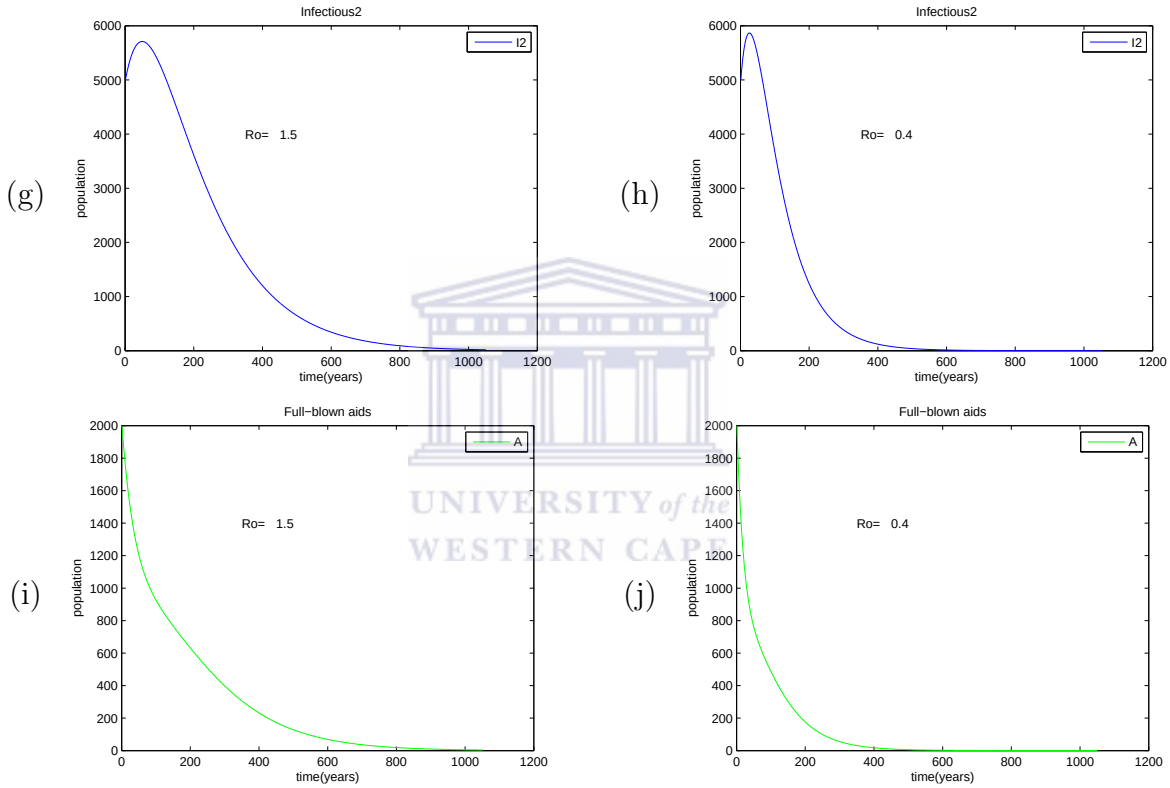


Figure 3.3: Variation of the HIV/AIDS population dynamics of the model system 3.1 when: $R_0 = 0.4$ in (g) and (i) and $R_0 = 1.5$ in (h) and (j).

Chapter 4

A 6-compartmental model of HIV model with education

The paper of Bhunu et. al. [7] presents a model of HIV/AIDS in which the classes are separated according to their HIV status and sexual activity levels, and which accommodates the effect of HIV/AIDS education programs. The entire population is divided into the following compartments:

- S : the susceptibles.
- I_1 : the individuals who are HIV positive and do not know their status.
- I_2 : the individuals who are HIV positive and know their status and reduce their risky sexual behavior as a result of knowing their status.
- I_3 : the individuals who are HIV positive and know their status and have increase in risky sexual behavior as a result of knowing their status.
- I_4 : HIV positive individuals who are sexually inactive.
- A : AIDS patients.

It is assumed that sexually inactive HIV positive individuals are no longer contributing new infections. Their total abstinence from sexual activities may be due to some of the fol-

lowing: effective public health education and HIV/AIDS information campaigns, a variety of sexual abstinence education programs, sexual isolation of individuals by some sexual means, individuals moral and religious reasons such as church, culture. We contributed in this model by means of simulations.
Thus the population size $N(t)$ is given by:

$$N(t) = S(t) + I_1(t) + I_2(t) + I_3(t) + I_4(t) + A(t).$$

Based on the fact that the infectious period is very long (≥ 10 years), we cannot regard the population size as staying constant. The model is described by the following system of equations:

$$\begin{aligned} S^{'}(t) &= \Lambda - (\lambda + \mu)S, \\ I_1^{'}(t) &= \lambda S - (\mu + \rho + \delta)I_1, \\ I_2^{'}(t) &= f\delta I_1 - (\mu + \theta + \rho)I_2, \\ I_3^{'}(t) &= (1-f)\delta I_1 - (\mu + \theta + \rho)I_3, \\ I_4^{'}(t) &= \theta(I_2 + I_3) - (\mu + \rho)I_4, \\ A^{'}(t) &= \theta(I_1 + I_2 + I_3 + I_4) - (\mu + \nu)A. \end{aligned} \tag{4.1}$$

Here λ is the rate at which susceptible individuals get infected with HIV, and

$$\lambda = \frac{\beta c(I_1(t) + \phi_1 I_2(t) + \phi_2 I_3(t))}{N}.$$

Thus, β is the probability of getting infected per sexual contact, the parameter c is the effective contact rate. The parameter $\phi_1 \in (0, 1)$ models of the effect of a positive behavioral change as a result of knowing one's HIV positive status while $\phi_2 > 1$ accounts for increase in risky behavior as a result of knowing one's HIV positive status. After infection with HIV, susceptible individuals infected with HIV will move into the class of HIV infected people not knowing their status (I_1). Individuals in the class (I_1) will know their HIV status through testing at a rate δ and counseling. A proportion f of HIV positive people knowing their status will move into the class I_2 and the complementary

$(1-f)$ will move onto the class I_3, respectively. HIV positive individuals who know their status will move into the sexually inactive class I_4 at a rate θ. For simplicity, we assume the same θ value in both I_2 and I_3 classes. HIV positive people in classes I_1, I_2, I_3 and I_4 progress to the AIDS class (A) at a rate ρ. In all classes individuals experience natural death at a constant rate μ which is proportional to the number in each class. Individuals in the AIDS class have an additional disease-induced death rate ν.

4.1 Disease-free equilibrium

The definition of a disease-free equilibrium has been stated in Chapter 2, so it follows that the model has the following disease-free equilibrium, E_0,

$$E_0 = (\frac{\Lambda}{\mu}, 0, 0, 0, 0, 0).$$

4.2 Basic reproduction number

By the method used in the previous section, due to Van den Driessche and Walmough [48], the basic reproduction number of the model (4.1) is calculated in [7] and is given by

$$R_0 = R_1 + R_2 + R_3, \tag{4.2}$$

where

$$R_1 = \frac{c\beta}{\mu+\rho+\delta}, R_2 = \frac{c\beta f\phi_1\delta}{(\mu+\theta+\rho)(\mu+\rho+\delta)}$$

and

$$R_3 = \frac{c\beta\delta\phi_2(1-f)}{(\mu+\theta+\rho)(\mu+\rho+\delta)}.$$

The numbers R_1, R_2 and R_3 can be considered to represent the average number of infected individuals as a contribution of each class I_1, I_2 and I_3 respectively.

The term $\frac{c\beta}{\mu+\rho+\delta}$ represents the new infections caused by infected individuals in the first stage I_1, where $\frac{1}{\mu+\rho+\delta}$ is the average time that infected individuals spend in the first stage

before progressing to the second stage or before dying due to natural causes.
The second term of R_0, $\frac{f\phi_1}{\mu+\rho+\delta}$ represents the fraction of individuals who progressed from stage one and are aware of their status (with presumed change of risky sexual behavior through abstinence or otherwise). The term, $\frac{c\beta}{\mu+\theta+\rho}$ represents the new infections caused by the infected individuals in the second stage.
The last term, $\frac{c\beta}{\mu+\theta+\rho}$, represents the number of new infections from infected individuals at the third stage, $\frac{(1-f)\phi_2}{(\mu+\theta+\rho)}$ is the proportion of individuals progress to the third stage who adopt risky sexual behavior and $\frac{\delta}{\mu+\rho+\delta}$ represents a proportion of those who receive education, its effect is to reduce R_0. The term, $\frac{1}{\mu+\theta+\rho}$ signifies the average time an infected individual will stay in the third stage.

Thus we have

$$R_0 = \frac{c\beta(\mu+\rho+\theta+(f\phi_1+(1-f)\phi_2)\delta)}{(\mu+\rho+\theta)(\mu+\delta+\rho)}.$$

4.3 Endemic equilibrium

Theorem 3.5. If $R_0 > 1$, the model given in (4.1) has a unique endemic equilibrium point given by

$$E^* = (S^*, I_1^*, I_2^*, I_3^*, I_4^* A^*),$$

given by the following:

$$\begin{aligned}
S^* &= \frac{\Lambda}{\mu} - \frac{(\mu+\rho+\delta)\Lambda(R_0-1)(\mu+\nu)(\mu+\rho)}{\mu(\mu++\theta+\rho)((\mu+\rho+\delta)[(\mu+\rho)(\mu+\nu)R_0-\rho\nu])},\\
I_1^* &= \frac{\Lambda(R_0-1)(\mu+\nu)(\mu+\rho)}{(\mu+\rho+\delta)[(\mu+\rho)(\mu+\nu)R_0-\rho\nu]},\\
I_2^* &= \frac{f\delta\Lambda(R_0-1)(\mu+\nu)(\mu+\rho)}{(\mu+\theta+\delta)((\mu+\rho+\delta)[(\mu+\rho)(\mu+\nu)R_0-\rho\nu])},\\
I_3^* &= \frac{(1-f)\delta\Lambda(R_0-1)(\mu+\nu)(\mu+\rho)}{(\mu+\theta+\delta)((\mu+\rho+\delta)[(\mu+\rho)(\mu+\nu)R_0-\rho\nu])},\\
I_4^* &= \frac{\theta\delta\Lambda(R_0-1)(\mu+\nu)(\mu+\rho)}{(\mu+\theta+\delta)((\mu+\rho+\delta)[(\mu+\rho)(\mu+\nu)R_0-\rho\nu])},\\
A^* &= \frac{\rho\Lambda(R_0-1)}{(\mu+\rho)(\mu+\nu)R_0-\rho\nu}.
\end{aligned}$$

4.4 Numerical Simulations

In this chapter, we will look at how can we numerically solve the system (4.1) using the fourth order of scheme Runge-Kutta. We will use the parameters in table 4.1 to numerically examine the effect of varying abstinence rate for the model in system (4.0.1). Figure 4.1(a) shows the effect of counseling and testing alone as an intervention approach as well as the combination of abstinence on HIV/AIDS disease. In figure 4.1(b), the graph illustrates what happens when there is a disease free equilibrium. It shows that the population growth is not affected by the disease as there will be in infection in the population. In figure 4.1(c), the graph denotes when HIV/AIDS exist in the population where counseling coupled with abstinence exist. In figure 4.1(d) and (e) shows when HIV/AIDS exist in the population where counseling and testing is the only strategy, as these simulations suggest that counseling and testing alone is not enough in the fight against the epidemic. In figure 4.1(f) shows a situation where HIV/AIDS exist in the abstinence of any public health campaign.

In these graphs, we note that in countries where the resources are limited when more people getting to know their status they increase the risky sexual behavior as a results of knowing their status. This tends to suggest that the epidermic is being influenced by people who know their status and have a negative change. We therefore suggest that public health health campaign programs are very important in reducing the effect of HIV/AIDS. We also suggest that counseling and testing with abstinence must also include the treatment in order to bring down the viral load of HIV/AIDS. The parameter have been taken from Bhunu et al. [7].

Table 4.1: Model parameters and their interpretations

Parameter description	Parameter	Estimated value
Recruitment rate	Λ	0.029
Natural mortality rate	μ	0.02
Rate of knowing one's HIV status through counseling and testing	σ	0.1
Natural rate rate of progression to AIDS	ρ	0.1
Modification parameter	ϕ_1	0.25
Modification parameter	ϕ_2	1.01
Proportion reducing risky sexual behavior as a result of knowing their HIV status	f	0.85
AIDS related death rate	ν	$0.333 - 0.4$
Product of effective contact rate for HIV infection and probability of HIV transmission per contact	βc	$0.011 - 0.95$
Abstinence rate	θ	0.2

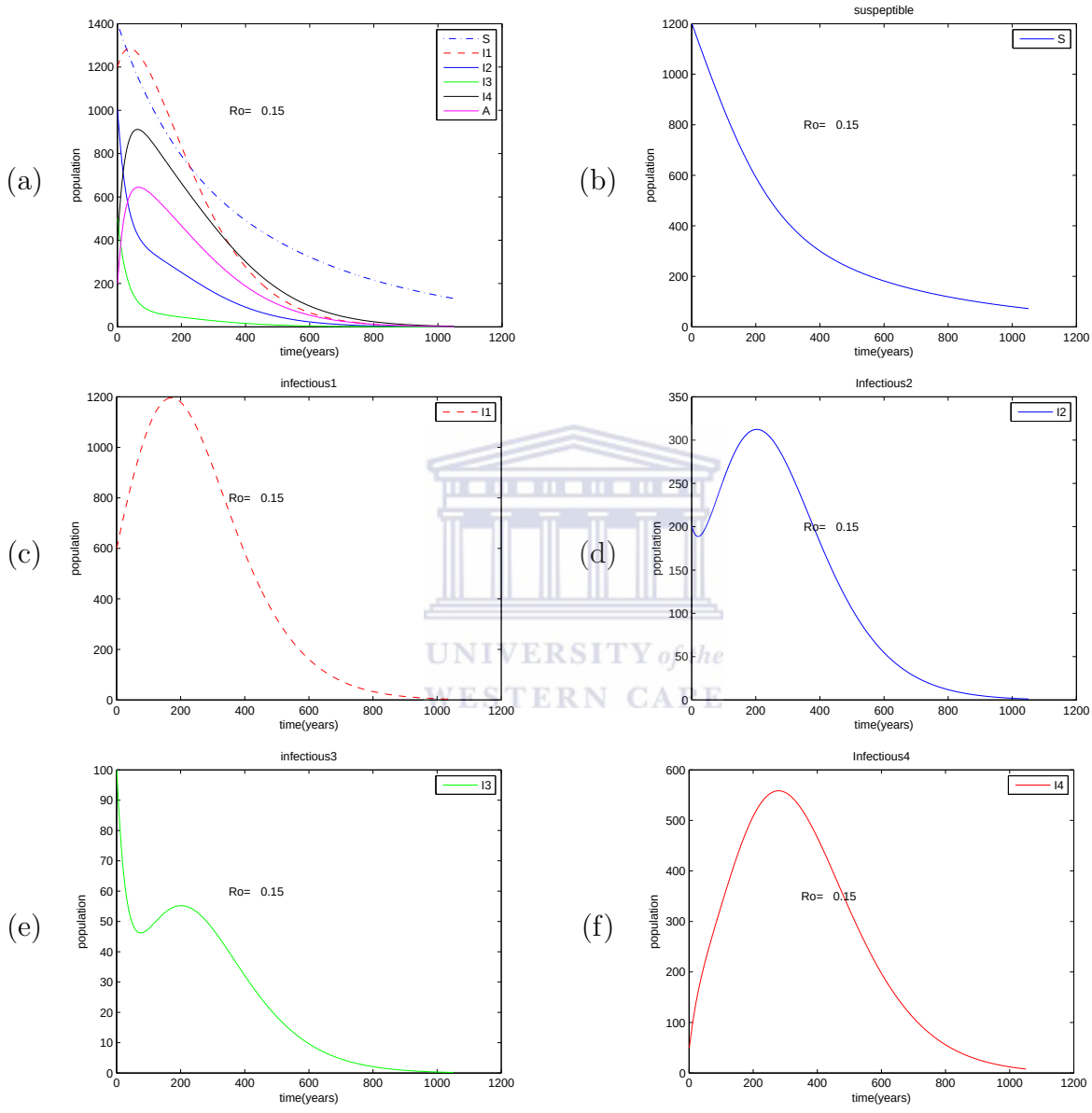


Figure 4.1: Variation of the HIV/AIDS population dynamics of the model system 4.1 when $R_0 = 0.15$.

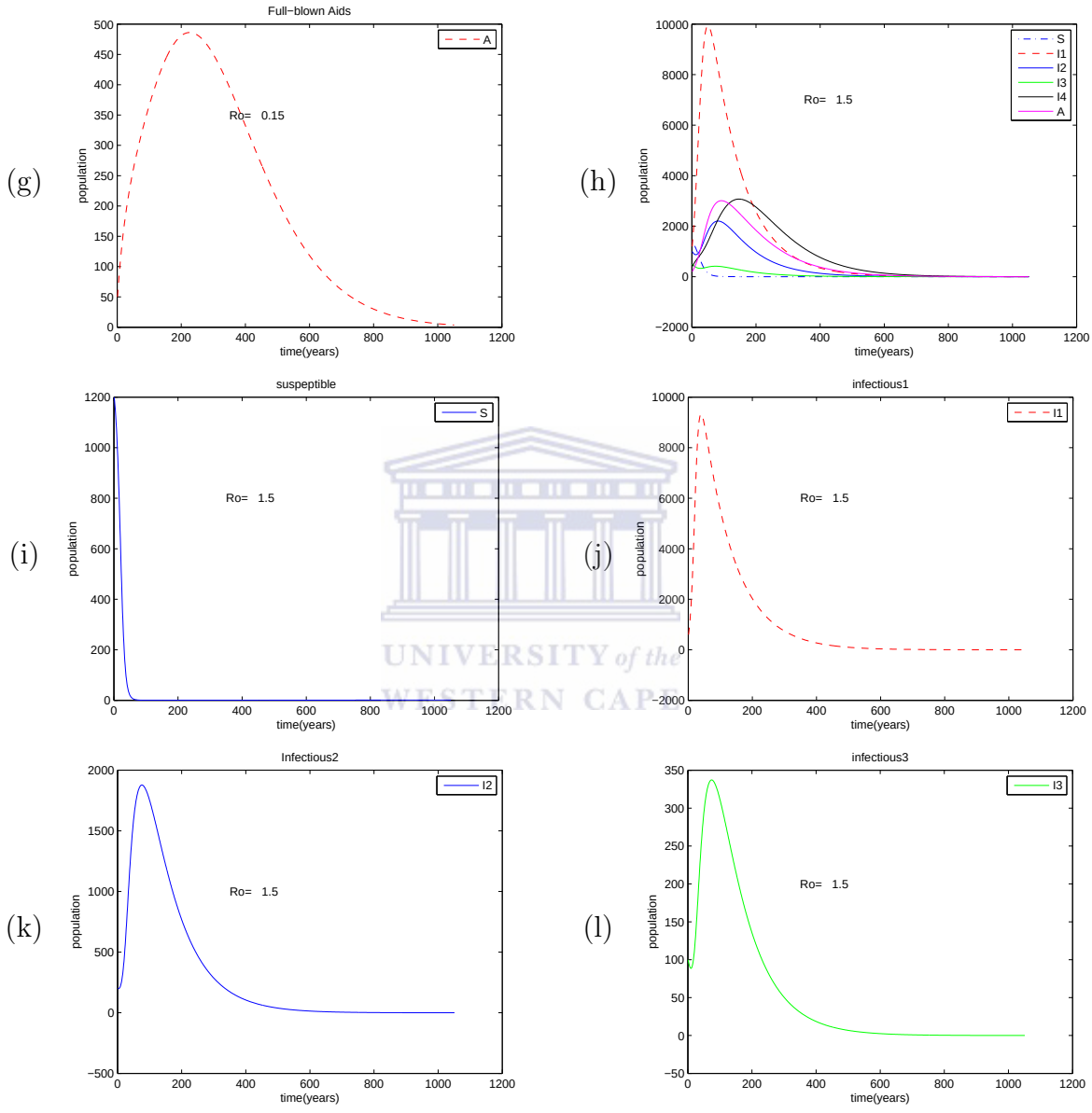
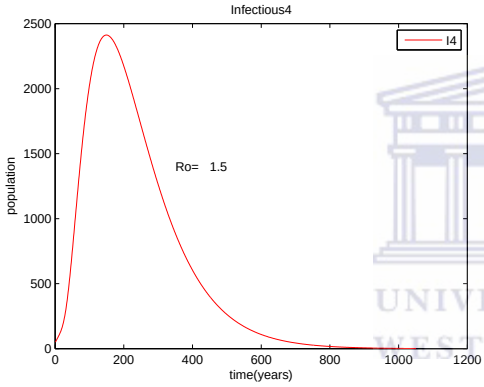


Figure 4.2: Variation of the HIV/AIDS population dynamics of the model system 4.1 when $R_0 = 0.025$ in (g) and $R_0 = 1.5$ in (h), (i), (j), (k) and (l).

(m)



(n)

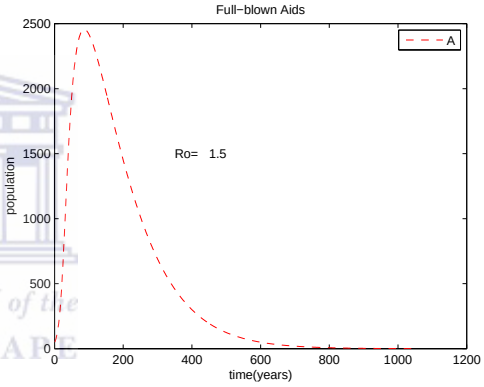


Figure 4.3: Variation of the HIV/AIDS population dynamics of the model system 4.1 when $R_0 = 1.5$ in (m) and (n).

Chapter 5

An HIV model with treatment and education

Based on the model of Cai et al. [12], which already includes treatment, we develop a model of HIV/AIDS that takes into account the effect of public health education. Our model is of the compartmental type and the population is divided into the four compartments which are the susceptible class (S), infectious classes that is for the asymptomatic phase (I), the symptomatic phase (J) and the AIDS patients class (A). Thus the total population is given by

$$N(t) = S(t) + I(t) + J(t) + A(t). \tag{5.1}$$

When susceptible individuals make sufficient contact with individuals in one of the other stages, new infections will result. All the newly infected individuals will join the asymptomatic stage. The individuals will stay in the asymptomatic phase or will progress to J-class if the symptoms are showing. They may die due to natural causes at each stage at a rate μ. They will then move to A class and this means full-blown AIDS with disease induced mortality.

The parameters used in this model are: μK the recruitment rate of sexually matured individuals into a susceptible class, c the contact rate of susceptible individuals with infected

individuals, μ the per-capita natural death rate of individuals in all classes, irrespective of being susceptible or infected. The factor β is the probability of disease transmission per contact by an infective in the first stage. The factor $b\beta$ is the probability of disease transmission per contact by an infective in the second stage. Furthermore, k_1 and k_2 are the transfer rate constants from the asymptomatic stage I to the symptomatic stage J and from the symptomatic stage to the AIDS cases, respectively. The factor α is the transfer rate rate from the symptomatic stage J to the asymptomatic stage I and δ is the disease related death rate of the AIDS cases. Suppose that public health information and education programs result in reduction of the coefficients c, k_1, and k_2 by the amounts $\epsilon_0, \epsilon_1, \epsilon_2$, respectively. Thus the term u denotes the education campaign effort. We assume maximum values: $\epsilon_0 u \leq c$, $\epsilon_1 u \leq k_1$, $\epsilon_2 u \leq k_2$.

The resulting system of equations is given by:

$$\begin{aligned}
\frac{dS}{dt} &= \mu K - \beta S(I + bJ)(c - \epsilon_0 u) - \mu S, \\
\frac{dI}{dt} &= \beta S(I + bJ)(c - \epsilon_0 u) - (\mu + k_1 - \epsilon_1 u)I + \alpha J, \\
\frac{dJ}{dt} &= (k_1 - \epsilon_1 u)I - (\mu + k_2 - \epsilon_2 u + \alpha)J, \\
\frac{dA}{dt} &= (k_2 - \epsilon_2 u)J - (\mu + \delta)A. \qquad (5.2)
\end{aligned}$$

5.1 Basic reproduction number

The basic reproduction number of our model (5.2) can be deduced from that of the model of Cai et al. [12]. Nevertheless we give the complete calculation. Since we have more than one infected compartment we will use the next generation matrix to find the basic reproduction number.

To calculate R_0 we first arrange the system (5.2) as follows,

$$\frac{dI}{dt} = \beta S(I + bJ)(c - \epsilon_0 u) - (\mu + k_1 - \epsilon_1 u)I + \alpha J,$$

$$\begin{aligned}\frac{dJ}{dt} &= (k_1 - \epsilon_1 u)I - (\mu + k_2 - \epsilon_2 u + \alpha)J, \\ \frac{dS}{dt} &= \mu K - \beta S(I + bJ)(c - \epsilon_0 u) - \mu S.\end{aligned}$$

The system (5.2) can be written as

$$x^{'} = F(x) - V(x)$$

which implies that

$$x_i^{'} = F_i - V_i, \qquad x_i^{'} = F_i - (V_i^{-} - V_i^{+}).$$

Thus F and V are the $m \times n$ matrix given by

$$F = \left(\frac{\partial F_i(x_0)}{\partial x_j} \right), \qquad V = \left(\frac{\partial V_i(x_0)}{\partial x_j} \right)$$

where F_i= the rate of appearance of new infections in compartment i,
V_i^{-} = the rate of transfer of individuals out of compartment i,
V_i^{+} = the rate of transfer of individuals out of compartment i.

From the system (5.2), $F_i = \beta S(I + bJ)(c - \epsilon_0 u)$,

$$F = \begin{pmatrix} \frac{\partial F_i}{\partial I} & \frac{\partial F_i}{\partial J} \\ 0 & 0 \end{pmatrix} = \begin{pmatrix} \beta S(c - \epsilon_0 u) & \beta b S(c - \epsilon_0 u) \\ 0 & 0 \end{pmatrix}$$

and

$$V = \begin{pmatrix} \frac{\partial V}{\partial I} & \frac{\partial V}{\partial J} \\ \frac{\partial V}{\partial I} & \frac{\partial V}{\partial J} \end{pmatrix} = \begin{pmatrix} V_1 & -\alpha \\ -k_1 - \epsilon_1 u & V_2 + \alpha \end{pmatrix}$$

where, for $i \in \{1, 2\}$, $V_i = \mu + k_i - \epsilon_i u$.

Thus we have F and V at the disease-free equilibrium E_0 respectively.

From the system (5.2), we have

$$F=\begin{pmatrix} \beta K(c-\epsilon_0 u) & \beta bK(c-\epsilon_0 u) \\ 0 & 0 \end{pmatrix}$$

and

$$V=\begin{pmatrix} V_1 & -\alpha \\ -(k_1-\epsilon_1 u) & V_2+\alpha \end{pmatrix}$$

at the disease-free equilibrium E_0.

Therefore FV^{-1} is the next generation of matrix of system (5.2), where

$$V^{-1}=\frac{(k_1-\epsilon_1 u)}{(\mu+k_1-\epsilon_1 u)(\mu+k_2-\epsilon_2 u+\alpha)-\alpha}\begin{pmatrix} V_2+\alpha & \alpha \\ (k_1-\epsilon_1 u) & V_1 \end{pmatrix}$$

Thus

$$FV^{-1}=\begin{pmatrix} \beta K(c-\epsilon_0 u) & \beta bK(c-\epsilon_0 u) \\ 0 & 0 \end{pmatrix}\begin{pmatrix} (\frac{V_2+\alpha}{P} & \frac{\alpha}{P} \\ \frac{(k_1-\epsilon_1 u)}{P} & \frac{V_1}{P} \end{pmatrix}$$

where $P=V_1(V_2+\alpha)-\alpha(k_1-\epsilon_1 u)$.

Thus FV^{-1} is the next generation of system (5.1). It follows that the spectral radius of matrix FV^{-1} is given by

$$\rho(FV^{-1})=\frac{\beta K(c-\epsilon_0 u)(V_2+\alpha+b(k_1-\epsilon_1 u))}{V_1V_2+\mu\alpha}.$$

Therefore $R_0=\rho(FV^{-1})$ is the threshold quantity, called the basic reproduction number for the system (5.2) and is also called the spectral radius of the matrix FV^{-1}.

5.2 The disease free equilibrium

If $R_0 < 1$, the model given by the system (5.2) has a unique feasible disease free equilibrium given by,

$$E_0 = (K, 0, 0, 0). \tag{5.3}$$

5.3 The endemic equilibrium

In addition to the disease-free equilibrium the model given (5.2) has a unique endemic equilibrium point given by

$$E^* = (S^*, I^*, J^*, A^*), \tag{5.4}$$

which we calculate as follows

$$\beta S(c-\epsilon_0 u)[(\frac{\mu+(k_2-\epsilon_2 u)+\alpha}{(k_1-\epsilon_1 u)})J + bJ]$$
$$-\frac{(\mu+(k_1-\epsilon_1 u))(\mu+(k_2-\epsilon_2 u)+\alpha)}{(k_1-\epsilon_1 u)}J + \alpha J = 0$$

$$\Rightarrow \frac{\beta S J(c-\epsilon_0 u)}{(k_1-\epsilon_1 u)}[(\mu+(k_2-\epsilon_2 u)+\alpha)+b(k_1-\epsilon_1 u)]$$

$$= \frac{J}{(k_1-\epsilon_1 u)}(\mu+(k_1-\epsilon_1 u))(\mu+(k_2-\epsilon_2 u)+\alpha) - \alpha(k_1-\epsilon_1 u) = 0$$

$$\beta S(c-\epsilon_0 u) = \frac{(\mu+(k_1-\epsilon_1 u))(\mu+(k_2-\epsilon_2 u)+\alpha)-\alpha(k_1-\epsilon_1 u)}{\mu+(k_2-\epsilon_2 u)+\alpha+b(k_1-\epsilon_1 u)}$$

$$S^* = \frac{(\mu+(k_1-\epsilon_1 u))(\mu+(k_2-\epsilon_2 u)+\alpha)-\alpha(k_1-\epsilon_1 u)}{\beta(c-\epsilon_0 u)(\mu+(k_2-\epsilon_2 u)+\alpha+b(k_1-\epsilon_1 u))}$$

$$S^* = \frac{(\mu+(k_1-\epsilon_1 u))(\mu+(k_2-\epsilon_2 u)+\mu\alpha)}{\beta(c-\epsilon_0 u)(\mu+(k_2-\epsilon_2 u)+\alpha+b(k_1-\epsilon_1 u))}.$$

From the first equation of (5.2) we have the following solution:

$$I^* = \frac{(\mu+(k_2-\epsilon_2 u)+\alpha)\mu K}{(\mu+(k_1-\epsilon_1 u))(\mu+(k_2+\alpha\mu))}(1-\frac{1}{R_0}).$$

The third equation of the system (5.2) gives

$$J^* = \frac{(k_1 - \epsilon_1 u)}{(\mu + k_2 - \epsilon_2 + \alpha)} I^*.$$

By solving the forth equation of (5.2) we have the following:

$$A^* = \frac{(k_2 - \epsilon_2 u)}{\mu + \delta} J^*.$$

The endemic equilibrium is given by $E^* = (S^*, I^*, J^*, A^*)$. □

5.4 Stability of disease free equilibrium

5.4.1 Global stability of E_0

In this section, we will now look at the global stability of the disease free equilibrium. We will use the Lyapunov function to prove the global stability of the disease free equilibrium.

Theorem 5.1.1 *If $R_0 \leq 1$, then the disease free equilibrium of the model given in (5.2) is globally asymptotically stable in the feasible domain.*

Proof. We define the Lyapunov function

$$\begin{aligned} L &= \frac{1}{2}[(K - S) + I + J + A]^2 + [\mu + (k_2 - \epsilon_2 u) + \alpha \\ &\quad + b(k_1 - \epsilon_1 u)]I + b[\mu + (k_1 - \epsilon_1 u) + \alpha]J. \end{aligned}$$

We obtain the following derivative of L

$$\begin{aligned} L' &= [(K - S) + I + J + A]\frac{d}{dt}[-S + I + J + A] \\ &\quad + [(\mu + (k_2 - \epsilon_2 u) + \alpha + b(k_1 - \epsilon_1 u))c\beta S \\ &\quad - ((\mu + (k_1 - \epsilon_1 u))(\mu + (k_2 - \epsilon_2 u) + \alpha\mu))](I + bJ) \end{aligned}$$

$$\begin{aligned} &= [(K - S) + I + J + A]\Big[2\beta S(I + bJ)(c - \epsilon_0 u) - \mu K + \mu S - \mu I \\ &\quad - \mu J - \delta A - \mu A\Big] + \Big[(\mu + (k_2 - \epsilon_2 u) + \alpha + b(k_1 - \epsilon_1 u))c\beta S \\ &\quad - ((\mu + (k_1 - \epsilon_1 u))(\mu + k_2 - \epsilon_2 u) + \alpha\mu))\Big](I + bJ) \end{aligned}$$

$$
\begin{aligned}
L^{'} &= [(K-S)+I+J+A]\Big[2\beta S(I+bJ)(c-\epsilon_0 u)-\mu[(K-S) \\
&\quad +I+J+A]-\delta A\Big]+\Big[(\mu+(k_2-\epsilon_2 u)+\alpha+b(k_1-\epsilon_1 u))c\beta S \\
&\quad -((\mu+(k_1-\epsilon_1 u))(\mu+k_2-\epsilon_2 u)+\alpha\mu))\Big](I+bJ).
\end{aligned}
$$

By writing $L^{'}$ in terms of basic reproduction number, we have

$$
\begin{aligned}
L^{'} &= -[(K-S)+I+J+A]\delta A-\Big[(K-S) \\
&\quad +I+J+A\Big]\Big[[\mu((K-S)+I+J+A)]-2\beta S(I+bJ)(c-\epsilon_0 u)] \\
&\quad +[(\mu+(k_1-\epsilon_1 u)(\mu+(k_2-\epsilon_2 u))+\alpha\mu)\Big](R_0-1)(I+bJ)
\end{aligned}
$$

If $R_0 \leq 1$, then $L^{'} \leq 0$. We note that, $L^{'}=0$ if and only if $S=K$, $I=J=A=0$ and this completes the proof. □

5.4.2 Local Stability of E^*

Lemma 5.1.2 *Let M be a 3×3 real matrix. If both* tr(M) *and* det($M^{[2]}$) *are negative, then all the eigenvalues of M have negative real parts.*

Theorem 5.1.3 *The positive equilibrium E^* of system (5.2) is locally asymptotically stable if $R_0>1$.* [12]

Proof. By evaluating the Jacobian of the system (5.2) at the endemic equilibrium, we get

$$
\frac{\partial f}{\partial x}(E^*)=\begin{pmatrix}
\frac{(wv+\alpha\mu)I^*}{(v+\alpha)S^*}-\mu & -\beta S^*(c-\epsilon_0 u) & -b\beta S^*(c-\epsilon_0 u) \\
\frac{(wv+\alpha\mu)I^*}{(v+\alpha)S^*} & \beta S^*(c-\epsilon_0 u)-w & b\beta S^*(c-\epsilon_0 u)+\alpha \\
0 & k_1-\epsilon_1 u & -(v+\alpha)
\end{pmatrix} \tag{5.1}
$$

where $w=\mu+k_1-\epsilon_1 u$, $v=\mu+k_2-\epsilon_2 u$ and
$\beta(I^*+bJ^*)(c-\epsilon_0 u)=\frac{(wv+\alpha\mu)I^*}{(v+\alpha)S^*}$.

Thus, we have the second additive compound of (5.1) as follows

$$\frac{\partial f^{[2]}}{\partial x}(E^*) =$$

$$\begin{pmatrix} -\mu - \frac{(wv+\alpha\mu)I^*}{(v+\alpha)S^*} + S^*l - w & bS^*l + \alpha & bS^*l \\ k_1 - \epsilon_1 u & -\mu - \frac{(wv+\alpha\mu)I^*}{(v+\alpha)S^*} - v - \alpha & S^*l \\ 0 & \frac{(wv+\alpha\mu)I^*}{(v+\alpha)S^*} & S^*l - w - v - \alpha \end{pmatrix}$$

By Lemma 5.1.2 above it is sufficient to prove that $\mathrm{tr}(\frac{\partial f}{\partial x}E^*)$, $\det(\frac{\partial f}{\partial x}E^*)$, and $\det(\frac{\partial f^2}{\partial x}E^*)$ are negative.

It follows from $w > \beta S^*(c - \epsilon_0 u)$ that

$$\mathrm{tr}(\frac{\partial f}{\partial x})(E^*) = -\mu - \frac{(wv+\alpha\mu)I^*}{(v+\alpha)S^*} + \beta S^*(c - \epsilon_0 u) - w - v - \alpha < 0.$$

Computing for the determinant of the system (5.2) we obtain the following

$$\det(\frac{\partial f}{\partial x}(E^*)) = -\frac{(wv+\alpha\mu)I^*}{(v+\alpha)S^*}(v + \alpha + k_1 - \epsilon_1 ub)\beta S^*(c - \epsilon_0 u).$$

Also, the determinant of $\frac{\partial f^{[2]}}{\partial x}(E^*)$ is as follows

$$\begin{aligned} \det \frac{\partial f^{[2]}}{\partial x}(E^*) &= -(v + \alpha + w - \beta S^*(c - \epsilon_0 u))\Big[(\mu + \frac{(wv+\alpha\mu)I^*}{(v+\alpha)S^*})^2 \\ &\quad + (\mu + (wv + \alpha\mu)I^*(v+\alpha)S^*)(w - \beta S^*(c - \epsilon_0 u))\Big] \\ &\quad - (v+\alpha)^2[\mu + \frac{(wv+\alpha\mu)I^*}{(v+\alpha)S^*}] - \mu[w - \beta S^*(c - \epsilon_0 u)](v+\alpha) \\ &\quad - [\frac{(wv+\alpha\mu)I^*}{(v+\alpha)S^*}] \times \Big[\beta S^*(c - \epsilon_0 u)((\mu + \frac{(wv+\alpha\mu)I^*}{(v+\alpha)S^*})) \\ &\quad + w - \beta S^*(c - \epsilon_0 u)\Big] - [\alpha(k_1 - \epsilon_1 u)\frac{(wv+\alpha\mu)I^*}{(\mathrm{v}+\alpha)\mathrm{S}^*}] < 0. \end{aligned}$$

We note that if $R_0 > 0$, then $w - \beta S^*(c - \epsilon_0 u) > 0$. Thus $\det \frac{\partial f^{[2]}}{\partial x}(E^*) < 0$.

This completes the proof of Lemma 3.4.3. □

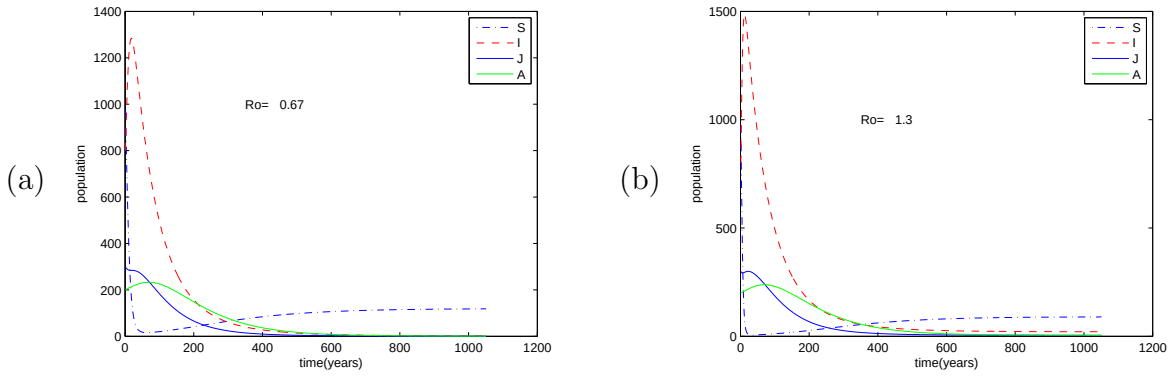


Figure 5.1: Deterministic trajectories of the HIV/AIDS population dynamics of the model system (5.2).

5.5 Numerical Simulation

In this section we present some numerical simulations for the system in (5.2) using the fourth order Runge-Kutta. We numerically analyze the effect of public health campaign for the model (5.2) using parameters described in Table (5.1). To illustrate the various theoretical results presented in system (5.2), various values of β are used. In Figure 5.1(a), 5.2(c), (e) and 5.3(g), (e), illustrates the dynamic behavior of the $SIJA$ model described by the deterministic system (5.2) when $R_0 < 1$. In Fig 5.1(b), 5.2(d), (f), and 5.3 (h), (j), illustrates the dynamic behavior of the $SIJA$ model described by the deterministic system (5.2) when $R_0 > 1$.

5.6 Sensitivity Analysis of R_0

The basic reproduction number is pivotal in determining the stability of the disease free equilibrium. It is thus important for us to understand the behavior of R_0 with respect to the different parameters it depends on. Sensitivity indeces allow us to measure the relative change in a state when a parameter changes. The normalized forward sensitivity index of a variable to a parameter is the ratio of the relative change in the variable to the relative change in the parameter. When the variable is a differentiable function of the

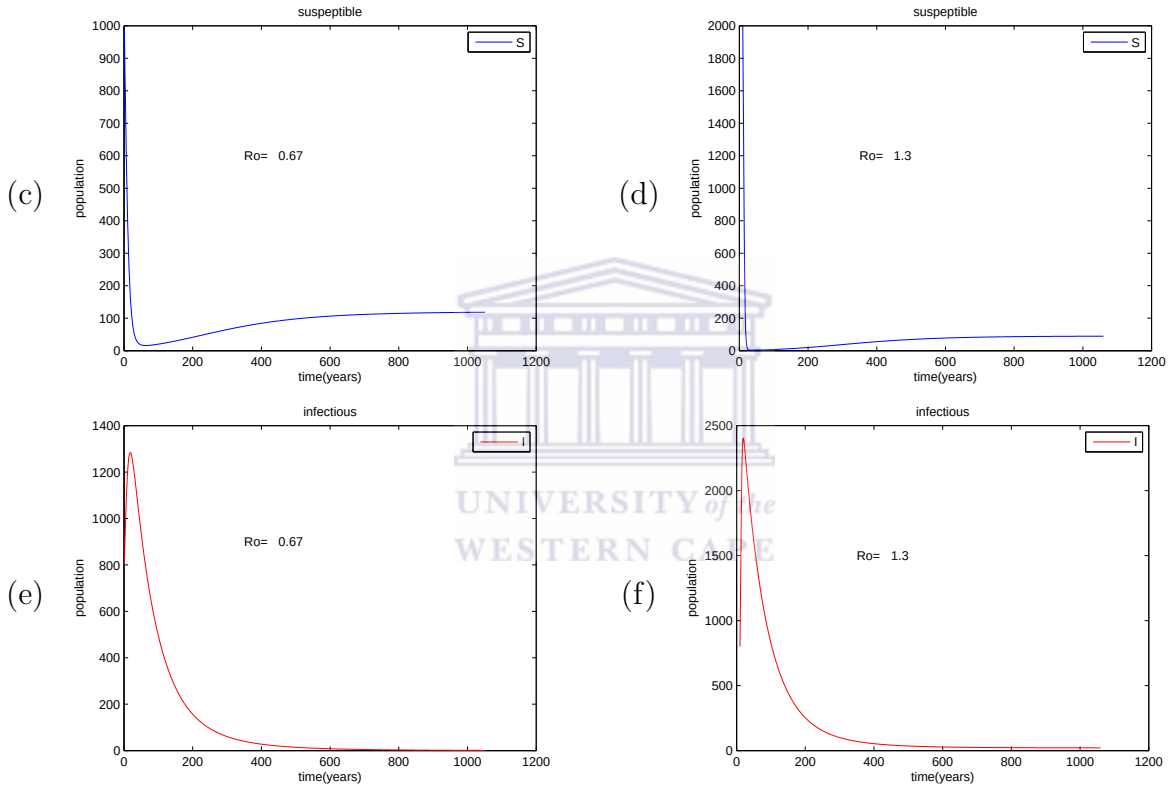


Figure 5.2: Deterministic trajectories of the HIV/AIDS population dynamics of the model system (5.2) when $R_0 = 0.67$ in (c) and (e) and when $R_0 = 1.3$ in (d) and (f).

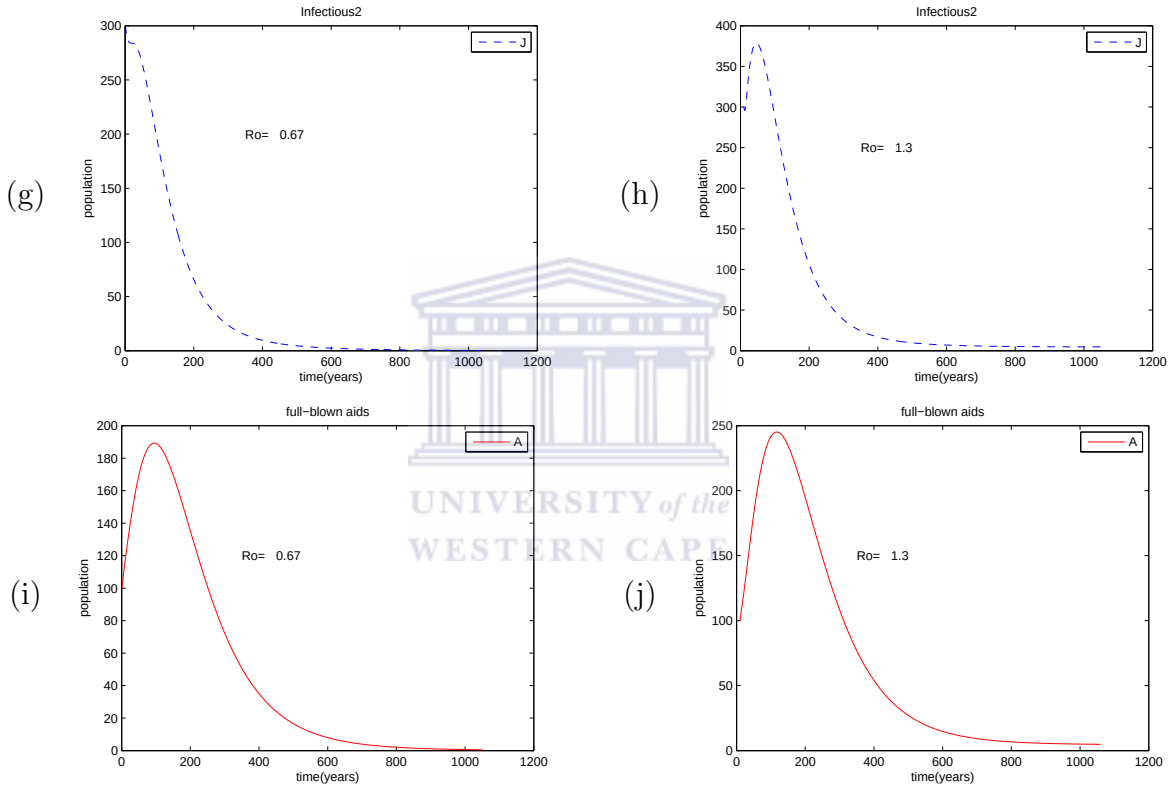


Figure 5.3: Deterministic trajectories of the HIV/AIDS population dynamics of the model system (5.2) when $R_0 = 0.67$ in (g) and (i) and when $R_0 = 1.3$ in (h) and (j).

Table 5.1: Model Parameters and their interpretations

Parameter	Parameter description	Estimated value
μ	Natural death rate of individuals	0.02
k_2	Transfer rate constant	0.02
k_1	Transfer rate constant	0.01
c	Contact rate of susceptible individuals	3
β	Probability of disease transmission	0.0005
K	Recruitment rate	120
u	Educational campaign effort	0.008
b	Probability of disease transmission	0.3
ϵ_1	Reduced Coefficient	0.008
ϵ_2	Reduced Coefficient	0.009
α	Treatment rate	0.01
ϵ_0	Reduced Coefficient	0.3

parameter, the sensitivity index may be alternatively defined using partial derivatives. We now derive the sensitivity of R_0 to each of the twelve different parameters described in Table 4.1

Let $v = \mu + (k_1 - \epsilon_1 u)$, $w = \mu + (k_2 - \epsilon_2 u)$, $a = \beta K(c - \epsilon_0 u)$ and $b_1 = \mu + \alpha + b(k_1 - \epsilon_1 u) + (k_2 - \epsilon_2 u)$

$$
\begin{aligned}
\frac{\partial R_0}{\partial \mu} \times \frac{\mu}{R_0} &= \frac{\mu[(vw + \mu\alpha) - (2\mu + \alpha + (k_1 - \epsilon_1 u) + k_2 - \epsilon_2 u)]}{b_1(vw + \mu\alpha)} \\
\frac{\partial R_0}{\partial c} \times \frac{c}{R_0} &= \frac{c}{c - \epsilon_0 u} \\
\frac{\partial R_0}{\partial b} \times \frac{b}{R_0} &= \frac{b(k_1 - \epsilon_1 u)}{\mu + \alpha + (k_2 - \epsilon_2 u) + b(k_1 - \epsilon_1 u)} \\
\frac{\partial R_0}{\partial \epsilon_0} \times \frac{\epsilon_0}{R_0} &= -\frac{\epsilon_0 u}{c - \epsilon_0 u} \\
\frac{\partial R_0}{\partial \beta} \times \frac{\beta}{R_0} &= 1 \\
\frac{\partial R_0}{\partial K} \times \frac{K}{R_0} &= 1 \\
\frac{\partial R_0}{\partial \epsilon_1} \times \frac{\epsilon_1}{R_0} &= -\frac{\epsilon_1[bu(vw + \mu\alpha) + b_1(\mu u + \epsilon_1 k_2)]}{b_1(vw + \mu\alpha)} \\
\frac{\partial R_0}{\partial \epsilon_2} \times \frac{\epsilon_2}{R_0} &= -\frac{\epsilon_2 u[(vw + \mu\alpha) + b_1(\epsilon_1 u - \mu - k_1)]}{b_1(vw + \mu\alpha)} \\
\frac{\partial R_0}{\partial \alpha} \times \frac{\alpha}{R_0} &= \frac{\alpha(vw + \mu\alpha) - \mu\alpha b_1}{b_1(vw + \mu\alpha)} \\
\frac{\partial R_0}{\partial k_1} \times \frac{k_1}{R_0} &= \frac{k_1[b(vw + \mu\alpha) - (\mu + (k_2 - \epsilon_2 u))]}{b_1(vw + \mu\alpha)} \\
\frac{\partial R_0}{\partial k_2} \times \frac{k_2}{R_0} &= \frac{k_2[(vw + \mu\alpha) - (\mu + (k_1 - \epsilon_1 u))]}{b_1(vw + \mu\alpha)} \\
\frac{\partial R_0}{\partial u} \times \frac{u}{R_0} &= \frac{-bKu\epsilon_0}{a} - \frac{u(\epsilon_2 + b\epsilon_1)}{b_1} + \frac{u(\mu + k_1\epsilon_2 + \epsilon_1\mu + k_2\epsilon_1 - 2\epsilon_1\epsilon_2 u)}{vw + \mu\alpha}
\end{aligned}
$$

The parameters shown in Table 5.2 are arranged from the most sensitive to the least from the given base of the parameters as in the list. The most sensitive parameter is the contact rate, c, the probability of disease transmission, β and the recruitment rate, K. The other important parameter include probability of disease transmission, b, reduced coefficient ϵ_1 and the treatment rate α. The least sensitive parameter is the natural death of individuals,

Table 5.2: Sensitivity indices of R_0

Parameter	Parameter description	Estimated value	Sensitivity index
c	Contact rate of susceptible individuals	3	+1.000800641
β	Probability of disease transmission	0.0005	+1
K	Recruitment rate	120	+1
b	Probability of disease transmission	0.3	+0.056338454
ϵ_1	Reduced Coefficient	0.008	+0.00219750
α	Treatment rate	0.01	+0.000456769
ϵ_0	Reduced Coefficient	0.3	−0.000800641
ϵ_2	Reduced Coefficient	0.009	−0.000183805
u	Educational campaign effort	0.008	−0.366116685
k_1	Transfer rate constant	0.01	−5.351471481
k_2	Transfer rate constant	0.02	−7.732353411
μ	Natural death rate of individuals	0.02	−21.25684921

μ. The sensitive index of R_0 with respect to the probability of disease transmission β is $+1$, implying that decreasing (or increasing) the β by 10 percent decreases (or increases) R_0 by 10 percent. Similarly increasing (or decreasing) the natural death rate of individuals μ by 10 percent, increases (or decreases) the R_0 by 212.57 percent.

Chapter 6

Optimal public education campaign

We now search for optimal rollout of the public education campaign, in terms of how much effort (or funding) to apply as a function of time. Thus in our model (5.2) we will consider u to be time dependent. i.e., $u = a(t)$. We want to see the classes I and J being as small as possible, and we want to balance that with the public education campaign effort. Thus we may want to consider a quantity of the form

$$u^2(t) + m_1 I(t) + m_2 J(t)$$

to be somehow kept as small as possible, for some balancing weight constants m_1 and m_2. Taking u in squared form is to ensure convexity of the problem. For more information see the book of Lenhart and Workman [30]. Let us consider a time horizon $[0, T]$,

let

$$V(u(t)) = \int_0^T u^2(t) + m_1 I(t) + m_2 J(t) dt. \tag{6.1}$$

Thus we shall seek to solve the following optimal control problem,

Problem (6.1.1.):

Minimize $V(u(t))$ subject to the conditions (5.2), and the initial conditions

$$S(0) = S_0 \geq 0, I(0) = I_0 \geq 0, J(0) = J_0 \geq 0, A(0) = A_0 \geq 0, \tag{6.2}$$

and terminal conditions

$$S(T),\ I(T),\ J(T) \text{ and } A(T) \tag{6.3}$$

are free, while the control variables is assumed to be bounded above,

$$0 \leq u(t) \leq \alpha \leq 1. \tag{6.4}$$

The Hamiltonian for this problem is given by

$$H(t, S, I, J, A, \lambda_1, \lambda_2, \lambda_3, \lambda_4) = u^2 + m_1 I + m_2 J + \lambda_1 \dot{S} + \lambda_2 \dot{I} + \lambda_3 \dot{J} + \lambda_4 \dot{A}$$

$$\begin{aligned} H(t, S, I, J, A, \lambda_1, \lambda_2, \lambda_3, \lambda_4) &= u^2 + m_1 I + m_2 J \\ &\quad + \lambda_1(\mu K - \beta S(I + bJ)(c - \epsilon_0 u) - \mu S) \\ &\quad + \lambda_2(\beta S(I + bJ)(c - \epsilon_0 u) \\ &\quad - (\mu + k_1 - \epsilon_1 u)I + \alpha J) \\ &\quad + \lambda_3((k_1 - \epsilon_1 u)I - (\mu + k_2 - \epsilon_2 u + \alpha)J) \\ &\quad + \lambda_4((k_2 - \epsilon_2 u)J - (\mu + d)A) \end{aligned}$$

Theorem 2.1.3 *Let S^*, I^*, J^*, A^* and u^* be optimal solutions for the optimal control problem (6.1), (6.2), (6.3) and (6.4). Then the costate variables satisfy the following differential equations:*

$$\begin{aligned} \frac{d\lambda_1(t)}{dt} &= \lambda_1\beta(I + bJ)(c - \epsilon_0 u) + \mu\lambda_1 - \lambda_2\beta(I + bJ)(c - \epsilon_0 u) \\ \frac{d\lambda_2(t)}{dt} &= -m_1 + \lambda_1\beta S(c - \epsilon_0 u) - \lambda_2\beta S(c - \epsilon_0 u) + (\mu + k_1 - \epsilon_1 u) \\ &\quad - \lambda_3(k_1 - \epsilon_1 u) \\ \frac{d\lambda_3(t)}{dt} &= -m_2 + \lambda_1\beta bS(c - \epsilon_0 u) - \lambda_2\beta bS(c - \epsilon_0 u) + \lambda_2\alpha + \lambda_3(\mu + k_2 - \epsilon_2 u) \\ &\quad -\lambda_4(k_2 - \epsilon_2 u) \\ \frac{d\lambda_4(t)}{dt} &= \lambda_4(\mu + d) \end{aligned} \tag{6.5}$$

with transversality conditions

$$\lambda_1(T) = 0, \lambda_2(T) = 0, \lambda_3(T) = 0 \text{ and } \lambda_4(T) = 0.$$

and the optimal control takes the form

$$u^*(t) = \min\left[\max\left(\frac{\beta S\epsilon_0(I + bJ)(\lambda_2 - \lambda_1) + \epsilon_1 I(\lambda_2 + \lambda_3) + \epsilon_2 J(\lambda_4 - \lambda_3)}{2}, 0\right), \alpha\right]. \quad (6.6)$$

Proof. We will use the Pontryagin maximum principle. For more information see Lenhart and Workman [30]. We calculate partial derivatives of the Hamiltonian with respect to the different state variables in order to obtain the time derivative λ_i of costate variables. Since $S(T), I(T), J(T)$ and $A(T)$ are free, the following terminal conditions hold:
$\lambda_1(T) = 0, \lambda_2(T) = 0, \lambda_3(T) = 0$ and $\lambda_4(T) = 0$.

We start by examining,

$$\frac{d\lambda_4(t)}{dt} = -\frac{\partial H}{\partial A} = (\mu + d)\lambda_4,$$

integrating both sides we get,

$$\lambda_4 = Me^{(\mu+d)t},$$

for some constant M. The terminal condition $\lambda(T) = 0$, forces M to disappear. Therefore λ_4 is equal to zero i.e., $\lambda_4 \equiv 0$. We now calculate the following:

$$\frac{d\lambda_1(t)}{dt} = -\frac{\partial H}{\partial S}, \frac{d\lambda_2(t)}{dt} = -\frac{\partial H}{\partial I}, \frac{d\lambda_3(t)}{dt} = -\frac{\partial H}{\partial J},$$

and obtain the equations stated in the theorem.

The function u^* must optimize H.
Thus we have,

$$\frac{\partial H}{\partial u} = 2u + \lambda_1\beta S(I + bJ)\epsilon_0 - \lambda_2(\beta S(I + bJ)\epsilon_0 + \epsilon_1 I) + \lambda_3(\epsilon_2 J - \epsilon_1 I) - \lambda_4(\epsilon_2 J).$$

Now if

$$2u + \lambda_1\beta S(I + bJ)\epsilon_0 - \lambda_2(\beta S(I + bJ)\epsilon_0 + \epsilon_1 I) + \lambda_3(\epsilon_2 J - \epsilon_1 I) - \lambda_4(\epsilon_2 J) = 0$$

for some values of $[0, \alpha]$ then the given value of u is optimal.
If for every value of $u \in [0, \alpha]$ we have

$$2u + \lambda_1\beta S(I + bJ)\epsilon_0 - \lambda_2(\beta S(I + bJ)\epsilon_0 + \epsilon_1 I) + \lambda_3(\epsilon_2 J - \epsilon_1 I) - \lambda_4(\epsilon_2 J) \geq 0,$$
$$2u + \lambda_1\beta S(I + bJ)\epsilon_0 - \lambda_2(\beta S(I + bJ)\epsilon_0 + \epsilon_1 I) + \lambda_3(\epsilon_2 J - \epsilon_1 I) - \lambda_4(\epsilon_2 J) \leq 0)$$

then we must choose $u = 0$ (respectively, $u = \alpha$).

Thus we must have

$$u^*(t) = \min\left[\max\left(\frac{\beta S\epsilon_0(I + bJ)(\lambda_2 - \lambda_1) + \epsilon_1 I(\lambda_2 + \lambda_3) + \epsilon_2 J(\lambda_4 - \lambda_3)}{2}, 0\right), \alpha\right].$$

The function $u_1^*(t)$ also must optimize H, and by a similar argument we obtain the definite expression for $u_1^*(t)$. This completes the proof. □

6.1 Numerical simulation for the Optimal Control

The optimality system is solved using an iterative method of Runge-Kutta forth order scheme. We note that in fig 6.1(a) the numerical results show that the number of susceptible individuals increase after the optimal control treatment and public health education campaign, leading to a smaller number of infected individuals. Fig 6.1(b), represents the population of infected individuals without optimal control treatment and public health educational programs, we observe that that the population is sharply increasing than the individuals with control. This shows that we need treatment and public health educational campaign to control the infected individuals. In fig 6.1(c), we note that the infected individual are decreasing due to optimal control treatment and public health educational campaigns. Fig 6.1(d) shows that there is a decrease of AIDS individuals due to the optimal control treatment and education that was implemented. The of the numerical

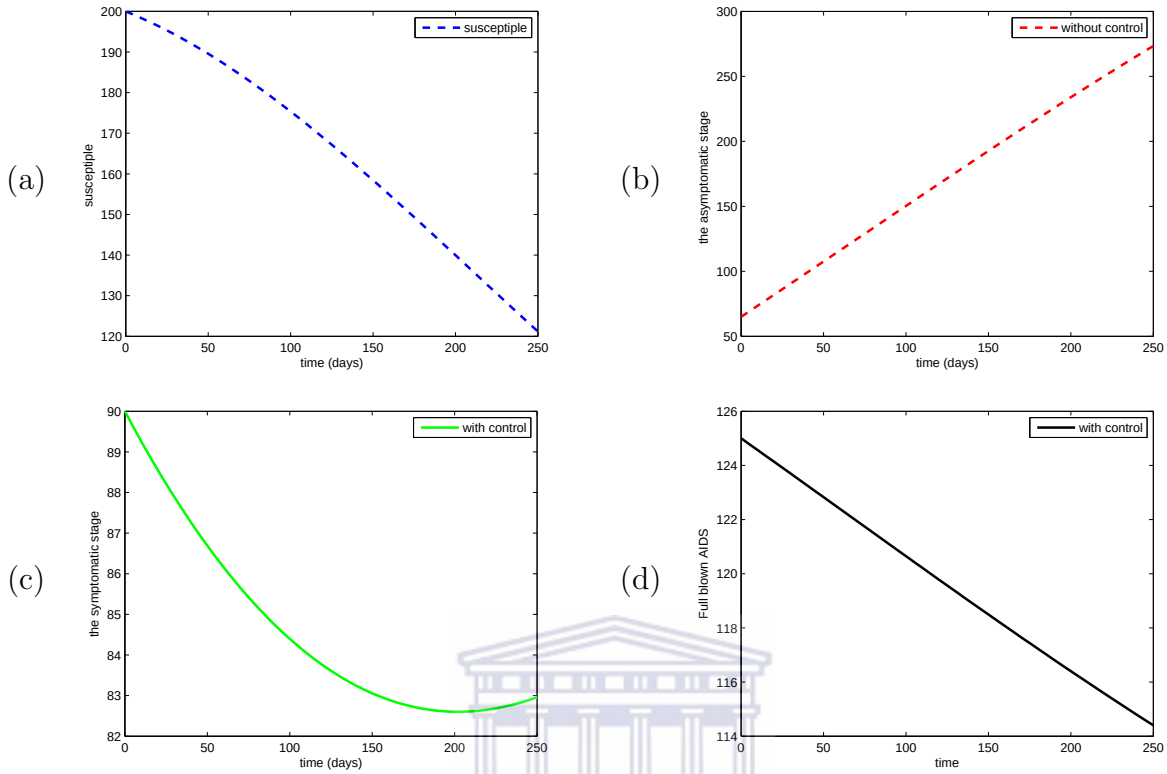


Figure 6.1: Plot of the HIV/AIDS population dynamics of the model (5.1) using optimal control strategies.

simulation shows that there is a small number of infected than before the optimal control. Thus we conclude that the rate of infected individuals decreases after the control treatment and public health education campaign.

Chapter 7

A stochastic HIV model

In this Chapter we study a Stochastic Differential Equation model of the HIV epidemic. The main results, Theorem 7.3, is on almost sure exponential stability and is included in the manuscript [1].

7.1 Types of models

The presence of stochastic perturbation in nature makes it desirable at times to introduce random variables into the modeling. Stochastic models assume that the response variables are a family of random variables indexed by time so that the epidemic is basically a stochastic process. Stochastic epidemic models are useful for small populations, possibly of isolated communities, in which the known heterogeneity inherent in the population is of importance. There are three different methods for formulating stochastic epidemic models that relate directly to their deterministic counterparts. The three popular types of stochastic modeling processes are described: discrete time Markov chain (DTMC) model, Continuous time Markov chain (CTMC) model and stochastic differential equation (SDE) model. These stochastic methods differ in the underlying assumptions regarding the time and the state variables. For more information the reader may consult Allen [4]

In a DTMC model, the time and the state variables are discrete. For example, let $S(t), I(t)$

and $R(t)$ denote discrete time stochastic process for the number of susceptible, infected and immune at time t, respectively. In a DTMC epidemic model, $t \in 0, \Delta t, 2\Delta t, \ldots$ and the discrete random variable satisfy

$$S(t), I(t), R(t) \in \{0, 1, 2, \ldots, N\}.$$

In a CTMC model, time is continuous, but the state variable is discrete. For example given $t \in [0, \infty)$, and the state $S(t), I(t)$ and $R(t)$ are discrete random variable, i.e.,

$$S(t), I(t), R(t) \in \{0, 1, 2, \ldots, N\}.$$

Finally, the SDE model is based on a diffusion process, where both the time and the state variables are continuous. In our model we will use the SDE approach. It has been applied in various papers, such as [29] by Lahrouz et al., [15] by Dalal et al., [17] by Ding et al. and [51] by Yang et al. The paper [26] of Jovanović and Krstić presents a stochastic model of vector-borne diseases. We have also looked at some of the models in which a stochastic perturbation has been inserted to each of the differential equations in the system and these models are [32] by Lu, [52], [25] and [26]. We also have found that there are instances where stochastic perturbation are introduced in such a way that the total population size is still a deterministic function of time and such models are found in [20] by Gray et al., [29] by Lahrouz et al. and [47] by Tornatore et al. We note that for systems of stochastic differential equations, different versions of stability are defined and studied in the literature. We refer to the book [33] of Mao and several papers, for instance, [17], [52], [25], [20], [29] and [47].

One of the most important differences between the deterministic and stochastic epidemic models is their asymptotic dynamics. It may happen that eventually stochastic solutions (sample paths) converge to the disease-free state even though the corresponding deterministic solution converges to an endemic equilibrium. For stochastic differential equations in general, this phenomenon is discussed in Mao's book [33] for instance. Other properties that are unique to the stochastic epidemic models include the probability of an outbreak,

the quasistationary probability distribution, the final size distribution of an epidemic and the expected duration of an epidemic.

7.2 A Stochastic differential equation model

Let us consider the model of Cai et al. [12] modified. Let us assume $(\Omega, \mathcal{F}, \{\mathcal{F}_t\}_{t\geq t_0}, P)$ be a complete probability space which is right continuous with a filtration $\{\mathcal{F}_t\}_{t\geq t_0}$. Let $B(t)$ be a one-dimensional Wiener process defined on this probability space. Let $g(S, I, J)$ be some function to be specified at a later stage. There are different ways of introducing randomnes into epidemic models, see the paper of [11] for a survey. For example, a discrete stochastic epidemic model is proposed in the paper [2] of Andersson and Lindenstrand to study the probability of outbreaks. An approximation of the discrete model by a system of stochastic differential equations is utilized to study the time to extinction of the disease. In this paper we study an epidemiological population model which can be described by a system of stochastic differential equations. For now let us refer to this form of randomness as stochastic perturbation with independent processes. In other cases, a stochastic perturbation is introduced in such a way that the total perturbation on the system is zero see the paper of Lahrouz et al. [29]. This type will be said to have stochastic perturbation with complementary processes. Thus we have the following complementary model:

$$\begin{aligned} dS &= [\mu K - c\beta(I + bJ)S - \mu S]\, dt - \sigma g(S, I, J) dB(t), \\ dI &= [c\beta(I + bJ)S - (\mu + k_1)I + \alpha J]\, dt + \sigma g(S, I, J) dB(t), \\ dJ &= [k_1 I - (\mu + k_2 + \alpha)J]\, dt, \\ dA &= [k_2 J - (\mu + \delta)A]\, dt. \end{aligned} \tag{7.1}$$

We describe the parameters. The term μK is the recruitment rate of the population and μ is the average death rate by natural causes, c is the average number of contacts of an individual per unit time, see Cai [12]. The term β is the probability of disease transmission per contact by an infective in the first stage. The term $b\beta$ is the probability of

disease transmission per contact by an infective in the second stage. By k_1 and k_2 we denote the transfer rates from the asymptomatic phase I to the symptomatic phase J and from the symptomatic phase to the AIDS cases, respectively. α is regarded as the treatment rate from symptomatic phase J to the asymptomatic phase I. The constant δ is the disease-related death rate of the AIDS cases. The parameter σ is referred to as the perturbation parameter.

The basic reproduction number for the deterministic model ($\sigma = 0$) has already been computed in the paper of Cai et. al [12], thus we have

$$R_0 = \frac{c\beta K(\mu + k_2 + \alpha + bk_1)}{(\mu + k_1)(\mu + k_2) + \mu\alpha}. \tag{7.2}$$

7.3 Stability of Solutions

Like with any ordinary and partial differential equations in a deterministic setting (ODE's and PDE's), the two most basic questions on an SDE system are those of existence and uniqueness of solutions. To obtain existence and uniqueness results, one has to impose reasonable regularity conditions on the coefficients occurring in the differential equation. Naturally stochastic differential equations (SDE's) contain all the complications of their non-stochastic counterparts and more.

Existence and positivity of global solutions are sometimes hard to prove. In special cases, those with independent perturbation, there is a method that works well. In other cases, mostly where the interest is in endemic equilibria, it is difficult to prove the positivity by similar methods. We shall avoid it here. Our aim is to study stability, assuming that we have positive global solutions.

The following lemma is useful in studying exponential stability. We quote it from [50].

Lemma 7.1. *For $k \in N$, let $X(t) = (X_1(t), X_2(t), \ ..., X_k(t))$ be a bounded $\mathbb{R}^k$-valued function and let $(t_{0,n})$ be any increasing unbounded sequence of positive real numbers. Then there is a family of sequences $(t_{l,n})$ such that for each $l \in \{1, 2, \ ..., k\}$, $(t_{l,n})$ is a*

subsequence of $(t_{l-1,n})$ *and the sequence* $X_l(t_{l,n})$ *converges to the largest limit point of the sequence* $X_l(t_{l-1,n})$.

The following numbers will play a key role in the main theorem. Let ξ_0, ξ_1, ξ_2, ξ_3 and ξ_4 be positive numbers, chosen as follows:

$$\xi_1 = \mu + k_2 + \alpha + bk_1,$$
$$\xi_2 = \alpha + b\mu + bk_1,$$
$$\xi_4 = (\mu + k_1)(\mu + k_2) + \mu\alpha.$$

The numbers ξ_0 and ξ_3 will be chosen later. For now we just bear in mind that they are both positive. Let $m = \xi_2\xi_1^{-1}$. In the sequel we shall consider only the case

$$g(S, I, J) = \sqrt{2}(I + mJ) \tag{7.3}$$

of the model above. Now for any $y \geq 0$, we define the number:

$$P(y) = c\beta K(1 - y\sigma^2)\frac{\xi_1}{\xi_4}.$$

The following number, which we shall denote by R_σ, will describe the almost sure exponential stability of model (7.1):

$$R_\sigma = \max\{P(1), P(m)\}.$$

We further expand R_σ to be:

$$R_\sigma = R_0(1 - \sigma^2 \min(1, \xi_2\xi_1^{-1})).$$

We continue by preparing notation and concepts for our main theorem, which is the theorem on almost sure exponential stability.

Suppose we have a positive solution $(S(t), I(t), J(t), A(t))$.
Let

$$Z(t) = \xi_0(K - S(t)) + \xi_1 I(t) + \xi_2 J(t) + \xi_3 A(t)$$

and let

$$V(t) = \ln Z(t),$$

Thus we have the following

$$V(t) = \ln\Big(\xi_0(K - S(t)) + \xi_1 I(t) + \xi_2 J(t) + \xi_3 A(t)\Big).$$

We now calculate LV, given by the formula.

$$LV = \frac{\partial V}{\partial t} + f^{\text{trp}}\frac{\partial V}{\partial x} + \frac{1}{2}\text{Trc}\left[g^{\text{trp}}\frac{\partial^2 V}{\partial x^2}g\right],$$

where Trc means *trace* and trp denotes the *transpose* of a matrix.

$$\begin{aligned} LV &= -\frac{1}{Z}\xi_0\left[\mu q - c\beta(I + bJ)S - \mu S\right] - \frac{1}{2}\left[\frac{\xi_0^2\sigma^2 g^2}{Z^2}\right] \\ &+ \frac{\xi_1}{Z}\left[c\beta(I + bJ)S - (\mu + k_1)I + \alpha J\right] - \frac{1}{2}\left[\frac{\xi_1^2\sigma^2 g^2}{Z^2}\right] \\ &+ \frac{\xi_0}{Z}\left[k_1 I - (\mu + k_2 + \alpha)J\right] + \frac{\xi_3}{Z}\left[k_2 J - (\mu + \delta)A\right] \\ &- \left[\frac{\xi_0\xi_1\sigma^2 g^2}{Z^2}\right] \end{aligned}$$

Now we define the following limits:

$$s = \lim_{n\to\infty} S(t_n), \quad i = \lim_{n\to\infty}\frac{I(t_n)}{Z(t_n)}, \quad j = \lim_{n\to\infty}\frac{J(t_n)}{Z(t_n)}, \quad a = \lim_{n\to\infty}\frac{A(t_n)}{Z(t_n)},$$

and

$$q = \lim_{n\to\infty}\frac{K - S(t_n)}{Z(t_n)}.$$

These limits exist due to Theorem 7.1.

In particular we note that $\xi_0 q + \xi_1 i + \xi_2 j + \xi_3 a = 1$ and $\xi_0 q, \xi_1 i, \xi_2 j, \xi_3 a \in [0,1]$.

Then we define $F(\xi)$ as:

$$F(\xi_0, \xi_1, \xi_2, \xi_3) = \limsup_{t\to\infty} LV(t).$$

Therefore $F(\xi)$ takes the form:

$$\begin{aligned} F(\xi) &= \xi_0\left[-\mu q + c\beta(i+bj)s\right] + \xi_1\left[c\beta(i+bj)s - (\mu+k_1)i + \alpha j\right] \\ &\quad + \xi_2\left[k_1 i - (\mu+k_2+\alpha)j\right] + \xi_3\left[k_2 j - (\mu+d)a\right] \\ &\quad - \frac{1}{2}\left[(\xi_0+\xi_1)\sqrt{2}\sigma(i+mj)\right]^2. \end{aligned}$$

7.4 The main theorem

Theorem 7.2. *The disease free equilibrium of the system (7.1) is almost surely exponentially stable if*

$$\limsup_{t\to\infty} LV(X(t)) < 0 \quad \text{(a.s.)}.$$

Proof. We start off by noting that

$$V(X(t)) = V(X(0)) + \int_0^t LV(X(u))du + (\xi_1-\xi_0)\sigma\int_0^t \frac{g(S(u),I(u),J(u))}{Z(X(u))}dW(u).$$

Note that the quadratic variation of the stochastic integral

$$\int_0^t \frac{g(S(u),I(u),J(u))}{Z(u)}dW(u)$$

is

$$\int_0^t \Big(\frac{g(S(u),I(u),J(u))}{z(X(u))}\Big)^2 du$$

In view of the condition on g in (7.3), it follows that

$$\frac{|g|}{z} \le \sum_{i=0}^{3}\frac{|g_{i+1}|}{\xi_i} \le \sum_{i=0}^{3}\frac{C_{i+1}}{\xi} = C,$$

and C is a uniform (finite) upper bound.

Consequently

$$\int_0^t \Big(\frac{g}{z(X(u))}\Big)^2 du \le Ct.$$

The strong law of large numbers for local martingales, see [33] for instance, implies that

$$\lim_{t\to\infty}\frac{1}{t}\int_0^t \frac{g(S(u),I(u),J(u))}{z(X(u))}dW(u)=0 \text{ (a.s.)}$$

Also, we observe that

$$\lim_{t\to\infty}\frac{1}{t}V(X(0))=0.$$

Therefore

$$\limsup_{t\to\infty}\frac{1}{t}V(X(t))=\limsup_{t\to\infty}\frac{1}{t}\int_0^t \mathcal{L}V(X(u))du \quad \text{(a.s.)}$$

This completes the proof. □

Theorem 7.3 *If $R_\sigma<1$, then restricted to the subset Ω_1, the infection-free equilibrium E_0 is almost surely exponentially stable, where*

$$\Omega_1=\{w\in\Omega \mid (S(t,w(t))),I(t,w(t)),J(t,(w(t))),A(t,w(t))\in\Delta \text{ for } t\geq 0\}$$

.

Proof. Let us assume that $R_\sigma<1$. It suffices to prove that $Z(t)$ a.s. converges exponentially to 0 since all the numbers ξ_i are positive. By definition (7.1) it suffices to prove that $F(\xi)<$. The idea is now to find values of ξ_0 and ξ_3, if possible, such that

$$F(\xi)<0.$$

The number ξ_0 is chosen sufficiently small such that the following two inequalities hold:

$$\xi_0(c\beta K+\sigma^2)+\left[(\mu+k_1)(\mu+k_2)+\mu\alpha\right](P(1)-1)<0.$$

$$\xi_0(bc\beta K+m\sigma^2)+b\left[(\mu+k_1)(\mu+k_2)+\mu\alpha\right][P(m)-1]<0.$$

Having chosen ξ_0, the number ξ_3 is chosen sufficiently small such that the following inequality holds:

$$\xi_0(bc\beta K+m\sigma^2)+b\left[(\mu+k_1)(\mu+k_2)+\mu\alpha\right][P(m)-1]+k_2\xi_3<0.$$

Noting that $s < K$, and rearranging the terms, we obtain the following inequality:

$$\begin{aligned} F(\xi) &\leq q(-\mu\xi_0) + i\left[c\beta K(\xi_0+\xi_1) - (\mu+k_1)\xi_1 + k_1\xi_2\right] \\ &\quad + j\left[c\beta K(\xi_0+\xi_1)b + \alpha\xi_1 - (\mu+k_2+\alpha)\xi_2 + k_2\xi_3\right] \\ &\quad + a(-(\mu+\alpha)\xi_3) - \left[(\xi_0+\xi_1)\sigma(i+mj)\right]^2. \end{aligned}$$

Now we simplify the term in the F-inequality that comes from the diffusion part. We denote it by D.

$$\begin{aligned} D &= -\sigma^2(\xi_0+\xi_1)^2(i+mj)^2 \\ &\leq -\sigma^2\xi_1^2[i+mj]^2 \\ &= -\sigma^2(\xi_1 i + \xi_2 j)^2. \end{aligned}$$

Since $\xi_1 i + \xi_2 j = 1 - \xi_0 q - \xi_3 a$ we get:

$$\begin{aligned} D &\leq -\sigma^2(\xi_1 i + \xi_2 j)(1 - \xi_0 q - \xi_3 a) \\ &= -\sigma^2(\xi_1 i + \xi_2 j) + \sigma^2(\xi_1 i + \xi_2 j)(\xi_0 q - \xi_3 a) \\ &\leq -\sigma^2(\xi_1 i + \xi_2 j) + \sigma^2(\xi_0 q - \xi_3 a), \end{aligned}$$

The latter inequality follows because $\xi_1 i + \xi_2 j \leq 1$. Therefore we can express $F(\xi)$ in an inequality as follows:

$$F(\xi) = C_0 q + C_1 i + C_2 j + C_3 a,$$

where

$$\begin{aligned} C_0 &= \xi_0(-\mu + \sigma^2), \\ C_3 &= \xi_3(-\mu + \alpha + \sigma^2), \\ C_1 &= \xi_0(c\beta K + \sigma^2) + c\beta K\xi_1 - (\mu+k_1)\xi_1 + k_1\xi_2 - \xi_1\sigma^2, \\ C_2 &= \xi_0(c\beta Kb + m\sigma^2) + c\beta Kb\xi_1 + \alpha\xi_1 - (\mu+k_2+\alpha)\xi_2 + \xi_3 k_2 - \xi_2\sigma^2 \ . \end{aligned}$$

By the assumptions we have $C_0 < 0$ and $C_3 < 0$. Regarding C_1, we note that

$$-(\mu+k_1)\xi_1 + k_1\xi_2 = -(\mu+k_1)(\mu+k_2) - \mu\alpha = -\xi_4,$$

and therefore

$$C_1 = \xi_0(c\beta K + \sigma^2) + [(\mu + k_1)(\mu + k_2) + \mu\alpha] \Big(P(1) - 1\Big) < 0.$$

Also note that

$$\alpha\xi_1 - (\mu + k_2 + \alpha)\xi_2 = -b\left[(\mu + k_1)(\mu + k_2) + \mu\alpha\right],$$

and thus

$$\begin{aligned} C_2 &= \xi_0(bc\beta K + m\sigma^2) + bc\beta K\xi_1 - b\left[(\mu + k_1)(\mu + k_2) + \mu\alpha\right] + \xi_3 k_2 - \xi_2\sigma^2 \\ &= \xi_0(bc\beta K + m\sigma^2) + b\left[(\mu + k_1)(\mu + k_2) + \mu\alpha\right][P(m) - 1] + k_2\xi_3 < 0. \end{aligned}$$

This implies that also $C_2 < 0$. Note that the limits q, i, j, a cannot all be zero. So $F < 0$ and this completes the proof. □

7.5 Numerical Simulation

In this section we simulate the model (7.1) at different set of parameters. The fig.(7.1) and (7.2) show the variation of $S(t), I(t), J(t), A(t)$ within time that is the disease free equilibrium and the endemic equilibrium. In the figures in (7.2)-(7.5), we use them to verify the greatness of a noise in cases where $R_0 < 1$ and $R_0 > 1$. The figures (7.4) and (7.5) shows that whenever $R_0 < 1$, then $(S(t), I(t), J(t), A(t))$ converge almost surely to E_0. In fig.(7.3) the endemic equilibrium becomes more unstable due to the noise and the solution of the model system (7.1) converges to almost surely to E_0 when $R_0 > 1$.

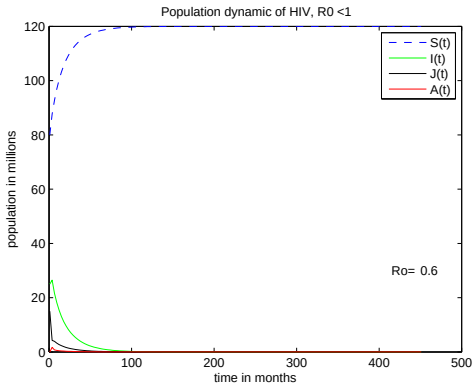


Figure 7.1: Stochastic trajectories epidemic model (7.1) for the parameters values: $K = 120$, $\delta = 0.2$, $\alpha = 0.2$, $\beta = 0.0099$, $b = 0.07$, $\mu = 0.098$, $c = 0.059$, $k_1 = 0.05$, $k_2 = 0.04$, $\sigma = 0$.

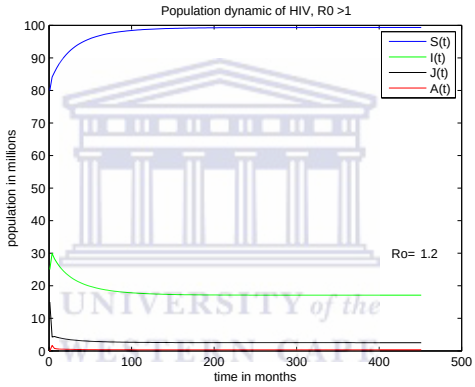


Figure 7.2: Stochastic trajectories of epidemic model (7.1) for the parameters values: $K = 120$, $\delta = 0.2$, $\alpha = 0.2$, $\beta = 0.02$, $b = 0.07$, $\mu = 0.098$, $c = 0.059$, $k_1 = 0.05$, $k_2 = 0.04$, $\sigma = 0$.

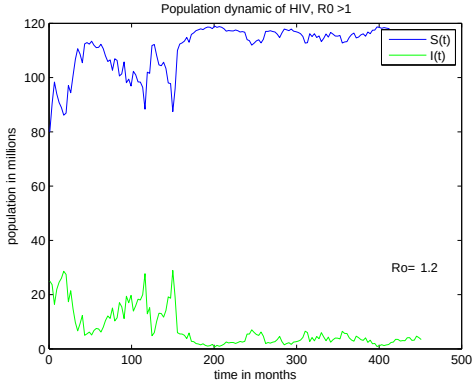


Figure 7.3: Stochastic trajectories of epidemic model (7.1) for the parameters values: $K = 120$, $\delta = 0.2$, $\alpha = 0.2$, $\beta = 0.02$, $b = 0.07$, $\mu = 0.099$, $c = 0.059$, $k_1 = 0.05$, $k_2 = 0.04$, $\sigma = 0.079$.

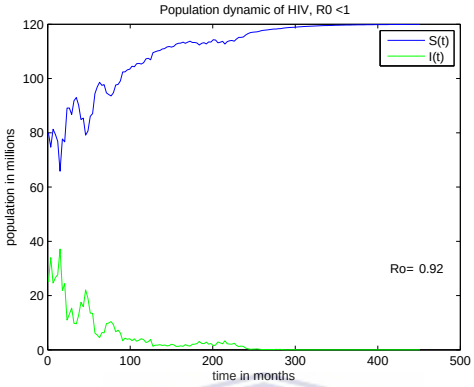


Figure 7.4: Stochastic trajectories of epidemic model (7.1) for the parameters values: $K = 120$, $\delta = 0.2$, $\alpha = 0.2$, $\beta = 0.01013$, $b = 0.85$, $\mu = 0.02$, $c = 0.03$, $k_1 = 0.08$, $k_2 = 0.09$, $\sigma = 0.060$.

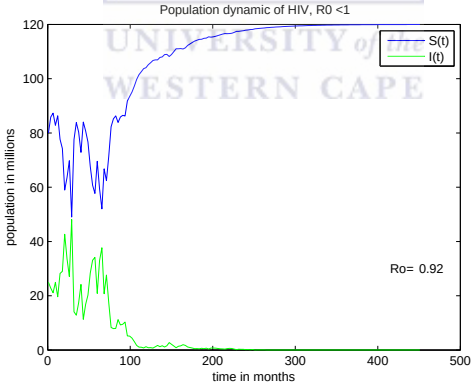


Figure 7.5: Stochastic trajectories of epidemic model (7.1) for the parameters values: $K = 120$, $\delta = 0.2$, $\alpha = 0.2$, $\beta = 0.01013$, $b = 0.85$, $\mu = 0.02$, $c = 0.03$, $k_1 = 0.08$, $k_2 = 0.09$, $\sigma = 0.080$.

Chapter 8

Conclusion

In this dissertation we have been dealing with HIV/AIDS treatment model with public health education. How can we find ways to stabilize the HIV/AIDS? We have seen throughout the paper that we were using R_0 as a threshold quantity that determines whether a disease can invade a population. In Chapter 3 we specifically considered global stability of the disease free equilibrium and simulations. By using all treatment methods, individuals with the symptomatic phases can be recovered back into the asymptomatic class. The dynamics behavior of the ordinary differential equation treatment model (5.2) can be determined by its basic reproduction number R_0, for example if $R_0 \leq 1$, the disease-free equilibrium is globally stable. If $R_0 > 1$, the disease persists and the unique endemic equilibrium is globally asymptotically stable. We use the optimal control theory to identify optimal roll-out of strategies to control the HIV/AIDS.

We looked also on the stochastic model describing the population dynamics of an HIV/AIDS epidemic. We proved the almost sure exponential stability of the system (7.1) under suitable conditions. We have proved in particular that the stochastic perturbation does not destabilize the disease free equilibrium, i.e., whenever $R_0 < 1$, then the disease free equilibrium is almost surely exponentially stable.

Instead of waiting for disease-related symptoms, creating awareness in the population

through campaigns about the disease is necessary for individuals to get tested early and know their HIV status. Depending on how much effort is invested and how the population responds to the information, campaigns help early testing. Once knowing their HIV status, the starting time of the treatment is decided by the countries policy on treatment. In our theoretical strategy, every HIV positive individual is eligible for treatment irrespective of the age of infection, in other words irrespective of the $CD4^+$ count. Introducing treatment at different ages of infection before developing AIDS-related diseases affects the dynamics to reduce the effective reproduction number even though it is greater than one and the disease remains endemic in the population.

In all the Models above public health Campaign plays a very important role in decreasing the spread of HIV/AIDS. In all the three model we have seen that total withdrawal from sexual activities of some HIV positive individuals has a great potential to tame the HIV/AIDS epidemic. Educating those infected with HIV/AIDS and those around them on the effects of the disease, how it is transmitted, safe sex practices may cause behavioral changes that can reduce HIV/AIDS infections. We have also noted that by giving free antiretroviral drug to HIV positive individuals in countries where the resources are limited can reduce HIV/AIDS. In Bhunu et al. [7], individual who are getting tested and changing the sexual behavior would mean being put to antiretroviral drug and having one's health improved. In all the three model education is the key to reduce the effect of HIV/AIDS, as individual turn to withdraw or decrease in sexual behavior.

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