MATHEMATICAL MODELING OF HIV/AIDS DYNAMICS AMONG THE FISHERFOLK AS A VECTOR FOR HIV: A CASE STUDY OF LAKE VICTORIA METAPOPULATIONS

BY

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DECLARATION

Declaration by the Student

I declare that this is my original work and has not been presented in any academic or other institution for academic award or other purposes. No part of this document should be copied or reproduced electronically or by other means without a written permission from the author, or the University of Eldoret.

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ABSTRACT

HIV/AIDS pandemic has remained the leading causes of death among the sexually transmitted diseases. To date, there has been no cure, and all the intervention measures involve preventive and reduction of the severity of the spread. Several dynamics related to HIV/AIDS have been studied using mathematical models, but the study of the spread of HIV by a vector has not been exhausted. In this study, HIV/AIDS is considered as a human 'vector borne' disease, where both the host and the vector is affected. This is possible with the definition of Fisherfolk, as a unique group of people with significantly different disease characteristics, and thus seen to play the role of a vector in the transmission of HIV. This is based on reported high prevalence of HIV among the Fisherfolk, of up to 4 times of the rest of the susceptible. A mathematical model will be formulated, and analyzed to arrive at the following objectives. The first task was to formulate a mathematical model using differential equations to describe human HIV/AIDS disease dynamics of Fisherfolk and normal population around Lake Victoria. The formulated model was then analyzed for the well posedness, in terms of stability, positivity and boundedness to ensure feasible and realistic solutions. In order to optimize the controls, the system was then expressed as a linear programming problem, and used to determine the threshold values of parameters for optimality of disease control measures. Finally, the system was coupled and tested for synchronization, stability and robustness under small perturbation, through All-to-All coupling topology. The achievement of these objectives were realized with the use of the following methods; compartmental formulation of mathematical model, coupling using nearest neighbor and all to all configuration, and use of Lyapunov type numbers to test stability and robustness under small perturbation. The study results found using a system of eight ordinary differential equations that two equilibrium points exists, disease free equilibrium (DFE) and endemic equilibrium point (EEP). DFE was found to be asymptotically stable whenever $R_0 < 1$. Intervention strategies like public health education and treatment were found to stabilize periodic solutions of EEP when $R_0 > 1$. Synchronization manifold of all to all coupling configuration was determined to be stable under small perturbations with a coupling strength of $k_0 \geq 1.1137$. This means interaction of a minimum of 12% of the population will lead to synchronization of metapopulations, and therefore any intervention strategy should exceed a threshold of 12% of the population. The findings are valuable to public health and government for planning and budgeting on the desired cost of treating the public, together with other strategies of minimizing interaction through creation of markets, control of fishing points through licensing bottlenecks, and other mitigation strategies to reduce the scourge. This will improve the human resource capacity and improve on fish production in the region.

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CHAPTER ONE

INTRODUCTION

1.1 Background of the study

Mathematical modeling involves the use of mathematical formula to create a system which mimics a real phenomenon. Mathematical biology, involves the use of mathematical relations and formula to represent a biological system. Mathematical epidemiology on the other hand, is a branch of mathematical biology, which deals with epidemics. Mathematical equations in this case should give information on the speed of the spread, sensitivity of factors causing the spread, the nature of the epidemic, whether it will persist or if it will die off, the effect of intervention strategies, for example isolation, vaccination, treatment, public health education, and use of contraceptives and many other intervention strategies.

Modeling infectious diseases is efficiently done using compartmental modeling.

1.2 Mathematical Modeling

Mathematical modeling is the process of representing a real physical phenomenon using mathematical equations, in order to mimic the reality. He purpose of modeling is to create an opportunity to assess the effects of varying parameters which represent a specific characteristic of the intended phenomenon. For example in modeling infectious diseases, a researcher may be interested in the effect of vaccination. A parameter is introduced in the model to account for the effect of vaccination, and this value is varied to determine, the minimum value that yields the desired results, in terms of herd immunity and cost.

During modeling, the process involves formulating a general model, then trimmed using Occam's razor theory (Domingos, 1999), to reduce complexity and represent the salient

features without affecting the qualitative dynamics of interest. In this regard, compartmental techniques were used to represent our model.

Suppose one considers a totally susceptible homogeneous population in an isolated community. The only changes expected are the recruitment rate through birth and the elimination rate through deaths. This can be represented by the diagram in Figure 1.1.

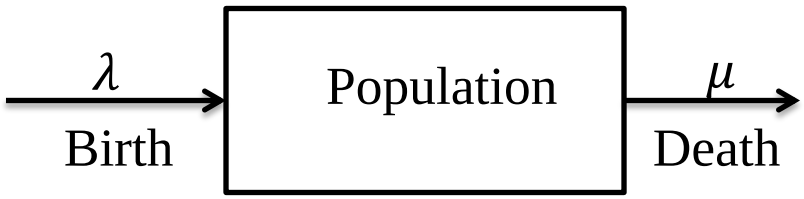

Figure 1.1 Simple Population model with Demographics

Notice that if the birth rate λ equals t the death rate μ, the population remains constant. Here, it is assumed that other sources of human population like migration and occurrence of catastrophes and natural phenomenon, which significantly affects the total population are not significantly affecting the dynamics.

An ordinary differential equation equivalent to the flow chart in Figure 1.1 is given by;

$$\frac{dP(t)}{dt} = (\lambda - \mu)P(t); \;\; P(0) = P_0 \tag{1.1}$$

which describes the population dynamics with demography. If the birth rate is greater than the death rate, that is, $\lambda > \mu$ the population grows exponentially, otherwise it decays exponentially, with the solution;

$$P(t) = P_0 e^{(\lambda-\mu)t} \tag{1.2}$$

Suppose one considers a situation of modeling disease dynamics in a population. In this case, we define unique disease stages that are of interest. These stages include susceptible class, infective class, and the removed class (which do not contribute to the dynamics of the others). This is commonly known as SIR model, and represented by a diagrammatic model with three compartments, and arrows showing the flow of individuals from one class to the other, as denoted in Figure 1.2.

Parameters defining the flow rate from one compartment to the other will be placed along the arrows joining the compartments. These parameters are either variable, to be investigated or fixed as obtained from data collection.

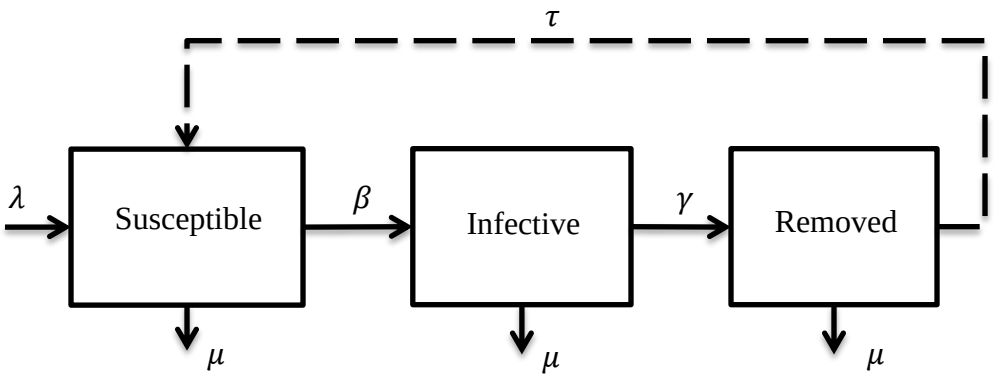

Figure 1.2 SIR Model with demographics

The removed class (R) represents all the group of people who were once infected but either became immune, treated, vaccinated or died, and thus do not contribute to the disease dynamics again. In Figure 1.2, the transmission parameters denote; λ constant recruitment rate, μ natural mortality rate, β force of infection, γ progression rate from infective state to removed state, and τ is the rate of loss of immunity and thus reinfection.

For some diseases, people once infected are conferred immunity temporarily, and once the immunity wanes, they become susceptible again, and therefore indicated by the dotted arrow in Figure 1.2, from the removed class back to the susceptible class. In other cases, the removed class is labelled as recovered, or death or for the case of HIV/AIDS, it may be labelled as AIDS class. This compartment represent the group of people who are at the last irreversible class, unless through loss of immunity. This model will be represented by a system of three ordinary differential equations, with mortality rate assumed to be equal in all compartments.

In this study, a similar model to the one in Figure 1.2 will be used, but with two sets of populations, the normal population and the vector population. In modeling vector borne diseases, it is important to analyze the population dynamics of the vector alongside the human population. This is because, the velocity of the disease spread depends on the number of vectors, or equally, depends on the probability of interaction of the humans and the vector. This probability is dependent on the population of the vector. The spread of diseases like malaria is dependent on the mosquito population and the control of mosquito vector will definitely lead to the control of malaria. The same case applies to all other vector borne diseases. This study explores the possibility of considering an isolated set of human population as a vector. This is qualified by the fact that the said isolated population have uniquely high prevalence of the disease, and in case of any interaction with the normal human population, there is always a one way spread of the disease from the ‘vector’ to the normal human population. The population under consideration here is the Fisherfolk community, which are known to have HIV prevalence up to more than four times higher than the normal population (Huang, 2002; Kissling et al., 2005).

A mathematical model is a description of a system using mathematical concepts and language. The process of developing a mathematical model is termed mathematical modeling. Mathematical models are used not only in the natural sciences (such as physics, biology, medicine, earth science, meteorology) and engineering disciplines (e.g. Computer science, artificial intelligence), but also in the social sciences(such as economics, psychology, sociology and political science); engineers, statisticians, operation research, analysts and economists use mathematical models quite extensively.

Simple models have additional value as they are the building blocks of models that include more detailed structure. Detailed models are difficult to solve analytically and hence their usefulness for theoretical purposes is limited, although their strategic value may be high.

One of the early triumphs of mathematical epidemiology was the formulation of a simple model that predicted behavior very similar to the behavior observed in countless epidemics. The Kermack McKendrick model (Murray, 2007) is a compartmental model based on relatively simple assumptions on the rates of flow between different classes of members of the population. The basic compartmental models to describe the transmission of communicable diseases are contained in a sequence of 3 papers in 1927, 1932 and 1933. The Kermack-McKendrick epidemic model is a special model. The general model included dependence on age of infection, that is, the time since becoming infected.

Many of the early developments in the mathematical modeling of communicable diseases date back to the late 18^{th} century. The first known result in mathematical epidemiology is a defense of the practice of inoculation against smallpox in 1760 by Daniel Bernoulli, a

member of a famous family of mathematicians (8 spread over 3 generations) who had trained as a physician. The first contributions to modern mathematical epidemiology are due to P.D En'ko between 1873 and 1894. The foundations of the entire approach to epidemiology based on compartmental models was laid by Sir Ross, Hamer, McKendrick, Kermack and Brownlee (Brauer, 2017; Murray, 2007). Sir Ross R.A. was awarded the second Nobel Prize in Medicine for his demonstration of the dynamics of the transmission of malaria between mosquitoes and humans. After Ross formulated a mathematical model that predicted that malaria outbreaks could be avoided if the mosquito population could be reduced below a critical threshold level, field trials supported his conclusions and led to brilliant successes in malaria control.

Mathematical modeling now plays a key role in policy making, including health-economic aspects; emergency planning and risk assessment; control-programme evaluation; and monitoring of surveillance data. In research, mathematical modeling is essential in study design, analysis (including parameter estimation) and interpretation.

With infectious diseases frequently dominating news headlines, public health and pharmaceutical industry professionals, policy makers, and infectious disease researchers, increasingly need to understand the transmission patterns of infectious diseases, so as to be able to interpret and critically-evaluate both epidemiological data, and the findings of mathematical modeling studies. Recently there has been rapid progress in developing models and new techniques for measurement and analysis, which have been applied to outbreaks and emerging epidemics, such as Influenza A (H1N1) and SARS (Keeling & Rohani, 2011). A simple but powerful new technique for assessing the potential of

different methods to control an infectious-disease outbreak was recently developed by course presenters.

A deterministic model describing of the spread of HIV infection of CD4+T cells was formulated and analyzed (Atangana & Doungmo Goufo, 2014). Investigations of the endemic equilibrium and disease free are done using the method of Jacobian matrix, where the iteration technique (homotopic decomposition method), was implemented to give an approximate solution of nonlinear ordinary differential equation systems and results compared with other techniques such as Runge-Kutta. The results stressed the trustworthiness of the iterative technique.

The study by (Perelson & Ribeiro, 2013) reviewed developments in HIV modeling, stressing quantitative findings about HIV biology uncovered by studying acute infection, the rate of generation of HIV variants and the response to drug therapy that escape immune responses. The study showed how modeling gave insight to dynamical features of HIV infection and gave clue to the ultimate cure for this infection.

The paper by (Brauer, 2017) presented review of works devoted to studies on Human Immunodeficiency Virus (HIV) and Acquired Immunodeficiency Syndrome (AIDS) dynamics through mathematical modeling (Buratto, Cesaretto, & Zamarchi, 2015). About a hundred papers were analyzed from 1989 to 2015. The models were distinguished according to the absence or presence of variables such as infected T Lymphocytes, precursors or immune effectors, and the absence or presence of differentiation in infected T cells, uninfected T cells and viruses. The study pointed the main features a

mathematical model should have in order to describe faithfully the complex interactions between HIV and the immune system.

The study by (Chacko, 2013), developed a mathematical model that predicts T cell/HIV dynamics by incorporating the three Lotka-Volterra interactions and other salient biological phenomena that influence the dynamics, such as T cells and the presence of viral reservoirs.

1.3 Epidemiology and HIV/AIDS

Epidemiology is the study of the spread of diseases in space and time. It involves tracing the casual factors responsible for or which contributed to their occurrences and dispersion. The threshold for many epidemiology models is the basic reproduction ratio R_0. The basic reproduction ratio is the average number of secondary infections produced when one infected individual is introduced into a host population where everyone is susceptible (Fulford, Roberts, & Heesterbeek, 2002). A disease becomes epidemic if it spreads to a large number of individuals in a given population within a short period of time (usually less than two years) and it is an endemic if it is constantly present to a greater or lesser degree in people of a certain class or certain geographical region. For many deterministic models, an infection can get started in a fully susceptible population if and only if $R_0 > 1$. The basic reproduction number is therefore considered as the threshold quantity that determined when an infection invaded and persisted in a new host population.

Despite improved sanitation, antibiotics and extensive vaccination programs, infectious diseases continue to be major causes of suffering and mortality. More importantly, infectious disease agents adapt and evolve so that new infectious diseases have emerged

and existing diseases have re-emerged. Diseases that have emerged in recent years include, Hepatitis C, Hepatitis E, Ebola hemorrhagic fever and Hantavirus (Dobson & Carper, 1996).. Human Immunodeficiency Virus (HIV) which is the etiological agent of Acquired Immune Deficiency Syndrome (AIDS) emerged in 1981 and has become the leading deadly sexually transmitted disease throughout the world. Drug and antibiotic resistance have become serious issues for diseases such as tuberculosis, malaria and gonorrhea. Malaria, dengue and yellow fever have re-emerged and are spreading into new regions as climate changes occur (Dobson & Carper, 1996).

Invasion of an infectious agent is considered to be successful if the agent is able to enter into a given patch and spread rapidly within a completely susceptible population that is, when an initially infected host is able to infect other hosts in the population. When such an invasion occurrs, then it could either go extinct after an initial epidemic or might become endemic in the population without subsequent re-invasion. In homogeneously mixing populations, infectious agents tend to become extinct when the host population size is below a critical community size (Matthew Jesse, Ezanno, Davis, & Heesterbeek, 2008). However, in metapopulations, the situation become more complex, due to the connectivity of the structure; the infection might become extinct in one patch but simultaneously invade other patches thereby increasing the risk of re-invasion in future. Inter and Intra patch dynamics in metapopulations therefore become important for the study of persistence of the infectious agent. In addition, to spatial dynamics, demographic and epidemiological processes are important factors that influenced persistence of infectious agent in metapopulations.

Acquired Immuno-Deficiency Syndrome (AIDS) is the final stage of Human-Immunodeficiency Virus (HIV) infection. It can take years for a person infected with HIV, even without treatment, to reach this stage. Having AIDS means that the virus has weakened the immune system to the point at which the body has a difficult time fighting infections. When someone has one or more of these infections and a low number of T cells, he or she has AIDS. Initial infection of HIV is usually in the macrophages. The antigen presenting cells and the phagocytes serve as a cloak for virus that can now be carried to all parts of the body through blood. Since infected CD4+ T die by apoptosis or due to lysis from infection, then as the infection develops, the immune system is depleted so that the host becomes susceptible to opportunistic diseases, (diseases that take advantage of the weakened immune system) and pathologies. AIDS is clinically diagnosed when the CD4 count is less than 200/mm^3 out of the normal range of between 800mm^3 to 1200mm^3.

The use of Highly Active Anti-Retroviral Therapy (HAART) does not treat the disease but reduces the impact of infection by controlling the levels of viruses in the body and increasing the CD4 count in the body. This increases the number of potential infectives, able to infect other individuals. There are two categories of Anti-Retrovirals (ARV's), namely; reverse transcriptase inhibitors (which interfere with the transcription of RNA to DNA thus halting cellular infection) and protease inhibitors (which interfere with post-translation viral particle assembly) Most chemotherapies reduce viral production in a dose based manner to the expense of multiple side effects and ineffectiveness after some time when the virus mutates.

According to (Kwena et al., 2019), achieving the United Nations AIDS Control (UNAIDS) goal of ending HIV by 2030 requires identifying HIV hotspots for targeted interventions to prevent new infections. The current HIV prevention approaches advocate for geographic and subpopulation targeting in investing available resources for maximum impact. Sub-Saharan Africa bears the greatest burden of the HIV epidemic described as generalized; but with substantial regional and subpopulation differences (Béné & Merten, 2008). According to (Béné & Merten, 2008) the most affected are countries in southern and eastern Africa, such as Kenya, as well as occupational subpopulations of migrant workers, sex workers, long distance truck drivers and others like injection drug users (IDU) and men who have sex with men (MSM). These populations, characterized by high HIV prevalence may sometimes act as important sources of new HIV infections to the general population.

The UNAIDS 90-90-90 targets (Sidibé, Loures, & Samb, 2016) outline that at least 90% of population should be aware of their HIV status as an entry point into care that acts both as prevention and treatment. This is more urgent in HIV hotspots to reduce transmission within the key populations and to the general population. To achieve these targets and the vision of an AIDS-free generation, it is essential to identify all most-at-risk subpopulations and provide services to increase awareness of their HIV status. Available literature from studies in small localized fishing communities from Kenya and Uganda show that Lake Victoria fishing communities, who comprise fishermen, fish traders/processors, boat owners and other traders selling assorted fishing commodities, as well as restaurant/bar workers and sex workers at the fish-landing beaches, are at a much higher risk of HIV infection compared to the general population. According to (Kwena et

al., 2019) HIV prevalence in the fish-landing beaches, defined as designated areas where fishing boats land with fish for sale, has been shown to range from anywhere between 12 to 32%.

The high risk of HIV infection among fishing communities has been attributed to many factors that are both behavioral and structural in nature. For instance, fisher-folk in many places, especially in sub-Saharan Africa including Kenya, are described as being highly mobile in pursuit of fish. As such, they are often away from homes and their families for long periods and interact with a lot of women fish traders in the course of their work.

According to (Kwena et al., 2019), in the process of these interactions, fishermen end up forming casual sexual relationships known as *jaboya (fish-for-sex)* with women fish traders, which take place within the context of perpetual low condom use and high consumption of alcohol and drugs in the fishing villages. (Kwena et al., 2019), observes that global efforts to end HIV by 2030 focus on reducing and eventually eliminating new infections in priority populations. Identifying these populations and characterizing their vulnerability factors helps in guiding investment of scarce HIV prevention resources to achieve maximum impact.

The study of infectious diseases does not only end in focusing on one particular population group. Assumptions of homogeneity of the population is not practical. There is need to look into the population in terms of patches, each with unique disease dynamics. This paves way to the analysis of coupling and arising scenarios of synchronization, stability and robustness.

(Culshaw & Ruan, 2000) studied a delay-differential equation model of HIV infection of $CD4^+$ T-cells using three compartments: the healthy $CD4^+$ T-cells, infected $CD4^+$ T-cells

and the free virus. The study examines the effects of time delay on the stability of endemically infected equilibrium. Numerical simulation to illustrate the effects of time delay is presented by the study. The study establishes that the infected steady state was stable for all $\tau \geq 0$. They also found out that under certain assumption for large values of N, the effect of delay is not as strong as for small N. This work has not considered effects of chemotherapy on the *in vivo* dynamics of HIV nor does it examine the effect of time delay on the disease free equilibrium.

(Perelson & Ribeiro, 2013) studied the dynamics of HIV infection of $CD4^+$T cells, using a system of linear ordinary differential equations. The study done by (Perelson & Ribeiro, 2013) studied various scenarios including the effects of AZT on HIV virus dynamics, but the effects of time delay on chemotherapy or on infection of $CD4^+$ T cells was not considered.

(Nelson & Perelson, 2002) studied a mathematical analysis of delay differential equation model of HIV-1 infection. This study considered delay in reference to protease inhibitor only. The study therefore has not considered time delay on HIV-1 *in vivo* dynamics in the presence of both protease and reverse transcriptase inhibitors or in the absence of treatment.

(Kirschner & Webb, 1996) studied a model for treatment strategy in the chemotherapy of AIDS. The study has looked at the interaction of HIV-1 and the immune system using a system of ODE's. A mechanistic description of chemotherapy was studied by age structuring of $CD4^+$T-cells. The effects of chemotherapy in this study was modeled using a scalar function which was assumed to be on during treatment and of

during off treatment. Two types of models were considered: age structured model and the other without age structure.

The results of the study were; one, periodicity of treatment during a given day does not reveal a significant difference in the overall effect, quantitatively or qualitatively. This means that whether one receives a 500mg dose once a day or 100mg dose five times a day, the overall result is the same. This is because the treatment serves only to perturb the system of AIDS into steady state. Two, chemotherapy should begin only after the second decline of $CD4^{+}$T-cells. Although this study has looked at various aspects in chemotherapy of AIDs, effects of time delay is not considered in the HIV-1 in vivo dynamics.

A mathematical model of HIV-1 infection including the saturation effect of healthy cell proliferation was studied under the assumption that that infection rate between healthy and infected cell is a saturating function of cell concentration (Kouche & Ainseba, 2010). Numerical simulation and stability analysis of the model was carried. The study revealed through simulation that, if less than 7.7% of infected cells survive the incubation period, the system converges to its healthy equilibrium. If between 7.7% and 30% of infected cells survive the incubation period, then system stabilize at infected equilibrium, and if more than 30% of infected cells survive the incubation period ,periodic oscillation of cell concentration was observed. Qualitatively under realistic parameter regimes, the model exhibits two Hopf-bifurcation and the infected steady state is locally asymptotically stable either when the average delay is high or small. The study also reported that the model exhibited stable periodic solutions for other delays due latency of infected cells.

Although the study looked at various scenarios on delay effects, effects of chemotherapy is not mentioned in the study.

Global dynamics of HIV infection model with two classes of target cells and distributed delays was considered in the study by (Elaiw, 2012). The study investigated the global dynamics of an HIV-1 infection with $CD4^+$T-cells and macrophages. The incidence rate is modeled by a saturation functional response. Two types of distributed delays describing the time needed for infection of target cells and virus replication has been considered. Lyapunov functional was constructed to establish the global stability of infected and uninfected steady states of the model. In this study numerical investigation is not done nor the specific effect of time delay investigated.

(Elaiw, 2012) studied a global stability models with intracellular delays. In the first of the model, delay odes are used to describe the dynamics of the interaction of HIV with two classes of target cells, $CD4^+$T-cells and macrophages taking into account the saturation infection rates. The second model is a generalization of the first one by assuming that the infection rate is given by (Bhardwaj & Das, 2020) functional response. Two time delays are used in each of the models to describe the time periods between viral entry into the two classes of target cells and the production of new virus particles. The study used Lyapunov functional and Lasalle-type theorem for delay differential equations (DDE) to establish the global asymptotic stability of the uninfected and infected steady states of the HIV infection models. The study of the effects of the time delays and the effects of chemotherapy was not considered in this study.

Infections are disorders caused by pathogenic agents such as bacteria, virus, fungi and protozoa. These are the major causes of morbidity and mortality mostly in low income nations and among children and the aged. This has elicited synergistic union of scientists in different disciplines to carry out research with the aim of understanding the spread of these infection causing pathogens in populations and also within the host. This would greatly help in the prevention and treatment of these infectious pathogens. The immune system is spread throughout the body and comprise of organs, tissues, cells and proteins that help the body fight these infectious agents and maintain the overall integrity of host's health. Human beings are always at risk invasion by these infectious agents and have therefore evolved a system to eliminate these infective agents in the body, which is the immune system defense. The immune system is essential for the survival of the host with over 15% of genes in human genome being associated to immune function (Saxena et al., 2012). Generally everyone's immune system has unique qualities different from another but in all hosts the immune system becomes stronger with age to some extent. This is partially because by the time of adulthood one will have encountered more pathogens and developed more immunity. A distinguishing and unique feature of the immune system is in its ability to differentiate an un offending pathogen like embryo in a mother and an offending pathogen like a virus. It is also able to identify pathogens previously encountered and those not previously encountered. This is a sophisticated process and is carried out by a host of cells each specialized in their functions in conjunction with biochemical substances such as enzymes and other proteins.

There are three distinct types of immunity in humans that are aimed at fighting pathogens: innate, specific adaptive and passive immunity. Innate immunity is present at

birth, it is nonspecific and offers the first line of defense. It is activated when an offending pathogen is encountered and recognized because of its specific molecular pattern. It includes exterior barriers like the skin, mucous membrane and secretions.

The adaptive immune system has two main branches that fight infectious agents, the Cell Mediated Immunity and the antibodies. Cell mediated immunity are those specific immune responses in which antibody plays only a minor or subsidiary role. This immunity mainly involves the lytic activity of cytotoxic T Lymphocytes (CTL) to fight and eliminate intracellular pathogens The CTL cells are produced in the bone marrow and matures in the thymus and are maintained in naive in secondary lymphoid organs. Cell mediated immunity is activated when a pathogen is presented by antigen presenting cells and identified as offending. This process leads to an immune response characterized by three phases: cellular expansion, contraction and memory cell generation (Rocha & Tanchot, 2004).

Cytotoxic T Lymphocytes Cells (CTL) cells mainly defend the host against virus in the intracellular phase and against intracellular bacteria and protozoa. The CTL cells detect pathogen driven groove of (Major Histocompatibility Cells) MHC-1 class I as presented by the Antigen Presenting Cells (APCs), key among them the Dendritic cells. It has also the ability to examine inside the cell to establish its status, whether it is damaged or healthy. Normally cells can not examine what could be happening inside other cells. By this cell-cell examination MHC class I provides a way of detecting cell normally allowing the immune system to expose the infected cells (Terry, Marvel, Arpin, Gandrillon, & Crauste, 2012). Passive immunity also called ’borrowed’ immunity happens when immunity is passed from one source to another as it happens during breast

feeding following birth or when the mother passes antibodies to an unborn child through the placenta. This immunity is short lived and is important in protection of a new born in the early years. However, it must be understood that technically mathematical model description and explanations of a biological behaviour are not necessarily the explanations given by Biosciences. Mathematical modeling and analysis is critical and must be used if any understanding will be converted from theoretical to predictive and quantitative science. The aim of mathematical modeling is not to develop a model that incorporates every aspect of the observed behaviour, if this was at all possible. If every detail was to be incorporated the resulting model would be too complex to give any meaning understanding of how crucial interactions within the system work. Rather it is to develop a model that incorporates important and critical interactions whose outcome cam be understood (Murray, 2007).

1.4 Metapopulations and Coupled Biological Oscillators

Many population models assume that individuals mix homogeneously implying that all individuals in the population are equally likely to encounter each other. In reality however, many populations are structured in space and are interconnected by human travel. The population may therefore be sub-divided into spatially separated patches also known as the subpopulations. These patches are connected to each other by migration of the hosts. Moreover, each patch has its own dynamics which are influenced by both immigration and emigration. Such a distinct group of sub-population is known as a metapopulation.(Jesse, et al 2008). Metapopulation is therefore a fragmented population in which population dynamics occurs at two distinct levels. These levels are;

i) Within patch dynamics and

ii) Between patch dynamics.

In a metapopulations, a patch is said to be infected if it contains at least one infected individual. In the simplest metapopulations models, individuals are assumed to migrate randomly among patches thus there is no spatial dimension. Such a model is known as spatially implicit model (Matthew Jesse et al., 2008).

In this type of model, metapopulations is assumed to be divided into separate patches but their spatial dimension between the patches is neglected. In contrast, the patches may also be structured in a network with explicit spatial dimension as seen in Figure 1.3. In this structure each patch is viewed as a node or an oscillator in the network and is connected to other patches/oscillators by an edge. These edges represent both immigration and emigration between the patches. These edge connections are called coupling. Different coupling yields various lattice structures. The nature of coupling determines the type of connection topology obtained. Frequently, systems of subpopulations are arranged in geometric structures, with nearest neighbour coupling; that is, the subpopulations are linked to their immediate neighbours (Wasike & Rotich, 2007).

According to (Wasike & Rotich, 2007), there were different forms of nearest neighbour coupling. Some of the various types of nearest neighbour coupling structures are as shown in Figure 1.3. That is (a) Coupling on a line; like in chemical reactors systems and neural networks, (b) Nearest neighbour coupling on a ring; like in chemical reactors, (c) Coupling on a two dimensional Bravais lattice, (d) One-to-all coupling, (e) All-to-all coupling and (f) subpopulations coupled to their nearest neighbour in a three dimensional Bravais lattice. Dynamics of the disease in a subpopulation can be described as an

oscillator. Oscillators can be modeled using ordinary differential equations (ODE's), partial differential equations (PDE's) or delay differential equations (DDE's). The scope of this study revolves around oscillators described by ordinary differential equations. Since there can be no oscillations in one state variable, for the case of an ordinary differential equation there must be at least two state variables.

Consider a biological oscillator governed by the solutions of the first order ordinary differential equation

$$\dot{z}(t) = g(z) \tag{1.3}$$

Where the dot "." denotes the derivative with respect to time t, and the z is the state variable and g is some function. The connection topology described in Figure 1.3 can be represented by the coupled system

$$\dot{z} = A(k)z + f(z) \tag{1.4}$$

Where $f(z) = g(z_1), g(z_2), \dots, g(z_n)$ and $A(k)$ is the coupling configuration matrix with k as the coupling strength. The Coupling matrix A is linear for nearest neighbour and all to all coupling. If the system (1.2) has a global attractor $\mathcal{A}_k$ for every $k > 0$, then it indicates that the system is synchronized. That is to mean that there exists a bounded invariant manifold, where

$$\mathcal{M}_1 \coloneqq (z \in \mathbb{R}^n : z_1 = z_2 = \cdots = z_n \neq 0) \tag{1.5}$$

This means the space $\mathcal{M}_1$ is not varying, so that solutions starting on $\mathcal{M}_1$ remains in the same space as time increases. The solutions are also bounded above and below.

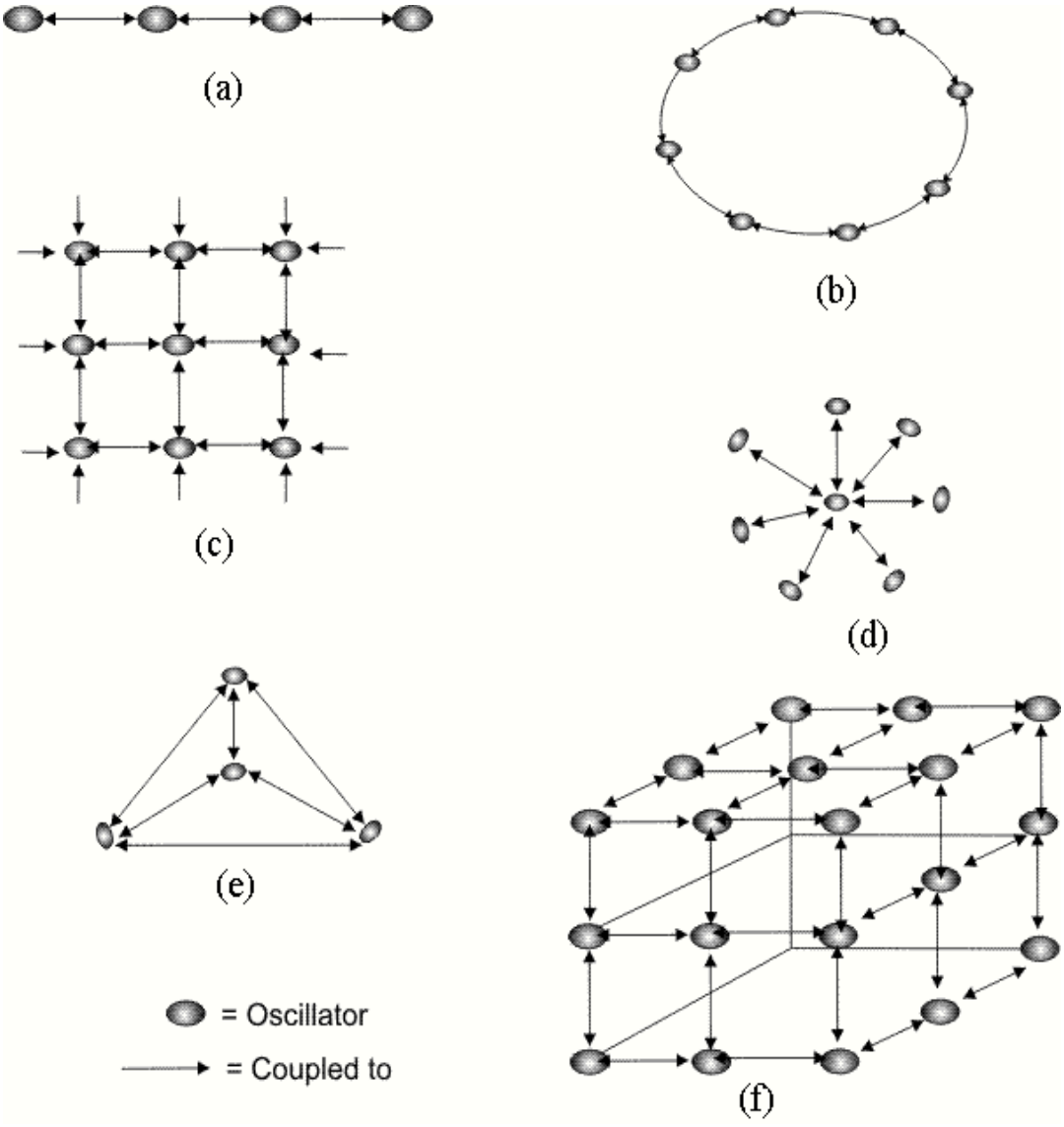

Figure 1.3 Oscillators Coupled in Different Coupling Topologies. Source: Author

An oscillator is defined as a set of differential equations which have a non-constant periodic solution, which changes from one point to another, and with respect to biological oscillators, refers to the set of differential equations which represents a biological phenomenon with non-constant repeating behavior. These includes for example the heart pacemaker, occurrence of diseases, menstrual cycle, hormone imbalance, flickering of fireflies, just to mention but a few. The subtle concept of study in this case is the

existence of invariant manifold and synchronization of coupled oscillators. Apart from synchronization, which refers to the situation in which each oscillator behaves in the same way as the others in such a way that the knowledge of one, infers to the behavior of the other, and the difference of the behavior of each oscillator is zero, it is also important to study robustness of the synchronization manifold.

In this study, the dynamics of HIV/AIDS among the Fisherfolk is considered as periodic, and thus forming an oscillator. Considering population patches, and their interaction, the dynamics of HIV/AIDS among Fisherfolk metapopulations in Lake Victoria region in Kenya is investigated. Lake Victoria is the source of river Nile, and around Lake Victoria, there are distinct patches of communities who live around the lake, and due to the geographical nature of the lake, the individual patches are separated by space and only interact due to common market or common fishing grounds. On the other hand, the HIV/AIDS prevalence among the Fisherfolk is significantly higher than that of the normal population, up to about four times higher (Kissling et al., 2005).

1.5 Statement of the Problem

HIV/AIDS pandemic is an infectious disease which has lasted over four decades, with no curative strategy available. All the chemotherapeutic strategies available are purely preventive, and treatment of opportunistic diseases. The scourge is still heavy and the spreading velocity still high, and thus affecting the workforce and general wellbeing of the population. This includes economic impact as a result of therapeutic cost. The disease prevalence is high, but alarming for a specific community (Fisherfolk), because of their behavior, which includes barter trade of fish in exchange of sexual intercourse (Béné & Merten, 2008). Besides the analysis of data on prevalence, it is necessary to consider the

prognostic dynamics of the diseases as to find a lasting intervention strategy on the control of the spread. Because the Fisherfolk have extraordinary prevalence rate as compared to the normal population, this community is considered as a kind of an agent that carries and transmits disease pathogens to the normal human population, thus the ley are labelled as ‘HIV vector’.

Considering Fisherfolk as HIV vector, the dynamics of coupling, interaction, synchronization, stability and robustness of the metapopulations is necessary in order to determine the optimal disease control parameters to curb the spread of the pandemic. As chemotherapy is sought, there is need for some preventive intervention strategy, which can be employed by the public health, apart from the usual ABC (Abstinence, Being faithful and Contraceptive). This does not suggest to propose a kind of isolation and imprisonment of HIV victims, but a way of understanding how interaction through coupling can permeate the spread of the disease into new population patches. This phenomenon can be understood through formulation of a mathematical model, with parameters describing control strategies. Due to the periodic solution of each system, coupling allows for the study of synchronization and stability of the invariant manifold. Occurrence of other dynamics like bifurcation will necessitate the analysis of stability and robustness of the manifold. Besides that, there is need to simulate results and determine the optimal threshold values of control parameters, like coupling strength, stability, persistence and diffusivity across the metapopulations.

It is for this reason that this study intended to study Fisherfolk as HIV vector, and the dynamics of coupled metapopulations.

1.6 Objectives of the study

1.6.1 General Objective of the Study

The general objective of this study was to formulate a mathematical model, which describes HIV/AIDS dynamics among the Fisherfolk, as a HIV vector and the impact of HIV prevalence rate All-to-All coupling with neighbouring and interacting Lake Victoria fishing metapopulations.

1.6.2 Specific Objectives

The specific objectives of this study were;

i) To formulate a mathematical model using differential equations to describe human HIV/AIDS disease dynamics of Fisherfolk and normal population around Lake Victoria.
ii) To analyze for the well posedness of the model, in terms of stability, positivity and boundedness of model solutions.
iii) To express the model in form of a linear programming problem, and determine the threshold values of parameters for optimality of disease control measures.
iv) To analyze the existence of synchronization manifold, study it's stability and robustness under small perturbation, through All-to-All coupling topology.

1.7 Significance of the Study

The success of the study produces results which are very important to the government on policy formulation of the control strategies of HIV pandemic. It is well known how the disease affects the workforce and the economy of the country, and such policies will

alleviate the population of the poverty situation which is arising due to heavy financial burden on ARV's and general care of people living with HIV/AIDS.

The other significance is to the researchers. This study produces results that forms the foundation to a new dimension of disease control. There is a possibility of controlling the levels of interaction of coupled metapopulations using methods like establishing fishing boundaries and creating markets for every community. This study provided information on the efficiency of such control methods on the spread of HIV/AIDS.

The other significance is the dimension of optimal control strategy. The study provides information on the minimum efforts required to control the pandemic. This information will guide on budgetary allocation to avoid a situation where unnecessary excess resources or insufficient resources are allocated to such intervention strategies.

1.8 Operational Definition of Terms

The following terms are used in the Thesis and are therefore defined.

Invariant Manifold

A set $\mathcal{M}_1$ is said to be invariant under the flow defined by equation (1.4) if picking any initial point on the ,manifold $z_0 \in \mathcal{M}_1$ the solution $z(t; z_0) \in \mathcal{M}_1$ for all $t \geq 0$.

Manifold

A Manifold is a set which locally has a structure of Euclidean space. They are m-dimensional surfaces embedded in the real space. If the function in equation (1.4) is describing a surface which has maximal rank, with non-zero Jacobian, then by implicit theory, this surface can be represented locally by a graph. The surface is a smooth manifold if the graph representing it is smooth.

CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

The World Health Organization (WHO) report of 2004 stated that, AIDS was discovered in 1981 and has become one of the leading causes of death, globally, affecting mostly impoverished people already suffering from poor nutrition and health (WHO, 2008). HIV stands for human immunodeficiency virus; it is a virus that attacks the immune system. While HIV does not kill, it causes the immune system to become defenseless against other opportunistic diseases it could normally fight off. According to (Abu-Radded, 2007), HIV/AIDS has killed an estimate of 25 million people globally. The HIV/AIDS epidemic has had a major impact throughout the world. In December 2007, the World Health Organization (WHO) and joint United Nations Programme on HIV/AIDS (UNAIDS) estimated that there are 33 million people living with HIV. Most of these people are unaware of their HIV infection and, as a result, unknowingly contribute to the spread of the infection (WHO, 2008). The epidemic has disproportionately affected people residing in areas of the world that have fewer resources to combat the disease. The (WHO, 2008) further estimated that there were 2.7 million people who were newly infected with HIV in 2007 and greater than 95% of these new infections occurred among persons residing in Low and Middle Income Countries (LMIC). Sub-Saharan Africa accounts for an estimated 22 million cases of HIV/AIDS and has an estimated prevalence of 5% in adults ages 15-49. In these LMIC, (WHO, 2008) says that the HIV/AIDS epidemic has often over-burdened the under-resourced health care infrastructure.

HIV/AIDS was first described from a Ugandan fishing Village on the shores of Lake Victoria in 1982 (Allison & Seeley, 2004). In the past recent decades, it is evident that HIV/AIDS-related illnesses and mortality are devastatingly high in some fishing communities. A synthesis of survey conducted since 1992 in ten low or middle-income countries in Africa, Asia and Latin America revealed that HIV/AIDS prevalence among fishers or fishing communities are between 4 and 14 times higher than the National average prevalence rate for adults aged 15-49 (Kissling et al., 2005). These considerable rates of HIV/AIDS infection place Fisherfolks among groups that are more usually identified as being at high risk (Olowosegun, Akangbe, Olowosegun, Iyilade, & Falaki, 2013).

The vulnerability of fishing communities to HIV/AIDS stems from complex interactions, mobility of many fishermen, the time they spend away from home, their access to cash income, demographic profile (they are often young and sexually active), low level of education (especially sex education), and readily available commercial sex hawkers in most of the fishing ports and shores of fishing grounds (Olowosegun et al., 2013). The sub-ordinate economic and social positions of women in many fishing communities make them even more vulnerable to the infection (Kissling et al., 2005). (Huang, 2002) also reported that due to poverty, women fishmongers have become victims of fishermen who demand for sexual favour on top of supplying fish. It is no longer gainsaying that people exchange sex for gift or economic gain for their up keep, commercial sex activities are thriving in the lake Victoria region, which may be one of consequences of effect of global warming on the water bodies which the desired attention has not been proffered (Béné & Merten, 2008).

(Kissling et al., 2005) compared HIV prevalence among Fisherfolks with both the wider population and with other groups generally considered at high risk of HIV infection. Their study yielded comparative data for ten low and middle income countries. In nine of those countries, Fisherfolk were more likely to have HIV than the general population, by factors ranging between 4.4 and 14.0. Three of the studies were conducted in Africa. Prevalence rates for Fisherfolk were 20.3% in the Democratic Republic of Congo (DRC), 30.5% in Kenya and 24.0% in Uganda, representing rates respectively 4.8, 4.5 and 5.8 times higher than in the general population. Moreover, in Kenya and Uganda, this incidence was respectively 2.1 and 1.8 times higher than for truck drivers, a known high-risk group. The absolute numbers were also higher: 44,000 Kenyan Fisherfolk infected as compared with 8,000 truck drivers, and 33,000 Ugandan Fisherfolk compared with 5,000 truck drivers. The Kenyan study suggests that rates of HIV infection are even slightly higher for Fisherfolk than for sex workers. Studies done in parts of Africa (e.g., Senegal, Ghana, Tanzania, Zambia, South Africa, Nigeria and Benin) (Abu-Radded, 2007) indicates that many fishing communities have high HIV/AIDS prevalence rates. Cash income, poverty, irregular working hours and being away from home places fishermen in a group with disposable income and time off (when not fishing), that favors the consumption of alcohol and prostitution; the corollary of this is that low-income women are drawn to fish landings or ports precisely because of the opportunities to sell food, alcohol or sex. The chance of being exposed to HIV is increased where a small number of women have unprotected sex with a larger number of men, or vice versa (Garnett & Anderson, 1996), cited in (Loevinsohn & Gillespie, 2003). In places where women compete intensely for the fish catch (for small-scale processing and local trade); “fish for

sex" is not uncommon; Gender inequality, compounded by poverty that puts women at risk of exploitation, makes it difficult for women to insist on condom use; and fishing communities have limited access to sexual health services. Africa's industrial fisheries and fish processing sub-sectors are also affected by HIV/AIDS, through the loss of skilled labor and high levels of absenteeism due to sickness or compassionate leave to attend funerals. In addition, Allison and Seeley (Allison & Seeley, 2004) highlight potential impacts on natural resource management, pointing out that: HIV/AIDS undermines the long-term perspective needed for successful co-management in fisheries, whilst deepening and desperate poverty may drive Fisherfolk towards increasingly short-sighted and unsustainable practices; and indigenous knowledge about resource management may also be lost, along with crucial capacities in universities and public services.

HIV/AIDS in the fisheries sector has much wider impacts too. Mobile and part-time fishing populations, moving in and out of the sector, along with interactions through trade and markets, permit HIV and its impacts to be spread outside the sector. The multiplier effects of the loss of productive labor and declining productivity may affect rural incomes more broadly. HIV/AIDS, moreover, threatens the ability of the fisheries sector to supply fish and fish products to the low-income groups for whom it represents an important and affordable source of animal protein and micronutrients.

HIV/AIDS disease studies done among fishing communities in Tanzania, Africa, found that fishers were most likely to die from any cause - AIDS or Non-AIDS. In fact, this study found that they were five times more likely to die of AIDS and of other causes than are farmers in the same region (Seeley & Allison, 2005). Their entire lifestyle also makes

them vulnerable to death due to infection from sexually transmitted diseases, including HIV/AIDS. One study among Malaysian fishers in the state of Kedah reported that 18.1% of the subjects had sex with commercial sex workers, 19.2% used various drugs and 14.4% consumed alcohol, all behaviors which put them at risk of being infected (Huang, 2002).

There is also an immediate need for action to tackle HIV/AIDS in fishing communities: to develop and implement policies; to translate the emerging lessons and approaches into programmes and activities on the ground, making sure that some of the key foundations are in place (including the availability of condoms, VCT centers, workplace policies, and other sensitization and education programmes); and to engage with donors, governments, the private sector and communities to harness the commitment and resources needed to fight the problem. Such action implies a variety of roles appropriate to different groups and professions working at different levels, from policy right down to the communities themselves.

2.2 Optimal Control

The HIV/AIDS epidemic has had a major impact throughout the world. In December 2007, the World Health Organization (WHO) and joint United Nations Program on HIV/AIDS (UNAIDS) estimated that there are 33 million people living with HIV. Most of these people are unaware of their HIV status and infectiousness, and as a result unknowingly contribute to the spread of the infection (WHO, 2008). The epidemic has disproportionately affected people residing in areas of the world that have fewer resources to combat the disease. WHO (WHO, 2008) also estimated that 2.7 million people were newly infected with HIV in 2007 and greater than 95% of these new

infections occurred among persons residing in Low and Middle Income Countries (LMIC). Sub-Saharan Africa accounts for an estimated 22 million cases of HIV/AIDS with an estimated prevalence of 5% in adults ages 15-49. Of these LMIC countries, HIV/AIDS epidemic has often over-burdened the under-resourced health care infrastructure worsening the situation.

In the past decade, it is evident that HIV/AIDS-related illnesses and mortality are devastatingly high in some fishing communities. A synthesis surveys conducted since 1992 in ten low or middle-income countries in Africa, Asia and Latin America revealed that HIV/AIDS prevalence among fishers or fishing communities are between 4 and 14 times higher than the National average prevalence rate for adults aged 15-49 years. These considerable rates of HIV/AIDS infection place Fisherfolks among groups that are usually identified as being at high risk (Olowosegun et al., 2013).

HIV/AIDS was first described from a Ugandan fishing Village on the shores of Lake Victoria in 1982 (Allison & Seeley, 2004). The vulnerability of fishing communities to HIV/AIDS stems from complex interactions, mobility of many fishers, the time they spend away from home, their access to cash income, demographic profile (they are often young and sexually active), low level of education (especially sex education), and readily available commercial sex hawkers in most of the fishing ports and shores of fishing grounds (Olowosegun et al., 2013). The sub-ordinate economic and social positions of women in many fishing communities make them even more vulnerable to the infection (Kissling et al., 2005). It has been reported that due to poverty women fishmongers have become victims of fishermen who demand for sexual favor on top of supplying fish (Awuonda, 2003; Duwal et al., 2015). It is no longer gain saying that people exchange

sex for gift or economic gain for their up keep, commercial sex activities are thriving in the area which may be one of consequences of effect of global warming on the water bodies which the desired attention has not been offered (Béné & Merten, 2008).

A comparative data for ten low and middle income countries on HIV prevalence among Fisherfolks with both the wider population and with other groups generally considered Fisherfolk at high risk of HIV infection (Kissling et al., 2005).

Among the HIV-associated pulmonary complications, opportunistic pneumonias are major causes of morbidity and mortality. Pneumonia refers to any inflammation of the lungs, usually caused by a germ. It can involve both lungs, one lung or one part of a lung. Pneumonia requires hospitalization and can even lead to death. The spectrum of HIV-associated opportunistic pneumonias is broad and includes bacterial, mycobacterial, fungal, viral, and parasitic pneumonias. Bacterial pneumonia is the most frequent opportunistic pneumonia.

While there is no cure for HIV, most drugs available are meant to boost immunity and treat opportunistic diseases. In addition to providing antiretroviral therapy to those with HIV infection, accurate diagnosis and appropriate treatment and prevention of HIV-associated opportunistic pneumonias are both important strategies for reducing the morbidity and mortality from HIV/AIDS. This paper, among other aspects, incorporates antiretroviral therapy for the AIDS cases and analyzes its implications on pneumonia.

It is not the AIDS that kills, but the opportunistic infections which take advantage of the body's weakened defense system(*The Columbia University Handbook of HIV and AIDS*, 2009). It is estimated that more than 34.3 million people in the world live with HIV

infection, out of which more than 24 million are in the developing world. Much of the research on anti-HIV vaccine is focused on the immune system because such a treatment if found can serve to help the body to fight HIV infection on its own. For this reason, the object of the new treatments is reducing the viral load while improving the immune response(H.R, 2011).

Human body organs called lymphoid, associated with the immune system is positioned throughout the body. The bone marrow is the ultimate source of all blood cells, including white blood cells. T-cells travel throughout the body through the blood vessels or lymphatic vessels. The exchange of cells and fluids between blood and lymphatic vessels makes it possible for the monitoring invasion by microbes(Institute, 2003).

The immune system keeps large stockpiles made up of lymphocytes and the cell-devouring phagocytes and their relatives. B-cells and T-cells are the main types of lymphocytes'-cells do their duty by secreting antibodies into the body's fluids. These antibodies attack antigens circulating the bloodstream but are unable to penetrate cells(Institute, 2003).

Unlike B-cells, T-cells do not recognize free-floating antigens. T-cells contribute to immune defenses through two ways: directing and regulating immune responses and directly attacking infected cells. Helper T-cells coordinate immune responses, by communicating with other cells or by stimulating B-cells to produce antibodies or by activating other T cells. Killer T-cells, also known as cytotoxic T-lymphocytes or CTLs directly attack other cells carrying certain foreign or abnormal molecules on their

surfaces. Killer T-cells are useful for attacking viruses that often hide and grow inside infected cells(Institute, 2003).

According to Zhu and Paul (2008), CD4 T-cells contribute to immunity through their capacity to help B-cells make antibodies; to induce macrophages to develop enhanced microbicide activity; to recruit neutrophils, eosinophils, and basophils to sites of infection and inflammation. They also help through their production of cytokines and chemokines that orchestrate immune responses.

According to("Virological and immunological features of long -term human immunodeficiency virus-infected individuals who have remained asymptomatic compared with those who have progressed to acquired immunodeficiency syndrome," 1998), most people mount an effective immune response to HIV during the first few months of infection. However, the effectiveness of their response wears down with time. The response to HIV infection comes in two forms: cellular and humoral. In the cellular response, the activity of the CD4 and the cytotoxic lymphocytes(also called CD8 T-cells) the lymphocytes directly attack infected cells. In the humoral response, the lymphocytes use antibody production and activity to fight HIV/AIDS.

("The viruses progression in early human immunodeficiency virus type 1 infection and their replication," 1997), asserts that the first few weeks after infection, experience an up to 20fold increases the number of CD8 T-cells and a sharp fall in CD4T-cell. This is paired with a decline in the immune functions governed by the CD4 T-cells. It sometimes results in the appearance of infections such as Candida, herpes and Pneumocystis pneumonia during seroconversion illness. About six months after infection, CD4 T-cell

function improves except in relation to HIV-specific antigen. The few people who maintain strong HIV-specific CD4 T-cell responses have lower viral loads than people with poor responses. This is due to the abundance of CD4 proteins on the surface of T cells.

As HIV infects and kills the CD4+ T cells the total number of healthyCD4+ T cells in the body. This is what is meant the lowering of CD4 counts in people living with HIV who are progressing to AIDS. The eventually depletion of CD4+ T cells weakens the ability of the human immune system to defend itself against attack from other pathogens. When HIV invades the body, the dendritic cells and macrophages attempt to do their usual job by engulfing HIV and displaying the antigen. But when CD4+ T cells respond they become infected by HIV. The HIV hijack CD4+ T cells and forces them to channel their activities into manufacturing more viruses. Medicines Australia (2014) traces the term vaccination from the Latin word "vice" that means "cow." They assert that the term was coined from the process of inoculating a naive patient with attenuated cowpox pathogens to induce immunity in subsequent attacks of the disease. They define a vaccine as a preparation whose intension is producing immunity to a disease by stimulating the production of antibodies. Vaccines include suspensions of killed or attenuated microorganisms, or derivatives of microorganisms. Vaccines are prophylactic medicines designed to prevent rather than treat disease.

Vaccination aims at eliciting a specific immune response to protect the immunized individual from a pathogen should he or she be exposed to it at a later date. The ability of a vaccine to do this is sometimes enhanced when combined with an adjuvant. An adjuvant is a substance that attracts additional inflammatory cells to the site of injury and

stimulates them to release more and different types of cytokines. These cytokines further stimulate and activate macrophages and lymphocytes to acquired additional protective functions (Abul Abbas, Lichtman, & Pillai, 2019).

According to (Delves & Roitt, 2000), vaccines provide a unique modern medication for they offer effective protection against the onset and progression of specific infections. Most of the other treatments are therapeutic. They are usually used to treat a disease and or its symptoms. Only a few are preventative. Vaccination is also unique in harnessing the cells, tissues and molecules of an individual's immune system so that they become able to offer protection through a variety of natural mechanisms and processes fundamental to human biology.

According to (Korobeinikov, 2007), mathematical models are valuable in understanding the dynamics of biological problems. Ianthe last decade, for instance, numerous mathematical models have been developed to describe immunological response to infection with Human Immunodeficiency Virus (HIV). Differential equations have been used to study the dynamical properties of HIV-1 infection models and provided much knowledge about the HIV-1 infection.

The mathematical study of epidemics reduces dependency on laboratory experiments which can be expensive. Further, the testing done in cases involving humans can be detrimental. Using a mathematical approach to describe the interaction between the Immune system with HIV viral pathogens in presence of vaccines will make a positive contribution to epidemiology.

2.3 Metapopulations and Epidemics

Although vaccines are available for many infectious diseases, these diseases continue to cause suffering in both developing and developed countries. In developed countries, chronic diseases such as cancer have received more attention than infectious diseases but the infectious diseases have continued to cause mortality in the world. The transmission mechanism from the infective to the susceptible is understood for many infectious diseases and the spread of the diseases through a chain of infections is known.

However, the transmission interactions in a population are very complex and are therefore difficult to understand the large scale dynamics of the disease spread without the formal structure of the mathematical model. In many sciences, it is possible to conduct experiments to obtain information, however experiments with infectious disease spread in human populations are often impossible, unethical or expensive. Data is sometimes available from naturally occurring epidemics or from natural incidence of endemic diseases (Rotich, 2013).

This data is however incomplete due to under reporting. The lack of reliable data makes accurate parameter estimation difficult so that it may only be possible to estimate a range of values for some parameters.

(Patel, Longini Jr, & Halloran, 2005) used an epidemic model to investigate which age groups should be vaccinated first to minimize the cost or deaths in an influenza epidemic. They established that the optimal vaccination strategy involves concentrating the vaccine on children with the left over vaccine going to the middle aged adults. Their study

revealed that given a population of 280 million people, it will be possible to prevent 31 million illnesses more by applying the optimal vaccination strategy when compared with the random mass vaccination.

(Lloyd & Jansen, 2004) studied an n-patch model with k different levels of individuals. Their study concentrated on the linear stability of the spatially homogeneous solutions of the model with population settings in which individuals migrated between patches according to a simple linear term. The dynamic behavior of the endemic SIR model was decomposed into spatial modes. They found out that for parameter values appropriate for childhood diseases, the out of phase modes decayed much more rapidly than the in-phase modes for a broad range of coupling strengths.

(Rotich, 2013) studied the dynamics of the immune system and the drug sensitive Wildtype HIV variant. Their study focused on the transient and steady state behavior of the mathematical model to assess the effects of time delay on the stability of the periodic oscillations.

The study showed that among the parameters which affects the management of HIV virus at very low levels, time delay and drug efficacy were shown to be the major contributors of stability condition. They also observed that since the lifespan of infected cell cannot be stretched beyond a certain limit. The minimum time delay before the infected cell become productive is given by τ_{min} and the maximum lifespan of the cell is $\tau_{\max}$ and in this range of time delay, the drug efficacy was effective within an interval of 50% and 70%.

(Marieke Jesse & Heesterbeek, 2011) investigated the effect of migration on the persistence of infectious agent in a metapopulation. Their study revealed that a higher migration rate would mean that an infectious individual would spend shorter time in one patch thus changing patches more frequently. By changing patches frequently, the infectious individual increases the number of contacts with susceptible individuals which increase the probability of the persistence of the infectious agent.

(Enagi & Ibrahim, 2011) studied the effects of combining immunization with treatment of latent tuberculosis in controlling the spread of TB in a population. Stability of DFE was discussed in this study using Routh Hurwitz theorem. Routh Hurwitz theorem (Clark, 1992) helped determine the sign of the eigenvalues of a matrix without necessarily computing their values. This work established that for DFE to be stable, the product of total contractions and total breakdown of latent class should be less than total rates from both latent and infectious classes. This work has studied the effects of immunization and treatment in a single population assumed to be closed. Effects of interactions with other near populations is not discussed, an assumption which is not practical.

(Sharma, 2014a) studied the effect of poverty and media coverage on the transmission of infectious diseases using numerical simulation. He found out that in life every individual usually takes preventive measures to protect themselves from infection as soon as the infected individuals are reported by media coverage thereby reducing the transmission rate, this research however showed that media coverage has very little effect on the transmission rate of infectious diseases to the population living below poverty line due to little access to media tools. He further observed that the unique disease free equilibrium

follows global asymptotic stability if $R_0 < 1$ but when $R_0 > 1$, the endemic equilibrium is asymptotically stable.

(Rahman & Zou, 2012) studied the dynamics of a vector-borne disease containing latency and non-linear incidence rates. They assumed that the population of vectors at a time t is proportional to the population of the infectious hosts and used the saturating incidence rate functions. They formulated a mathematical model to describe the dynamics of a vector borne disease with two-strains and with latency delays. They determined the global dynamics by selecting suitable Lyaponov functional. They showed that when the basic reproduction number is less than one then the disease dies out but when $R_o > 1$ then the disease will persist in one or both the strains will become endemic.

Time series data for the Ebola virus disease cases in Guinea, Sierra Leone and Liberia up to September 8, 2014 and employed novel methodology to estimate how the rate of exponential rise of new cases had changed over the outbreak using piecewise fit of exponential curves to the outbreak data. They found that in Liberia and Guinea the effective reproduction number rose around the time that the outbreak spread to densely populated cities (Towers, Patterson-Lomba, & Castillo-Chavez, 2014). The authors further observed that the enforced quarantine measures were not effective control measures.

Existing data from Liberia and Sierra Leone were used to parameterize a mathematical model of Ebola and used the model to forecast the progression of the epidemic, as well as the efficacy of the several interventions including increased contact tracing, improved infection control practices, the use of hypothetical pharmaceutical intervention to

improve survival in hospitalized patients. Modeling results showed that increased contact tracing and improved infection control or the combination of the two can have a substantial impact on the number of Ebola cases but the interventions were not sufficient to halt the progress of the epidemic. The hypothetical pharmaceutical intervention while impacting mortality had a smaller impact on the forecasted trajectory of the epidemic (Rivers, Lofgren, Marathe, Eubank, & Lewis, 2014).

A mathematical model for a Lassa fever was developed with three compartments of susceptible humans (S), infected humans (I) and the rodents carrying the virus (V) and incorporated infection contact rates. They obtained the basic reproduction ratio (R_o) and established conditions for local stability of both the disease free and endemic equilibria (Okuonghae & Okuonghae, 2006).

(Bawa, Abdulrahman, Jimoh, & Adabara, 2014) extended the work of (Okuonghae & Okuonghae, 2006) by developing a mathematical model with five compartments of susceptible humans (SH), infected humans (IH), infant reservoirs (IR), adult reservoirs (AR) and the Lassa virus in the environment (V). The authors also incorporated the demographic factors, disease induced deaths, human-to-human contact rate (β_1), rodent-to-human contact rate (β_2) and infection contact rate (β_3). Their model results showed that Lassa fever could be controlled if the basic reproduction ratio (R_0) was less than one regardless of the initial population profile.

(Ullah, Zaman, & Islam, 2013) investigated the stability of the general SIR epidemic model of infectious disease. The authors showed that the local dynamic of the general SIR model is determined by the basic reproduction ratio(R_0). They used the Lyapunov

theory to show that disease free equilibrium is globally asymptotically stable when $R_o < 1$ while the endemic equilibrium is locally asymptotically stable when $R_o > 1$. Here local means around the fixed points, while global is at any other point away from the fixed points.

In the literature reviewed above, the disease dynamics were analyzed in a homogeneous population, where individuals are expected to interact freely and randomly. Boundaries were nonexistent between subpopulations and individuals mingled freely amongst themselves. In this study, the researcher introduced subpopulations and analyzed the disease dynamics in a metapopulation, where boundaries are assumed to exist between homogeneous subpopulations. The dynamics between and within subpopulations were analyzed.

Epidemiology is the study of the disease distribution in a population and seeks to determine the causes and patterns of the disease. The main object of epidemiological study is to establish preventive and control methods and therefore prevent the transmission of the disease in a given population. One of the main area of epidemiological study is the disease surveillance which monitors the spread of a disease by establishing patterns of progression of the disease. The goal of the surveillance is to predict, observe and minimize the harm caused by the epidemic to the population. Epidemic modeling is a tool used to study the mechanism through which an infectious disease spreads, predict the future course of the epidemic and identify the possible strategies for controlling the epidemic. Thus epidemic modeling has three main goals;

i) To understand the mechanism through which the disease spreads. The most important part here is the set of mathematical equations that describe the model i.e. the mathematical structure of the model.

ii) To predict the future trend of the disease transmission in the population. In order to make a model that can give reliable prediction of the future course of the epidemic, the model must describe the epidemic closely and must contain all the specific features of the epidemic.

iii) To identify possible control measures of the epidemic. The threshold for many epidemiology models is the basic reproduction Number R_o.

Basic Reproduction Number is defined as the average number of secondary infections produced when one infected individual is introduced into a host population where everyone is susceptible (Diekmann & Hesterbeek, 2003).

The number R_o is used to measure the transmission potential of an infectious disease. It is usually affected by several factors including contact rate in the population, the probability of infection in a given contact and the time duration at which an individual who has contracted the disease remains infectious.

The global basic reproduction number R_0 and if $R_0 < 1$ then an index case introduced into a population which is fully susceptible will produce less than one other infection on average during its entire infectious period thus the epidemic will die out. However if $R_0 > 1$ then each index case introduced into a population of susceptible individual will produce on average more than one infection during the period that it remains infectious thus the epidemic will occur. The disease reproduction number in a sub-population is also known as the local reproduction number is denoted by $R_i;\ i \in [1,2,3\ldots]$ and measures

the number of secondary infections produced in the sub-population i when Epidemic refers to one infected case is introduced in the sub-population i when everyone in that sub-population is susceptible.

Epidemic –the sudden increase in the number of cases of an infectious disease above the expected number of cases in a given population within a short duration of time (usually less than two years) (Beer, McCree, Jeffries IV, Lemons, & Sionean, 2019).

Endemic – A disease is said to be endemic in a population if it is constantly present to a lesser or greater extent to people of a certain class or of certain geographical region. For many infectious diseases, the basic reproduction number is considered to be the threshold quantity determining when an infection could invade a fully susceptible population.

In general, the infection can invade and persist in a population which is wholly susceptible if and only if R_0 is less than one.

Despite extensive vaccination programs, use of antibiotics and improved sanitation, infectious

diseases continue to be major causes of morbidity and mortality throughout the world. More importantly, pathogens evolve and adapt to new environments leading to emergence of new infectious diseases and spreading of the existing diseases to new geographical regions Levin's, Awerbuch and Brinkman, 1994. Diseases that have emerged in recent years include Lyme (1975), Hepatitis C (1989), Legionnairer (1976), Hepatitis E (1990), Ebola hemorrhagic fever (1976), Hantavirus (1993) and Coronavirus disease 2019 (COVID 19).

Drug resistance by pathogens has become a serious issue in the control of diseases such as malaria, tuberculosis and gonorrhea and with occurrence of the climatic changes some

diseases such as malaria, yellow fever and dengue are spreading into new regions. Recently, new pathogens known as prions have joined the previously known pathogens (protozoa, worms, viruses and bacteria). A prion is a misfolded protein with the ability to infect normal proteins of the same variant and cause them to be misfolded. They are responsible for neuro-degenerate diseases such as Bovine Spongiform Encephalopathy (BSE) in variety of mammals. An outbreak of foot and mouth disease in the United Kingdom in 2001 caused great economic hardships in the United Kingdom (Ferguson, Donnelly, & Anderson, 2001; Woolhouse et al., 2001). Avian influenza has devastated bird population in South East Asia. Moreover, it is feared that a recombination of human influenza strain with Avian influenza strain might give rise to a novel influenza strain. In future therefore, the world is likely to face new challenges as a result of the emergence of novel infectious diseases.

Invasions of new ecosystems by animals and human beings, environmental degradation, global warming, changes in economic and social patterns and increased international travel will continue to provide opportunities for the transmission of new and existing infectious diseases (Martens et al., 1999). The growth of the world population, changes in the global climatic conditions, emergence and re-emergence of new infectious diseases and deadly strains of the existing infectious diseases have continued to increase the need for better methods to guide disease control and prevention.

2.4 The n-Patch Metapopulation Modeling

The influence of spatial structure in population dynamics have been studied intensively in the recent years. One way to incorporate structure is to consider metapopulations consisting of well-mixed, coupled patches also known as sub-populations or households.

In metapopulation models, the patches are thought to be homogeneously mixed and contain individuals in different states of the disease. There are several choices for the underlying local dynamics and they can be classified according to the considered phases of the disease (compartments) and the reaction between them. Individuals within each sub-population are assumed to be well mixed. Metapopulation models allow explicit mathematical expressions and straight forward numerical solutions, and hence play an important role in mathematical epidemiology. Hierarchical metapopulation models are a special type of general metapopulation models.

Research done by (Shattuck-Hufnagel & Ren, 2018) considered the hierarchy involved in human movements (i.e. that sub-populations have some non-random pattern of connections) Simulations from these models show that disease spreading is significantly influenced by multilevel movements. New studies based on real human mobility data also provide evidence to support the argument that individual movements occur at different levels (Schlosser & Brockmann, 2021). Another thing to consider is the way individuals interact with each other.

Interactions between individuals involve both within-patch interactions and between patch interactions. It is assumed that the contacts between individuals on each patch are frequent and hence random mixing applies within the sub-population. Between-patch interactions are of more interest and usually modeled by two methods, depending on the frequency of movements. If the interaction between two patches is dominated by frequent movements such as people commuting to and from work, the sub-populations are said to be interacting with each other in a random manner thus any infection occurring on one

patch has the force of infection on the susceptible individuals in the closely related patches.

Lloyd and Jansen (2004). The force of infection is defined as the per capita rate that the infected individuals transmit the disease to susceptible individuals. Alternatively, if the movements between two patches mainly take the form of migration, it means that individuals migrate to the host population with the disease status they get from the home patch first and then take part in the disease transmission process in the host patch (Lloyd & Jansen, 2004). These two scenarios were studied separately in the past. In real populations, it is obvious that both scenarios occur simultaneously.

In this study, we will build a metapopulation model based on multilevel movements including both patch coupling and migration. At the lowest level, where the population movements between the patches are most frequent, the patches will be coupled by the force of infection while patches with less frequent movements in between will be linked by migration. In this research, these two kinds of patch relationships will be referred to as close-related patches and non-close-related patches. Moreover, it will not necessarily mean that well-connected patches are geographically close, in contrast to previous work.

Human interaction tends to be more complex than animal migration or plant dispersal and is not necessarily related to geographic distances (Burnside et al., 2012). A hierarchical system to describe a metapopulation model consisting of m levels of movement and having a total of n patches was set up. Individuals were assumed to mix homogeneously within each patch. All patches will be assumed to have identical within-patch population dynamics and environmental conditions. Transmission of infection occurs when an infectious individual meets a susceptible individual in one of the n

patches. Interaction of patches is either through coupling or migration. We assumed that the population was distributed evenly across all the n patches and one infectious individual was introduced into one of the patches.

Vaccines are available for many infectious diseases, but these diseases continue to cause mortality and morbidity in both developing and developed countries. Although infectious diseases have continued to cause morbidity and mortality throughout the world, chronic diseases such as hypertension and cancer have received more attention in developed countries. For many infectious diseases, the spreading mechanism through a chain of infection and also the transmission mechanism from the infectious to the susceptible individuals are understood. However, it is difficult to understand the disease transmission on a large scale dynamics without a formal structure of a mathematical model due to the complexity of the human to human interplay. In many sciences, it is usually possible to obtain data by conducting repeated experiments. However, with transmission of infectious diseases in human population, such experiments are often expensive, unethical or even impossible. Sometimes epidemiological data is available from naturally occurring epidemics but due to under reporting, the data is usually incomplete in many instances. This lack of reliable data makes it difficult to accurately estimate parameter values and therefore in many instances, parameter estimation is only possible over a range of values. Because repeatable experimental data is not readily available in epidemiological study, theoretical experiments are usually carried out using mathematical modeling and computer simulations to provide data that can be used to predict the future cause of the epidemic.

Epidemiological models are useful when it is required to determine the effect of the control methods to the transmission of the disease in the population. The models are also useful when comparison of the effect of the control or prevention procedures are required and may be used in the comparison of the control procedures of different diseases in the same population, same disease in different populations or even the same disease in the same population but at different times.

Compartmental mathematical modeling can be traced back to Kermack and McKendrick model (Brauer, 2005) of 1927 formulated a Susceptible-Infectious-Recovered (SIR) compartmental model to study the outbreak of plague of Mumbai in 1906 and the outbreak of bubonic plague of London between the years 1665 and 1666 (Brauer et al., 2019). They formally introduced the concept of thresholds that determines whether a disease can invade a given population (Volz & Meyers, 2009). This concept established the fundamental theory of epidemic modeling. More intensive studies on epidemic modeling have taken place in recent years. A two-region metapopulation model by (Nakata & Röst, 2015) used to study stability of influenza with respect to the rate of human travel from one region to the next found that the disease approached the disease-free equilibrium in one region and an endemic equilibrium in the other region when there was no movement of individuals between the patches. When small movement of individuals between the patches was introduced then the disease approached the endemic equilibrium state in both patches.

On further increasing the rate of human travel between the patches, the disease died out in all the patches. The study conducted by (Isdory, Mureithi, & Sumpter, 2015) was designed to study the effect of human travel in different parts of Kenya on the

transmission of Human Immunodeficiency Virus (HIV) using an SIR metapopulation model that incorporated different regions within the country. They parameterized the model using HIV data, census data and mobile phone data. The data on mobile phones was adopted to track the mobility of individuals in different parts of the country. Their model results showed that movement between different regions had relatively small overall effect on the rise of HIV cases in Kenya. However, the most important consequence of movement patterns was transmission of the disease from high prevalence areas to low prevalence areas. They observed that mobility slightly increased HIV incidences in regions with initially low HIV prevalence and slightly decreased incidences in regions with initially high HIV prevalence. On the other hand, (Marieke Jesse & Heesterbeek, 2011) investigated the effect of migration on the persistence of infectious agent in a metapopulation. Their study revealed that a higher migration rate would mean that an infectious individual would spend shorter time in one patch thus changing patches more frequently. By changing patches frequently, the infectious individual increases the number of contacts with susceptible individuals which increases the probability of the persistence of the infectious agent. The study conducted by (Phaijoo & Gurung, 2017) to investigate the effect of temperature and human movement on the persistence of dengue disease using a multi-patch Susceptible-Exposed-Infectious-Recovered (SEIR) - Susceptible-Exposed-Infectious (SEI) model showed that temperature plays a significant role in the transmission of dengue disease while human travel helped in spreading the disease to new areas. Stability analysis of the model showed that the disease-free equilibrium was locally asymptotically stable when the basic reproduction number is less than one and unstable otherwise. Simulation results on the other hand showed that the

basic reproduction number of the disease was a function of temperature and human travel. In their study to assess the risk of yellow fever importation into urban areas when healthy individuals visit forests where yellow fever is endemic, (Esteva, Vargas, & Yang, 2019) noted that migration of individuals plays a significant role in the distribution and persistence of yellow fever. The authors used an ordinary differential equation (ODE) model that considered human beings living in urban centers and incorporating migration of healthy persons to forests where yellow fever was endemic. They based their study on three reproduction numbers of human migrants, humans in the urban centers and monkeys in the forests. The results of their model showed that an increase in migration leads to increased risk of acquiring the disease. Further, they found that an epidemic of yellow fever could occur in urban areas if a large number of individuals visited forest areas.

(Patel et al., 2005) carried out a study to investigate the optimal age group for vaccination against influenza in order to minimize the deaths due to influenza epidemic or the cost of immunization. They established that the optimal vaccination strategy involves concentrating the vaccine on children with the left over vaccine going to the middle aged adults. Their study revealed that given a population of 280 million people, it will be possible to prevent 31 million illnesses more by applying the optimal vaccination strategy when compared with the random mass vaccination.

An n-patch model with $k-$ different levels of individuals studied by (Lloyd & Jansen, 2004) concentrated on the linear stability of the spatially homogeneous solutions of the model with population settings in which individuals migrated between patches according to a simple linear term. The dynamic behaviour of the endemic SIR model was

decomposed into spatial modes. The authors found that for parameter values appropriate for childhood diseases, the out of phase modes decayed much more rapidly than the in-phase modes for a broad range of coupling strengths. (Rotich, 2013) on the other hand studied the dynamics of the immune system and the drug sensitive wild-type HIV variant. Their study focused on the transient and steady state behaviour of the mathematical model to assess the effects of time delay on the stability of the periodic oscillations. The study showed that among the parameters which affects the management of HIV virus at very low levels, time delay and drug efficacy were the major contributors of stability condition. They also observed that since the lifespan of infected cell cannot be stretched beyond a certain limit. The minimum time delay before the infected cell become productive is given by the maximum lifespan of the cell is maximum and in this range of time delay, the drug efficacy was effective within an interval of 50% and 70%. Studies done by (Olaniyi, Okosun, Adesanya, & Areo, 2018) used a non-autonomous system of ordinary differential equations that incorporated four control methods of liver and blood stage therapies, mosquito reduction technique by personal protection using treated mosquito nets and the use of insecticide sprays to study the dynamics of malaria transmission between two interacting populations. The authors used Lyapunov methods to analyze the global dynamics of the system. Model analysis was performed by the use of the Pontryagin's Maximum principle coupled with numerical simulation. The results of their study revealed that combination of the four control methods may be adopted to prevent the spread of malaria in the population. The authors further showed that effective control of malaria transmission in the community depends largely on the value of the

basic reproduction number (R_0) and therefore recommended that efforts be made to reduce the value of R_0 to less than one.

The study conducted by (Titus, Robert, Omulimi, & Jeptanui, 2016) to investigate the n-patch metapopulation model using SIR-HIV epidemic model in a one dimensional nearest neighbour coupling lattice showed that the basic reproduction number was a function of the coupling strength and affected the stability characteristics of the equilibrium points. The authors showed that the disease free equilibrium was asymptotically stable regardless of the value of the coupling strength but the endemic equilibrium point depends on the value of the coupling strength. It was however shown that the endemic equilibrium point could be eliminated by reducing the coupling strength to less than the critical value of $k = 0.15$. Modeling results further showed that restriction of movement of infected individuals is key to the control of the disease because lower values of coupling strength results to lower values of R_0. (Colizza & Vespignani, 2008) investigated the behaviour of infectious diseases in metapopulation characterized by heterogeneous connectivity and mobility patterns. They derived the basic reaction–diffusion equations that describe the metapopulation system at the mechanistic level and obtained the early stage dynamic approximation for the subpopulation invasion dynamics. The authors showed that along with the usual single population epidemic threshold, the metapopulation network exhibits a global threshold for the subpopulation invasion and obtained an explicit analytic expression for the invasion threshold that determines the minimum number of individuals traveling among subpopulations in order to have the infection of a macroscopic number of subpopulations. The invasion threshold was found to be a function of factors such as the basic

reproductive number, the infectious period and the mobility process and decreases with increasing network heterogeneity.

(Wanjau, Titus, & Isaac, 2019) studied the SIRS metapopulation model with vital dynamics. The author described a new approach to study various control strategies of compartmental disease transmission models. The method was based on the construction of alternative next generation matrices and made use of the type reproduction number and the target reproduction number. Each alternative next generation matrix was designed for a specified control strategy. Using this technique it was possible to understand the dependence of the disease transmission on targeted parameters even in high-dimensional models where the relations are usually complex.

(Sharma, 2014b) studied the effect of poverty and media coverage on the transmission of infectious diseases using numerical simulation. He found out that in life every individual usually takes preventive measures to protect themselves from infection as soon as the infected individuals are reported by media coverage thereby reducing the transmission rate, his research however showed that media coverage has very little effect on the transmission rate of infectious diseases to the population living below poverty line due to little access to media tools. He further observed that the unique disease free equilibrium follows global asymptotic stability if $R_0 < 1$ but when $R_0 > 1$, the endemic equilibrium is asymptotically stable.

Studies done by (Rahman & Zou, 2012) investigated the dynamics of a vector-borne disease containing latency and non-linear incidence rates. They assumed that the population of vectors at a time t is proportional to the population of the infectious hosts and used the saturating incidence rate functions. They formulated a mathematical model

to describe the dynamics of a vector-borne disease with two-strains and with latency delays. They determined the global dynamics by selecting suitable Lyapunov functional. They showed that when $R_0 < 1$ then the disease dies out but when $R_0 > 1$ then the disease will persist in one or both the strains will become endemic.

In their study to investigate how the rate of exponential rise of the Ebola Virus Disease (EVD) had changed over the outbreak period, (Towers et al., 2014) used the EVD data in Guinea, Liberia and Sierra Leone and used the negative binomial likelihood fit to account for over dispersion in the data. The results of their analysis showed that the value of the effective basic reproduction number rose at the time when the disease spread to densely populated regions of Guinea and Liberia. The authors further observed that the enforced quarantine measures were not effective in the control of the Ebola virus disease. (Rivers et al., 2014) on the other hand used data for the Ebola virus disease from Liberia and Guinea to parameterize a mathematical model for the disease. The authors used the model to predict the future progression of the disease and also to determine the efficacy of various intervention methods.

The analysis of their model showed that improved infection control and an increase in contact tracing could have a significant impact on the spread of the epidemic. They however noted that the two intervention methods were not sufficient in the control of the epidemic. The authors recommended a long time commitment of resources in the fight against the Ebola virus disease.

(Obabiyi & Onifade, 2017; Okuonghae & Okuonghae, 2006) developed a mathematical model for a Lassa fever with three compartments of susceptible humans (S), infected humans (I) and the rodents carrying the virus (V) and incorporated infection contact rates.

They obtained the basic reproduction number (R_0) and established conditions for local stability of both the disease free and endemic equilibria. (Bawa, Abdulrahman, Jimoh, & Adabara, 2013) extended the work of (Okuonghae & Okuonghae, 2006) by developing a mathematical model with five compartments of susceptible humans (*SH*), infected humans (*IH*), infant reservoirs (*IR*), adult reservoirs (*AR*) and the Lassa virus in the environment (V).

The authors also incorporated the demographic factors, disease induced deaths, human to human contact rate (*1*), rodent-to-human contact rate (*2*) and infection contact rate (*3*). Their model results showed that Lassa fever could be controlled if the basic reproduction number (R_0) was less than one regardless of the initial population profile.

(Dumrongpokaphan, Kaewkheaw, & Ouncharoen, 2010) studied the SIR epidemic model with and constant immigration rate and a population size which was variable. He derived the sufficient conditions on model parameters under which the equilibrium points of the system were locally or globally asymptotically stable. If the disease free equilibrium (DFE) is stable, then the disease will not invade the population. On the contrary, if the endemic equilibrium point is stable, then the number of infectious individuals will remain constant which means that the transmission rate would be equal to the recovery rate. Consequently the prevention program can be instituted efficiently.

Research done by (Ullah, Zaman, & Islam, 2014) investigated the stability of the general SIR epidemic model of infectious disease. The authors showed that the local dynamic of the general SIR model is determined by the basic reproduction number (R_0). They used the Lyapunov theory to show that disease free equilibrium is globally asymptotically

stable when *R*0 Ç 1 while the endemic equilibrium is locally asymptotically stable when *R*0 less than1.

Potential spread of H1N1 influenza was studied by (Flahault, Vergu, & Boëlle, 2009) and used several values of the reproduction number and generation interval to model the potential spread of influenza A (H1N1) virus across a network of 52 cities while also attempting to predict the effect of vaccination program. Their research showed that the attack rate was 46% when the basic reproduction number was 1.5 and the generation interval of 2 days while a basic reproduction number of 2.2 with a generation interval of 3.1 days resulted to an attack rate of 77%. They concluded that a mass vaccination program of the disease with reproduction number of 1.5 resulting in 50% of the population being vaccinated and starting at most 6 months after the start of the epidemic could reduce the total number of cases by 91% while a similar vaccination program with a basic reproduction number of 2.2 would reduce the number of cases by approximately 44%.

(Agrawal, 2014) used a four-compartmental model of susceptible, exposed, infectious and recovered individuals with limited resources for treatment. The treatment rate of infected members of the population was assumed to be proportional to the number of patients provided that the number of patients does not exceed the treatment capacity. When the threshold treatment capacity was exceeded, the rate of treatment was assumed to be a constant. The analysis of the model showed that the treatment rate would lead to the existence of multiple endemic equilibrium states. The results of the model analysis showed that when $R_0 \leq 1$, there exist no positive equilibrium and the DFE is globally asymptotically stable thus the disease dies out. However, an endemic equilibrium X^e

exist, where $X^e \in (S\ E\ I\ R)$ when $1 \leq R_0 \leq P_0$ for some P_0 which is globally asymptotically stable. Two more endemic equilibria X^0 and X^e were found to exist when $R_0 > P_1$ and $R_0 < P_2$ respectively. The two equilibrium points were found to be locally asymptotically stable.

The object of the study by (Allen, 2008) was to compare the dynamics of deterministic and stochastic SIR and SIS epidemic models for an infectious disease. For stochastic model, the authors obtained the ultimate disease extinction criteria that were not a function of the basic reproduction number. However, when the time to extinction of the disease was long, the authors found that there existed a quasi-stationary probability distribution and that the mean of this distribution agreed with the endemic equilibrium state for a deterministic model whenever the basic reproduction number exceeded unity. The study by (Fierro, 2010) designed to study the similarities between the deterministic and the stochastic mathematical models for infectious diseases showed that the results for the two models differed significantly for small populations of about 10 individuals.

However, for larger populations with more than 1,000 individuals, the author showed that the results obtained by the use of deterministic model were consistent with the results obtained by the use of a stochastic model. For a novel infectious disease with unknown parameter values, (Brauer, 2017) recommended the use of a deterministic model to model the outbreak. The analysis of the deterministic model showed results which were consistent with stochastic models presented by (Halloran et al., 2008).

Although spatially separated populations have been studied widely in the past, the analysis of the control strategies has received little attention. In general, it is difficult to understand the effect of human movement on the disease transmission without a formal

mathematical structure. Further, pathogens responsible for the transmission of infectious diseases often mutate to produce two or more strains of the same pathogen. The management strategy for multiple strains of an infectious disease in a metapopulation setup is a challenging task and yet studies on the management of multiple strains in a metapopulation setup has not been documented. The goal of mathematical modeling of infectious diseases is to determine the parameters necessary to reduce the value of the basic reproduction number to less than one by changing the model parameters. In many models however, the complexity of the expression for the basic reproduction number makes such analysis difficult. In homogeneous populations, the basic reproduction number gives the strength of the control measure needed to control the epidemic provided that all model parameters accommodate change. However, in many cases limitations exist because some of the model parameters may not accommodate change. The object of this study is to address the research gap in previous work by presenting a mathematical model of infectious disease in a metapopulation setup with both migration and random movement of individuals between patches and also a model that incorporates the mutation of the pathogen. The study computes the target reproduction number which is a measure of the strength of the control measure required to reduce the basic reproduction number to less than one.

2.5 Coupling and Synchronization

Mathematical modeling of infectious diseases and analytic techniques have given great insights into the study of the evolution and control of epidemics (Allen, Brauer, Van den Driessche, & Wu, 2008). The occurrence of most epidemics is seasonal and therefore periodic. Infectious diseases can be therefore be modeled as biological oscillators using

differential equations (Keeling & Rohani, 2011; Murray, 2007; Olsen, Truty, & Schaffer, 1988; Strogatz & Mirollo, 1990). Many interesting dynamics occur in the study of oscillators, but most interesting phenomena, physically significant is the stability and robustness of oscillators under perturbation (Wasike & Rotich, 2007). In this regard, the epidemic focused in this study is HIV/AIDS. The World Health Organization (WHO) report of 2004 states that, AIDS has been a problem for the last four decades since it was first reported and labeled as AIDS (Control & Prevention, 2006). According to (Abu-Radded, 2007). It was estimated that over 33 million people were living with HIV, most of whom are unaware of their HIV status, and as a result, unknowingly contribute to the spread of the infection (WHO, 2008). The epidemic has disproportionately affected people residing in areas of the world that have fewer resources to combat the disease. The (WHO, 2008) further estimated that there were 2.7 million people who were newly infected with HIV in 2007 and greater than 95% of these new infections occurred among persons residing in Low and Middle Income Countries. Sub-Saharan Africa accounts for an estimated 22 million cases of HIV/AIDS and has an estimated prevalence of 5% in adults ages 15-49. In these Low and Middle Income Countries, (WHO, 2008) says that the HIV/AIDS epidemic has often over-burdened the under-resourced health care infrastructure. In Kenya for example, the worst affected community is the Fisherfolk as compared to the other populations (Kamali et al., 2016; Kissling et al., 2005; Olowosegun et al., 2013; Tanzarn & Bishop-Sambrook, 2003; Woodhead, Abernethy, Szaboova, & Turner, 2018). Surveys conducted since 1992 in ten low or middle-income countries in Africa, Asia and Latin America revealed that HIV/AIDS prevalence among fishers or fishing communities are between 4 and 14 times higher than the National

average prevalence rate for adults aged 15-49 (Béné & Merten, 2008; Huang, 2002). These considerable rates of HIV/AIDS infection place Fisherfolks among groups that are more usually identified as being at high risk (Allison & Seeley, 2004; Awuonda, 2003; Duwal et al., 2015; Olowosegun et al., 2013). It is for this reason that this study focuses on dynamics of HIV/AIDS among the Fisherfolk community around Lake Victoria Kenya, as a problem of coupled metapopulation patches, stability and robustness under small disease parameter perturbation.

2.6 Summary and Knowledge Gap

In this chapter, a review of related research studies in terms of the scope and methodology was explored. These include research on mathematical model formulation of communicable diseases, together with the analysis of the model stability around the fixed points, and their stability. Also, the sensitivity of the model parameters on the reproductive ratio R_0 was reviewed. This sensitivity analysis helps in analyzing the significance of the model parameters on the effect of the basic reproductive ratio.

Additional review was made on the formulation of a linear programming model, for the purpose of studying evaluating the optimality of disease control intervention strategies, like treatment, public health educational campaign, and isolation. An extension was made on coupling dynamics of identical oscillators representing adjacent independent population patches, and studying the dynamics which arise as a result of All-to-All coupling topology. These included the study of the existence of synchronization manifold, its stability and robustness under small perturbation.

There are several research studies that have been carried out on epidemiological mathematics, model formulation, coupling, synchronization, stability and robustness, of

diffusively coupled lattice oscillators, together with optimization studies, but most of these studies have been done independently, and none has integrated the distinct areas in one study. In this research study, the various analytic methods are put together on a mathematical model that is original, and not used before in previous studies.

CHAPTER THREE

METHODOLOGY

3.1 Introduction

This chapter gives details of the methods used in this research. The research design is described under the following subheadings; model formulation, model flow chart, model assumptions, variables and parameters, and model analytic and numerical methods.

3.2. Model Formulation

HIV/AIDS as described in chapter two, has been in existence for more than 4 decades, and numerous studies and mathematical models have been formulated, to describe the dynamics of HIV/AIDS under different scenarios. In this study, the dynamics of HIV epidemic as a vector borne disease is investigated.

Most commonly known diseases transmitted by vector include Malaria, with anopheles mosquito being the vector. Other vectored transmissions include rodents for Bubonic plaque, tsetse flies for Trypanosomiasis, snails for bilharzia, just to mention but a few.

Fisherfolk is here used as a special transmission vector. This is because Fisherfolk has been known to have uniquely high prevalence of HIV, and because of their barter trade behavior of having sex for fish, it can be compared to a vector, which transmits disease as it feeds. Apart from being a vector, the transmission also occurs between the vectors and also between the rest of the population.

The dynamics of infectious diseases is generally studied using compartmental model. Here, the human population is categorized into distinct groups, each with similar disease characteristics. In the initial case, the entire populations is considered initially susceptible

($N = S$), and once one individual is exposed to the virus, he or she becomes infected and able to infect others, here referred to as infective (I). The disease will then progress towards full blown AIDS (A), unless therapeutic intervention is taken. A new compartment of those who seek medication, will have low levels of viral load, and less infective, thus labeled as treated class (T). This gives four compartments, $N = S + I + T + A$ thus we employ a $SITA - SITA$ paradigm.

The mathematical model here used represents the flow rates of individuals from one compartment to the other. The flow is assumed to be instantaneous and all depends on the time elapsed, thus we use ordinary differential equations to represent the rate of change or the flux, from one level to the other. A system of 8 differential equations was formulated, each representing the dynamics of the population of each of the eight compartments. The underlying condition is that, the total population is conserved, so that the only changes in the entire population is due to demographic factors, death and births. It is assumed here that the entire population is homogeneous, so that all the members of one compartment have the same characteristics in terms of the disease progression. It is also assumed that all the individuals prescribe to the same cultural beliefs and therefore act in the same way.

3.3 Model Assumptions

For the purpose of studying the dynamics of HIV/AIDS with Fisherfolk as a vector, it is inevitable to make assumptions for the purpose of plausible model formulation and analysis. It is hereby assumed that the Fisherfolk population is strongly coupled, that all the members have common and distinct characteristics from the rest of the members. The new members of Fisherfolk are recruited from the rest of the community members, and

also fall back to the community and at determined rate. They are also assumed to spend most of the time in the lake fishing, away from the others and thus considered as a separate community from the rest of the people. The transmission dynamics between the compartments will be described by probabilities assigned to the chances of interaction sufficient to transmit HIV disease, and the probabilities describing the chances of getting treatment, natural and accelerated mortality rates due to infection, together with the probabilities associated with interacting with the vectors. It is also assumed that, the rate of transfer from one compartment to the other is described by parameters, which can be determined from data available, or calculated from the previous experiences.

Further assumptions made include the fact that once an individual is infected, he or she becomes infective immediately. The provision of window period or the delay between infection and being infective is assumed. The rest of the transfer terms are also assumed to be instantaneous, so that once infected, one progresses immediately to AIDS class or seek treatment, or die. The passage of time between one event and the other is assumed. This can be improved using difference equations, with a unit time change equivalent to the amount of time enough to cause changes. But it should be noted here that, the qualitative characteristics of the model, like eigenvalues, eigenvectors, stability among others remains the same.

Additionally, it is also assumed that environmental, psychological and biological factors cannot interfere with the value of parameters used in the model. For example, the force of infection β remains constant whether many individuals are sick or no one is sick. The only factors considered here to be affecting the dynamics is public health education and treatment. All the other factors are assumed to have no significant contribution.

In the model, it is also assumed that, no other unique characteristics are evidenced. That is, apart from the mentioned classes, of Susceptible, Infective, Treated and AIDS, there is no other class of people with unique characteristics. This assumption is made so as to monitor the population changes in the said classes only.

It should also be noted that, contributions of other opportunistic diseases or underlying factors like lifestyle diseases or hereditary diseases like diabetes, hepatitis, cancer, acute pneumonia, among others, which are known to accelerate the progression of HIV status to AIDS are also assumed. This is the extent to which the term homogeneity of individuals reaches.

3.4 Model Flow Chart

Considering compartmental modeling, the SITA paradigm is illustrated by the flowchart shown in Figure 3.1. The compartments represent the subset of the population, and the arrows show the flow of population into or out of a compartment, with the flow rate parameters indicated.

From the law of conservation of mass, it is here assumed that the total population is split into two groups; the normal population and the Fisherfolk population, denoted by N and N_v respectively. Due to disease prognostic characteristics, each category is subdivided into four subgroups, Susceptible, Infective, Treated and AIDS classes denoted by $SITA$ for the normal population and $S_v I_v T_v A_v$ for the vector Fisherfolk community. Thus, the total population will be given as;

$$N = S + I + T + A; \qquad N_v = S_v + I_v + T_v + A_v$$

Each of the subgroups, also referred to as compartments are affected by factors which either adds or reduces the number of individuals in each compartment. Some of these dynamics leads to the transfer of individuals from one compartment, to the other. For simplicity, Figure 3.1 below shows briefly the flow dynamics of the two subgroups, and how the vector population augments the disease prevalence among the normal population.

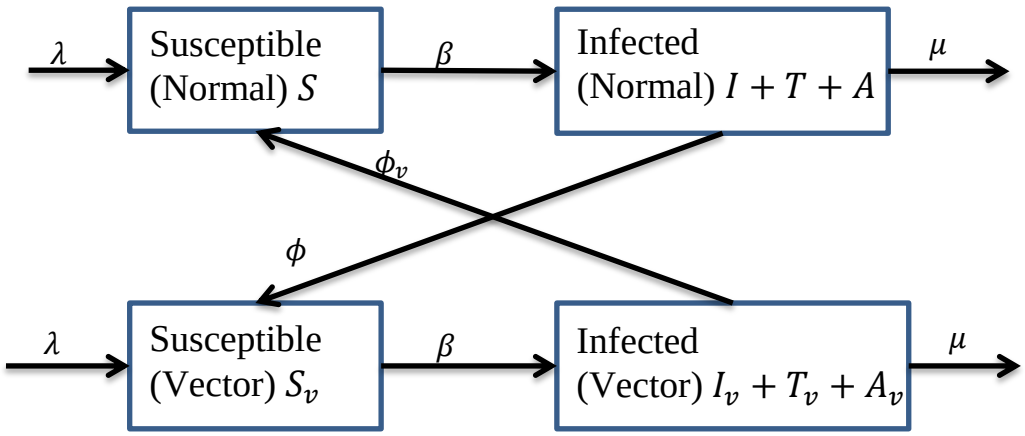

Figure 3.1 Flow chart showing interactions between members of different compartments

The detailed graph with more compartments and respective parameters and their meaning are outlined in chapter four. In this chapter, all the infected class (I, T, A) is lumped together, because all contribute proportionately to new transmission of disease to the susceptible. The crossed arrows with probabilities $\phi,\ \phi_v$ denote crossed infection by the vector population to the normal population and vise-versa.

3.5. Model Analysis

Let $X = X(S, I, T, A)$ where $S(t)$ is a function of time t denoting susceptible population, $I(t)$ denoting the infective population, $T(t)$ denotes the treated class and $A(t)$ the AIDS class, with $X' = \frac{dX}{dt}$ representing (S', I', T', A'). To show the dependence on time, the model is represented by the function $G(X, t)$, thus, the model under study will be of the form;

$$X' = G(X, t) \tag{3.1}$$

where, the function $G(X, t)$ describes the dynamics involved in infection of new members, transfer of infected to treated class, and to AIDS classes together with the coupling configuration and the interaction dynamics. The function $G(X, t)$ can be split into three, that is,

$$G(X, t) = f(X, t) + g(X, t) + M(X, t) \tag{3.2}$$

Where $f(X, t)$ describes the new infections, $g(X, t)$ describes the other transfer terms and $M(X, t)$ represents the coupling configuration between the Fisherfolk and the rest of the community members.

3.6. Fixed Point Analysis

Without loss of qualitative characteristics of the model, the nature of the dynamics of the model in Equation (3.1) are studied using a linearized function about the equilibrium points. Equilibrium is the point where the characteristics of a system changes. It is also called the turning point or the critical points. There are usually two types of equilibrium points of disease models, namely; disease free equilibrium (DFE) and endemic equilibrium point (EEP). DFE is the point where the entire population is susceptible, and

nobody is infected or has ever been infected by the disease. The entire population N equals to the number of susceptibles S and the number of individuals in the other compartments is zero $(I, T, A) = (0, 0, 0)$. EEP is the type of equilibrium point where an infected individual has been introduced to a purely susceptible population, and thus there are non-zero population of infectives, treated and AIDS cases. In this case, the disease coexist in the population, and therefore the entire population $N = S + I + T + A$, where $I \geq 0, T \geq 0, A \geq 0$.

Equilibrium points are computed by evaluating the points where the derivative of the model equations equal to zero. Equating the right hand side of the model in equation (3.1) to zero and evaluating, to obtain the equilibrium points $\bar{x}$ the equation $G(\bar{X}, t) = 0$ is solved. Using the model equation (3.1), two equilibrium points DFE and EEP were evaluated as discussed in the next subsection.

3.6.1. Disease Free Equilibrium (DFE)

Sometimes, instead of studying the stability of a system in the entire domain, without loss of generality, the stability of dynamics around the fixed point is enough to give a picture of the entire system. The equilibrium in absence of the disease called DFE, is defined as,

$$G(\bar{X}_0, t) = \tilde{0} \tag{3.3}$$

Where $\bar{X}_0 = (S_0, I_0, T_0, A_0) = (N, 0, 0, 0)$ denoting the state when the infected, treated, and AIDS compartments are empty and everybody $N = S + I + T + A$ is susceptible.

3.6.2. Endemic Equilibrium Point (EEP)

The other existing equilibrium point, where the disease exists in the population is the Endemic equilibrium point. This is defined as

$$G(\bar{X}_e, t) = \tilde{0} \tag{3.4}$$

Where $\bar{X}_e = (S_e, I_e, T_e, A_e) \neq (0,0,0,0)$. The subscript X_e denotes the endemic equilibrium point and X_0 is the disease free equilibrium point. This is a point when each compartment has non zero population, because of the progress and the existence of the disease amongst the population.

3.6.3 Stability of the Equilibrium Points

Apart from the model existence and well boundedness, it is necessary to study its' stability, with respect to perturbation. The model stability depends on the nature of the spectral values around the fixed point. Stability is determined by the eigenvalues of community matrix obtained by evaluating the Jacobian of the system, evaluated at the fixed point.

$$M = \frac{\partial G(X,t)}{\partial X}\Big|_{X_i} \quad i = 0, e \tag{3.5}$$

Let the spectrum of the matrix M be defined as

$$|M| = \lambda_j, j = 1, 2, 3, \dots, n$$

Then the system (3.1) is classified as stable, unstable or can't be determined at the equilibrium point as follows;

$$\left.\begin{matrix} Unstable \\ Stable \\ Undetermined \end{matrix}\right\} \; if\ for\ all\ i, \quad \begin{cases} \lambda_i > 0 \\ \lambda_i < 0 \\ \lambda_i = 0 \end{cases}$$

If the nature of eigenvalues are zero, the stability of the system can be determined using Lyapunov type numbers (eigenvalue functionals), or using the Poincare map (describing

the proximity of periodic solutions to each other after one period), if the solution is periodic.

3.7. Reproductive Ratio R_0

The condition on the dominant spectral radius $\max \lambda_i$ yields a very important parameter denoted by R_0. It is used to describe the rate at which new infectives are created from one primary infective, introduced into a purely susceptible population. It therefore measures the velocity at which the disease is spreading.

If $R_0 \leq 1$, the disease will die off, if $R_0 = 1$, the disease remains persistent, unless intervention is taken. If $R_0 > 1$, the pandemic will persist in the population and become epidemic, and the disease coexist in the population.

Using the method of next generation matrix as proposed by (Diekmann & Hesterbeek, 2003; Van Den Driesche & Watmought, 2003), the value of the reproductive ratio will be determined as,

$$R_0 = \rho(FV^{-1}) \tag{3.6}$$

Where $F = \frac{\partial f(X,t)}{\partial X}\Big|_{X_i}\ i = 0, e$ and $V = \frac{\partial g(X,t)}{\partial X}\Big|_{X_i}\ i = 0, e$. The value of R_0 will always be equal to the condition on the dominant eigenvalue, for the matrix M to be stable.

3.8 Positivity and Boundedness

The necessary and sufficient condition for a model to be well posed is the requirement on the solution of equation (3.1) to be positive and bounded. Since the model (3.1) describes human population dynamics, the variables $S(t), I(t), T(t)$ and $A(t)$ need to remain

positive and bounded for all time $t \geq 0$. We require that for all initial values in $\mathbb{R}_0$, the solutions $X(t)$ remains in $\mathbb{R}_{0+}$, that is, $\mathbb{R}_{0+}$ is positively invariant.

Boundedness is a condition which requires that solutions have lower and upper bounds. In this case, for all future time $t \geq 0$, we require that $X(t) \in (0, \infty]$.

This argument is valid if we can find the solution of the form

$$X(t) = X_0 e^{G(X(t),t)}; \;\; t \geq 0, \qquad 0 \leq X < \infty$$

3.9 Sensitivity Analysis

Sensitivity analysis of variables and parameters used in the model helps in revealing the key variables or parameters which significantly affect the spread or control of the epidemic. Using the method proposed by (Perumal & Gunawan, 2011), sensitivity of parameters to reproductive ratio R_0 were computed as;

$$p_i|_{R_0} = \frac{\partial R_0}{\partial p_i}\frac{1}{R_0}, \;\; i = 1, 2, 3, \ldots$$

where p_i denotes parameter $i = 1, 2, 3, \ldots$ and $p_i|_{R_0}$ means sensitivity of parameter p_i on the reproductive ratio R_0. Once sensitivity is done, insignificant parameters will be lumped together, while sensitive ones are varied to determine their threshold values. These parameters account for intervention strategies, coupling strength, stability, and robustness of the model.

3.10 Coupling configurations

Basing on the location and area of operation of the Fisherfolk, with respect to the rest of the community, the following coupling configuration lattice will be more appropriate.

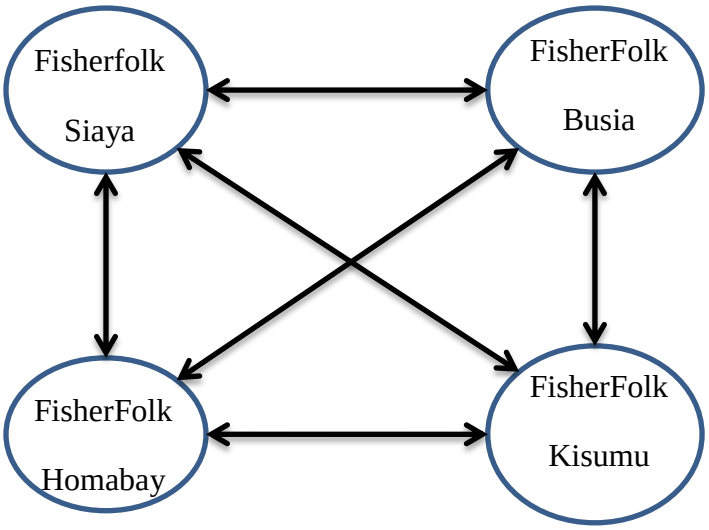

Figure 3.2 All-to-all Coupling Configuration in a Bravais Lattice. Source: Author

In the diagram of Figure 3.2, the arrows shows diffusive coupling of one lattice point to the other, and circles represent the unique groupings of human population.

3.10.1. Coupling and Coupling Configuration

Biological oscillators are common in real life situation, where a system behaves in a non-constant state, displaying a repetitive pattern. This is mostly due to coupled action and reaction forces which act with an aim of bringing equilibrium.

When oscillators are represented using differential equations, the repetitive behavior is represented by non-constant derivative with respect to time t. Coupling of oscillators involve placing them in proximity so as to allow them transmit a signal to one another. The most common coupling configuration include nearest neighbour and all-to-all presented in one, two or three dimensional Bravais lattice.

Consider the case where there are identical oscillators, with the dynamics of each described by equation (3.1), which is presented again in equation (3.7) for the purpose of emphasizing the number of oscillators.

$$X_j' = G_j(X_j, t);\ \ j = 1, 2, 3, \dots, n \tag{3.7}$$

Suppose that for each j, there exist a compact set which is invariant under the flow defined by the solution to equation (3.1), and the ω limit set of each of (3.1) belongs to this set (Strogatz & Mirollo, 1990). Coupling these subsystems with linear terms, one obtains

$$X, = A(k)X + G(X, t) \tag{3.8}$$

Where $A(k)$ is a real symmetric matrix depending upon the parameter $k \in \mathbb{R}^d$ representing the coupling strength, and $A(k)$ the coupling matrix.

3.10.2 Nearest Neighbour Coupling

In everyday life, coupled oscillators influences each other through transmission of signal from one oscillator to the other. The common coupling configurations include nearest neighbour and all to all.

The choice of coupling function $A(k)$ in Equation (1.4) is defined as $A(k) - k\Delta_1 \otimes I_N$, where $k \geq 0$ is the coupling strength parameret and I_N is the $N-$dimensional identity matrix, while Δ represents symmetric nearest neighbour diffusive coupling on one dimensional Bravais lattice with Neumann boundary conditions, given by;

$$\Delta_1 = \begin{pmatrix} -1 & 1 & 0 & 0 & \dots & 0 & 0 & 0 \\ 1 & -2 & 1 & 0 & \dots & 0 & 0 & 0 \\ 0 & 1 & -2 & 1 & \dots & 0 & 0 & 0 \\ \vdots & \vdots & \vdots & \vdots & \ddots & \vdots & \vdots & \vdots \\ 0 & 0 & 0 & 0 & \dots & 1 & -2 & 1 \\ 0 & 0 & 0 & 0 & \dots & 0 & 1 & -1 \end{pmatrix} \in \mathbb{R}^{n \times n}$$

Here, the elements of the matrix describes the number of signals in and out of the adjacent oscillators in the arrangement. The fist loses one and gains one signal from the next oscillator, while the second losses two and gains on from the fisrt oscillator, and another from the third oscillator, and so forth.

3.10.3 All-to-all Coupling Configuration

On the other hand, the coupling parameter $A(k)$ in equation (1.4) for an all-to-all coupling configuration in a one dimensional Bravais lattice is chosen to be $A(k) = k\Delta_A \otimes I_N$, where like in the first case, $\otimes$ is the Knonecker product and Δ_1 is an all-to-all coupling matrix defined as

$$\Delta_{\mathrm{A}} = \begin{pmatrix} -(n-1) & 1 & 1 & \dots & 1 & 1 \\ 1 & -(n-1) & 1 & \dots & 1 & 1 \\ 1 & 1 & -(n-1) & \dots & 1 & 1 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\ 1 & 1 & 1 & \dots & -(n-1) & 1 \\ 1 & 1 & 1 & \dots & 1 & -(n-1) \end{pmatrix} \in \mathbb{R}^{n\times n}$$

The analysis on the system equation (3.8) will be done to determine the existence of a compact global attractor A_k for each k. Conditions on the value of the coupling strength k, will be determined to guarantee synchronization. Further analysis of perturbed system will be done to determine cases of robustness or oscillator death (Jack H., 1997).

Other coupling configurations like one-to-many, many-to-one, small world, random, and all-to-all will be considered.

3.11. Synchronization

In general, synchronization of coupled systems means that systems which previously had different patterns of behavior begin to behave in the same way and simultaneously so that the difference in their dynamics is zero.

In mathematical models, one considers an oscillator represented by z_i whose dynamics are governed by;

$$\dot{z}_i = g(z_i)$$

where the dot denotes the derivative with respect to time t. Suppose the oscillators are coupled by some function $A(k)$ depending on the parameter k for the coupling strength. Then the connection topology is represented by the equation (1.4) reproduced as

$$\dot{z} = A(k)z + f(z)$$

where $f(z) = \big(g(z_1), g(z_2), \dots, g(z_n)\big)$.

Suppose for Equation (1.4), there is a compact global attractor $\mathcal{A}_k$ for every $k > 0$ which is invariant under the flow defined by Equation (1.3) which contains the ω −limit sets of the oscillator. The coupled system (1.4) is synchronized if there exist a smooth invariant manifold

$$\mathcal{M}_1 \coloneqq \{z \in \mathbb{R}^{nd} : z_i = z_{i+1} \neq 0, i = 1, 2, 3, 4, \dots, n\}$$

Synchronization is experienced if z belongs to the attractor $\mathcal{A}_k$ so that the difference $z_j(t) - z_{j+1}(t) \to 0$ as $t \to \infty$ for all $1 \leq j \leq n - 1$.

3.12 Stability and Persistence

It is not sufficient to study synchronization per-se. It is pertinent to study synchronization together with the stability and persistence of the synchronization manifold.

Stability relates to the attractivity of the manifold, linearized about the invariant manifold $\mathcal{M}_1$. This is determined by the sign of generalized Lyapunov exponents.

Persistence is a measure of robustness or the ability of the manifold to be insensitive to small perturbations. A necessary and sufficient condition for synchronization and persistence of invariant manifold is normal hyperbolicity. A manifold is normally hyperbolic if, under the dynamics linearized about the invariant manifold, the growth rate of vectors transverse to the manifold dominates the growth rates of vectors tangent to the manifold.

The rate of contraction or growth of vectors in the direction normal to the manifold $\mathcal{M}$ and the ratio of the exponential rate of contraction or growth of vectors normal versus vectors transverse to the manifold are measured using Lyapunov exponents; namely α and β respectively, defined as;

$$\alpha(z_0) = \lim_{n\to\infty} \frac{1}{t} \ln\|\Phi_s(t; z_0)\|$$

$$\beta(z_0) = \lim_{t\to\infty} \frac{\ln\|\Phi_s(t; z_0)\|}{\ln m\, \|\Phi_c(t; z_0)\|}$$

Where for a linear operator L, $m(L) \coloneqq \min\big(|Lx||x| = 1, x \in \mathcal{D}(L)\big)$ and $\Phi_c(t; z_0)$ is the linearization of the flow parallel to the manifold while $\Phi_s(t; z_0)$ is the linearization of the flow normal to the manifold.

3.13 Analysis of Transversal and Tangential Flows

In order to study stability of an invariant manifold, coordinate transformation is made to take care of transversal and tangential flows. Consider the transformation

$$z = ye + \tilde{e}w, \qquad w = (w_1, w_2, w_3, \dots, w_{n-1})^T, w \in \mathbb{R}^{nd-d}, \qquad y \in \mathbb{R}^d$$

$$w_j = z_j - z_{j+1}, \qquad 1 \le j \le n-1$$

$$y = \frac{1}{n}\sum_{j=1}^{n} z_j$$

Where $e = (1, 1, 1, 1, \dots, 1)^T \in \mathbb{R}^{nd}$ is th generalized eigenvector and e_j is the j^{th} column of an $n \times n$ identity matrix, while $\tilde{e} = (\tilde{e}_1, \tilde{e}_2, \tilde{e}_3, \dots, \tilde{e}_{n-1})$ and

$$\tilde{e}_j = \sum_{i=1}^{j} e_i - \frac{j}{n}e$$

For a nearest neighbour coupling of 4 oscillators, the transformation is given by

$$e = \begin{pmatrix} 1 \\ 1 \\ 1 \\ 1 \end{pmatrix}, \qquad \tilde{e} = \frac{1}{4}\begin{pmatrix} 3 & 2 & 1 \\ -1 & 2 & 1 \\ -1 & -2 & 1 \\ -1 & -2 & -3 \end{pmatrix}$$

Using this transformation, the system of four 2-dimensional oscillators will be defined by the equation

$$\begin{pmatrix} \dot{z_1}(t) \\ \dot{z_2}(t) \\ \dot{z_3}(t) \\ \dot{z_4}(t) \end{pmatrix} = k\begin{pmatrix} -1 & 1 & 0 & 0 \\ 1 & -2 & 1 & 0 \\ 0 & 1 & -2 & 1 \\ 0 & 0 & 1 & -1 \end{pmatrix} \otimes \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} \begin{pmatrix} z_1(t) \\ z_2(t) \\ z_3(t) \\ z_4(t) \end{pmatrix} + \begin{pmatrix} g(z_1(t)) \\ g(z_2(t)) \\ g(z_3(t)) \\ g(z_4(t)) \end{pmatrix}$$

Where the identity matrix I_2 is a 2×2 matrix due to the existence of two unique metapopulations; the normal and the Fisherfolk populations. Clearly, the eigenvalues of the coupling matrix are given by

$$\lambda_s = -2 - 2\cos\frac{s\pi}{4}, \quad s = 1,2,3,4$$

each occurring twice. Note that for $s = 4$, $\lambda_4 = 0$. The existence of zero eigenvalue shows that the corresponding eigenvector is $e = (1, 1, 1, 1)$ which spans the diagonal in $\mathbb{R}^{nd}$. This eigenspace forms the invariant manifold.

Using the transformation, one obtains the system

$$\begin{pmatrix} \dot{w}_1(t) \\ \dot{w}_2(t) \\ \dot{w}_3(t) \end{pmatrix} = k\begin{pmatrix} -2 & 1 & 0 \\ 1 & -2 & 1 \\ 0 & 1 & -2 \end{pmatrix} \otimes \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} \begin{pmatrix} w_1(t) \\ w_2(t) \\ w_3(t) \end{pmatrix} + \begin{pmatrix} g(z_1(t)) - g(z_2(t)) \\ g(z_2(t)) - g(z_3(t)) \\ g(z_3(t)) - g(z_4(t)) \end{pmatrix}$$

$$\dot{y}(t) = \frac{1}{4}\{g(z_1(t)) + g(z_2(t)) + g(z_3(t)) + g(z_4(t))\}$$

The first equation describes motion transverse to the manifold $\mathcal{M} = \{z | \, z_1 = z_2 = z_3 = z_4\}$ while the second equation describes motion tangential to the manifold $\mathcal{M}$.

3.14. Optimization

The endeavor of modeling infectious diseases is to ultimately understand its dynamics and possibly control the pandemic. The spread of infectious diseases can be controlled either through prevention or treatment. Some of the preventive measures include vaccination, quarantine, public health education, or restricted movement among others. In the model under study, the set of equations governing the disease dynamics can be modified to include a control parameter $u_i(t); \ i = 1,2$ which is a function of time. In

this study, the control measure of public health education campaign is denoted by $u_1(t)$ and treatment denoted by $u_2(t)$. Here, public health campaign refers to any form of education which changes the living styles and cultures of Fisherfolk so that they are moved from the high risk of infection compartment to low risk compartment. The methods under consideration include awareness, use of contraceptives for example condom, being faithful, having one partner, abstain from using sex for cultural practices, drop of beliefs that having sex before fishing brings success, change in mode of dressing and fishing styles among others (Kissling et al., 2005). All these are combined as a set of measures which reduces the rate of transmission of HIV among the Fisherfolk and also across the entire community. The other set of control using chemotherapy is denoted by $u_2(t)$. These include use of ARVs among PLWHA and treatment of opportunistic diseases among the newly infected people and use of emergency pills when on suspicion of exposure, among others.

In order to simulate the effect of controls on the system of equations in (3.1), a control variable $U = \left(u_1(t), u_2(t)\right)$ is introduced as the control variable and obtain the following system.

$$X' = G(X, U, t) \tag{3.10}$$

where $U \coloneqq \left(u_1(t), u_2(t)\right)$ denotes the set of control measures which satisfy the condition $0 \leq U \leq 1 \ a.e. \ t \in [0, \ T]$ where T is some final time $0 \leq T \leq +\infty$. In this study, we consider a linear L^1 cost function, which is more appropriate for problems with biological and biomedical background (Schättler, Ledzewicz, & Maurer, 2014). Optimal

control is defined in the form similar to Lagrange formulation (Lenhart & Workman, 2007) as;

$$\begin{aligned} max \quad & J(X,U,t) = \int_0^T f(X,U,t)dt \\ s.t. \quad & X' = G(X,U,t) \\ & 0 \leq U(t) \leq 1 \\ & X(0) = X_0 \end{aligned} \tag{3.11}$$

With the function $f(.)$ being a continuous and differentiable function. Define the Hamiltonian function of equation (3.11) as

$$H(X,U,t,\lambda) = f(X,U,t) + \lambda\big(G(X,U,t)\big) \tag{3.11}$$

Then using Pontryagin's Maximum principle (Pontryagin, 1987; Sharomi & Malik, 2017), which is the 20th century novel results used to append the differential equations as constraints to the objective functional, equation (3.11) is analyzed for optimality condition and the associated state. This principle converts the efforts of finding controls of maximizing objective function subject to the set of ordinary differential equations as constraints, to a simpler and straightforward of optimizing the Hamiltonian.

Since it is tedious and difficult, almost impossible to find analytic solution to the optimal control problem, the numerical solution of equation (3.11) is obtained using the inbuilt Runge-Kutta of order 4 – 5 method in MATLAB.

CHAPTER FOUR

RESULTS AND DUSCUSSION

4.1 Introduction

In this chapter, a specific model is formulated using differential equations, and the analysis discussed in chapter three is re-evaluated numerically. Data collected from the study area is then used to simulate the results following the analytic discussion is chapter three. Graphs are then plotted to depict the simulated results and for visual interpretation. This chapter is divided into three sections, namely; the model formulation and analysis, model optimization and graphical simulation of the model.

4.2 Model flow chart

From the general model flow chart in Figure 3.1, the parameters accounting for the transmissions across each compartment are placed as shown in Figure 4.1. The parameters and variables are all positive in the open octagonal domain $\mathbb{R}^+ = \{S \geq 0, I \geq 0, \geq 0, A \geq 0, S_v \geq 0, I_v \geq 0, T_v \geq 0, A_v \geq 0\}$ with positive initial conditions $S(0) = S_0 \geq 0, I(0) = I_o \geq 0, T(0) = T_0 \geq 0, A(0) = A_0(0) = A_{v0} \geq 0, S_v(0) = S_{v0} \geq 0, I_v(0) = I_{v0} \geq 0, T_v(0) = T_{v0} \geq 0, A_v(0) = A_{v0} \geq 0.$

The Fisherfolk is considered as high risk group of people, who interact freely with the general masses. Since their HIV prevalence is over 14%, infectivity amongst themselves is negligible, but infection transmission across to other individuals is so high. This is the reason why they are considered as HIV human vectors in the community. Through intervention strategies however, transfer of individuals from the high risk to low risk compartments is witnessed, despite the continued attachment to traditional occupation of fishing.

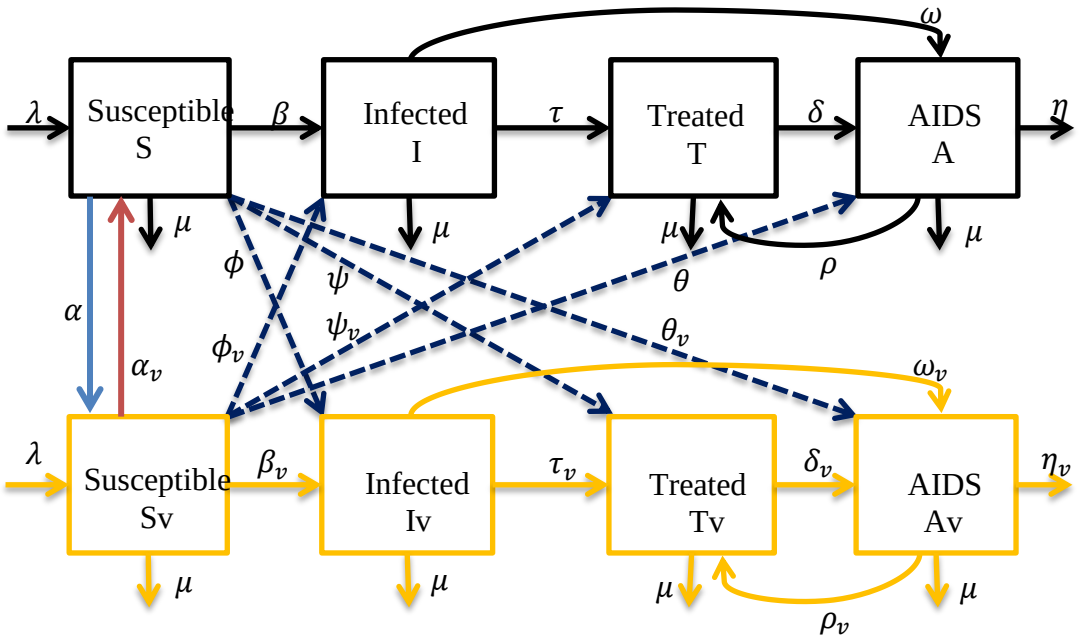

Figure 4.1. Model Flow chart showing SITA-SITA compartments for the normal community and the Fisherfolk

4.3 Model Description and Equations

From the model flow chart in figure 4.1 above, we note the following; There are two sets of population, namely; the normal population and the Fisherfolk population. The Normal population is subdivided into four disease subgroups, Susceptible, Infected, Treated and AIDS case. These subgroups are also witnessed in the Fisherfolk subpopulation. The recruitment rate of individuals into the susceptible population is constant, described by the parameter λ. From this group, population may transfer from the normal to the Fisherfolk through a constant parameter a and a_v respectively. These parameters are denotes transmission probability, and are always positive but less than one.. Natural death in each class is denoted by μ, and it is uniform in all the classes. Accelerated death rate due to the disease or due to AIDS status are represented by the parameter η for the

normal population and η_v for the Fisherfolk population. Individuals in the susceptible class are moved to the infected class through a force of infection denoted by β and β_v. These values are not equal, and it is considered here that there is a higher probability for a Fisherfolk to infect a normal population than vice versa, so it is here taken $\beta_v \geq \beta$. The interaction and the contribution of infection by the infected class, the treatment class and the AIDS class is not uniform, and it is modified by the parameters ϕ, ψ and θ respectively. It should therefore be noted that, the probability of a normal susceptible population to be infected by a treated individual in the fisherfolk population is defined as $\psi\beta_v ST_v$. The rest are equally defined. An infected individual seeks treatment, and therefore classified under treatment class at a rate τ and progress to AIDS class, due to ineffective treatment at a rate δ. It should also be noted that individuals in the treatment class and those in AIDS class have the capacity of infecting the susceptible. It also happens that before an individual seeks treatment, they can progress to AIDS class at a rate ω, however, those in AIDS class still go back seeking treatment at a rate ρ. With these descriptions, and together with the assumptions stated above, we can formulate a system of differential equations representing the model flow chart using eight ordinary differential equations to obtain,

$$\begin{aligned}
S' &= \alpha_v - \alpha + \lambda - \beta SI - \beta_v \phi SI_v - \mu S \\
I' &= \beta SI + \beta_v S_v I \phi_v - \mu I - \tau I \\
T' &= \tau I - \mu T - \delta T \\
A' &= \delta T - (\mu + \eta) A \\
S_v' &= \alpha - \alpha_v + \lambda - \beta_v S_v I_v - \beta_v S_v \phi_v I - \mu S_v \\
I_v' &= \beta_v S_v I_v + \beta \phi SI_v - (\mu + \tau) I_v \\
T_v' &= \tau I_v - (\mu + \ \delta) T_v \\
A_v' &= \delta T_v - (\mu + \eta) A_v
\end{aligned} \tag{4.1}$$

where:

β is the force of infection, with β_v being the vector folk infection rate.

λ is the natural recruitment rate to the susceptible group. λ_v is the corresponding recruitment rate to the vector folk group

μ natural death rate. It is here assumed to be equal in all compartments

θ is the modification parameter accounting for the difference in the infection rate by the infected class.

ψ is the modification parameter accounting for the difference in the infection rate by the treated class.

ϕ is the modification parameter accounting for the difference in the infection rate by the AIDS class.

τ is the rate at which infected class seek treatment. This comes either after a HIV test or at the onset of AIDS, or when opportunistic diseases symptoms occur.

δ is the proportion of those under treatment, who will not be cured and therefore progress to AIDS class

ρ is the rate at which AIDS and PLWHA seeks treatment. Note that the treatment class is also referred to as PLWHA.

ω is the rate at which infected individuals progress to AIDS class without seeking treatment

η is the accelerated death rate due to opportunistic diseases or AIDS

4.4 Stability of the System

In order to determine the stability of the system in equation (4.1), the characteristic equation and the characteristic roots are evaluated. In order to study the qualitative dynamics of the system, the behavioral dynamics locally around the fixed points are evaluated to give a general picture. Stability of the system is determined by the sign of the eigenvalues around a fixed point. Fixed points were described earlier as the set of points which satisfy the differential equation $\frac{d\bar{x}}{dt} = 0$, thus they are determined by equating the right hand side of system 4.1 to zero, and evaluate the fixed points. The system is stable if the eigenvalues of a linearized system about the fixed point are all negative, and unstable if positive. The stability of the system is undetermined from the nature of eigenvalues if some of them equals to zero. This will call for other methods, which include the use of Lyapunov exponents.

4.5 Equilibrium Points

There are two sets of fixed points; disease free equilibrium (DFE) and endemic equilibrium points (EEP).

4.5.1. Disease Free Equilibrium (DFE)

DFE occurs in absence of disease. This is realized before the onset of the disease, or when everybody has been healed or cured and thus the number of individuals in the infective class, treatment class or AIDS class is zero. In this case, since the entire population is $N(t) = S(t) + I(t) + T(t) + A(t)$, it means that at DFE, $N(t) = S(t)$.

The disease free equilibrium point (DFE) is defined as;

$$DFE = (S^0, I^0, T^0, A^0, S_v^0, I_v^0, T_v^0, A_v^0) = \left\{\frac{\lambda}{\mu}, 0, 0, 0, \frac{\lambda_v}{\mu}, 0, 0, 0\right\} \quad (4.2)$$

4.5.2 Endemic Equilibrium Point (EEP)

This is the alternative equilibrium point realized in presence of the disease. In this case, all the compartments are not empty, and the equilibrium point is defined as;

$$EEP := (S^e, I^e, T^e, A^e, S_v^e, I_v^e, T_v^e, A_v^e) \quad (4.3)$$

Where the values of the endemic equilibrium points is computed and given below.

The computation of the equilibrium point is evaluated by equating system (4.1) to zero and solving for equation (4.3). In this case, the equilibrium points obtained are defined as,

$$S^e = \frac{(1-\phi_v)(\mu+\tau)}{\beta(1-\phi\phi_v)}, I^e = \frac{\lambda(\beta_v - \sigma\phi\beta) - \mu\sigma(\beta_v - \phi\beta)S_v^e}{\sigma\beta\beta_v(1-\phi\phi_v)S_v^e}, T^e = \frac{\tau I^e}{(\mu+\delta)}, \quad A^e = \frac{\tau\delta I^e}{(\mu+\delta)(\mu+\eta)}$$

$$S_v^e = \frac{(1-\phi)(\mu+\tau)}{\beta_v(1-\phi\phi_v)}, I_v^e = \frac{\lambda(\sigma\beta - \phi_v\beta_v) - \mu\sigma(\beta - \phi_v\beta_v)S_v^e}{\sigma\beta\beta_v(1-\phi\phi_v)S_v^e}, T_v^e = \frac{\tau I_v^e}{(\mu+\delta)}, \quad A_v^e = \frac{\tau\delta I_v^e}{(\mu+\delta)(\mu+\eta)}$$

with $\sigma = \frac{\beta_v(1-\phi_v)}{\beta(1-\theta)}$

Stability of system (4.1) is determined by examining the sign of the eigenvalues of community matrix, also called stability matrix, linearized about the fixed points. Linearization matrix M is defined as;

$$M = \begin{pmatrix} -a_{11} & -\beta S & 0 & 0 & 0 & -\beta S\phi & 0 & 0 \\ \beta I & a_{22} & 0 & 0 & \beta_v I\phi_v & 0 & 0 & 0 \\ 0 & \tau & -a_{33} & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \delta & -a_{44} & 0 & 0 & 0 & 0 \\ 0 & -\beta_v S_v\phi_v & 0 & 0 & -a_{55} & -\beta_v S_v & 0 & 0 \\ \beta\phi I_v & 0 & 0 & 0 & \beta_v I_v & a_{66} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \tau & -a_{77} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \delta & -a_{88} \end{pmatrix}$$

where $a_{11} = \beta I + (\beta\phi I_v) + \mu$, $a_{22} = \beta S + \beta_v S_v\phi_v - \mu - \tau$, $a_{33} = a_{77} = (\mu + \delta)$, $a_{44} = a_{88} = (\mu + \eta)$, $a_{55} = \beta_v I_v + \beta_v\phi_v I + \mu$, and $a_{66} = \beta_v S_v + \beta S\phi - \mu - \tau$

4.5.3 Stability of Disease Free Equilibrium (DFE) point

Stability at DFE is determined by substituting DFE into the stability matrix M. Using the values in equation (4.2), where in absence of the disease, stability matrix becomes;

$$M|_{DFE} = \begin{pmatrix} -\mu & -\beta\frac{\lambda}{\mu} & 0 & 0 & 0 & -\beta\phi\frac{\lambda}{\mu} & 0 & 0 \\ 0 & a_{22} & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \tau & -(\mu+\delta) & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \delta & -(\mu+\eta) & 0 & 0 & 0 & 0 \\ 0 & -\beta_v\phi_v\frac{\lambda}{\mu} & 0 & 0 & -\mu & -\beta_v\frac{\lambda}{\mu} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & a_{66} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \tau & -(\mu+\delta) & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \delta & -(\mu+\eta) \end{pmatrix}$$

Where $a_{22} = (\beta + \beta_v\phi_v)\frac{\lambda}{\mu}$, $a_{66} = (\beta_v + \beta\phi)\frac{\lambda}{\mu}$, Stability of DFE is determined by the nature of the characteristic roots of matrix $M|_{DFE}$ which yields the roots;

$\Lambda_1 = -\mu$, $\Lambda_2 = (\beta + \phi_v\beta_v)\frac{\lambda}{\mu} - (\mu + \tau)$, $\Lambda_3 = -(\mu + \delta)$, $\Lambda_4 = -(\mu + \eta)$, $\Lambda_5 = -\mu$, $\Lambda_6 = (\beta_v + \phi\beta)\frac{\lambda}{\mu} - (\mu + \tau_v)$, $\Lambda_7 = -(\mu + \delta_v)$, $\Lambda_8 = -(\mu + \eta)$. Note that all eigenvalues $\Lambda_s, s = 1,3,4,5,7,8$ are clearly negative. The only non-negative eigenvalues

are Λ_2 and Λ_6. In order to guarantee stability, it is required that Λ_2, Λ_6 are also negative. This is satisfied if the following conditions are fulfilled.

From Λ_2, negativity is obtained if the condition below is satisfied; that is

$$\frac{(\beta+\phi_v\beta_v)\lambda}{\mu(\mu+\tau)} < 1 \coloneqq R_{0v} \tag{4.4a}$$

While from Λ_6, the condition for negativity is given by;

$$\frac{(\beta_v+\phi\beta)\lambda}{\mu(\mu+\tau_v)} < 1 \coloneqq R_{0n} \tag{4.4b}$$

The conditions in equation (4.4a) and equation (4.4b) are called the basic reproductive ratio. It is a measure of the ratio of newly infected individuals over those transferred by other terms. The dimensionless parameter represents the proportion of the infected individuals due to introduction of one infective into a purely susceptible population. If the ratio is greater than one, the disease replaces itself, and thus remains persistent in the community. This is because it means one infected individual is able to infect more than one other susceptible in its lifetime, thus the disease spreads. If the ratio is less than one, the disease will die off with time. This is because the infected individual cannot be able to replace itself.

We say that the equilibrium point DFE is stable if condition (4.4) is satisfied.

4.5.4 Stability of Endemic Equilibrium Point (EEP)

The analysis of the stability of EEP is determined by aligning linearization matrix about the EEP point in equation (4.3). An equilibrium point is stable if all the eigenvalues of a linearized matrix (about the fixed point) have the value lying on the left side of the

imaginary axis. That is, the value of the real part is less than zero. The linearization matrix about the EEP is given by;

$$M_{EEP} = \begin{pmatrix} -a_{11} & -\beta S^e & 0 & 0 & 0 & -\beta S^e \phi & 0 & 0 \\ \beta I^e & a_{22} & 0 & 0 & \beta_v I^e \phi_v & 0 & 0 & 0 \\ 0 & \tau & -a_{33} & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \delta & -a_{44} & 0 & 0 & 0 & 0 \\ 0 & -\beta_v S_v^e \phi_v & 0 & 0 & -a_{55} & -\beta_v S_v^e & 0 & 0 \\ \beta \phi I_v^e & 0 & 0 & 0 & \beta_v I_v^e & a_{66} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \tau & -a_{77} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \delta & -a_{88} \end{pmatrix}$$

where $a_{11} = \beta I^e - \beta \phi I_v^e + \mu,\ a_{22} = \beta S^e + \beta_v S_v^e \phi_v - \mu - \tau,\ \ a_{33} = (\mu + \delta),\ \ a_{44} = (\mu + \eta),\ \ a_{55} = \beta_v I_v^e + \beta_v \phi_v I^e + \mu,$ and $\ a_{66} = \beta_v I_v^e + \beta S^e \phi - \mu - \tau,\ a_{77} = (\mu + \delta)$ and $a_{88} = (\mu + \eta)$ with the equilibrium points being given in equation (4.3), and for convenience repeated below.

The equilibrium points stated in equation (4.3) are defined by; $(S^e, I^e, T^e, A^e, S_v^e, I_v^e, T_v^e, A_v^e)$ equals to;

$S^e = \frac{(1-\phi_v)(\mu+\tau)}{\beta(1-\phi\phi_v)},\ I^e = \frac{\lambda(\beta_v - \sigma\phi\beta) - \mu\sigma(\beta_v - \phi\beta)S_v^e}{\sigma\beta\beta_v(1-\phi\phi_v)S_v^e},\ \ T^e = \frac{\tau I^e}{(\mu+\delta)},\ \ A^e = \frac{\tau\delta I^e}{(\mu+\delta)(\mu+\eta)},\ S_v^e = \frac{(1-\phi)(\mu+\tau)}{\beta_v(1-\phi\phi_v)},\ \ I_v^e = \frac{\lambda(\sigma\beta - \phi_v\beta_v) - \mu\sigma(\beta - \phi_v\beta_v)S_v^e}{\sigma\beta\beta_v(1-\phi\phi_v)S_v^e},\ \ T_v^e = \frac{\tau I_v^e}{(\mu+\delta)},$ and $\ A_v^e = \frac{\tau\delta I_v^e}{(\mu+\delta)(\mu+\eta)}$

where $\sigma = \frac{\beta_v(1-\phi_v)}{\beta(1-\theta)}$. The sign of these eigenvalues will be used to determine stability of the endemic equilibrium point (EEP). Stability of this equilibrium point is determined by the nature of the eigenvalues of matrix M_{EEP} above. Without loss of qualitative characteristics, we can assume homogeneity of the normal and the Fisherfolk population and analyze stability of a system of four equations. Here, it is assumed that $S(t) = S_v(t)$, and due to the same human nature, the biological procedures like infectivity, progression

to AIDS class, treatment rate and the rest are equal, thus considering a system of four equations, we analyzed stability conditions and showed that the eigenvalues $\Lambda_i \ i = 1,2,3,4,5,6,7,8$ are;

$$\Lambda_1 = -\frac{\beta(I^e - S^e)(1+\phi) - 2\mu - \tau}{2}$$

$$- \frac{[\beta^2(I^e - S^e)^2(1+\phi)^2 - 2\beta\tau(1+\phi)(I^e + S^e) + \tau^2]^{\frac{1}{2}}}{2}$$

$$\Lambda_2 - \frac{\beta(I^e - S^e)(1+\phi) - 2\mu - \tau}{2} + \frac{[\beta^2(I^e - S^e)^2(1+\phi)^2 - 2\beta\tau(1+\phi)(I^e + S^e) + \tau^2]^{\frac{1}{2}}}{2}$$

$$\Lambda_3 = -(\mu + \delta), \qquad \Lambda_4 = -(\mu + \eta)$$

$$\Lambda_5 = -\tfrac{1}{2}[\beta(I^e - S^e)(1+\phi) - 2\mu - \tau] - \tfrac{1}{2}[\beta^2(I^e - S^e)^2(1+\phi)^2 + 16\beta^2\phi I^e S^e -$$

$$2\beta\tau(1+\phi)(I^e + S^e) + \tau^2]^{\frac{1}{2}}, \ \ \Lambda_6 = -\tfrac{1}{2}[\beta(I^e - S^e)(1+\phi) - 2\mu - \tau] +$$

$$\tfrac{1}{2}[\beta^2(I^e - S^e)^2(1+\phi)^2 + 16\beta^2\phi I^e S^e - 2\beta\tau(1+\phi)(I^e + S^e) + \tau^2]^{\frac{1}{2}}, \ \Lambda_7 =$$

$$-(\mu + \delta), \ \Lambda_8 = -(\mu + \eta)$$

Clearly, some eigenvalues $\Lambda_s, s = 3,4,7,8$ are negative since all the parameters are positive, and the rest $\Lambda_s, s = 1,2,5,6$ require additional conditions to determine their sign.

The condition for the rest of the eigenvalues to be negative is if $S^e - I^e \geq 0$. This is naturally expected, unless the pandemic sweeps every susceptible individual, and thus it is declared that the EEP is stable.

4.6 Positivity and Boundedness of Solutions

When dealing with biological models, it is necessary to show that the solutions fall within the feasible space. Solutions are feasible if they are always positive and bounded. Positivity and boundedness is proven for every solution of equations in system (4.1). Beginning with equation one, we show that from

$$S' = \lambda - \beta SI - \beta_v \phi SI_v - \mu S;\ \lambda > 0$$

$$\dot{S} \leq -\beta SI - \beta_v \phi SI_v - \mu S \leq -(\beta I + \phi I_v + \mu)S$$

Let $\beta I + \phi I_v + \mu = A$, then

$\dot{S} \leq -AS \Longrightarrow \frac{\dot{S}}{S} \leq -A.$

Integrating both sides gives $lnS(t) \leq -At + c \ \Longrightarrow S(t) \leq S_0 e^{-At}$ where $S_0 = e^c$.

Clearly, the solution of equation one of system (4.1) $S(t) \leq S_0 e^{-At}$ is bounded for all $t \geq 0$ and positive.

Similarly, the analysis of equation two yields

$$I' = \beta SI + \beta_v S_v I \phi_v - \mu I - \tau I = (\beta S + \beta_v S_v \phi_v - \mu - \tau)I$$

Let $B = \beta S + \beta_v S_v \phi_v - \mu - \tau$, then $I' = BI \Longrightarrow I(t) = I_0 e^{Bt}$

For boundedness, we require that $B < 0 \Longrightarrow \beta S + \beta_v S_v \phi_v - \mu - \tau < 0$

Positivity is guaranteed if the condition $\beta S + \beta_v S_v \phi_v < \mu + \tau$. At the fixed points, this condition is equivalent to equation (4.4a), and therefore the solution is always positive and bounded whenever $R_{0i} < 1,\ \ i = v, n.$

The third equation on treatment class is given by $T' = \tau I - \mu T - \delta T$ which reduces to

$$\dot{T} \leq -(\mu + \delta)T$$

Solving this gives $T(t) \leq T_0 e^{-(\mu+\delta)t}$ which is positive and bounded for all $0 \leq t \leq \infty^+$.

The fourth equation on

$$\frac{dA}{dt} = \delta T - (\mu + \eta)A$$

$$\dot{A} \leq -(\mu + \eta)A$$

Solving, gives $A(t) \leq A_0 e^{-(\mu+\eta)t}$ which is positive and bounded for all $0 \leq t \leq \infty^+$.

The set of equations representing the vector population can be analyzed in the same way to obtain

$$S_v' = \lambda - \beta_v S_v I_v - \beta_v S_v \phi_v I - \mu S_v$$

$S_v' \leq -(\beta_v I_v + \beta_v S_v \phi_v I + \mu)S_v$ with $S_v(t) \leq S_{v_0} e^{-(\beta_v I_v + \beta_v S_v \phi_v I + \mu)t}$ which is positive and bounded.

The infective equation $\frac{dI_v}{dt} = \beta_v S_v I_v + \beta\phi S I_v - (\mu + \tau)I_v$ yields the solution

$$I_v(t) \leq I_{v_0} e^{-(\beta_v S_v + \beta\phi S - (\mu+\tau))t}$$

Which is always positive and bounded whenever $\beta_v S_v + \beta\phi S < (\mu + \tau)$or whenever $R_{0n} < 1$.

The third equation on treatment class yields $\frac{dT_v}{dt} = \tau I_v - (\mu + \delta)T_v$ or $\dot{T_v}(t) \leq -(\mu + \delta)T_v$.

Solving, gives $T_v(t) \leq T_{v_0} e^{-(\mu+\delta)t}$ which is positive and bounded for all positive time t.

Lastly, the eighth equation on AIDS class is analyzed as $\frac{dA_v}{dt} = \delta T_v - (\mu + \eta)A_v$ or $\dot{A_v}(t) \leq -(\mu + \eta)A_v$. Solving, gives $A_v(t) \leq A_{v_0} e^{-(\mu+\delta)t}$ which is positive and bounded.

Clearly, system (4.1) is positive and bounded on the interval $[0,\ \infty^+]$ for all positive time $t \in [0,\ \infty^+]$.

4.7. Sensitivity

Due to the presence of many parameters in the system, it is necessary to determine the sensitivity of parameters, so as to focus on the study of those that make significant change whenever they are varied. Suppose the perturbation parameters are represented by letter P, say $P_i, i = 1,2,3,4,$ ... Their sensitivity is defined as

$$\frac{1}{P_i}\frac{\partial R_0}{\partial P_i} = [0\ , 1] \tag{4.5}$$

The sensitivity of the parameters $\mu, \tau, \phi, \phi_v, \beta, \beta_v, \lambda$ with respect to the reproductive ratio R_0 is evaluated, to check which of them can significantly create a big change. Here, the reproductive ratio is defined as;

$R_{0_1} = \frac{(\beta+\beta_v\phi_v)\lambda}{\mu(\mu+\tau)}$ and $R_{0_2} = \frac{(\beta_v+\beta\phi)\lambda}{\mu(\mu+\tau)}$ for the property that $\tau = \tau_v$. Then, the following are sensitivity ratios of various parameters.

Sensitivity of β on $R_{0_1} = \frac{1}{\beta}\frac{(\partial R_{0_1})}{\partial \beta} = \frac{1}{\beta}\left(\frac{\lambda}{\mu(\mu+\tau)}\right)$

Sensitivity of β on $R_{0_2} = \frac{1}{\beta}\frac{\partial R_{0_2}}{\partial \beta} = \frac{1}{\beta}\left(\frac{\phi\lambda}{\mu(\mu+\tau)}\right)$

Sensitivity of β_v on $R_{0_1} = \frac{1}{\beta_v}\frac{\partial R_{0_1}}{\partial \beta_v} = \frac{1}{\beta_v}\left(\frac{\phi_v\lambda}{\mu(\mu+\tau)}\right)$

Sensitivity of β_v on $R_{0_2} = \frac{1}{\beta_v}\frac{\partial R_{0_2}}{\partial \beta_v} = \frac{1}{\beta_v}\left(\frac{\lambda}{\mu(\mu+\tau)}\right)$

Sensitivity of ϕ on $R_{0_1} = \frac{1}{\phi}\frac{\partial R_{0_1}}{\partial \phi} = \frac{1}{\phi}(0) = 0$

Sensitivity of ϕ on $R_{0_2} = \frac{1}{\phi}\frac{\partial R_{0_2}}{\partial \phi} = \frac{1}{\phi}\left(\frac{\beta\lambda}{\mu(\mu+\tau)}\right)$

Sensitivity of ϕ_v on $R_{0_1} = \frac{1}{\phi_v}\frac{\partial R_{0_1}}{\partial \phi_v} = \frac{1}{\phi_v}\left(\frac{\beta_v\lambda}{\mu(\mu+\tau)}\right)$

Sensitivity of ϕ_v on $R_{0_2} = 0$

Sensitivity of λ on $R_{0_1} = \frac{1}{\lambda}\frac{\partial R_{0_1}}{\partial \lambda} = \frac{1}{\lambda}\left(\frac{(\beta+\beta_v\phi_v)}{\mu(\mu+\tau)}\right)$

Sensitivity of λ on $R_{0_2} = \frac{1}{\lambda}\frac{\partial R_{0_2}}{\partial \lambda} = \frac{1}{\lambda}\left(\frac{(\beta_v+\beta\phi)}{\mu(\mu+\tau)}\right)$

Sensitivity of τ on $R_{0_1} = \frac{1}{\tau}\frac{\partial R_{0_1}}{\partial \tau} = \frac{-\lambda(\beta+\beta_v\phi_v)}{\mu^2(\mu+\tau)^2}$

Sensitivity of τ on $R_{0_2} = \frac{1}{\tau}\frac{\partial R_{0_2}}{\partial \tau} = \frac{-\lambda(\beta_v+\beta\phi)}{\mu^2(\mu+\tau)^2}$

Sensitivity of μ on $R_{0_1} = \frac{1}{\mu}\frac{\partial R_{0_1}}{\partial \mu} = \frac{-\lambda(\beta+\beta_v\phi_v)(2\mu+\tau)}{\mu^3(\mu+\tau)^2}$

Sensitivity of μ on $R_{0_2} = \frac{1}{\mu}\frac{\partial R_{0_2}}{\partial \mu} = \frac{-\lambda(\beta_v+\beta\phi)(2\mu+\tau)}{\mu^3(\mu+\tau)^2}$

4.8 Optimization and Control

In this study, we analyze public health educational campaign denoted by the net transfer rates of susceptible between the two categories $u_E(t) = \alpha(t) - \alpha_v(t)$ and treatment $u_T(t) = \tau(t) + \rho(t)$ of the system (4.1),where $0 \leq U \leq 1$, with the objective of minimizing treatment cost and reducing the number of infectives.

4.8.1 Public Health Educational Campaign and Treatment

Through public health educational campaigns, susceptible individuals become aware and become cautious and therefore avoid high risk behaviours, which expose them to

contracting HIV. Those already infected will also avoid careless behaviours which can potentially infect others, and take treatment so as to avoid progressing to AIDS class. The variable $0 \leq u_E(t) \leq 1$ represents the proportion of those effectively transformed to low risk class, while the variable $0 \leq u_T(t) \leq 1$ denotes the proportion of individuals treated, so that they don't progress to PLWHA and also reduce the virus load and infectivity.

In order to analyze the potential effect of control strategies, this study forcused on the control of the vector population using a system of two equations, the susceptible $S(t)$ and the infected class $I(t)$ as shown in equation 4.6.

$$\begin{aligned} S_v' &= \lambda - \beta_v S_v I_v - \mu S_v - u_E(t) \\ I_v' &= \beta_v S_v I_v - \mu I_v - u_T(t) I_v \end{aligned} \tag{4.6}$$

The set of equations in (4.6) represent the high risk population, responsible for the high transmission of HIV, and the control of the pandemic among this population is as good as controlling the disease in the entire population. Notice also that control parameters are introduced in terms of $U = (u_T,\ u_E)$ in all the affected equations.

In this model, the AIDS class is ignored because HIV is irreversible, and once someone has developed AIDS, their fate is either death or long live treatment commonly called PLWHA. This is catered for in equation (4.6) as mortality due to HIV and the transfer due to treatment respectively. It is therefore considered that the total population $N(t) = S(t) + I(t)$.

From system (4.6), the number of treated individuals is monitored and the number of individuals transformed due to public health education, who are now low risk to HIV is also monitored by the equations $T_v' = u_T(t) I_v$ and $S_v' = u_E(t) S_v$ respectively.

4.8.2 Optimal Control Problem Model

In order to account for the control of the disease both through public health education and treatment, optimal control problem of two variables is modelled using equation 4.7. With this in mind, and considering a linear cost functional, the optimal control problem will be of the form

$$\max J(X,U,t) = \int_0^T (A_1 I(t) + A_2 S(t) + A_3 u_E(t) + A_4 u_T(t))\, dt - B_1 I(T) - B_2 S(T) \tag{4.7}$$

where $(A_i, B_i > 0, i = 1,2,\dots)$ subject to the constraints in equation (4.1) together with their positivity and boundedness conditions $0 \le U \le 1$. Here, A_1, A_2, A_3 and A_4 are linear constants used to balance the units and measurement as well as indicating the amount of effort on the type of intervention strategy applied. In this study, the constants will be assumed to be $A_1 = A_2 = A_3 = A_4 = B_1 = B_2 = 1$.

Maximization of the objective function of the optimal problem in equation 4.7 can be expressed as;

$$\max_{0 \le U \le 1} J(U),$$

Subject to the constraints:

$$\begin{aligned} S_v' &= \lambda - \beta_v S_v I_v - \mu S_v - u_E(t) S_v, \qquad I(0) = 1, \\ I_v' &= \beta_v S_v I_v - \mu I_v - u_T(t) I_v, \;\; S(0) = N, \end{aligned}$$

and:

$$0 \le u_T \le 1, \;\; 0 \le u_E \le 1$$

Applying Pontryagin principle in (Di Liddo, 2016), the Hamiltonian H is defined by:

$$H(I, S, U, \lambda) = \lambda_1(t)I(t, u_T) + \lambda_2 S(t, u_E) - I - S$$

which in explicit form, the Hamiltonian is defined as

$$H = -I - S - U + \lambda_1(\lambda - \beta_v S_v I_v - \mu S_v - u_E(t)S_v) + \lambda_2(\beta_v S_v I_v - \mu I_v - u_T(t)I_v) \tag{4.8}$$

There are several cost functions that can be employed in analyzing the optimal control. These include linear and quadratic state dependent or independent cost functions, as used in many literature (see for instance (Francis, 2004), (Buonomo & Vargas-De-León, 2014), (Jung, Iwami, Takeuchi, & Jo, 2009), (Jana, Haldar, & Kar, 2016)). These cost functions are independent on the number of treated people, and thus making it unsuitable. For the purpose of this study, a blowing up cost function $U = \frac{\hat{B}puI}{\hat{B}-puI}$ is chosen since it accommodates the characteristics of the number of people treated and the total cost if all people are treated (Di Liddo, 2016). The cost function U can be expressed for both public health educational campaigns and treatment as;

$$u_E(t) = \frac{\hat{B}puS_v}{(\hat{B}-pu_E S_v)^2} \tag{4.9a}$$

And

$$u_T(t) = \frac{\hat{B}puI_v}{(\hat{B}-pu_E I_v)^2} \tag{4.9b}$$

Using the blowing up cost functions presented in equation (4.9) on the objective function in equation (4.7) together with the Hamiltonian in equation (4.8), the adjoin condition for equation (4.8) is obtained to be of the form

$$\begin{aligned} \lambda_1'(t) &= -\frac{\partial H}{\partial I} = 1 + \lambda_1\beta_v S_v - \lambda_2\beta_v S_v + \mu + u_T(t) \\ \lambda_2'(t) &= -\frac{\partial H}{\partial S} = 1 - \lambda_1\beta_v I_v + \mu + u_E(t) - \lambda_2\beta_v I_v \end{aligned} \tag{4.10}$$

And the transversality conditions given by

$$\begin{aligned} \lambda_1(T) &= 1 + (\lambda_1 - \lambda_2)\beta_v N + \mu + u_T(T) \\ \lambda_2(T) &= 1 + \mu + u_E(T) \end{aligned} \tag{4.11}$$

And the optimality conditions given by

$$\begin{aligned} \frac{\partial H}{\partial u_E} &= \left(-\frac{\hat{B}^2 p}{(\hat{B} - p u_E S_v)^2} - \lambda_1\right) S_v \\ \frac{\partial H}{\partial u_T} &= \left(-\frac{\hat{B}^2 p}{(\hat{B} - p u_T I_v)^2} - \lambda_2\right) I_v \end{aligned} \tag{4.12}$$

Equating equation (4.12) to zero and solving for the cost function U gives the solutions

$$\hat{u}_E = \frac{\hat{B} - \sqrt{\frac{\hat{B}^2 p}{-\lambda_1}}}{p S_v}, \quad \text{and} \quad \hat{u}_T = \frac{\hat{B} - \sqrt{\frac{\hat{B}^2 p}{-\lambda_2}}}{p I_v},$$

From the Pontryagin maximum principle, the blowing up cost function is expressed as;

$$u_E(t) = \begin{cases} 0 & if\ \lambda_1 \geq 0 \\ \hat{u}_E & if\ \lambda_1 \geq 0 \quad and\ 0 \leq \hat{u_E}(t) \leq 1 \\ 1 & if\ \lambda_1 \geq 0 \quad and\ \hat{u}_E \geq 1 \end{cases} \tag{4.13}$$

$$u_T(t) = \begin{cases} 0 & if\ \lambda_2 \geq 0 \\ \hat{u}_T(t) & if\ \lambda_2 \geq 0 \quad and\ 0 \leq \hat{u_T}(t) \leq 1 \\ 1 & if\ \lambda_2 \geq 0 \quad and\ \hat{u}_T \geq 1 \end{cases} \tag{4.14}$$

4.9 Simulation and Numerical Results

Numerical solutions verify analytic solutions and graphically depict the specific picture of a particular zone or area. In this section, numerical results are presented using data collected from Kisumu, Homabay, Siaya and Busia fishing sites. Table 1 summarizes the parameter values as per the data collected.

Table 1: Parameter values from data collected from Samia, Kisumu, Homabay and *Mbita.*

No	Symbol	Description	Value
1	λ	Recruitment rate of normal community	0.7
2	λ_v	Recruitment rate of individuals into the Fisherfolk	0.9
3	μ	Natural death rate	0.00124
4	β	Probability of infectivity given sufficient contact	0.00033
5	β_v	Probability of infectivity by Fisherfolk community	0.00133
6	c	Number of sexual partners or contact rate of normal population	0.18624
7	c_v	Number of sexual partners or contact rate of Fisherfolk population	0.20835
7	τ	Rate of seeking treatment by HIV infected patients	0.024
8	τ_v	Rate of seeking treatment by Fisherfolk HIV patients	0.021
9	σ	Progression rate of HIV patients to AIDS status	0.023
10	σ_v	Fisherfolk Progression rate of HIV patients to AIDS status	0.032
11	η	Accelerated death rate due to HIV/AIDS	0.00124

The parameters in Table 1 were computed from population data available. Using the parameter values in Table 1. above, the following HIV/AIDS dynamics of the normal population and the Fisherfolk population are obtained.

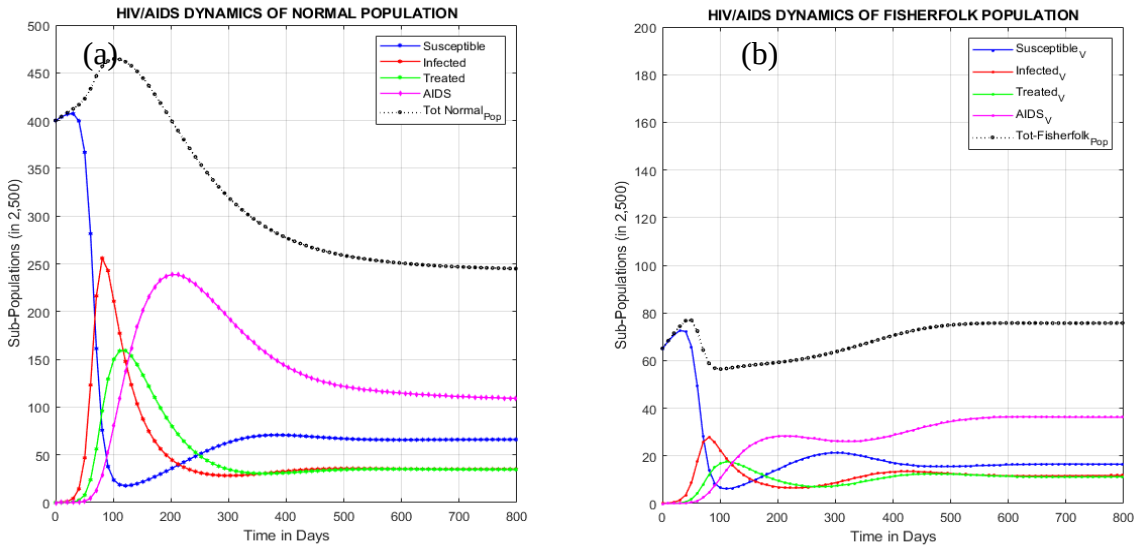

Figure 4.2 HIV/AIDS dynamics in Lake Victoria region for the Normal and the Fisherfolk Population in absence of control.

In Figure 4.2, the dynamics of HIV/AIDS in absence of control strategies and with full interaction of the normal population and the Fisherfolk is depicted. It is noted that from the onset of HIV pandemic, both the normal population and the Fisherfolk are affected. After the first quarter, wild dynamics gently begin to vanish so that by one year, the dynamics begin to settle and steady state is achieved after two years (700 days).

With the consideration of Fisherfolk as HIV vector, the parameters representing the interaction between the two communities can be controlled, and when c_v and ϕ_v are adjusted to zero, the dynamics of the new system is as shown in Figure 4.3.

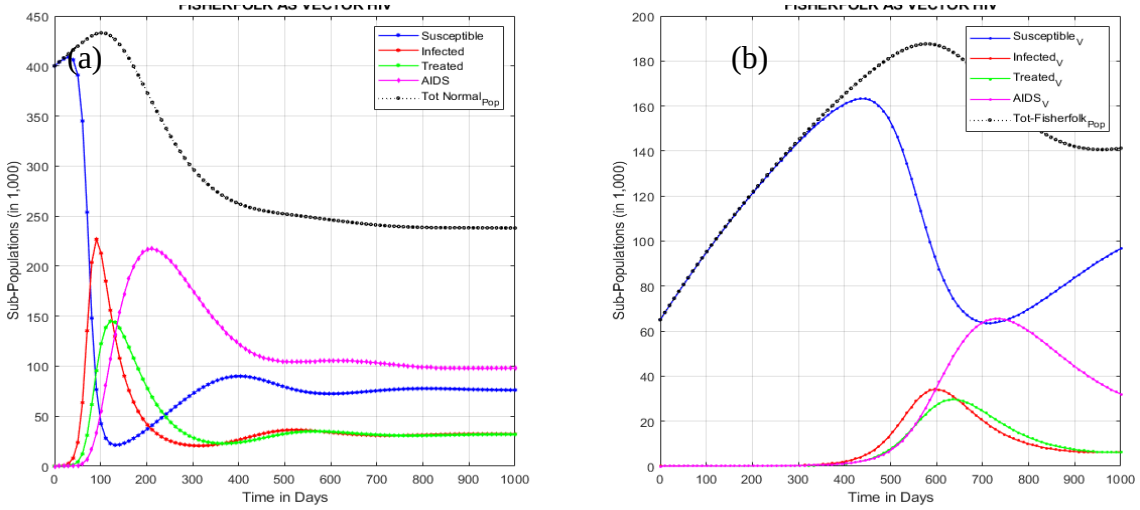

Figure 4.3. HIV/AIDS dynamics among normal and fisherfolk communities with no interaction.

The disease dynamics of the Fisherfolk community are prolonged and intensified, while the normal population experience improved health status, with lesser infectivity and accelerated achievement of a higher steady state.

4.10 Coupling and Synchronization of Coupled Oscillators

In this section, the concept of allowing independent oscillators to influence each other was considered. Here, identical oscillators are all allowed to influence each other, so that the action of one, leads to a proportional reaction of all the other $n-1$ oscillators. It was studied in a view that, the independent oscillations may be influenced so that in future time, all the oscillators behave in the same way. This phenomenon is called synchronization. Various forms of coupling configurations discussed before includes nearest neighbour coupling, ring coupling, one to many coupling and all-to-all coupling. The latter is further analyzed in this study.

4.10.1 All-to-All Coupling Topology

Diffusive coupling is an arrangement, where oscillators are allowed to influence each other (Wasike & Rotich, 2007). In terms of the biological oscillators under study, the periodic dynamics of HIV/AIDS pandemic in four distinct population patches around Lake Victoria are interacting through people entering and leaving each patch, together with interacting in the markets and common fishing grounds. The interaction referred to here is the relationship which leads to unprotected sexual intercourse. The level of interaction which leads to sexual relationship, significant to cause transfer of disease is here considered. All-to-all coupling, also called global coupling is represented geometrically as in Figure 4.1 (Heagy, Carroll, & Pecora, 1994). Each terminal point represents an oscillator, while the arrows joining the oscillators represent bidirectional coupling where oscillators are allowed to influence each other simultaneously.

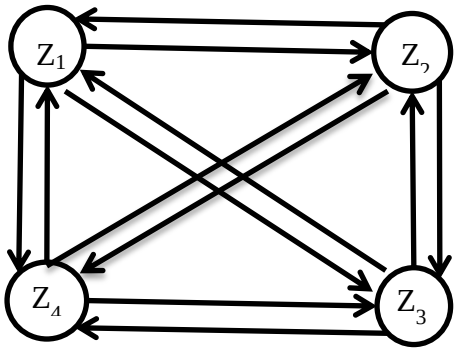

Figure 4.4. All-to-All Coupling configuration

Each oscillator is represented by a system of ordinary differential equations, denoting a dissipative system of four variables, described by the second set of four differential equations in equation (4.1), describing the dynamics of Susceptible, Infective, Treated and AIDS cases of Fisherfolk. Using the notation of $Z_i,\ i = k, s, h, b$ (Kisumu, Siaya, Homabay and Busia) to

represent the fours oscilators, we derive the system of coupled oscillators as in equation (3.8) given by

$$\begin{pmatrix} \dot{z_1}(t) \\ \dot{z_2}(t) \\ \dot{z_3}(t) \\ \dot{z_4}(t) \end{pmatrix} = k \begin{pmatrix} -3 & 1 & 1 & 1 \\ 1 & -3 & 1 & 1 \\ 1 & 1 & -3 & 1 \\ 1 & 1 & 1 & -3 \end{pmatrix} \otimes (I_4) \begin{pmatrix} z_1 \\ z_2 \\ z_3 \\ z_4 \end{pmatrix} + \begin{pmatrix} g_1(z_1) \\ g_2(z_2) \\ g_3(z_3) \\ g_4(z_4) \end{pmatrix} \qquad (4.15)$$

where the matrices are given in detail as;

$$\mathrm{k}\Delta \otimes I_4 = k \begin{pmatrix} -3I_4 & I_4 & I_4 & I_4 \\ I_4 & -3I_4 & I_4 & I_4 \\ I_4 & I_4 & -3I_4 & I_4 \\ I_4 & I_4 & I_4 & -3I_4 \end{pmatrix} \qquad (4.16)$$

and

$$\dot{z_i}(t) = \begin{pmatrix} \dot{S}_i(t) \\ \dot{I}_i(t) \\ \dot{T}_i(t) \\ \dot{A}_i(t) \end{pmatrix} = \begin{pmatrix} \lambda S_i - c\beta\phi S_i I_i - \mu S_i \\ c\beta\phi S_i I_i - (\mu + \tau + \omega) I_i \\ \tau I_i - (\mu + \delta) T_i + \rho A_i \\ \delta T_i - (\xi + \sigma + \rho) A_i + \omega I_i \end{pmatrix} \qquad (4.17)$$

where the subscripts $i = k, h, s, b$ for Kisumu, Homabay, Siaya and Busia respectively. In compact vector form, equation (4.19) is expressed equivalent to equation (1.4) as;

$$\dot{Z} = k(\Delta \otimes I_4)Z + G(Z) \qquad (4.18)$$

where Z and $G(Z)$ are defined in equation (1.4) above. The coupled system (4.18) is said to be synchronized, if there exist a manifold

$$\mathcal{M} := \{Z \in \mathbb{R}^{nd} : z_i = z_{i+1} \neq 0, \qquad i = k, s, h, b\}$$

That is, there exist an invariant attractor $\mathcal{A}_k \forall\, k > 0$ invariant under the flow defined by equation (1.13) which contains the ω- limit set of the oscillator, so that the difference $z_i(t) - z_{i+i}(t) \to 0$ as $t \to \infty, \forall\, i$.

4.10.2 Construction of Synchronization manifold

Synchronization manifold $\mathcal{M} \coloneqq (Z \in \mathbb{R}^{nd}: z_i = z_{i+1} \neq 0,\ i = 1,2,3,\dots,n-1\}$ is always guaranteed when identical oscillators are coupled, and thus the diagonal is invariant (Sun, Bollt, & Nishikawa, 2009). The task at hand is therefore to show that one of the eigenvalues of the coupling topology matrix Δ is $\lambda_0 = 0$ and the corresponding generalized eigenvector spans the diagonal in $\mathbb{R}^{nd}$ while the other eigenvalues $\lambda_s, s = 1,2,..,n-2$ are bounded to the left side of the imaginary axis.

Clearly, the eigenvalues of the matrix $\sigma(\Delta)$

$$\Delta = \begin{pmatrix} -3 & 1 & 1 & 1 \\ 1 & -3 & 1 & 1 \\ 1 & 1 & -3 & 1 \\ 1 & 1 & 1 & -3 \end{pmatrix}$$

are; $\lambda_0 = 0$ and $\lambda_s = -n_s,\ s = 1,2,3,\dots n-1,$ with the corresponding generalized eigenvectors as; $v_0 \coloneqq (1,1,1,1,\dots,1) \in \mathbb{R}^d$ which spans the diagonal and the other eigenvectors are;

$v_i \coloneqq [(-1,1,0,0,\dots,0),(-1,0,1,0,0,\dots,0),(-1,0,0,1,0,\dots,0),\dots,(-1,0,0,\dots,0,1)].$

The existence of a global attractor, (the diagonal) in a bounded set $U \in \mathbb{R}^{nd}$, we define a transformation, that splits the system into transverse flow and tangential flow to the manifold. Consider the transformation in (Wasike & Rotich, 2007) defined below.

$$\begin{gathered} z = ye + \tilde{e}w, w = (w_1, w_2, \dots, w_{n-1})^T, \qquad w \in \mathbb{R}^{nd-d}, y \in \mathbb{R}^d \\ w_j = z_j - z_{j+1}, 1 \leq j \leq n-1, \\ y = \frac{1}{n}\sum_{j=1}^{n} z_j, \end{gathered} \tag{4.19}$$

where e_j is the j^{th} column of an $n \times n$ identity matrix and $\tilde{e} = \sum_i^j \left(e_i - \frac{j}{n}e\right)$, with $\tilde{e} = (\tilde{e}_1, \tilde{e}_2, \dots, \tilde{e}_{n-1})$. The set e , $\tilde{e}_j$ is an orthogonal basis for $\mathbb{R}^n$.

Using transformation (4.19) in equation (4.18), yields

$$\begin{aligned} \dot{w} &= k(\Delta_1 \otimes I_d)w + F(w, y) \\ \dot{y} &= \frac{1}{n}\sum_{j=1}^{n} g(z_j) \end{aligned} \tag{4.20}$$

where $F(w, y) = (F_1(w, y), F_2(w, y), F_3(w, y))$ with $F_i(w, y) = g(z_i) - g(z_{i+1})$, $1 \leq i \leq n - 1$ and the matrix Δ_1 is given by $\Delta_1 = -knI_n \otimes I_d$.

The first equation in (4.20) describes the dynamics transverse to the synchronization manifold, and the second equation describes the dynamics tangential to the synchronization manifold.

4.10.3 Stability of the Synchronization Manifold

Synchronization means the deviations $z_i - z_{i+1}$ as $t \to \infty$ dies out, that means the solution of the first equation in (4.20) is expected to be exponentially stable, the property that $w = 0$ (Josic, 2000). This research is interested in local synchronization, and thus the fundamental matrix solution $\Phi(t; z_0)$, $z_0 \in \mathcal{M}$ of the linearization of equation (4.18) about $\mathcal{M}$ defined as $\dot{Z} = A\big(z(t; z_0)\big)Z$ is considered.

Let

$$\Phi(t; z_0) = \Phi_c(t; z_0) \oplus \Phi_s(t; z_0);$$

be the invariant splitting where $\Phi_c(t; z_0)$ and $\Phi_s(t; z_0)$ are restrictions of $\Phi(t; z_0)$ of the tangent bundle vector $T_{z_0}\mathcal{M}$ to the manifold at z_0 and N_{z_0} bundle of vectors normal to the manifold at z_0.

Linearizing equation (4.20) along the solution $\big(0, y_0(t)\big)$ on the manifold $\mathcal{M}$ yields

$$\begin{pmatrix} \dot{w} \\ \dot{y} \end{pmatrix} = \begin{pmatrix} k(\Delta_1 \otimes I_4 + I_3 \otimes D_z g(y_0(t)) & 0 \\ 0 & D_z g\big(y_0(t)\big) \end{pmatrix} \begin{pmatrix} w \\ y \end{pmatrix} \tag{4.21}$$

Whose solution is of the form

$$\begin{aligned} w(t) = \Phi_s(t; z_0) \approx e^{(k\lambda_\zeta + \lambda_i)t}, \zeta = 1, 2, 3,\ i = 1, 2,\ 3 \\ y(t) = \Phi_c(t; t_0) \approx e^{\lambda t} \end{aligned} \tag{4.22}$$

The invariant manifold $\mathcal{M}$ is attracting and stable if the maximum of $k\big(\lambda_\zeta + \lambda_i\big)$ is less than zero. In our case, $\max\big(\lambda_\zeta\big) = -4k$ and $\max(\lambda_i) = 1.6361$, thus the generalized Lyapunov exponent

$$\alpha(z_0) = \max\big(k\lambda_\zeta + \lambda_i\big) = -4k + 1.6361$$

Giving the optimal coupling strength $k_0 = 0.409025$

If $\alpha(z_0) < 0$, it is required for persistence that $\beta(z_0) < 1$, that is

$$\beta(z_0) \coloneqq \lim_{t\to\infty} sup\, \frac{\ln\|\Phi_s(t, z_0)\|}{\ln m\big(\Phi_c(t, z_0)\big)} < 1$$

From calculation, the value of $\beta(z_0)$ obtained is $\beta(z_0) = 0.1993 < 1$ as required.

4.11 Coupling of Oscillators

All-to-All coupling configuration described in section 3.9 is presented for four oscillators each of dimension four, making a system of sixteen ordinary differential equations, in equation 4.23(a-d). Consider the choice of $\dot{z}(t) = g\big(z(t)\big)$ defined in equation (4.1) for Kisumu (k), Homabay (h), Siaya (s) and Busia (b) as;

$$\dot{z}_k(t) = \begin{bmatrix} \dot{S_k} = & \lambda S_k - c\beta\phi S_k I_k - \mu S_k \\ \dot{I_k} = & c\beta\phi S_k I_k - (\mu + \tau + \omega) I_k \\ \dot{T_k} = & \tau I_k - (\sigma + \delta) T_k + \rho A_k \\ \dot{A_k} = & \delta T_k - (\xi + \sigma + \rho) A_k + \omega I_k \end{bmatrix} \tag{4.23a}$$

$$\dot{z}_h(t) = \begin{bmatrix} \dot{S}_h = & \lambda S_h - c\beta\phi S_h I_h - \mu S_h \\ \dot{I}_h = & c\beta\phi S_h I_h - (\mu + \tau + \omega) I_h \\ \dot{T}_h = & \tau I_h - (\sigma + \delta) T_h + \rho A_h \\ \dot{A}_h = & \delta T_h - (\xi + \sigma + \rho) A_h + \omega I_h \end{bmatrix} \tag{4.23b}$$

$$\dot{z}_s(t) = \begin{bmatrix} \dot{S}_s = & \lambda S_s - c\beta\phi S_s I_s - \mu S_s \\ \dot{I}_s = & c\beta\phi S_k I_k - (\mu + \tau + \omega) I_s \\ \dot{T}_s = & \tau I_s - (\sigma + \delta) T_s + \rho A_s \\ \dot{A}_s = & \delta T_s - (\xi + \sigma + \rho) A_s + \omega I_s \end{bmatrix} \tag{4.23c}$$

$$\dot{z}_b(t) = \begin{bmatrix} \dot{S}_b = & \lambda S_b - c\beta\phi S_b I_b - \mu S_b \\ \dot{I}_b = & c\beta\phi S_b I_b - (\mu + \tau + \omega) I_b \\ \dot{T}_b = & \tau I_b - (\sigma + \delta) T_b + \rho A_b \\ \dot{A}_b = & \delta T_b - (\xi + \sigma + \rho) A_b + \omega I_b \end{bmatrix} \tag{4.23d}$$

Coupling equations (4.23a-d) as described in equation (4.15), and transforming to a form similar to equation (4.20), yields the system which satisfies the criteria for synchronization and persistence.

4.12 Graphical presentation of Coupled Oscillators

In order to represent graphically the dynamics of HIV/AIDS in the four patches, namely Kisumu, Busia, Siaya and Homabay, the following data collected from the study area are presented in Table 2 below. Some data were approximated within plausible range.

Table 2. Parameter values of data collected from Siaya, Kisumu, Homabay and Busia.

No	Symbol	Description	Value
1	λ	Recruitment rate of normal community	0.01385
2	μ	Natural death rate	0.00124
3	β	Probability of infectivity given sufficient contact	0.00033
4	ϕ	Modification parameter describing sexual interaction probability	0.00177
5	c	Contact rate of susceptible with infective, sufficient to transmit HIV	0.18624
6	τ	Progression rate of Treatment class to HIV patients	0.24
7	σ	Progression rate of HIV patients to AIDS status	0.023
8	η	Accelerated death rate due to HIV/AIDS	0.00124
9	δ	Accelerated death rate due to HIV infection, while on treatment	0.00496
10	ρ	Rate of seeking treatment by AIDS class	0.00354
11	ω	Direct progression to AIDS class from the time of infection	0.003218
12	p	Perturbation multiplier	0.01
13	k	Coupling strength	[0 , 1]
14	ξ	Accelerated death rate due to full blown AIDS status	0.00321

Parameters presented in Table 2 were collected and computed from the secondary data from Kisumu regional Kenya Population and Census office.

The fourth order Runge-Kutta numerical algorithm inbuilt in MATLAB is used to evaluate the trajectories of system 4.23 with initial conditions $(S_0, I_0, T_0, A_0) = (300, 0.1, 0.01, 0.01)$. The dynamics of system (4.23) are shown in the subsequent figures. Figure 4.4 and subsequent figures will have (a) Top left – shows the orbit where we pick the initial conditions, (b) Top right – shows the invariant manifold or the diagonal, (c) Bottom left – shows the four graphs representing the dynamics of each class of disease dynamics, and (d) Bottom right – shows the differences of each oscillator versus time.

Clearly, the first graph (a) shows existence or periodic orbit, which is the characteristic of an oscillator, meaning that the solutions of the system is periodic. This is evidenced in all the four equations of the SITA model. Notice the smooth diagonal and absence of deviations from the synchronization manifold as depicted in figure (b) and (d) respectively.

4.13 Perturbation and Coupling Strength

In biological oscillators under study, perturbation is considered here as the small changes that arise due to changes in the intensity of interaction, for example changes in market forces, shift of fish populations, change in tidal waves, among others which contributes to more or less interaction of the Fisherfolk in the four population patches. Now adding a small perturbation of $p \ll 1$ to uncoupled system ($k = 0$) yields the system (4.24) below.

$$\begin{aligned} \dot{S}_\iota &= \lambda S_i - c\beta\phi S_i I_i - \mu S_i + k\left(-3S_i + \textstyle\sum_j S_j\right) + p(a_{i1})S_i \\ \dot{I}_\iota &= c\beta\phi S_i I_i - (\mu + \tau + \omega)I_i + k\left(-3I_i + \textstyle\sum_j I_j\right) + p(a_{i2})I_i \\ \dot{T}_\iota &= \tau I_i - (\sigma + \delta)T_i + \rho A_i + k\left(-3T_i + \textstyle\sum_j T_j\right) + p(a_{i3})T_i \\ \dot{A}_\iota &= \delta T_i - (\xi + \sigma + \rho)A_i + \omega I_i + k\left(-3A_i + \textstyle\sum_j A_j\right) + p(a_{i4})A_i \end{aligned} \tag{4.24}$$

Where the index $i = k, s, b, h$ denotes the metapopulations of Kisumu, Siaya, Busia and Homabay respectively, while the elements $a_{ij}\ i = k, s, b, h;\ j = 1,2,3,4$ represents various values of perturbation parameter $a_{ij} \in \mathbb{R}$. Equation (4.24) is equivalent to;

$$\dot{Z}_\iota = k(\Delta \otimes I_4)Z_i + G(Z_i) + p(Z_i)$$

Simulations are run with various values of the coupling strength $k \geq 0$ for the purpose of achieving the threshold coupling strength which eliminates all deviations from the diagonal.

With small perturbation, it is noted that there is a loss of synchronization manifold (the diagonal) and deviations in the dynamics as shown in Figure 4.5 (a, b, d). As the coupling

strength is increased gradually, it is found that the chaotic behavior is lost and synchronization is achieved again. This is achieved at $k \geq 1.1137$ as seen in Figure 4.6 below.

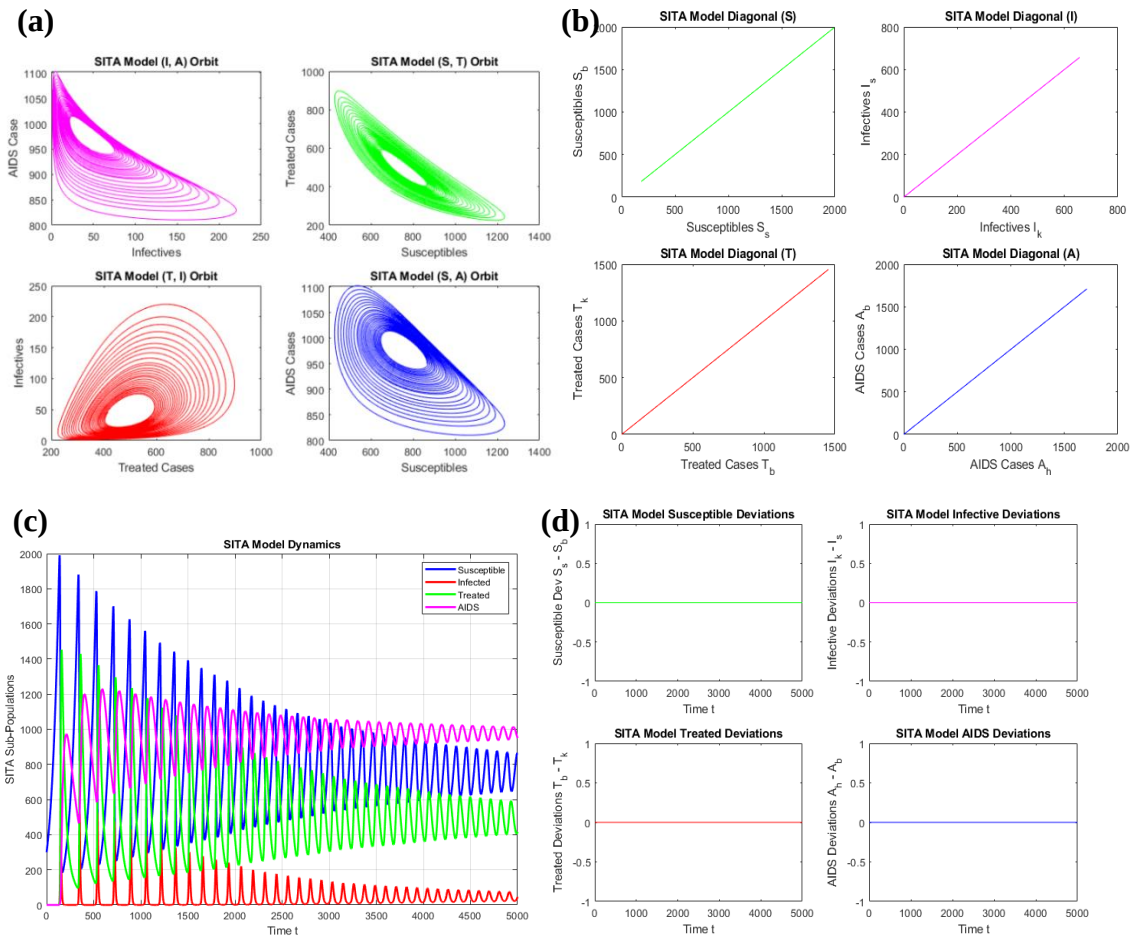

Figure 4.4 HIV/AIDS interaction dynamics of Coupled Oscillators with k=0,p=0.

Figure 4.4 describes the dynamics of the population without coupling. It is noted that Figure 4.4 (a) portrays periodic solutions which tends to a specific limit set, as it is seen in Figure 4.4 (c) with time evolution. Figure 4.4(b) describes the diagonal, which in this case is the synchronization manifold, and figure 4.4(d) describes the deviations in the

synchronization manifold. Clearly, the synchronization manifold is stable and there are no deviations.

In the next figure 4.5. perturbation is introduced, with a unit coupling strength, to determine the effect on the stability of synchronization manifold and deviations om the manifold. Figure 4.5 is similar to Figure 4.4 but it is noted that the periodic solutions are perturbed, and also the diagonal is slightly perturbed. The perturbation is evidenced by the deviations in figure 4.4(d).

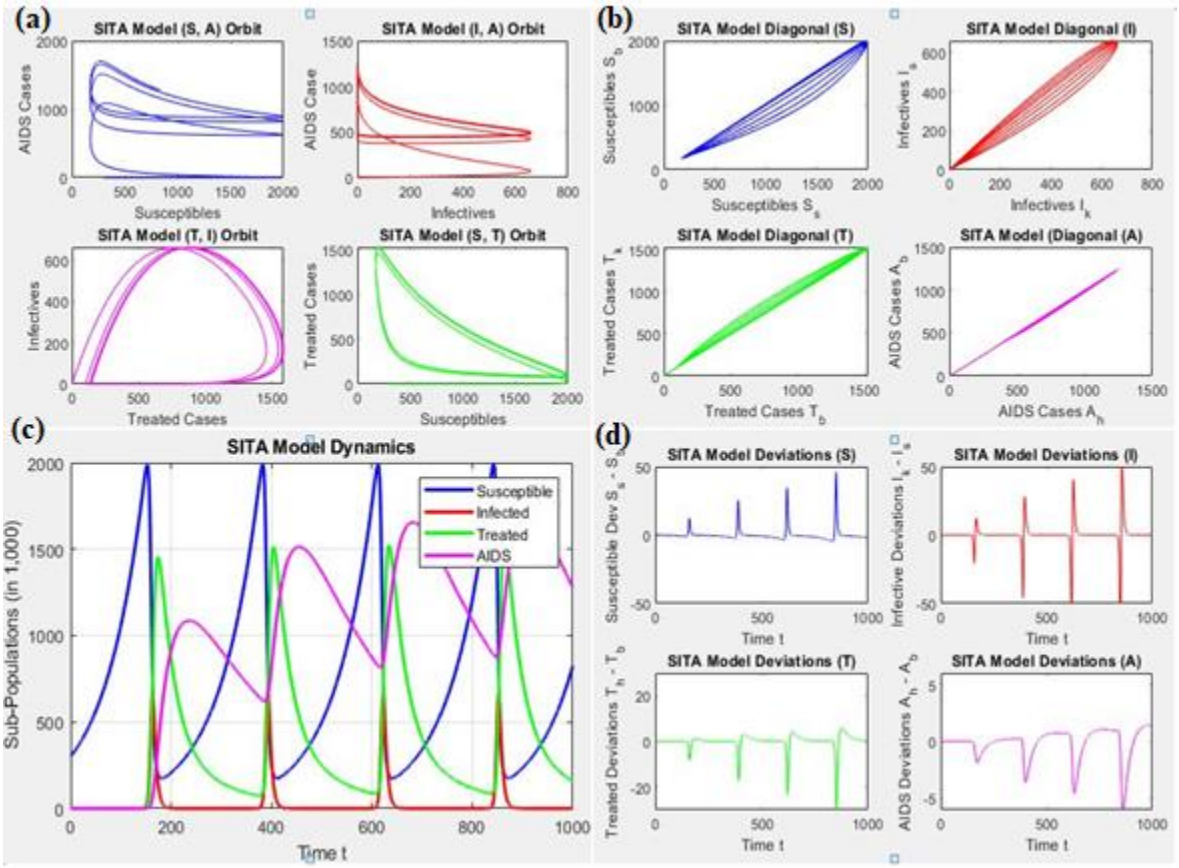

Figure 4.5 HIV/AIDS interaction dynamics of Coupled Oscillators with k=0,p=1.

The analysis of the effect of coupling strength is depicted in Figure 4.6. Various values of the coupling strength k are simulated and at $k = 1.1137$, it is noted that stability of the

synchronization manifold is achieved, and the deviations is very minimal. Here, the value of perturbation constant $p \neq 0$ is positive but small $p \ll 1$. The ω-limit set is seen in figure 4.6 (a)

And the synchronization manifold in figure 4.6 (b) is stable as seen by insignificant deviations in figure 4.6 (d). All the deviations which were seen in Figure 4.5 (d) have died off at a minimum value of 12% coupling strength. This indicates that at any coupling more that 12%, the disease dynamics in the four coupled metapopulations is synchronized and behaves the same way.

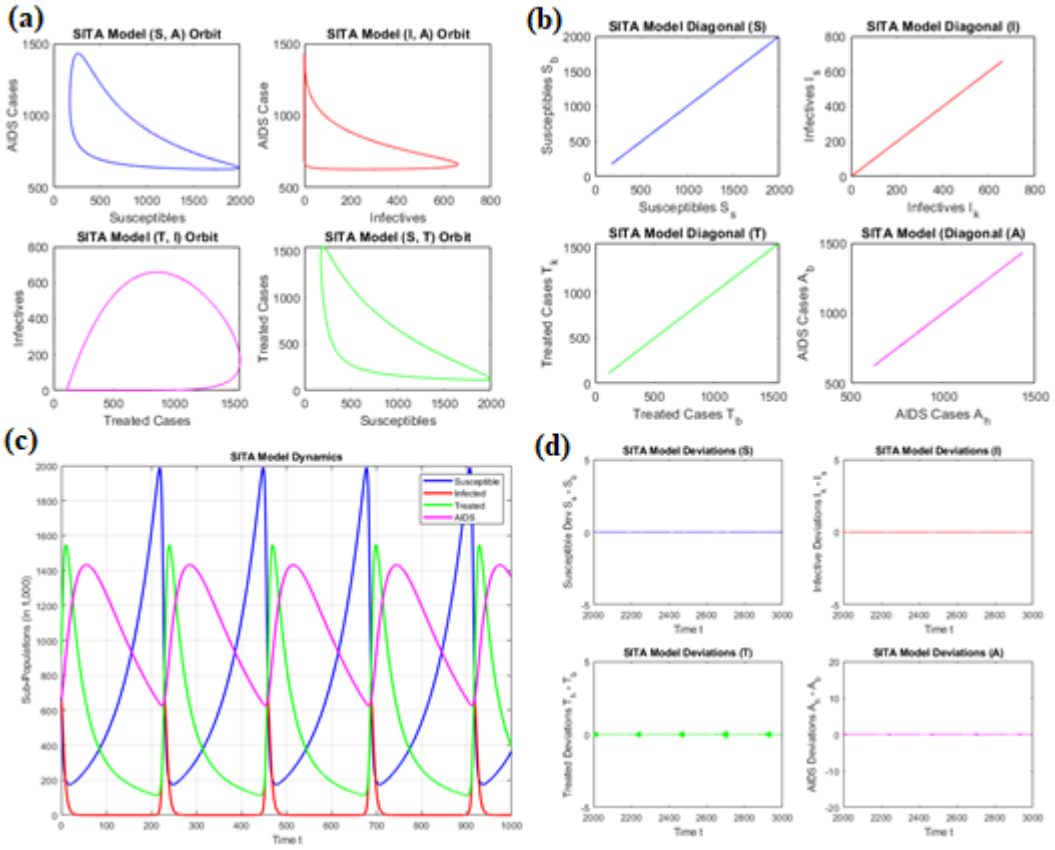

Figure 4.6 HIV/AIDS interaction dynamics of coupled oscillators with k=1.1137, p ≠ 0

CHAPTER FIVE

CONCLUSION AND RECOMMENDATION

5.1. Conclusion

From the results obtained a Mathematical model was formulated, and analyzed for positivity and boundedness of solutions. It was established that all solutions are bound to the domain $\Phi \in \mathbb{R}^{nd}, n, d > 0$. This facilitated further analysis of equilibrium points DFE and EEP, which were obtained and determined that DFE was stable if the reproductive ratio $R_0 < 1$. For $R_0 \geq 1$, a new equilibrium is born that is; EEP, which is periodic. EEP yields an oscillatory behavior of results, which are further analyzed. The analysis of periodic solutions is the sensitivity to control parameters. It was found that control factors such as educational campaigns, public health efforts, treatment and use of ABC are all significant, and their optimality condition evaluated. The study monitored the number of treated individuals and the number of the transformed individuals due to public health education, who are now low risk to HIV by the equations $T_v' = u_T(t)I_v$ and $S_v' = u_E(t)S_v$ respectively. For the purpose of this study, a blowing up cost function $U = \frac{\hat{B}puI}{\hat{B}-puI}$ is chosen since it accommodates the characteristics of the number of people treated and the total cost if all people are treated. The study looks at transversality conditions given by equations (4.11) and optimality conditions given by equations (4.12) and blowing up cost function in equations (4.13) and (4.14). The criteria on optimality condition obtained in equation (4.13) and (4.14) showed that the minimum Education campaign and treatment using ARV to reduce HIV/AIDS incidences and spread among the fisher-folk and the neighbouring population was $u_T = 0.34$ and $u_E = 0.47$ repsectively.

Further analysis of the model showed the existence of oscillating solutions. These were then placed into independent patches and coupled. The coupling configuration used was All-to-all topology, which was analyzed for the existence of synchronization manifold, stability and robustness under small perturbation.

It was found that the coupled system remains stable under small perturbation if the coupling strength is $k_0 \geq 1.1137$. This is interpreted to mean that approximately 12% of the population should be allowed to interact. This translates to about 50 sexual interactions significant to transmit HIV, in a population of about 400 individuals.

Numerical solutions were also carried using MATLAB which generated results using 4^{th}-order Runge-Kutta Scheme. It generated the required graphs. It looked at 2 scenarios: HIV/AIDS dynamics in Lake Victoria region for the Normal and the Fisherfolk Population in absence of control and HIV/AIDS dynamics among normal and fisherfolk communities with no interaction. The numerical results agree with the analytical results. The values of minimum treatment control strategy of $u_T(t) = 0.34$ and that of educational public health campaign of $u_E(t) = 0.47$ indicates that it requires more effort to offer education campaign than treatment, but considering the cost of the two strategies, a decision can be easily made. Suppose it is assumed that the cost of treatment is one and a third that of public health campaign, then the best strategy would still be treatment at $u_T(t)C = 0.34 * 1\frac{1}{3} = 0.44$ lesser than public health campaign of $u_E(t) = 0.47$.

5.2. Recommendation

The following recommendations are made from the study. Following the scope and the assumptions of the study, it is recommended that;

Education and treatment play a very important role in reducing the spread of HIV between the Fisherfolk and the normal population. The government should allocate more funds to the ministry of Health and the affected counties; that is, Kisumu, Homabay, Siaya and Busia counties in control of HIV/AIDS. Also the strategy of economically empowering the women who practice sex-for-fish trade in other trades should also be looked at. Other campaign strategies like distribution of free condoms, free testing, provision of controlled markets and fishing timings, as well as treatment services of PLWHA will synergize to bring better results.

More research on HIV/AIDS among Fisherfolk and the normal population should be done on coupling in other counties like Baringo, Turkana and other counties in Kenya where fishing is a source of livelihood.

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APPENDICES

Appendix I: MATLAB CODES FOR MODEL SIMULATION

```
function SITA_Coupled_model
tf = 2000;
tspan = [0,tf];
%IC = [S;  I;   T;   A]
IC = [97; 0.1;  0.01;  0.01; 99; 0.01;  0.01;  0.01];

sol = ode45(@sita,tspan,IC);
t = linspace(0,tf,1000);

S = deval(sol,t,1);
I = deval(sol,t,2);
T = deval(sol,t,3);
A = deval(sol,t,4);
S2 = deval(sol,t,5);
I2 = deval(sol,t,6);
T2 = deval(sol,t,7);
A2 = deval(sol,t,8);

%-------------------------------------------------------------
figure

subplot(2,2,1);
plot(S,T,A2,I,A,I,A2,I2,...
   'LineWidth',1,'MarkerSize',2)
title('Orbit around Initiial Conditions');
xlabel('Popn of AIDS cases')
ylabel('Popn of Infectives')
legend('(S, T)','(A_2, I)','(A, I)','(A_2, I_2)')
grid,hold on;

subplot(2,2,2);
plot(A,A2,'r',I,I2,'b',T,T2,'c',...
    'LineWidth',1,'MarkerSize',2)
title('Invariant Manifold or the Diagonal');
xlabel('Z_1')
ylabel('Z_2')
legend('AIDS cases','Infected Cases','Treated Cases')
grid,hold on;

subplot(2,2,3);
plot(t,S,t,I,t,T,t,A,...
    'LineWidth',1,'MarkerSize',2)
title('Patch Epidemic Dynamics');
xlabel('Time in Days')
ylabel('S, I, T, A Sub-Pops')
legend('Susceptible','Infectives','AIDS','Treated')
grid,hold on;

subplot(2,2,4);
plot(t,S-S3,t,I-I2, t,T4-T2,t,A3-A2,'-dm',...
    'LineWidth',1,'MarkerSize',2)
```

```
title('Graph of the Deviations');
xlabel('Time in Days')
ylabel('Diff in Sub-Pops')
legend('I-I_2','T-T_2','A - A_2')
grid,hold on;


%-------------------------------------------------------------
function dv = sita(~,v)
dv = zeros(16,1);
%Parameters
mu = 0.00124; %  Death rate due to the disease
lambdav = 0.325;% Testing rate

deltav = 0.01524;
%phi = 0.20835; phiv = 0.157;
phiv = 1.2;
k = 0.00653; % Coupling strength
cv = 1.2;
betav = 0.00033; %  Force of infection
tauv = 0.04;
etav = 0.00154;

%-------------------------------------------------
%S_h = dv(1); S_l = dv(2)  E = dv(3);  I = dv(4); R = dv(5); Q = dv(6);
J = dv(7);  H = dv(8);  D = dv(9);

%equations
dv(1) = lambdav - cv*betav*phiv*v(1)*v(2) - mu*v(1);
dv(2) = cv*betav*phiv*v(1)*v(2) - (tauv + mu)*v(2);
dv(3) = tauv*v(2) - (mu + deltav)*v(3);
dv(4) = deltav*v(3) - (mu + etav)*v(4);

dv(5) = lambdav - cv*betav*phiv*v(5)*v(6) - mu*v(5);
dv(6) = cv*betav*phiv*v(5)*v(6) - (tauv + mu)*v(6);
dv(7) = tauv*v(6) - (mu + deltav)*v(7);
dv(8) = deltav*v(7) - (mu + etav)*v(8);
%-------------------------------------------------
```

Appendix II. MATLAB Code for Model Coupling Simulation

```
function SITA_Coupled_model
tf = 2000;
tspan = [0,tf];
%IC = [S;  I;   T;   A]
IC = [97; 0.1;  0.01;  0.01; 99; 0.01;  0.01;  0.01; 97; 0.1;  0.01;
0.01; 99; 0.1;  0.01;  0.01];

sol = ode45(@sita,tspan,IC);
t = linspace(0,tf,1000);

S = deval(sol,t,1);
I = deval(sol,t,2);
T = deval(sol,t,3);
A = deval(sol,t,4);
S2 = deval(sol,t,5);
I2 = deval(sol,t,6);
T2 = deval(sol,t,7);
A2 = deval(sol,t,8);
S3 = deval(sol,t,9);
I3 = deval(sol,t,10);
T3 = deval(sol,t,11);
A3 = deval(sol,t,12);
S4 = deval(sol,t,13);
I4 = deval(sol,t,14);
T4 = deval(sol,t,15);
A4 = deval(sol,t,16);
%-------------------------------------------------------------
figure

subplot(2,2,1);
plot(S,T,A2,I,A,I,A2,I2,...
   'LineWidth',1,'MarkerSize',2)
title('Orbit around Initiial Conditions');
xlabel('Popn of AIDS cases')
ylabel('Popn of Infectives')
legend('(S, T)','(A_2, I)','(A, I)','(A_2, I_2)')
grid,hold on;

subplot(2,2,2);
plot(A,A2,'r',I,I2,'b',T,T2,'c',...
    'LineWidth',1,'MarkerSize',2)
title('Invariant Manifold or the Diagonal');
xlabel('Z_1')
ylabel('Z_2')
legend('AIDS cases','Infected Cases','Treated Cases')
grid,hold on;

subplot(2,2,3);
plot(t,S,t,I,t,T,t,A,...
    'LineWidth',1,'MarkerSize',2)
title('Patch Epidemic Dynamics');
xlabel('Time in Days')
ylabel('S, I, T, A Sub-Pops')
legend('Susceptible','Infectives','AIDS','Treated')
```

```
grid,hold on;

subplot(2,2,4);
plot(t,S-S3,t,I-I2, t,T4-T2,t,A3-A2,'-dm',...
    'LineWidth',1,'MarkerSize',2)
title('Graph of the Deviations');
xlabel('Time in Days')
ylabel('Diff in Sub-Pops')
legend('I-I_2','T-T_2','A - A_2')
grid,hold on;


%-------------------------------------------------------------
function dv = sita(~,v)
dv = zeros(16,1);
%Parameters
mu = 0.00124; %  Death rate due to the disease
lambdav = 0.325;% Testing rate

deltav = 0.01524;
%phi = 0.20835; phiv = 0.157;
phiv = 1.2;
k = 0.00653; % Coupling strength
cv = 1.2;
betav = 0.00033; %  Force of infection
tauv = 0.04;
etav = 0.00154;

%-----------------------------------------------
%S_h = dv(1); S_l = dv(2)  E = dv(3);  I = dv(4); R = dv(5); Q = dv(6);
J = dv(7);  H = dv(8);  D = dv(9);

%equations
dv(1) = lambdav - cv*betav*phiv*v(1)*v(2) - mu*v(1) + k*(v(5) + v(9) +
v(13) - 3*v(1));
dv(2) = cv*betav*phiv*v(1)*v(2) - (tauv + mu)*v(2) + k*(v(6) + v(10) +
v(14) - 3*v(2));
dv(3) = tauv*v(2) - (mu + deltav)*v(3) + k*(v(7) + v(11) + v(15) -
3*v(3));
dv(4) = deltav*v(3) - (mu + etav)*v(4) + k*(v(8) + v(12) + v(16) -
3*v(4));

dv(5) = lambdav - cv*betav*phiv*v(5)*v(6) - mu*v(5) + k*(v(1) + v(9) +
v(13) - 3*v(5));
dv(6) = cv*betav*phiv*v(5)*v(6) - (tauv + mu)*v(6) + k*(-3*v(6) + v(10)
+ v(14) + v(2));
dv(7) = tauv*v(6) - (mu + deltav)*v(7) + k*(-3*v(7) + v(11) + v(15) +
v(3));
dv(8) = deltav*v(7) - (mu + etav)*v(8) + k*(v(4) + v(12) + v(16) -
3*v(8));
dv(9) = lambdav - cv*betav*phiv*v(9)*v(10) - mu*v(9) + k*(v(1) + v(5) +
v(13) - 3*v(9));
dv(10) = cv*betav*phiv*v(9)*v(10) - (tauv + mu)*v(10) + k*(v(2) +v(6) +
v(14) - 3*v(10));
```

```
dv(11) = tauv*v(10) - (mu + deltav)*v(11) + k*(v(3) + v(7) + v(15) -
3*v(11));
dv(12) = deltav*v(11) - (mu + etav)*v(12) + k*(v(4) + v(8) + v(16) -
3*v(12));

dv(13) = lambdav - cv*betav*phiv*v(13)*v(14) - mu*v(13) + k*(v(1) +
v(5) + v(9) - 3*v(13));
dv(14) = cv*betav*phiv*v(13)*v(14) - (tauv + mu)*v(14) + k*(v(2) + v(6)
+ v(10) - 3*v(14));
dv(15) = tauv*v(14) - (mu + deltav)*v(15) + k*(v(3) + v(7) + v(11)-
3*v(15));
dv(16) = deltav*v(15) - (mu + etav)*v(16) + k*(v(4) + v(8) + v(12) -
3*v(16));

%-----------------------------------------------
```

Appendix III. MATLAB Code for Model Perturbation Simulation

```
function SITA_model2_Coupled
% clear all
tf = 3000;
tspan = [0,tf];
%IC = [Sk;  Ik;   Tk;   Ak; Ss;  Is;   Ts;   As; Sh;  Ih;   Th;   Ah;
Sb;  Ib;   Tb;   Ab]
IC = [300; 0.01;  0.01;  0.01; 300; 0.01;  0.01;  0.01; 300; 0.01;
0.01;  0.01; 300; 0.01;  0.01;  0.01];

sol = ode45(@sita2,tspan,IC);
t = linspace(2000,tf,10000);

Sk = deval(sol,t,1); %v1
Ik = deval(sol,t,2); %v2
Tk = deval(sol,t,3); %v3
Ak = deval(sol,t,4); %v4
Ss = deval(sol,t,5); %v5
Is = deval(sol,t,6); %v6
Ts = deval(sol,t,7); %v7
As = deval(sol,t,8); %v8
Sh = deval(sol,t,9); %v9
Ih = deval(sol,t,10); %v10
Th = deval(sol,t,11); %v11
Ah = deval(sol,t,12); %v12
Sb = deval(sol,t,13); %v13
Ib = deval(sol,t,14); %v14
Tb = deval(sol,t,15); %v15
Ab = deval(sol,t,16); %v16

%-------------------------------------------------------------
figure % Dynamics
plot(t,Sk,'-b',t,Ih,'-r',t,Ts,'-g',t,Ab,'-m',...
    'LineWidth',2,'MarkerSize',2)
title('SITA Model Dynamics');
xlabel('Time t')
ylabel('Sub-Populations (in 1,000)')
legend('Susceptible','Infected','Treated', 'AIDS');grid,hold on;

figure % Orbit
subplot(2,2,1)
plot(Sh,Ah,'b')
title('SITA Model (S, A) Orbit');
xlabel('Susceptibles')
ylabel('AIDS Cases')
subplot(2,2,2)
plot(Ik,Ak,'r')
title('SITA Model (I, A) Orbit');
xlabel('Infectives')
ylabel('AIDS Case')
subplot(2,2,3)
plot(Tb,Ib,'m')
title('SITA Model (T, I) Orbit');
xlabel('Treated Cases')
```

```
ylabel('Infectives')
subplot(2,2,4)
plot(Ss,Ts,'g')
title('SITA Model (S, T) Orbit');
xlabel('Susceptibles')
ylabel('Treated Cases')


figure % Diagonal
subplot(2,2,1)
plot(Ss,Sb,'b')
title('SITA Model Diagonal (S)');
xlabel('Susceptibles S_s')
ylabel('Susceptibles S_b')
subplot(2,2,2)
plot(Ik,Is,'r')
title('SITA Model Diagonal (I)');
xlabel('Infectives I_k')
ylabel('Infectives I_s')
subplot(2,2,3)
plot(Ts,Tk,'g')
title('SITA Model Diagonal (T)');
xlabel('Treated Cases T_b')
ylabel('Treated Cases T_k')
subplot(2,2,4)
plot(Ak,As,'m')
title('SITA Model (Diagonal (A)');
xlabel('AIDS Cases A_h')
ylabel('AIDS Cases A_b')

figure % Deviations
subplot(2,2,1)
plot(t,Sh-Sb,'b')
title('SITA Model Deviations (S)');
xlabel('Time t')
ylabel('Susceptible Dev S_s - S_b')
subplot(2,2,2)
plot(t,Ik-Ib,'r')
title('SITA Model Deviations (I)');
xlabel('Time t')
ylabel('Infective Deviations I_k - I_s')
subplot(2,2,3)
plot(t,Th-Tb,'g')
title('SITA Model Deviations (T)');
xlabel('Time t')
ylabel('Treated Deviations T_h - T_b')
subplot(2,2,4)
plot(t,Ah-Ab,'m')
title('SITA Model Deviations (A)');
xlabel('Time t')
ylabel('AIDS Deviations A_h - A_b')

%-------------------------------------------------------------------
function dv = sita2(~,v)
dv = zeros(16,1);
%Parameters
```

```
mu = 0.00124; %  Natural Death rate due to the disease
lambda = 0.01385; % Recruitment rate
delta = 0.023; % Progression rate of Treatment class to AIDS
beta = 0.00033;  %  Force of infection
tau = 0.24;    % Rate of seeking and obtaining effective treatment
rho = 0.00354;  % Rate of seeking treatment of AIDS class
omga = 0.003218;  % Direct progression to AIDS class
sig = 0.00496;  % Accelerated death rate due to the disease
mu1 = 0.00321;
k = 1.11357;  % Coupling strength
p = 0;%.0001;  % Perturbation parameter
p0 = 0.01;  % Perturbation parameter
p1 = 0;%.0001;  % Perturbation parameter
p2 = 0;%.0001;  % Perturbation parameter
p3 = 0;%.0001;  % Perturbation parameter

%-----------------------------------------------
%S_h = dv(1); S_l = dv(2)  E = dv(3);  I = dv(4); R = dv(5); Q = dv(6);
J = dv(7);  H = dv(8);  D = dv(9);

%equations
dv(1) = lambda*v(1) - beta*v(1)*v(2) - mu*v(1) + k*(v(5) + v(9) + v(13)
- 3*v(1)) + p*(0.01*v(1));
dv(2) = beta*v(1)*v(2) - (tau + mu1 + omga)*v(2) + k*(v(6) + v(10) +
v(14) - 3*v(2))  + p0*(-0.001*v(2));
dv(3) = tau*v(2) - (sig + delta)*v(3) + rho*v(4) + k*(v(7) + v(11) +
v(15) - 3*v(3)) + p0*(0.005*v(3));
dv(4) = delta*v(3) - (mu1 + sig + rho)*v(4) + omga*v(2) + k*(v(8) +
v(12) + v(16) - 3*v(4)) + p0*(0.0021*v(4));

dv(5) = lambda*v(5) - beta*v(5)*v(6) - mu*v(5) + k*(v(1) + v(9) + v(13)
- 3*v(5)) + p0*(-0.002*v(5));
dv(6) = beta*v(5)*v(6) - (tau + mu1 + omga)*v(6) + k*(-3*v(6) + v(10) +
v(14) + v(2))  + p0*(0.015*v(6));
dv(7) = tau*v(6) - (sig + delta)*v(7) + rho*v(8) + k*(-3*v(7) + v(11) +
v(15) + v(3)) + p0*(-0.0015*v(7));
dv(8) = delta*v(7) - (mu1 + sig + rho)*v(8) + omga*v(6) + k*(v(4) +
v(12) + v(16) - 3*v(8)) + p1*(0.003*v(8));

dv(9) = lambda*v(9) - beta*v(9)*v(10) - mu*v(9) + k*(v(1) + v(5) +
v(13) - 3*v(9)) + p0*(0.0013*v(9));
dv(10) = beta*v(9)*v(10) - (tau + mu1 + omga)*v(10) + k*(v(2) +v(6) +
v(14) - 3*v(10))  + p2*(- 0.005*v(10));
dv(11) = tau*v(10) - (sig + delta)*v(11) + rho*v(12) + k*(v(3) + v(7) +
v(15) - 3*v(11)) + p0*(0.00125*v(11));
dv(12) = delta*v(11) - (mu1 + sig + rho)*v(12) + omga*v(12) + k*(v(4) +
v(8) + v(16) - 3*v(12)) + p0*(0.0021*v(12));

dv(13) = lambda*v(13) - beta*v(13)*v(14) - mu*v(13) + k*(v(1) + v(5) +
v(9) - 3*v(13)) + p0*(0.0017*v(13));
dv(14) = beta*v(13)*v(14) - (tau + mu1 + omga)*v(14) + k*(v(2) + v(6) +
v(10) - 3*v(14))  + p0*(0.00525*v(14));
dv(15) = tau*v(14) - (sig + delta)*v(15) + rho*v(16) + k*(v(3) + v(7) +
v(11)- 3*v(15)) + p0*(0.002*v(15));
dv(16) = delta*v(15) - (mu1 + sig + rho)*v(16) + omga*v(16) + k*(v(4) +
v(8) + v(12) - 3*v(16)) + p0*(0.0017*v(16));
%-----------------------------------------------
```

Appendix IV: MATLAB code for Parameter Elasticity Computation

```
function SITA_parameter_Elasticity

%Parameters
mu = 0.00124; muv = 0.00124;%  Death rate due to the disease
lambda = 2; lambdav = 2;% Testing rate

delta = 0.023; deltav = 0.02304;
phi = 0;%0.022;
phiv = 0; %0.02205;
beta = 0.00033; betav = 0.00033; %  Force of infection
theta = 0.021; thetav  = 0.02103;
tau = 0.024; tauv = 0.02405;
psi = 0.0214; psiv = 0.0215;
al = 0;   alv = 0;
k1 = 0.25;   k2 = 0.25;
rho = 0.03;  rhov = 0.03;
omga = 0.00218;   omgav = 0.00218;
eta = 0.0124;  etav = 0.0124;

figure
for beta = 0:0.01:1
R0 = (beta + phiv*betav)*lambda/(mu*(mu + tau));
R0v = (betav + phi*beta)*lambda/(mu*(mu + tauv));

subplot(4,2,1)
plot(beta,R0,'r*',beta,R0v,'b*','MarkerSize',2); hold on
legend('Effects of \beta on R_0', 'Efects of \beta on R_0v')
title('Elasticity of \beta on Reproductive Ratio');
xlabel('Value of Parameter')
ylabel('Reproductive Ratio')
end

hold on

for betav = 0:0.01:1
  R0 = (beta + phiv*betav)*lambda/(mu*(mu + tau));
R0v = (betav + phi*beta)*lambda/(mu*(mu + tauv));

subplot(4,2,2)
plot(betav,R0,'r*',betav,R0v,'b*','MarkerSize',2); hold on
legend('Effects of \beta_v on R_0', 'Efects of \beta_v on R_0v')
title('Elasticity of \beta_v on Reproductive Ratio');
xlabel('Value of Parameter')
ylabel('Reproductive Ratio')
end

hold on
for phi = 0:0.01:1
  R0 = (beta + phiv*betav)*lambda/(mu*(mu + tau));
R0v = (betav + phi*beta)*lambda/(mu*(mu + tauv));

subplot(4,2,3)
plot(phi,R0,'r*',phi,R0v,'b*','MarkerSize',2); hold on
```

```
title('Elasticity of \phi on Reproductive Ratio');
legend('Effects of \phi on R_0', 'Efects of \phi on R_0v')
xlabel('Value of Parameter')
ylabel('Reproductive Ratio')
end
hold on

for phiv = 0:0.01:1
  R0 = (beta + phiv*betav)*lambda/(mu*(mu + tau));
R0v = (betav + phi*beta)*lambda/(mu*(mu + tauv));

subplot(4,2,4)
plot(phiv,R0,'r*',phiv,R0v,'b*','MarkerSize',2); hold on
title('Elasticity of \phi_v on Reproductive Ratio');
legend('Effects of \phi_v on R_0', 'Efects of \phi_v on R_0v')
xlabel('Value of Parameter')
ylabel('Reproductive Ratio')
end

for lambda = 0:0.01:1
R0 = (beta + phiv*betav)*lambda/(mu*(mu + tau));
R0v = (betav + phi*beta)*lambda/(mu*(mu + tauv));

subplot(4,2,5)
plot(lambda,R0,'r*',lambda,R0v,'bo','MarkerSize',2); hold on
legend('Effects of \lambda on R_0', 'Efects of \lambda on R_0v')
title('Elasticity of \lambda on Reproductive Ratio');
xlabel('Value of Parameter')
ylabel('Reproductive Ratio')
end

hold on

for mu = 0:0.01:1
  R0 = (beta + phiv*betav)*lambda/(mu*(mu + tau));
R0v = (betav + phi*beta)*lambda/(mu*(mu + tauv));

subplot(4,2,6)
plot(mu,R0,'r*',mu,R0v,'bo','MarkerSize',2); hold on
legend('Effects of \mu on R_0', 'Efects of \mu on R_0v')
title('Elasticity of \mu on Reproductive Ratio');
xlabel('Value of Parameter')
ylabel('Reproductive Ratio')
end

for tau = 0:0.01:1
R0 = (beta + phiv*betav)*lambda/(mu*(mu + tau));
R0v = (betav + phi*beta)*lambda/(mu*(mu + tauv));

subplot(4,2,7)
plot(tau,R0,'r*',tau,R0v,'b*','MarkerSize',2); hold on
legend('Effects of \tau on R_0', 'Efects of \tau on R_0v')
title('Elasticity of \tau on Reproductive Ratio');
xlabel('Value of Parameter')
ylabel('Reproductive Ratio')
```

```
end

hold on
for tauv = 0:0.01:1
  R0 = (beta + phiv*betav)*lambda/(mu*(mu + tau));
R0v = (betav + phi*beta)*lambda/(mu*(mu + tauv));

subplot(4,2,8)
plot(tauv,R0,'r*',tauv,R0v,'b*','MarkerSize',2); hold on
legend('Effects of \tau_v on R_0', 'Efects of \tau_v on R_0v')
title('Elasticity of \tau_v on Reproductive Ratio');
xlabel('Value of Parameter')
ylabel('Reproductive Ratio')
end
%-------------------------------------------------------------
```

Appendix V: MATLAB code for Eigenvalue and Inverse Computation

```
function symbolicSITA_EEP
syms a b m t q
A = [-a*(1+q)-m -b 0 -b*q; a b*(1+q)-m-t a*q 0;0 -b*q -a*(1+q)-m -b;a*q
0 a b*(1+q)-m-t];
A
D = eig(A)
B=[-2 3 0 4;5 1 6 0;0 4 -2 3;6 0 5 1]
d=eig(B)
```

Appendix VI: Similarity Report