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Using Atanackovic and Stankovic Numerical Method to Investigate Fractional Order Cholera Model

By

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Declaration

I hereby declare that this submission is my own work towards the award of the M. Phil degree and that, to the best of my knowledge, it contains no material previously published by another person nor material which had been accepted for the award of any other degree of the university, except where due acknowledgement had been made in the text.

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Dedication

This work is rst of all dedicated to Almighty ALLAH (S.W.T), the creator of the heavens and the earth and all that is in-between them. I further dedicate it to my beloved parents, my Mum, Okunade Elizabeth Modupe Idayat and my Dad, Abdulai Olagoke Oni.

Abstract

In this work, we investigate the dynamical behavior of a fractional order cholera model. Here, we developed interest in the use of the deterministic model proposed by Codeco in 2001. The fractional order cholera model is converted to a system of ordinary di erential equations of integer order by using Atanackovic and Stankovic numerical method and is then solved numerically by using the fourth order well-known Runge-Kutta method. All the feasible equilibria for the system are obtained and the conditions for the existence of interior equilibrium are determined. Local stability analysis of the cholera model is studied by using the fractional Routh-Hurwitz stability conditions. The ndings reveal that, the disease dies out at the disease free equilibrium state but will persist at the endemic state and that the concentration of toxigenic vibrio cholerae in water largely depends on (i) the rate of exposure to contaminated water (parameter a) and (ii) the contribution of each e ected person to the aquatic environment (parameter e).

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Chapter 1

Introduction

1.1 Background

Cholera is an acute intestinal infection caused by ingestion of food or water contaminated with the bacterium Vibrio cholerae. It has a short incubation period, from less than one day to ve days, and produces an enterotoxin that causes copious, painless, watery diarrhoea that can quickly lead to severe dehydration and death if treatment is not promptly given. Vomiting also occurs in most patients. Cholera is an extremely ancient and virulent disease that continues to cause epidemic and pandemic infection despite ongoing e orts to limit its spread. It a ects both children and adults and can kill within hours. About 75% of people infected with Vibrio cholerae do not develop any symptoms, although the bacteria are present in their faeces for 7-14 days after infection and are shed back into the environment, potentially infecting other people.

If left untreated, cholera can be fatal in a matter of hours, even in previously healthy people. Most people exposed to the cholera bacterium do not become ill and never know they have been infected. Yet because they shed vibrio cholerae in their stool for 7 to 14 days, they can still infect others through contaminated water. Only about 1 in 10 infected people develop the typical signs and symptoms of cholera, usually within a few
days of infection.

Diarrhoea: Cholera-related diarrhoea comes on suddenly and may quickly cause dangerous uid loss as much as a quart (about 1 liter) an hour. Diarrhoea due to cholera often has a pale, milky appearance that resembles water in which rice has been rinsed (rice-water stool).

Nausea and vomiting: Occurring especially in the early stages of cholera, vomiting may persist for hours at a time.

Dehydration: Dehydration can develop within hours after the onset of cholera symptoms. Depending on how many body uids have been lost, dehydration can range from mild to severe. A loss of 10 percent or more of total body weight indicates severe dehydration.

Signs and symptoms of cholera dehydration include irritability, lethargy, sunken eyes, a dry mouth, and extreme thirst, dry and shriveled skin that's slow to bounce back when pinched into a fold, little or no urine output, low blood pressure, and an irregular heartbeat (arrhythmia). Dehydration may lead to a rapid loss of minerals in your blood (electrolytes) that maintain the balance of uids in your body. This is called an electrolyte imbalance. Modern sewage and water treatment has virtually eliminated cholera in industrialized countries but cholera is still present in Africa, Southeast Asia, Haiti and central Mexico. The risk of cholera epidemic is highest when poverty, war or natural disasters force people to live in crowded conditions without adequate sanitation. Cholera is easily treated and death results from severe dehydration that can be prevented with a simple and inexpensive rehydration solution. Historically, six out of the seven cholera pandemics have swept the globe since 1816. Most recently, the seventh pandemic started from Indonesia in 1961, spread into Europe, South Paci c and Japan in the late 1970s, reached South America in 1990s, and has continued to the present. The last few years have witnessed many cholera outbreaks in developing countries, including Liberia (2002), Mali (2003), Senegal and Chad (2004), West Africa (2005), Angola and Sudan (2006), India (2007), Iraq and Congo (2008), Zimbabwe (2008 and 2009), Vietnam (2009), Nigeria, Central Africa, Pakistan and Haiti (2010), Sierra Leone (2012) and Ghana (2014). Every year there are an estimated 3 to 5 million cholera cases and 100 000 to 120 000 deaths and that is the reason why cholera represents a signi cant public health burden to developing countries in recent years.

In the last decades, attention to cholera epidemiology increased, as cholera epidemics became a worldwide health problem. Detailed investigation of V. cholerae interactions with its host and with other organisms in the environment suggests that cholera dynamics is much more complex than previously thought. Though many mathematical models have been proposed to investigate the complex epidemic and endemic behavior of cholera in the past,

notable example among these is the deterministic model proposed by Codeco in 2001 which, in the rst time, explicitly incorporated the environmental component, i.e. the V.cholerae concentration in the water supply (denoted by B), into a regular SIR system to form a combined human-environment (SI-B) epidemiological model. This model enables a careful study on the complex interaction between human hosts and environmental pathogen towards better understanding the cholera transmission mechanism, and, as such, it has motivated the development of several other cholera

models.

Fractional-order di erentiation is regarded as the generalization of classical integer-order di erentiation to real or complex orders. Fractional di erential equations have gained considerable importance due to their application in various sciences, such as physics, mechanics, chemistry, and engineering. In the recent years, the dynamic behaviors of fractional-order di erential systems have received increasing attention. The existence of solutions of initial value problems for fractional order di erential equations will be discussed in this work. Here, we will introduce a fractional order Codeco cholera model. The researcher will discuss an e cient numerical method to converting the system of fractional di erential equations to system of ordinary di erential equations. Finally, numerical simulations are presented to illustrate the obtained results.

Just when it is assumed that cholera outbreak has been brought under check, the Ghana Health Service (GHS) reported cholera outbreak in Ghana has hit a record over 28,000 cases with over 243 deaths. The last time Ghana su ered such a staggering number of cholera cases was in 1982. A report published by the World Health Organisation (WHO) says by the end of 2011 a total number of 589,854 cholera cases had been

reported globally, out of which 7,816 deaths were recorded.

This gure represents an increase of 85% in the number of cases reported in 2010 and a 16% increase in the number of countries. However, a total of 188,678 cases were reported from Africa only, representing an increase of 64% compared with the 2010 gure of 115,106 cases. The rest of the total gure was taken up by Asia˘38,298;Oceania˘1,514; and Europe˘71. The

Americas, however, took the largest chunk of 361,266, owing to the epidemic that hit Haiti as a result of the earthquake that struck on January 12, 2010.

Haiti alone reported 340,311 cases, which resulted in 2,869 deaths during the period. For Africa, countries that had reported cases during the period were Somalia, Nigeria, Democratic Republic of Congo, Cameroon, Niger, Angola, Benin, Burkina Faso, Ghana, and Central African Republic.

The rest were Chad, Congo, Cote d'Ivoire, Djibouti, Guinea, Kenya, Liberia, Mali, Mauritania, Malawi, Mozambique, Senegal, Somalia, Togo, Tanzania, Zambia, and Zimbabwe.The chunk of cases recorded on the African continent was taken by ve

countries, with Somalia's 77,636 reported cases, 1,130 deaths and 1.46% case fatality rate (CFR) topping the African chart.

Nigeria followed at a great distance with 23,377 reported cases, 742 deaths and a rather high CFR of 3.17%. On its heels was Cameroon with 22,433 reported cases, but with a larger number of deaths 783 and, not surprising, the highest CFR of 3.49% for the period.

The Democratic Republic of Congo placed fourth with 21,700 cases, 584 deaths and a CFR of 2.69% while Ghana came fth, having reported a total of 10,628 cases by the close of 2011 and a total of 105 deaths with a CFR of 0.99%.

Four countries from Central Africa, the Great Lakes region, and the Horn of Africa accounted for 145,164 cases (Cameroon, Democratic Republic of Congo, Nigeria and Somalia), or 77% of cases reported from the continent. There was a sharp increase in cases reported from the Horn of Africa, with 127 cases (and one death) reported from Djibouti. No cases were reported from Ethiopia, Sudan or Uganda. A total of 2,295 cases were, however, reported from Kenya (74), Mozambique (1,279) and Tanzania (942). In southern Africa the number of reported cases declined to levels never previously reported during the current millennium, with 2,949 cases reported: Malawi (120), Mozambique (1,279), Zambia (330) and Zimbabwe (1,220).

In West Africa, reported cases increased to the levels of 2006 to 2008 with a total of 16,088 cases compared with 3,074 in 2010. Ghana's 10,628 cases accounted for 66% of cases reported from West Africa. Increasing numbers of cases were reported from C te d'Ivoire

(1261), Mali (2220), and Niger (2324). Cases were also reported from Benin (755), Burkina Faso (20), Guinea (3), Liberia (1,146), Mauritania (46), Senegal (ve), and Togo (four). The CFRs were high for Burkina Faso (10%), Mali (4.3%), and Mauritania (6.5%).

1.1.1 Problem Statement

Just when it was assumed that cholera outbreak had been brought under check, the Ghana Health Service (GHS) has reported that cholera outbreak has hit a record of over 28,000 cases with over 243 deaths from June 2014 to April 2015. The last time Ghana su ered such a staggering number of cholera cases was in 1982.

Since this report, the world health Organisation (WHO) and others have provided several technical supports to ght cholera outbreak in the country. However, cholera as a disease is beyond the health sector alone and there is a need for multi-sectorial approach involving ministry of water and resources, work and housing, department of environmental health and last but not the least the research institutions to help investigate and educate the public on cholera outbreak.

Though many mathematical models have been proposed to investigate the complex epidemic and endemic behavior of cholera in the past, most of these researches has focused only on the human-human transmission of the disease using SIR cholera model. On this note, the researchers developed interest in the use of the deterministic model proposed by Codeco in 2001 which, for the rst time, explicitly incorporated the environmental component, i.e. the V.cholerae concentration in the water supply (denoted by B), into a regular SIR system to form a combined human-environment (SI-B) epidemiological model. This model enables a careful study of the complex interaction between human hosts and environmental pathogen towards better understanding the cholera transmission mechanism. There is also the need to investigate the use of fractional order di erential equations instead of an ordinary di erential equations model especially because an epidemic like cholera must have memory.

1.1.2 Objectives

The objectives of the study are;

1. To formulate the dynamics of fractional-order Codeco cholera model
2. To solve a fractional-order Codeco cholera model by means of Atanackovic and Stankovic numerical method and Runge-Kutta fourth order method.
3. To use simulations to study the behavior of cholera at the disease free equilibrium state compared to the endemic state as well as under various scenarios.

1.1.3 Methodology

In the study, the researcher intends to investigate a fractional-order Codeco cholera model by means of an e cient (Atanackovic and Stankovic) numerical method, based on an idea of transforming the proposed model to a system of ordinary di erential equations with initial conditions by using the well-known Runge-Kutta method of fourth order. All the feasible equilibria for the system will be discussed.

Also, local stability analysis of the cholera model will be carried out by applying the fractional Routh-Hurwitz criterion. To facilitate the interpretation of the mathematical results developed for the model; this is investigated by numerical simulations. Matlab will be involved in the nal stages to simulate the results. Information is obtained both from the internet and the library for the purpose of this work.

1.1.4 Fractional-order Codeco model

This model explicitly incorporated the environmental component, i.e. the V.cholerae concentration in the water supply (denoted by B), into a regular SIR system to form a combined human-environment (SI-B) epidemiological model.

1.1.5 Justi cation

The study investigates the complex epidemic and endemic behavior of cholera on the fact that cholera outbreak recurs yearly in Africa killing thousands and sickening many more. Cholera has become a signi cant public health burden in Africa but this has been eliminated from industrialized countries by water and sewage treatment over a century ago. A erce cholera epidemic has hit Ghana in 2014, killing over 243 people despite all e orts to curb it. The last time Ghana su ered such a staggering number was in 1982. Recently, there has been a call from the government of Ghana that the public should engage in regular clean-up exercises all in an e ort to control the current cholera outbreak in this country. Also, several organizations, such as Actionaid, World Health Organisation (WHO), China Red Cross (CRC), Mind Development Foundation (MDF) and many others have o ered both nancial and technical support in an e ort to

eradicate, prevent and treat cholera.

However, it is obvious that solutions to outbreaks of communicable disease like cholera go beyond poor environmental attitude and poor eating habits. Cholera is beyond health sector alone and there is a need for multi-sectorial approach involving ministry of water and resources, work and housing, department of environmental health and last but not the least the research institutions to help investigate and educate the public on cholera outbreak. With early detection and the timely and e ective management of cholera cases, health education and researches on cholera epidemiology will prevent the re-emergence of cholera in highly endemic settings.

Though, great progress has been made in mathematical models on cholera transmission dynamics in recent years, little interest has been made on models that incorporate the environmental component of cholera infection. On this basis, the study will investigate

the cholera dynamics using model developed by Codeco which employed both the environment-human and human-human infection routes.

Cholera is a global threat to public health and one of the key indicators of social

development, and with the consequent increase in the reporting of cholera cases in yearly, almost every developing country is facing either an outbreak or the threat of an epidemic.

Cholera outbreaks bring fear and anxiety in populations and this may have adverse e ects on the social and economic structure of communities, thereby blocking developmental growth in many sectors of a country, (WHO, 2010). In the implementation of national economic development, aspects of the environment, climate, culture, medical management, political intention and individual behavioral patterns, as well as researches on cholera must be considered because they are related. Nevertheless, cholera will continue thriving in endemic regions, survived by its strong links to maritime environment, alongside social determinants of poor sanitary conditions, if the situation is not addressed with much urgency. Also, the use of Atanackovic and Stankovic numerical method is an e cient method for solving the fractional-order cholera model equations and this will bring analytically to the oor level better understanding cholera outbreak and its dynamics.

1.1.6 Thesis Organisation

This thesis is made up of ve (5) chapters; chapter one deals with the introduction of the study. Here, detailed explanations and discussions on cholera is given, key words in the title of the thesis are all well explained. This chapter also talks about the purpose and justi cation of the study. In chapter two is the relevant literature review of the study, this section review relevant previous studies done by others in the past either published or not. Come next is chapter three which contains the methodology of this work, here, Codeco cholera model and an e cient numerical (Atanackovic and Stankovic) method is well discussed. Finally in this section the well-known Runge-Kutta of order fourth is used to solve the obtained ordinary di erential equations. Next is the chapter four where the given model is studied numerically and results, ndings and discussions are presented. And the fth and last chapter of this work talks about conclusion and recommendation. That is, whether or not the topic is properly dealt with and the outlined objectives achieved.

Chapter 2

Literature Review

2.1 Introduction

In this chapter we reviewed the work of other researchers related to the topic.

2.2 Literature Relevant to this thesis

Most mathematical modeling of infectious diseases has been restricted to the use of a system of integer-order ordinary di erential equations. But of late, fractional calculus has been widely applied in many elds, for instance many mathematicians and researchers have tried to use fractional calculus to model real life process.

2.3 Literature on Mathematical models

According to Das and De (2000), diseases like cholera (+ve) and non-choleric diarrhoea break out regularly in greater Calcutta and occasionally in epidemic form. It is interesting to note that in the classical susceptible-infected removal (SIR) models for infectious diseases, the epidemic can persists only if the susceptibles are being supplied steadily; for example, through birth and immigration. Such are the cases which occur in this part of west Bengal, the city areas of Calcutta and its neighborhood. Therefore, it is an obvious reason to study epidemic disease for this with such a mathematical model. Within this framework of SIR epidemic model with time-dependent recovery rate, the time-behaviour of infectives for cholera (+ve) and non-choleric diarrhoea has been studied. Here, the population of greater Calcutta has been considered. The infectivity curves for these diseases as computed from this model have been tted with the data available up to 1991 and have been extrapolated up to 2000 years. The steady number

of infectives for the forthcoming year is being predicted here.

Leah (2006) studied the patterns of infection of cholera in a human population and understood what factors in uence transmission of the disease as well as the dynamics of the bacteria in their aquatic environment. In this dissertation, he explore the dynamics of cholera on three scales. First, Leah introduced a fairly simple model for cholera in a human population coupled to an environmental reservoir of bacteria. This model demonstrates the need to understand more fully how V. cholerae survives and evolves in the aquatic environment. Next, Leah explored the life histories of bacteria, in particular how aging and environmental factors in uence bacterial tness. Finally Leah examined

the implications of various types of inter-cellular interactions during surface colonization for the structure and composition of bacterial communities using an individual based model, as well as examining under what conditions living in communities of various sizes would be optial.

Mark et al, (2006) researched on the epidemiological and environmental observations of a cholera outbreak in Dhaka, Bangladesh, suggest that lytic bacteriophage speci c for V. cholerae may limit the severity of cholera outbreaks by killing bacteria present in the reservoir and in infected individuals. To quantify this idea and generate testable hypotheses, they analyzed a mathematical model that combines the epidemiology of cholera with the population dynamics of the bacteria and phage. Under biologically reasonable conditions, they found that vibrio phage can ameliorate cholera outbreaks. If phage predation limits bacterial density before an outbreak, a transient reduction in phage density can disrupt that limitation, and subsequent bacterial growth can initiate a cholera outbreak. Our analysis also suggests that either bacteria in the environmental reservoir are hyper infectious or most victims ingest bacteria ampli ed in food or drinking water contaminated by environmental water carrying few viable V. cholerae. Their theoretical results make a number of empirically testable predictions.

Richard et al, (2008) reported that there are numerous examples of human pathogens which persist in environmental reservoirs while infectious outbreaks remain rare. In this manuscript, they consider the dynamics of infectious diseases for which the primary mode of transmission is indirect and mediated by contact with a contaminated reservoir. they evaluate the realistic

scenario in which the number of ingested pathogens must be above a critical threshold to cause infection in susceptible individuals. This minimal infectious dose is a consequence of the clearance e ect of the innate immune system. Infected individuals shed pathogens back into the aquatic reservoir, indirectly increasing the transmutability of the pathogen to the susceptible. They devised two new measures of how likely it is that an environmentally persistent pathogen will cause an outbreak: (i) the minimum fraction of infected individuals; and (ii) the minimum uctuation size of in-reservoir pathogens. They also nd an additional control parameter involving the shedding rate of infected individuals, which they term the pathogen enhancement ratio, which determines whether outbreaks lead to epidemics or endemic disease states. Their model predicts that in the case of waterborne diseases, suppressing the pathogen density in aquatic reservoirs may be more e ective than minimizing the number of infected

individuals.

According to Yibeltal(2009),Since 2005, the reoccurrence of cholera is linked with the ever-increasing size of the population living in unsanitary conditions. For instance, from August 2008 to February 2009, more than 79,000 cases and 3,700 deaths were reported from a single country Zimbabwe. Regardless of the advancement of medical science and health care service, cholera remains a global threat to public health and one of the key indicators of social development. While the disease is not an issue in the developed nations where minimum hygiene standards are met, it still remains a threat in developing countries. In this essay, a new mathematical model for cholera transmission dynamics was developed and rigorously analysed. Historical pandemics of the disease, transmission means and global impact of the disease and control mechanisms of cholera disease were brie y discussed. Since the survival rate of the vibrio cholerae is often a function of time delay, the researcher incorporated a time delay in the V. cholerae population. He found a threshold condition, Ro, in terms of the parameters of the model. It is shown that the disease free equilibrium is locally and globally stable for no time delay. Furthermore, for the case with time delay $\tau > 0$, it was shown that a disease free equilibrium is globally asymptotically stable if $Ro < 1$. The model has an endemic equilibrium when $Ro > 1$. Bertuzzo et al, (2009) generalized a recently proposed model for

cholera epidemics that accounts for local communities of susceptibles and infectives in a spatially explicit arrangement of nodes linked by networks having di erent topologies. The mathematical tools used are borrowed from general schemes of reactive transport on river networks acting as the environmental matrix for the circulation and mixing of waterborne pathogens. Using the di usion approximation, they analytically derived the speed of propagation for travelling fronts of epidemics on regular lattices (either one-dimensional or two-dimensional) endowed with uniform population density. Power laws are found that relate the propagation speed to the di usion coe cient and the basic reproduction number. they numerically obtained the related, slower speed of epidemic spreading for more complex, yet realistic river structures such as Peano networks and optimal channel networks. The relevance of their results lie in the major di erences potentially arising between the predictions of spatially explicit models and traditional compartmental models of the susceptible infected recovered (SIR) like type. This suggest that in many cases of real-life epidemiological interest, time scales of disease dynamics may trigger outbreaks that signi cantly depart from the predictions of compartmental models.

Jianjun et al, (2010) reported that recent years have seen a strong trend of cholera outbreaks in developing countries, including, among others, those in Kenya (2010), Vietnam (2009), Zimbabwe (2008/2009), Iraq (2008), Congo (2008) and India (2007). According to the World Health Organization (WHO), there are an estimated 3 - 5 million cholera cases and 100,000 - 120,000 deaths due to cholera every year , among which only a small portion were o cially reported because of poor surveillance and incomplete records. Due to its huge impacts on public health and social and economic development, cholera has been a subject of extensive studies in clinical, experimental and theoretical elds .Here, Conducted rigorous stability analysis for the well-known cholera model proposed by Codeco using theory of monotone dynamical systems, they proved that the endemic equilibrium, when it exists, of the model is globally asymptotically stable, implying the persistence of the disease in the absence of interventions. They then modi ed Codeco's model by incorporating various control strategies, and study the subsequent dynamics. Jianjun et al found that with strong control measures, the basic reproduction number will be reduced below one (1) so that the disease-free

equilibrium is globally asymptotically stable. With weak controls, instead, a unique and globally stable endemic equilibrium would still occur, though at a lower infection level. The analytical predictions were con rmed by numerical simulation results.

Andrews and Badu (2011) O cial projections of the cholera epidemic in Haiti have not incorporated existing disease trends or patterns of transmission, and proposed interventions have been debated without comparative estimates of their e ect. They used a mathematical model of the epidemic to provide projections of future morbidity and mortality, and to produce comparative estimates of the e ects of proposed interventions. They designed mathematical models of cholera transmission based on existing models and tted them to incidence data reported in Haiti for each province from Oct 31,2010, to Jan 24,2011. They then simulated future epidemic trajectories from March 1 to Nov 30,2011, to estimate the e ect of clean water, vaccination, and enhanced antibiotic distribution programmes. They also projected 779,000 cases of cholera in Haiti and 11,100 deaths between March 1 and Nov 30,2011. The researchers expected that a 1% per week reduction in consumption of contaminated water would avert 105,000 cases and 1,500 deaths. They predicted that the vaccination of 10% of the population, from March 1, will avert 63000 cases and 900 deaths. The proposed extension of the use of antibiotics to all patients with severe dehydration and half of patients with moderate dehydration is expected to avert 9,000 cases and 1,300 deaths.

Wang et al, (2011) researched that Cholera is a severe water-borne infectious disease caused by the bacterium Vibrio cholerae. The dynamics of cholera involve multiple interactions between the human host, the pathogen, and the environment which contribute to both direct human-to-human and indirect environment-to-human transmission pathways. In an e ort to gain deeper understanding of the complex dynamics of cholera, several mathematical models have been published. In this paper, they presented and analyzed a cholera epidemiological model with control measures incorporated. This model is extended from the one proposed by Mukandavire et al in 2008/2009 and included the e ects of vaccination, therapeutic treatment, and water sanitation. Equilibrium analysis is conducted in the case with constant controls for both epidemic and endemic dynamics. Optimal control theory is applied to seek cost-e ective solution of multiple time-dependent intervention strategies

against cholera outbreaks. The results in this study showed that the vaccination cost is kept the same as before.They again conducted simulations for the optimal strategy of the three controls combined and that for vaccination only. The results are presented with the reduced costs for therapeutic treatment. Finally it was observed that both the strength and e ective period of the optimal vaccination rate are decreased. And the optimal treatment rate shows a signi cant increase to achieve the optimal balance between controls.

According to Mukandavire et al, (2011), beginning in August 2008, a major cholera epidemic occurred in Zimbabwe, with 98,585 reported cases and 4,287 deaths. The dynamics of such outbreaks, particularly in non-estuarine regions, are not well understood. They explored the utility of mathematical models in understanding transmission dynamics of cholera and in assessing the magnitude of interventions necessary to control epidemic disease. Weekly data on reported cholera cases were obtained from the Zimbabwe Ministry of Health and Child Welfare (MoHCW) for the period from November 13, 2008 to July 31, 2009. A mathematical model was formulated and tted to cumulative cholera cases to estimate the basic reproductive numbers and the partial reproductive numbers from all 10 provinces for the 2008/2009 Zimbabwe cholera epidemics. Estimated basic reproductive numbers were highly heterogeneous, ranging from a low value of just above unity to 2.72. Partial reproductive numbers were also highly heterogeneous, suggesting that the transmission routes varied by province; human-to-human transmission accounted for 41-95% of all transmission. Their models suggest that the underlying patterns of cholera transmission varied widely from province to province, with a corresponding variation in the amenability of outbreaks in di erent provinces to control measures such as immunization.

According to Tuite et al, (2011), Haiti is the poorest country in the Western Hemisphere , is in the midst of a cholera epidemic that has reportedly killed more than 4,000 people and infected about 217,000 (as of 30 January 2011). Approximately one half of those infected have been hospitalized and case-fatality rates in both community and hospital settings have been approximately 2%. With respect to epidemic spread as a function of population mass and distance. They used a gravity model to accurately predict the sequence and timing of regional cholera epidemics in Haiti by using publicly available data. They also used a model

based on the best available data and calibrated to reproduce the initial reported epidemic curve for Haiti and then evaluate the probable time course of Haiti's cholera epidemic in the absence of e ective intervention and explore the potential e ects of competing and complementary control strategies, including vaccine distribution and provision of clean water. The model projects that the epidemic is likely to last well into 2011 and suggest that adaptive strategies for vaccination may provide a modest reduction in morbidity and mortality in the economically challenged

country.

Saeed et al, (2011) reported that Lytic bacteriophages are hypothesized to contribute to the seasonality and duration of cholera epidemics in Bangladesh. In this study, they isolated and sequenced the genomes of 15 bacteriophages from stool samples from cholera patients spanning a 10-year surveillance period in Dhaka, Bangladesh. Their results indicated that a single novel bacteriophage type, designated ICP1 (for the International Centre for Diarrhoeal Disease Research, Bangladesh cholera phage 1) is present in all stool samples from cholera patients, while two other bacteriophage types, one novel (ICP2) and one T7-like (ICP3), are transient. ICP1 is a member of the Myoviridae family and has a 126-kilobase genome comprising 230 open reading frames. Comparative sequence analysis of ICP1 and related isolates from this time period indicated a high level of genetic conservation. The ubiquitous presence of ICP1 in cholera patients and the nding that the O1 antigen of lipopolysaccharide (LPS) serves as the ICP1 receptor suggest that ICP1 is extremely well adapted to predation of human-pathogenic V. cholerae O1.

According to Manju et al, (2012), Epidemic models have been studied by several researchers [Anderson et al. (1979), Bailey (1975) and Hsu et al. (2004)]. The e ects of the presence of bacteria and carriers in the environment on the spread of infectious disease have not been studied using mathematical models [Gonzalez-Guzmem (1989)]. Hethcote (1976) discussed an epidemic model in which the carrier population is assumed to be constant. Although, Codeco et al. (2006) have discussed Trends in Cholera Epidemiology and Ghose et al. (2005) and Shukla et al. (2006) have studied the spread of infectious diseases with bacteria in the environment they have ignored the role of carriers present in the environment. In this paper,

a nonlinear delayed mathematical model with immigration for the spread of infectious disease cholera with carriers in the environment was proposed and analyzed. The model is analyzed by stability theory of di erential equations and computer simulation. This study shows that the spread of the infectious disease cholera increases due to growth of carriers in the environment and disease becomes more endemic due to immigration.

Understanding, predicting, and controlling outbreaks of waterborne diseases are crucial goals of public health policies, but pose challenging problems because infection patterns are in uenced by spatial structure and temporal asynchrony.According to Marino et al, (2012), Networked connectivity models, describing the interplay between hydrology, epidemiology, and social behavior sustaining human mobility, thus prove to be key tools for emergency management of waterborne infections. Here we show that the requirement that all the local reproduction numbers R0 be larger than unity is neither necessary nor su cient for outbreaks to occur when local settlements are connected by networks of primary and secondary infection mechanisms. They showed that geographical outbreak patterns in complex environments are linked to the dominant eigenvector and to spectral properties of G0. Tests against data and computations for the 2010 Haiti and 2000 KwaZulu-Natal cholera outbreaks, as well as against computations for metapopulation networks, demonstrate that eigenvectors of G0 provide a synthetic and e ective tool for predicting the disease course in space and time. Hailegiorgis and Andrew (2012) wrote that the displacement of people in times of crises represents a challenge for humanitarian agencies. This challenge is especially acute within developing countries, which home the majority of displaced people. Within this paper, they demonstrated a spatially explicit agent based model that explores the spread of cholera in the Dadaab refugee camps. Poor sanitation and housing conditions contribute to frequent incidents of cholera outbreaks. They modeled the spread of cholera by

explicitly representing the interaction between humans (host) and their environment, and the spread of the epidemic using Susceptible-Exposed-Infected-Recovered (SEIR) model. Infected agents spread cholera bacteria through excretion of faeces to the environment and this can then be spread throughout the system. Results from the model showed that the spread of cholera grows radially from contaminated water sources. This modeling e ort also

highlights the potential of agent based modeling to explore the spread of cholera in a humanitarian context and its impact on service provision.

According to Cheng and Xiuxiang,(2012),Over the last decade, quite a few mathematical models have been published to investigate the transmission dynamics of cholera. For example, Codeco in 2001 proposed a model that explicitly accounted for the environmental component, i.e. the V. cholerae concentration in the water supply, into a regular SIR epidemiological model. In this paper, They conducted a careful global stability analysis for a generalized cholera epidemiological model. Cholera is a water and food-borne infectious disease whose dynamics are complicated by the multiple interactions between the human host, the pathogen, and the environment. Using the geometric approach, they rigorously proved the endemic global stability for the cholera model in three-dimensional (when the pathogen component is a scalar) and four-dimensional (when the pathogen component is a vector) systems. This work uni es the study of global dynamics for several existing deterministic cholera models.

In 2005,131,943 cases including 2,272 deaths have noti ed from 52 countries. Liman et al,(2012) said the year was marked by a particular signi cant series of outbreaks in West Africa, which a ected 14 countries and accounted for 58% of all cholera cases world-wide (WHO 2006). In the same year Nigeria had 4,477 cases and 174 deaths. There was

reported case of cholera in 2008 in Nigeria in which 429 death out of 6,330 cases. In this essay, a new mathematical model (S, I, R and B) for cholera transmission dynamics is developed and analyzed. Transmission means, global impact of the disease and control mechanisms of cholera disease are brief discussed. They established the existence of equilibrium states and analyzed the disease free equilibrium state for stability using linearization theorem. The disease died out when the rate at which people are exposed to contaminated water and food, and the contribution of those infected with cholera to concentration of V.cholerae are checked. i.e $T < 0$ and $D > 0$ had given disease- free

state to be asymptotically stable.

Motassem et al, (2013) wrote in their paper that recent years have seen a strong trend of cholera outbreaks in developing countries, including Haiti (2010/2011), Cameroon

(2010/2011), Kenya (2010), Vietnam (2009), Zimbabwe (2008/2009), Iraq (2008), the Democratic Republic of Congo (2008) and India (2007). Due to its huge impact on public health, and social and economic development, cholera has been the subject of extensive studies in clinical, experimental and theoretical eld. Haiti o ers the most recent example of the tragedy that can befall a country and its people where cholera striked. While cholera has been a recognized disease for two centuries, there is no strategy for its e ective control. They formulated and analyzed a mathematical model that includes two essential and a ordable control measures: water chlorination and education. They calculated the basic reproduction number and determine the global stability of the disease-free equilibrium for the model without chlorination. They used Latin Hypercube Sampling to demonstrate that the model is most sensitive to education. The researchers also derived the minimal e ective chlorination period required to control the disease for both xed and variable chlorination. Numerical simulations suggest that education is more e ective than chlorination in decreasing bacteria and the number of

cholera cases.

Many mathematical models have been proposed to investigate the complex epidemic and endemic behavior of cholera. The earliest mathematical model was proposed by Capasso and Paveri-Fontana to study a cholera epidemic occurred in the Mediterranean in 1973. Codeco in 2001 extended the work in and explicitly accounted for the role of the aquatic reservoir in cholera dynamics. In this work, Javidi and Ahmed (2013) investigated the dynamical behavior of a fractional order cholera model. All the feasible equilibria for the system were obtained and the conditions for the existence of interior equilibrium were all determined. Local stability analysis of the cholera model was studied by using the fractional Routh-Hurwitz stability conditions. Results in this study indicate the potential of fractional-order cholera models to cope with modern epidemics.

Cholera is said to be the epidemic that urge health education in the early nineteenth century, due to its contagious nature which if allow deteriorating, it has no respect to class of people, and it is still maintaining this threatening gesture. Mathematical modeling being the main stay of epidemiological theory is crucial to apply in studying cholera dynamics because ability

to model disease dynamics can be used to forecast the danger of a major epidemic. Outbreaks of cholera occur suddenly, if not controlled, can spread like wild bush re. In this work,Sani et al, (2013) formulated a deterministic mathematical model of cholera from some modi cations of previous cholera models. Analysis was performed on the Jacobian matrix assuming zero Vibrio Cholerae environments. The basic reproduction number R_0 was obtained as $\frac{k(\gamma+\tau)(g-l+\omega)}{\varepsilon\alpha}$ and the critical number or threshold S_0 was also obtained as $\frac{\varepsilon\alpha p}{k(\gamma+\tau)(g-l+\omega)}$. These two values are used to predict

occurrence of cholera outbreak in a community. Zero equilibrium state is stable when

$R_0 < 1$ and unstable when $R_0 > 1$.

Ochoche (2013) researched that Cholera is generally a disease of the poor, a ecting regions that lack a heightened sense of hygiene and access to safe drinking water. In this research, a mathematical model for the control of cholera transmission dynamics using water treatment as a control strategy is proposed. The model is designed by dividing the system into compartments leading to corresponding di erential equations. The model is built on the assumption that cholera is contracted only through the ingestion of contaminated water. Conditions are derived for the existence of the disease free and endemic equilibria. They proved that the disease free equilibrium is locally asymptotically stable under prescribed conditions on the given parameters. This means that cholera can be eradicated under such conditions in nite time. Numerical simulations are carried out using parameter values from published data to investigate the e ect of transmission parameters on the dynamics of the infection. They simulated cases with no control, weak and strong control. Their results showed that water treatment is an e ective method of controlling cholera however cholera cases will continue to be present in the population if the contribution of the each infected person to the aquatic environment and the contact rate with contaminated water is high.

Cholera remains a public health threat in many countries around the world where outbreaks occur sporadically and punctuate periods of disease extinction or fade-out. This epidemic behaviour is characterized by dramatic variation in the size of individual outbreaks including large intermittent and unpredictable events. According to Manojit et al,(2013), Cholera is on the rise globally, especially epidemic cholera which is characterized by intermittent and

unpredictable outbreaks that punctuate periods of regional disease fade-out. These epidemic dynamics remain however poorly understood. Here, they examined records for epidemic cholera over both contemporary and historical time lines, from Africa (1990/2006) and former British India (1882/1939). They found that the frequency distribution of outbreak size is fat-tailed, scaling approximately as a power-law. This pattern which shows strong parallels with wild res is incompatible with existing cholera models developed for endemic regions, as it implies a fundamental role for stochastic transmission and local depletion of susceptible hosts. Application of a recently developed forest- re model indicates that epidemic cholera dynamics are located above a critical phase transition and propagate in similar ways to aggressive wild res. These ndings have implications for the e ectiveness of control measures and the mechanisms that ultimately limit the size of outbreaks.

Finger et al, (2014) wrote that Mathematical models of cholera dynamics can not only help in identifying environmental drivers and processes that in uence disease transmission, but may also represent valuable tools for the prediction of the epidemiological patterns in time and space as well as for the allocation of health care resources. Cholera outbreaks have been reported in the Democratic Republic of the Congo since the 1970s. They have been ravaging the shore of Lake Kivu in the east of the country repeatedly during the last decades. Here they employed a spatially explicit, inhomogeneous Markov chain model to describe cholera incidence in eight health zones on the shore of the lake. The e ect of human mobility is also modeled

mechanistically. The researchers tested several models on a multiyear data set of reported cholera cases. The best fourteen models, accounting for di erent environmental drivers, and selected using the Akaike information criterion, are formally compared via proper cross validation. Among these, the one accounting for seasonality, El Niæo Southern Oscillation, precipitation and human mobility outperforms the others in cross validation. Some drivers (such as human mobility and rainfall) are retained only by a few models, possibly indicating that the mechanisms through which they in uence cholera dynamics in the area will have to be investigated further.

Crooks and Atesmachew (2014) in their paper reported that Cholera is an intestinal disease and is characterized by diarrhea and severe dehydration. While cholera has mainly been eliminated in regions that can provide clean water, adequate hygiene and proper sanitation; it remains a constant threat in many parts of Africa and Asia. Within this paper, they developed an agent-based model that explores the spread of cholera in the Dadaab refugee camp in Kenya, Poor sanitation and housing conditions contributed to frequent incidents of cholera outbreaks within this camp. For example, 10,000 Rwandan refugees died from cholera in 1994 (Waldor and Chairat,2010). They modeled the spread of cholera by explicitly representing the interaction between humans and their environment, and the spread of the epidemic using Susceptible-Exposed-InfectedRecovered model. Results from the model show that the spread of cholera grows radially from contaminated water sources and seasonal rains can cause the emergence of cholera outbreaks. This modeling e ort highlights the potential of agent-based modeling to explore the spread of cholera in a humanitarian context .

According to Sani et al,(2014), in recent years, cholera outbreaks have been on increase, there are more than 250,000 cases of cholera each year worldwide. Factors that in uence cholera outbreak include ood, draught and river height. Codeco (2001) ''Flooding and draught are likely to a ect cholera dynamic in a complex way. Flooding washes contaminated faeces and sewage into the river. It can also disrupt water distribution service and aggravate hygiene conditions. Draught on the other hand shortens the availability of potable water, aggravates hygiene condition, by increasing the number of people sharing the same water supply and may increase per capita water contamination . The dynamics of cholera is analysed using a system of four di erential equations with two control measures τ and ω, which are; therapeutic treatment and sanitary measures respectively. A zero Vibrio Cholerae bacteria environment was rst assumed and analysed establishing disease free equilibrium state (DFE), which is interpreted as $R_0 < 1$. Epidemic equilibrium state assumed as $R_0 > 1$ was then obtained after

analysing the non-zeroVibrio Cholerae bacteria environment. This established the fact that; measures aimed at reducing Vibrio Cholerae bacteria in the environment will in turn reduce or control cholera.

Limited access to safe water and sanitation resources is common in developing countries, leaving them vulnerable to cholera outbreaks.Posny and Wang (2014) wrote that Cholera is an intestinal infection caused by ingesting food or water contaminated with the bacterium Vibrio cholerae. If left untreated, an infected individual may become severely dehydrated and die within several days. Besides the transmission route based on environment human interaction, the human-to-human direct transmission is also found important in shaping a cholera epidemic. A recent cholera outbreak in Zimbabwe, a land-locked country in Africa, during 2008/2009 underscores such a direct transmission pathway. They proposed a deterministic compartmental model for cholera dynamics in periodic environments. The model incorporates seasonal variation into a general formulation for the incidence (or, force of infection) and the pathogen concentration. The basic reproduction number of the periodic model is derived, based on which a careful analysis is conducted on the epidemic and endemic dynamics of cholera. Several speci c examples are presented to demonstrate this general model, and numerical simulation results are used to validate the analytical prediction. In Nigeria, outbreaks of the disease have been occurring with increasing frequency since the rst outbreak in modern times in 1970 (Epstein, 1993 Osemwenkhae et al, 2009).

Since then, cholera has continued to cause high mortality in humans, in Nigeria. The year 1999 saw the highest number of reported cases (WHO, 2009). Since then, cholera cases have been persistent in the country. Recently, in Kano, on September 22nd 2008, the United Nations o ce for the coordination of Humanitarian A airs unit reported that cholera outbreak killed 97 persons in Kano. In this work two mathematical models that described the dynamics of cholera in Nigeria were presented. The rst model examined the bacteria population using a logistic de nition for its growth in the expected habitat and their interaction with the susceptible population. The second model is an optimal control model that includes two time-dependent control functions with one minimizing the contact between the susceptible and the bacteria and the other, the population of the bacteria in the water. The results from the numerical solutions of the models presented showed that increasing the susceptible pool and the infected population above some threshold values were responsible for epidemic cholera. It also showed that the di erence between the growth rate (r) and the loss rate (n) of the

bacteria plays a huge role in the outbreak as well as the severity of the disease according to Isere et al,(2014).

In 2005, Nigeria had 4,477 cases and 174 deaths. In 2008, Nigeria recorded 429 deaths out of 6,330 cases. Furthermore, in 2009, Nigeria reported 13,691 cases and 431 deaths (WHO, 2012). In summary, the United Nation (UN) unit, reports: despite Nigeria's oil wealth, more than 70% of the country's 126 million people live below the poverty line and cholera outbreaks are common in poor urban areas which lack proper sanitation

and clean drinking water (UN O ce for the Coordination of Humanitarian A airs Integrated Regional Information Networks (IFIN), 2005). In this research, Sulayman et al,(2014) presented and analyzed a mathematical model for the control of cholera in Nigeria with modi cations as compared to previous cholera models. Their model incorporates treatment, water hygiene and environmental sanitation in curtailing the disease. A system of ordinary di erential equations is used. Numerical simulation of the full model using maple shows that improvement in treatment, water hygiene and the environmental sanitation o ered to about fty percent is e ective to eradicate cholera

epidemic.

2.4 Literature on Statistical models

Erin et al, (2002) reported that recently, the role of the environment and climate in disease dynamics has become a subject of increasing interest to scientists. Much of the interest has been stimulated by the growing problems of antibiotic resistance among pathogens, emergence and/or reemergence of infectious diseases worldwide. First, the disease has a historical context linking it to speci c seasons and biogeographical zones. In addition, the population dynamics of V. cholerae in the environment are strongly controlled by environmental factors, such as water temperature, salinity, and the presence of copepods, which are, in turn, controlled by larger-scale climate variability. In this review, the association between plankton and V. cholerae that has been documented over the last 20 years is discussed in support of the hypothesis that cholera shares properties of a vector-borne disease. In addition, a model for environmental transmission of cholera to humans in the context of climate variability is presented. The cholera model provides a template for future

research on climate-sensitive diseases, allowing de nition of critical parameters and o ering a means of developing more sophisticated methods for prediction of disease outbreaks.

Chingayipe (2008) wrote that in Malawi, outbreaks of varying intensities have occurred each year especially during rainy season. Like other districts in the country, Chiradzulu has been experiencing cholera outbreaks notably since 2001/2002 rainy season with high case fatality rates of 4.5%. Despite the e orts to control cholera it has caused unnecessary panicking among the communities and health workers whenever it strikes which has led to loss of lives. This was a cross sectional study using both qualitative and quantitative methodologies. A total of 150 households were sampled in four

villages from two traditional authorities. The traditional authorities (TAs) were selected randomly depending on their distances from the main hospital. The study suggests that about 70% of the respondents had knowledge on cholera. In villages where cholera occurred frequently people were more knowledgeable than where it seldom occurred. Inadequate and mistimed messages due to lack of commitment of health workers to guide communities and cultural beliefs were the factors which contributed to poor detection of the disease.

According to Said (2006), Cholera made an unforeseen appearance on the eastern coast of South Africa in the province of KwaZulu-Natal (KZN) in August 2000. Having started from the more urban centres of the coastal region of the province, cholera proceeded unabated to the interior of the province where no community was spared from the scourge. Despite prompt medical intervention, health education and media awareness campaigns, cholera continued to spread throughout KZN. Thus GIS was used as a

research tool to facilitate the comparison of the disease trends and risk factors on a spatial level in order to determine the possible role(s) played by the di erent environmental and socio-economic drivers. At the spatial level, the characteristics of the epidemic as revealed by the GIS maps and spatial modeling highlighted possible relationships between the incidence of cholera and the various socio-economic and climatic variables. The results give an altogether holistic portrayal of the cholera epidemic from all perspectives and also supported the hypothesis that cholera is a function of social and environmental factors. Spatial modeling o ered more insight that the statistically supported climatic and socio-

economic aspects were indeed important factors in guiding cholera outbreak predictions in the future.

In Zimbabwe, gradual economic collapse over the last 10 years culminated in the creation of a complex humanitarian emergency state in 2008, with massive loss of health and water infrastructure. This situation put the country at risk for one of the largest and most severe cholera outbreaks in the past 10 years. Missing data was an issue in the analysis, and imputation methods were compared and contrasted in the development of nal logistic and multiple linear regression models. Despite the limited availability of timely point-of-use water treatment in the Zimbabwean cholera outbreak, a characteristic inherent to many response e orts, there was suggestive but inconclusive evidence that water quality at the source may reduce cholera morbidity by itself.Here, David (2009) paper has important implications not only for eld outbreak data methodology, but for water and sanitation promotion as well. While simple imputation methods seem to be the norm in outbreaks in the eld, there was value in multiple imputation methods for improving the validity and precision of the model estimates.

The cholera epidemic has been a huge burden in the world in recent times, with the disease still thriving with much energy in Asia, Africa and South America. The occurrence and severity of cholera outbreaks in endemic areas is greatly enhanced by human behaviour with regards to the practice of healthy hygiene, sanitation and health education. However, information ow in the delivery of health education on the practice of healthy hygiene and sanitation in cholera endemic regions, during or prior to cholera outbreaks has been a great handicap in the prevention and control of cholera. In this regard, a study protocol has been designed to determine the barriers to the practice of healthy hygiene and sanitation by residents in Douala, a cholera-endemic region in Cameroon. The proposed study was done in two phases. The rst phase was knowledge, attitude and practice (KAP) study to measure the knowledge, attitudes and practices of the residents in response to health education on cholera prevention and control. The second phase was qualitative study to explore unclear concepts or phenomenon to understand particular aspects of actions and behaviour, while paying attention to the social mechanisms in the population that lead to risk behaviour. The KAP

study will provide rst-hand information about possible disease determinants, leading to the formulation of a hypothesis that can be tested using an analytical study design. The results of this study will be useful for planning health care interventions on cholera prevention and control according to Njol (2010).

A recent study on cholera reveals that local environmental parameters are intensely associated with cholera dynamics. In particular, increase in ocean chlorophyll concentration; sea surface temperature and river height play a signi cant role on the occurrence of cholera and the magnitude of the epidemic. Cholera, a man-environment disease is transmitted through drinking water which is contaminated from improper treatment of sewage. Further, it may be noted that if the degree of infectivity increases, sociological or other mechanisms which tend to saturate the e ect that a large number of infectives may have often come into play. Therefore they are interested in exploring the e ects of environmental uctuations by considering the saturation incidence term. The study focuses on randomly uctuating phenomena of cholera deterministic model by incorporating white noise stochastic perturbation. For the deterministic model, stability of the equilibria and persistent aspects of population are discussed. Variances of population are evaluated for the model system at the endemic equilibrium. They concluded from the study that the inclusion of environmental uctuation does not change substantially the dynamical behaviour of the system although it induces some initial random oscillations according to Gazi et al, (2010).

Global cholera incidence is increasing, particularly in sub-Saharan Africa. Reyburn et al, (2011) examined the impact of climate and ocean environmental variability on cholera outbreaks, and developed a forecasting model for outbreaks in Zanzibar. Routine cholera surveillance reports between 1997 and 2006 were correlated with remotely and locally sensed environmental data. A seasonal autoregressive integrated moving average (SARIMA) model determined the impact of climate and environmental variability on cholera. The SARIMA model shows temporal clustering of cholera. A 1^0C increase in temperature at 4 months lag resulted in a 2-fold increase of cholera cases, and an increase of 200 mm of rainfall at 2 months lag resulted in a 1.6-fold increase of cholera cases. Temperature and rainfall

interaction yielded a signi cantly positive association ($P < 0.04$) with cholera at a 1-month lag. These results may be applied to forecast

cholera outbreaks, and guide public health resources in controlling cholera in Zanzibar. Started in late October 2010, cholera epidemic peaked during January 2011, with more than 344,000 reported cases and about 5,400 deaths within the period of three months. Mari et al, (2011) investigated the role of human mobility as a driver for longrange spreading of cholera infections, which primarily propagate through hydrologically controlled ecological corridors. They build a spatially explicit model of a disease epidemic, which is relevant to both social and scienti c issues. They presented a twolayer network model that accounts for the interplay between epidemiological dynamics, hydrological transport and long-distance dissemination of the pathogen Vibrio cholerae owing to host movement, described here by means of a gravity-model approach. The researchers also tested their model against epidemiological data recorded during the extensive cholera outbreak occurred in the KwaZulu-Natal province of South Africa during 2000/2001. They showed that long-range human movement is fundamental in

quantifying otherwise unexplained inter-catchment transport of V. cholerae, thus playing a key role in the formation of regional patterns of cholera epidemics. They also showed quantitatively how heterogeneously distributed drinking water supplies and sanitation conditions may a ect large-scale cholera transmission.

Heidi,(2012) researched that many communities in the Dominican Republic have little or no access to safe drinking water or sanitation. The recent introduction of cholera from Haiti further highlights these limitations and their impact on human health. This research focused on two communities; a rural mountainous village and a periurban batey, which is a settlement community constructed by sugar cane companies to house primarily Haitian immigrant laborers. Research methods included community observations, household interviews, and interviews with local leaders. The results showed two dramatically di erent types of water access and sanitation. The mountainous village had regular access to local springs, consistent piped water, functioning latrines, and low population density. Community members voiced

no dissatisfaction with their water system or waste disposal and reported no diarrheal disease. In contrast, the batey

reported chronic diarrhea disease, high population density, and inconsistent access to safe water or latrines. Residents in the batey voiced frustration with the water infrastructure, with their inability to mobilize as a community, and with government run water services. In 2005, there were 31,719 cholera cases, with 458 deaths in the Republic of Senegal. Guillaume et al,(2012) retrospectively investigated the climate origin of the devastating oods in mid-August 2005, in the Dakar Region of Senegal and the subsequent outbreak of cholera along with the pattern of cholera outbreaks in three other regions of that country. They compared rainfall patterns between 2002 and 2005 and the relationship between the sea surface temperature (SST) gradient in the tropical Atlantic Ocean and precipitation over Senegal for 2005. Results showed a speci c pattern of rainfall throughout the Dakar region during August, 2005, and the associated rainfall anomaly coincided with an exacerbation of the cholera epidemic. Comparison of rainfall and epidemiological patterns revealed that the temporal dynamics of precipitation, which was abrupt and heavy, was presumably the determining factor. Analysis of the SST gradient showed that the Atlantic Ocean SST variability in 2005 di ered from that of 2002 to 2004, a result of a prominent Atlantic meridional mode. Thus, high resolution rainfall forecasts at sub seasonal time scales should provide a way forward for an early warning system in Africa for cholera and, thereby, trigger epidemic preparedness.

The growing number and increased frequency of major cholera outbreaks, especially in African countries, have heightened concerns about the disease in particular about its spatial and temporal characteristics and their underlying risk factors.According to Osei (2010), Cholera is transmitted mainly through contaminated water and food; however, demographic and geographic factors can predispose inhabitants to infection. Socioeconomic and environmental factors like environmental sanitation can in uence the vulnerability of a population to cholera infection. Here, a steepest downhill path analysis using a 3D elevation model and refuse dumps location to delineate potential cholera reservoirs. Using proximity to the potential cholera reservoir as explanatory variables, statistical models are developed and implemented to assess the e ects of surface water pollution on cholera. Finally the results

show that the distribution exhibits a distinct spatial and temporal variation. Such variation is in uenced by demographic risk factors like urbanization, overcrowding, migration, sanitation and use of drinking water. Open space refuse dumps and surface water pollution on cholera are important environmental risk factors for cholera transmission. Cholera outbreaks can start from multiple geographical locations that actually have no spatial connection.

Sara et al, (2010) reported an increase in temperatures and changes in patterns of rainfall as a result of climate change are widely recognized to entail serious consequences for human health, including the risk of diarrheal diseases. Indeed, there is strong evidence that temperature and rainfall patterns a ect the disease pattern. This paper presents the rst study that links the incidence of cholera to environmental and socioeconomic factors and uses that relationship to predict how climate change will a ect the incidence of cholera. Speci cally, the paper integrates historical data on temperature and rainfall with the burden of disease from cholera in Tanzania, and uses socioeconomic data to control the impacts of general development on the risk of cholera. Based on these results they estimated the number and costs of additional cholera cases and deaths that can be attributed to climate change by year 2030 in Tanzania. The result shows a signi cant relationship between cholera cases and temperature and predicts an increase in the initial risk ratio for cholera in Tanzania in the range of 23 to 51 percent for a 1 degree Celsius increase in annual mean temperature.

Since the initial transmission mechanism of Cholera was revealed by John Snow in 1854, the cause and spread of this disease has been under continuous research. Snow's study showed how disease incidences can be linked to a source based on the spatial distribution of the patients. However, Snow's work did not address the question of di usion mechanisms. The predominant transmission mechanism of Cholera is via the fecal-oral route but in recent years several scientists have pointed toward a number of other transmission mechanisms that might contribute to the prevalence of the disease. The model presented in this research is a geographically explicit agent-based Cholera simulation. It is a micro scale, hydrology-driven model that di ers from already existing ones in that it consists of four di erent sub-models: (i) a hydrological model for the transport of the V. cholerae pathogen (ii) an epidemic model (iii) a house y model for modeling ies as disease carriers (iv) a human interaction model. In the

study, EllenWien et al, (2011) presented the conceptual design and the initial ndings of the model.

Findings here include the comparison of di erent transmission mechanisms.

2.5 Literature on Biological models

During spring and late summer in Bangladesh, phytoplankton blooms occur, followed by zooplankton, with heaviest blooms occurring in September and October. Each year, the seasonal zooplankton blooms, in turn, are followed by cholera outbreaks. It has been determined that a During spring and late summer in Bangladesh, phytoplankton blooms occur, followed by zooplankton, with heaviest blooms occurring in September and October. Each year, the seasonal zooplankton blooms, in turn, are followed by cholera outbreaks. It has been determined that a single copepod, depending on species and size, can carry up to 10^4 cells of V. cholerae. Thus, a copepod bloom can result in the number of V. cholerae per ml of water comprising an infective Thus, a copepod bloom can result in the number of V. cholerae per ml of water comprising an infective dose, showing that $\approx 10^4$ to 10^6 V. cholerae O1 can produce clinical cholera. Patchiness in copepod distribution, often species speci c in the aquatic environment, can result in signi cant variability in the number of copepods in water taken directly from a pond or river for drinking. Based on results of ecological studies demonstrating that Vibrio cholerae, the etiological agent of epidemic cholera, is commensal to zooplankton, notably copepods, a simple ltration procedure was developed whereby zooplankton, most phytoplankton, and particulates > $20\mu m$ were removed from water before use. E ective deployment of this ltration procedure, from September 1999 through July 2002 in 65 villages of rural Bangladesh, of which the total population for the entire study comprised $\approx 133{,}000$ individuals, yielded a 48% reduction in cholera ($P < 0.005$) compared with the control according to Colwell et al,(2003).

Roseman et al, (2003) wrote that Chitin, an insoluble polymer of GlcNAc, is an abundant source of carbon, nitrogen, and energy for marine microorganisms. Microarray expression pro ling and mutational studies of Vibrio cholerae growing on a natural chitin surface,

or with the soluble chitin oligosaccharides $(GlcNAc)_{2-6}$, GlcNAc, or the glucosamine dimer $(GlcN)_2$ identi ed three sets of di erentially regulated genes. They showed that (i) ChiS, a sensor histidine kinase, regulates expression of the $(GlcNAc)_{2-6}$ gene set, including a $(GlcNAc)_2$ catabolic operon, two extracellular chitinases, a chitoporin, and a PilA-containing type IV pilus, designated ChiRP (chitin-regulated pilus) that confers a signi cant growth advantage to V. cholerae on a chitin surface; (ii) GlcNAc causes the coordinate expression of genes involved with chitin chemotaxis and adherence and with the transport and assimilation of GlcNAc; (iii) $(GlcN)_2$ induces genes required for the transport and catabolism of nonacetylated chitin residues; and (iv) the constitutively expressed MSHA pilus facilitates adhesion to the chitin surface independent of surface chemistry. Collectively, these results provide a global portrait of a complex, multistage V. cholerae program for the e cient utilization of chitin. V. cholerae Expression Pro ling Studies Identify Three Classes of Chitin-Regulated Genes.

Bacteriophage VP4 is a lytic phage of the Vibro cholerae serogroup O1, and it is used in phage subtyping of V. cholerae biotype El Tor. Studies of phage infection mechanisms promoted the understanding of the basis of phage subtyping as well as the genetic di erences between sensitive and resistant strains. In this study, they investigated the receptor that phage VP4 uses to bind to El Tor strains of V. cholerae and found that it infects strains through adsorbing the O antigen of V. cholerae O1. In some natural isolates that are resistant to VP4 infection, mutations were identi ed in the *wb*∗ cluster (O-antigen gene cluster), which is responsible for the biosynthesis of O antigen. Mutations in the *man*B, *wbe*E, and *wbe*U genes caused failure of adsorption of VP4 to these strains, whereas the observed amino acid residue mutations within *wbe*W and *man*C have no e ect on VP4 infection. Although mutations in two resistant strains were found only in *man*B and *wbe*W, complementing both genes did not restore sensitivity to VP4 infection, suggesting that other resistance mechanisms may exist. Therefore, the mechanism of VP4 infection may provide a basis for subtyping the phage. Elaborate mutations of the O antigen may imbue V. cholerae strains with resistance to phage infection according to Jialiang et al, (2013).

The ever increasing challenge of pathogenic bacteria becoming resistant to multiple antibiotics has spawned the search for new antibacterial drugs and new targets for antibacterial drugs.Henrik (2009) reported that Virulence factors could be such new drug targets. Here he presented an in vivo model of the infectious disease cholera using the bacteria grazing nematode Caenorhabditis elegans. He showed that the non-pathogenic (CTX-) Vibrio choleraeO1 El Tor strain 2740-80 is ingested by C. elegans and establishes a lethal infection in the intestinal tract of the worm. The study found out that the virulence of V. cholerae, determined as its ability to kill C. elegans, was induced by growth of the bacteria under anaerobic conditions. A library of an estimated 14,000 clones was constructed, each clone expressing a di erent peptide. In order to test the individual clones a killing/rescue assay in liquid medium was set up in 96-well microtiter plates. This simple system was used to screen 350 clones/peptides. None of the clones promoted survival of the worms, but he atributed this to the low number of clones tested. Despite the lack of a positive outcome, the experiments indicate that this assay could be used to screen for peptides that target bacterial virulence

Chapter 3

Methodology

3.1 Introduction

In this chapter, we recall some de nitions and a model for cholera transmission is formulated in respect of the dynamics of the disease and an e cient numerical method used to solve the fractional-order nonlinear system.

3.2 Basic Concepts and De nitions

Fractional-order di erentiation is regarded as the generalization of classical integer-order di erentiation to real or complex orders. There has been much interest in developing the theoretical analysis and numerical methods for fractional di erential equations as fractional calculus is found to be a valuable tool in various elds of science and engineering. Indeed, we can nd numerous applications in polymer rheology, regular variation in thermodynamics, biophysics, blood ow phenomena, aerodynamics, electrodynamics of complex medium, viscoelasticity, Bode analysis of feedback ampli ers, capacitor theory, electrical circuits, electro-analytical chemistry, biology, control theory, tting of experimental data, etc. It has been mainly due to the reason that fractionalorder equations are naturally related to systems with memory which exists in most biological systems. Also they are closely related to fractals which are abundant in biological systems.

3.2.1 The Gamma Function

This function is basically tied to fractional calculus by de nition. Its explanation is simply the generality of the factorial for all real numbers. The de nition of the gamma function is given by

$$\Gamma(z) = \int_0^\infty e^{-u} u^{z-1} du, \forall z \in R$$

This function is the only one of its kind in that the value for any quantity is, by consequence of the form of the integral, equivalent to that quantity z minus one times the gamma of the quantity minus one.

$\Gamma(z+1) = z\Gamma(z)$, also when $z \in N_+$, then $\gamma(z) = (z-1)!$

. This can be shown through a simple integration by parts.

3.2.2 Riemann-Liouville De nition

$$D_t^\alpha f(t) = \frac{1}{\Gamma(n-\alpha)} (\frac{d}{dt})^n \int_a^t \frac{f(s)ds}{(t-s)^{\alpha-n+1}}, n-1 \leq \alpha < n$$

3.2.3 Fractional integral according to Riemann-Liouville

According to Riemann-Liouville the notion of fractional integral of order $\alpha(\alpha > 0)$ for a function f (t), is a natural consequence of the well-known formula (Cauchy-Dirichlet), that reduces the calculation of the n-fold primitive of a function f (t) to a single integral of convolution type

$$J_{a+}^n f(t) := \frac{1}{(n-1)!} \int_a^t (t-s)^{n-1} f(s)ds, n \in N$$

Vanishing at $t = a$ with its derivatives of order $1,2,\ldots,n-1$. Require $f(t)$ and $J_t^\alpha f(t)$ to be causal functions, that is, vanishing for $t < 0$

Extend to any positive real value by using the Gamma function, $(n-1)! = \Gamma n$

Fractional integral of order $\alpha > 0$ (right sided)

$$J_{a+}^n f(t) := \frac{1}{\Gamma(\alpha)} \int_a^t (t-s)^{\alpha-1} f(s)ds, \alpha \in N$$

De ne $J_{a+}^0 f(t) := I,\ J_{a+}^0 f(t) := f(t)$

Alternatively

$$J_{b-}^\alpha f(t) = \frac{1}{\Gamma(\alpha)} (\frac{d}{dt})^n \int_b^t (s-t)^{\alpha-1} f(s)ds, \alpha \in R$$

$(a = 0, b = +\infty)$ Riemann

$(a = -\infty, b = +\infty)$ Liouville

3.2.4 Caputo fractional derivative

There is another option for computing fractional derivatives; the Caputo fractional derivative. It was introduced by M. Caputo in his 1967 paper. In contrast to the Riemann Liouville fractional derivative, when solving di erential equations using Caputo's de nition, it is not necessary to de ne the fractional order initial conditions.

Caputo's de nition is illustrated as follows.

$$D_{to}^{\alpha} f(t) = \frac{1}{\Gamma(1-\alpha)} \int_a^t \frac{f^{(n)}(s)}{(t-s)^{\alpha+1-n}} ds, 0 < \alpha < 1$$

3.3 Components of mathematical models

Mathematical model: is a set of formulas and or equations based on a quantitative description of real phenomena and created in the hope that the behavior it predicts will resemble the real behavior on which it is based.

Mathematical quantities in models can be classi ed as variables, constants, parameters and input functions. An independent variable is a quantity that takes on a range of values. Usually, independent variables are measures of time or position. The set of all possible values of the independent variable is the domain of the problem. A dependent variable is a quantity that changes during a given problem, depending on the value(s) of the independent variable(s).

A constant is a quantity that has a single xed value. And a parameter is a quantity whose value is xed throughout the domain of the model but can be varied to a family of related problems.

3.3.1 Purposes of Epidemiological Modeling

The following are some purposes of epidemiological modeling

1. The model formulation process clari es assumptions, variables and parameters.

2. The behavior of precise mathematical models can be analyzed using mathematical methods and computer simulations.

3. Modeling provides concepts such as a threshold, reproduction number, etc.

4. Modeling is an experimental tool for testing theories and assessing quantitative conjectures.

5. Modeling can be used to estimate key parameters by tting data.

6. Models can be used in comparing diseases of di erent types or at di erent times or in di erent populations.

7. Models can be used to theoretically evaluate, compare or optimize various detection, prevention, therapy and control programs.

8. Model can suggest crucial data which needs to be collected.

3.3.2 Limitations of Epidemiological Modeling

The following are some of the limitations of epidemiological modeling.

1. An epidemiological modeling is not reality; it is an extreme simpli cation of reality.

2. Deterministic models do not re ect the role of chance in disease spread and do not provide con dence interval on results.

Before we start with our Codeco cholera model, let us analyze some of the shortcomings of SIR model as we are aware that a model should simulate the spread of the disease as accurate as possible, which means that the resulting graph of the model should t the empirical data. Above all, an accurate prediction of the disease dynamics will allow us to evaluate the e ectiveness of the control measures.

3.4 SIR Model

Almost all epidemiological models start from this same basic model. The SIR model is used for modeling general epidemics and to know how the spread of a disease is in a particular population and some possible ways of controlling such a disease.

3.4.1 Some SIR Model Assumptions

Here the population is divided into three compartments, namely Susceptible, Infectious and Recovered population as represented below .

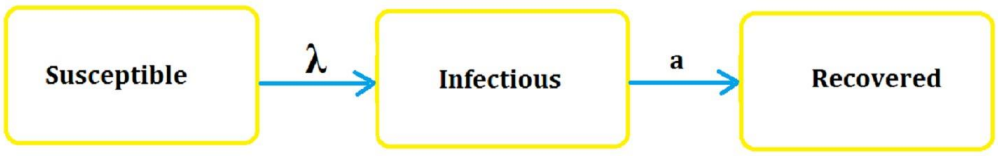


Figure 3.1: A diagram showing Susceptible, Infectious and Recovered group

The above model has a few assumptions:

1. It is assumed that if the infected person did not die from the disease, then he/she becomes immune upon recovery.
2. In addition, the model assumes that the population is mixing homogenously. ie there is an interaction within the population.
3. The total population at any time is assumed to be constant.
4. It is also assumed that, at any given day a xed fraction of the infected group will recover. For example, if the average duration of infection (infectious period) is four days, then, on average, one-fourth of the currently infected population recovers each day.

3.4.2 Equations for SIR Model

In this model the total population is divided into three distinct groups. We rst have the Susceptible(S), Infected (I) and the Recovered (R). The total population is assumed to be constant. That is, $S + I + R = N$

Assuming the disease spreads into a population that is totally susceptible, the susceptible individuals have never come into contact with the disease and are able to catch the disease, after which they move into the infectious class. Infectious individuals spread the disease to the susceptible, and remain in the infectious class for a given period of time (the infectious period) before moving into the recovered/removed class.

This description of the SIR model was made more mathematical by a formulated di erential equation for the proportion of individuals in each class.

Table 3.1: Variables and de nitions of sub-populations of Sir Model

Variables	De nitions
S(t)	The number of susceptible individuals at time, t
I(t)	The number of infected individuals at time, t
R(t)	The number of recovered individuals at time, t

Table 3.2: Parameters and their de nitions of Sir Model

Parameters	De nitions
Λ	Rate of infection per unit time
A	The rate at which an infectious individual recovered per unit time

3.4.3 Di erential Equations

The di erential equations for the SIR model are given by the following

$$\frac{dS}{dt} = -\lambda S(t)I(t)$$
$$\frac{dI}{dt} = \lambda S(t)I(t) - \alpha I(t)$$
$$\frac{dR}{dt} = \alpha I(t)$$

Where, S stands for Susceptible (those who can contract the disease), I stands for Infectious (those who have the disease and can infect others) and R represents Recovered or Removed. The parameters λ and α characterize the propagation of the disease and can also be used as control parameters in order to stop the epidemic.

3.4.4 Limitations of the SIR Model

Even though the SIR model provides a general framework to understand the spread of a disease, it may be too simple to accurately model a real epidemic like the outbreak of cholera worldwide. There are various limitations or shortcomings in this model, which are explained as follows:

There should be an environmental component, i.e. the vibrio cholerae concentration in the water supply. In fact, this is the case for cholera outbreak. A cholera patient becomes infectious or develops the symptoms only after being in contact with contaminated water supply.

Therefore, the limitations and aws in the SIR model can be modi ed and extended to the Codeco model.

3.5 Codeco model

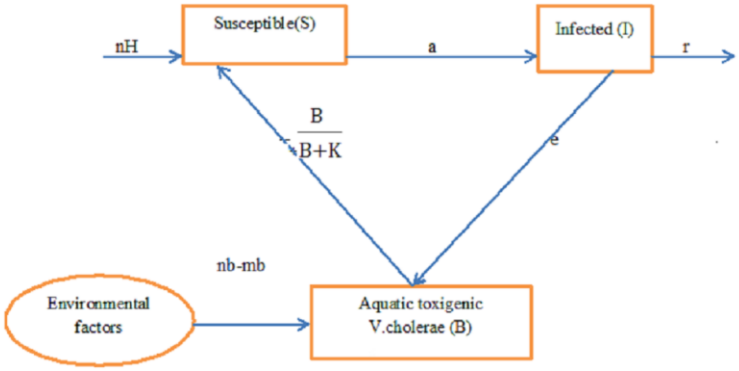
This model explicitly incorporated the environmental component, i.e. the V.cholerae concentration in the water supply (denoted by B), into a regular SIR system to form a combined human-environment (SI-B) epidemiological model.

Figure 3.2: the deterministic Codeco cholera model diagram

3.5.1 Assumptions of the Codeco Cholera Model

The only route for infection is the injection of contaminated water from non-treated sources.

individuals in the population H are born susceptible



Susceptible people(S) become infected as they are exposed to contaminated water

Infected individuals recover at the rate r

Recovered individuals are not explicitly included but its size can be estimated as H-I-S.

Infected individuals contribute to the enhancement of bacteria population through excretion.

Bacteria population in the aquatic reservoir (B) may also grow in the water at a rate determined by environmental factors

3.5.2 Model Formulation

The assumptions of the model lead to the following system of di erential equations

$$\frac{dS}{dt} = n(H - S) - a\frac{BS}{K + B}$$
$$\frac{dI}{dt} = a\frac{BS}{K + B} - rI$$
$$\frac{dB}{dt} = B(nb - mb) + eI, nb > mb$$

By fractionalizing the system above, where $D^{\alpha}S$, $D^{\alpha}I$ and $D^{\alpha}B$ are the derivatives of S (t), I (t) and B (t) respectively, of arbitrary order α in the sense of caputo and $0 < \alpha < 1$,

then the system leads to fractional di erential equations given by,

$$D^{\alpha}S = n(H - S) - a\frac{BS}{K + B} \tag{3.1}$$

$$D^{\alpha}I = a\frac{BS}{K + B} - rI \tag{3.2}$$

$$D^{\alpha}B = B(nb - mb) + eI, nb > mb \tag{3.3}$$

$$S(0) = S_0, I(0) = I_0 > 0, B(0) = B_0 > 0$$

The reason for considering a fractional order system instead of its integer order matching part is that fractional order di erential equations are generalization of integer order di erential equations. Also, using fractional order di erential equations can help us to decrease the errors arising from the neglected parameters in modeling real life phenomena.

Table 3.3: Variables and de nitions of Codeco model

SYMBOL	DESCRIPTION
State variables	
S	number of susceptible individuals
I	number of infected individuals
B	Concentration of toxigenic V. cholerae in water (cells/ml)

Table 3.4: Parameters and de nitions of Codeco model

SYMBOL	DESCRIPTION
Parameters	
H	total human population
n	human birth and death rates (day^{-1})
a	rate of exposure to contaminated water (day^{-1})
K	concentration of V.cholerae in water that yields 50% of catching cholera (cells/ml)
r	rate at which people recover from cholera (day^{-1})
$nb-mb$	di erence between the growth and loss rates of V.cholerae in the aquatic environment
e	contribution of each infected people to the population of V.cholerae in the aquatic

3.5.3 Basic Reproductive Number (R_0) of the Model

A fundamental concept in epidemiology is the basic reproduction number, which measures the average number of secondary infections that occur when one infective is introduced into a completely susceptible host population. The basic reproduction number R_0 is de ned as the average number of Secondary cases generated by a typical infective (patience) within a population with no immunity to the disease, in the absence of interventions produced by a single infected individual introduced into a population of N susceptible. It is denoted by R_0 (Kermack and McKendrick, 1927).

If $R_0 < 1$, then there is no epidemics, that is the disease dies out. If $R_0 > 1$, then it implies that the disease spreads in the susceptible population. Following the standard next-generation matrix (NGM) theory, the disease-free equilibrium is given by $E_0 = (S_0, I_0, B_0) = (H, 0, 0)$. From the next generation matrix theory;

$$F = \begin{bmatrix} 0 & \frac{aH}{k} \\ 0 & 0 \end{bmatrix}$$

And

$$V = \begin{bmatrix} r & o \\ -e & nb - mb \end{bmatrix}$$

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

But

$$V^{-1} = \frac{1}{r(nb-mb)} \begin{bmatrix} nb-mb & 0 \\ e & r \end{bmatrix}$$

$$\Rightarrow V^{-1} = \begin{bmatrix} \frac{1}{r} & 0 \\ \frac{e}{r(nb-mb)} & \frac{1}{nb-mb} \end{bmatrix}$$

$$FV^{-1} = \begin{bmatrix} 0 & \frac{aH}{k} \\ 0 & 0 \end{bmatrix} \begin{bmatrix} \frac{1}{r} & 0 \\ \frac{e}{r(nb-mb)} & \frac{1}{nb-mb} \end{bmatrix}$$

$$\frac{eaH}{} \quad \frac{aH}{} \quad ? \quad ?$$

Hence FV^{-1} = ? $rK(nb-mb)$ $K(nb-mb)$?

? 0 0 ?

Hence the Next Generational Matrix (NGM) is $\begin{bmatrix} \frac{eaH}{rK(nb-mb)} & \frac{aH}{K(nb-mb)} \\ 0 & 0 \end{bmatrix}$

And since R_o is the most dominant eigenvalue of the NGM, then this implies that

$$R_o = \frac{eaH}{rK(nb-mb)}$$

3.5.4 Equilibrium point and Stability

To determine the stability analysis of the model, we rst evaluate the equilibrium point(s) or steady states of the system of fractional di erential equations (1), (2), and (3). The equilibrium points involved determine the disease-free (where $I = 0$) and endemic (where $I \neq 0$) Consider the initial value problem (1)-(3) with $0 \leq \alpha \leq 1$.To evaluate the equilibrium points of (1)-(3),

$$D^{\alpha}S = 0, D^{\alpha}I = 0, D^{\alpha}B = 0$$

3.5.5 Existence of the Disease Free Equilibrium State

Here, we discuss the existence and stability of the equilibrium state of the model. At the equilibrium state $D^{\alpha}S, D^{\alpha}I$ and $D^{\alpha}B$, all vanish. Therefore, equating the right hand sides of the model equations (1), (2) and (3) to zero, we have

$$n(H-S) - a\frac{SB}{B+K} = 0 \tag{3.4}$$

$$a\frac{SB}{B+K} - Ir = 0 \tag{3.5}$$

$$B(nb-mb) + Ie = 0 \tag{3.6}$$

(3.7)

At the disease Free State (DFE), there are no infections, that is $I = 0$. Substituting this into (3.6), we have

$$B(nb - mb) = 0$$

Therefore $B = 0$ provided $(nb - mb)\ 6{=}\ 0$. Putting $B = 0$ into (3.4)

$$n(H - S) = 0$$

$$\Rightarrow n = 0 \text{ and } S = H$$

Hence, there exists a disease free equilibrium state given by $E_o(H,0,0)$.

3.5.6 Stability of the Disease Free Equilibrium State

To investigate the local behavior of the system about each of the equilibrium points, the Jacobian matrix J of the equilibrium point $E = (S,I,B)$ is computed using RouthHurwitz criteria as illustrated below.

$$J(E_0) = \begin{pmatrix} -n - \frac{aB}{K+B} & 0 & \frac{-aSK}{(K+B)^2} \\ \frac{aB}{K+B} & -r & \frac{aSK}{(K+B)^2} \\ 0 & e & (nb-mb) \end{pmatrix}$$

Now we consider the asymptotically stability of the system at the equilibrium point E_0.

The equilibrium point E_0 is asymptotically stable if $R_0 < 1$.
At the disease Free State (DFE),

When $S = H, I = 0$ and $B = 0$

$$J(E_0) = \begin{pmatrix} -n & 0 & \frac{-aH}{K} \\ 0 & -r & \frac{aH}{K} \\ 0 & e & -(nb - mb) \end{pmatrix}$$

The equilibrium point is asymptotically stable if one of the following conditions holds for polynomial P and it's determinant.

1. determinant $P(x) > 0, b_1 \geq 0, b_2 \geq 0, b_3 \geq 0$ and $b_1 b_2 > b_3$, (Routh-Hurwitz conditions)

2. determinant $P(x) > 0, b_1 \geq 0, b_2 \geq 0, b_3 \geq 0$ and $a < \frac{2}{3}$

But $P|J(E_o) - \lambda I| = 0$

$$\Rightarrow \begin{vmatrix} -n-\lambda & 0 & \frac{-aH}{K} \\ 0 & -r-\lambda & \frac{aH}{K} \\ 0 & e & mb-nb-\lambda \end{vmatrix} = 0$$

$$\Rightarrow (-n-\lambda)\begin{vmatrix} -r-\lambda & \frac{aH}{K} \\ e & mb-nb-\lambda \end{vmatrix} - 0\begin{vmatrix} 0 & \frac{aH}{K} \\ 0 & mb-nb-\lambda \end{vmatrix} - \frac{aH}{K}\begin{vmatrix} 0 & -r-\lambda \\ 0 & e \end{vmatrix} = 0$$

$$\Rightarrow (-n-\lambda)\begin{vmatrix} -r-\lambda & \frac{aH}{K} \\ e & mb-nb-\lambda \end{vmatrix} = 0$$

$$\Rightarrow (-n-\lambda)[(-r-\lambda)(mb-nb-\lambda) - \frac{eaH}{K}] = 0$$

$$\Rightarrow (-n-\lambda)(-rnb + rmb + r\lambda - nb\lambda + mb\lambda + \lambda^2 - \frac{eaH}{K}) = 0$$

By factorization,

$$\lambda^3 + (nb - mb + r + n)\lambda^2 + ((mb - nb)(n + r) + nr - \frac{eaH}{k})\lambda - \frac{eaH}{K} + nr(mb - nb) = 0$$

With the characteristic equation as; $p(\lambda) = \lambda^3 + b_1\lambda^2 + b_2\lambda + b_3 = 0$, using Routh-Hurwitz criteria

$$\begin{aligned} b_1 &= mb - nb + n + r \\ b_2 &= (mb - nb)(n + r) + nr - \frac{eaH}{k} \\ &= n(mb - nb + r) + r(mb - nb)(1 - R_0) \\ b_3 &= \frac{-eaH}{K} + nr(mb - nb) \\ &= rn(mb - nb)(1 - R_0) \end{aligned}$$

Where

,

$$b_1b_2 - b_3 = n(mb - nb + n + r)(mb - nb + r) + (mb - nb + r)r(mb - nb)(1 - R_0)$$

Therefore the eigenvalues corresponding to the equilibrium E_0 are

$$\lambda_1 = -n$$

$$\lambda_{2,3} = \frac{-(mb - nb + r)\sqrt{(mb - nb + r)^2 + 4\frac{eaH}{K}}}{2}$$

Thus if $R_0 < 1$ then all the roots are negative and given that $R_0 < 1$, the disease free equilibrium state (DFE) of the model is asymptotically stable.

3.5.7 Existence of the Endemic Equilibrium State

For this stage, thus an endemic equilibrium solution, we consider the case where there is infection.

From equation (3.6)

$$I = \frac{B(nb - mb)}{e}$$

Substitute I into equation (3.5) to nd S, then we have

$$\begin{aligned} a\frac{SB}{B+K} &= Ir \\ \Rightarrow a\frac{SB}{B+K} &= r\frac{B(nb-mb)}{e} \\ \Rightarrow a\frac{S}{B+K} &= r\frac{(nb-mb)}{e} \\ \Rightarrow aS &= r\frac{(nb-mb)(B+K)}{e} \end{aligned}$$

Hence

$$S = r\frac{(nb-mb)(B+K)}{ae}$$

Substituting $S = r\frac{(nb-mb)(B+K)}{ae}$ into equation (3.4) gives

$$B = \frac{n(aeH - rK)(nb-mb)}{er(n+a)}$$

Let $R_0 = \frac{aeH}{rk(nb-mb)}$ be the basic reproduction number.

Hence, substituting R_0 into the above equations gives

$$\begin{aligned} S &= \frac{H(a+R_0)}{R_0(a+n)} \\ B &= \frac{nK(nb-mb)(R_0-1)}{e(n+a)} \\ I &= \frac{nK(nb-mb)^2(R_0-1)}{e^2(n+a)} \end{aligned}$$

Hence at endemic equilibrium we have the point,

$$(S^*, I^*, B^*) = \frac{H(a+R_0)}{R_0(a+n)}, \frac{nK(nb-mb)^2(R_0-1)}{e^2(n+a)}, \frac{nK(nb-mb)(R_0-1)}{e(n+a)}$$

3.5.8 Stability Analysis of Endemic Equilibrium Point

The system has an endemic infection because of the introduction of those with secondary infections. To determine this, we linearized the Jacobian matrix J evaluated at the endemic equilibrium point. The Jacobian matrix of the system is,

$$J(E_1) = \begin{pmatrix} -n - \frac{aB^*}{K+B^*} & 0 & \frac{-r(nb-mb)}{e}\frac{K}{K+B*} \\ \frac{aB*}{K+B*} & -r & \frac{r(nb-mb)}{e}\frac{K}{K+B*} \\ 0 & e & -(nb-mb) \end{pmatrix}$$

The equilibrium point is asymptotically stable if one of the following conditions holds for polynomial P and its determinant.

1. determinant $P(x) > 0, b_1 \geq 0, b_2 \geq 0, b_3 \geq 0$ and $b_1 b_2 > b_3$, (Routh-Hurwitz conditions)
2. determinant $P(x) > 0, b_1 \geq 0, b_2 \geq 0, b_3 \geq 0$ and $a < \frac{2}{3}$

But $P|J(E_1) - \lambda I| = 0$

$$\Rightarrow \begin{vmatrix} -n - \frac{aB^*}{K+B^*} - \lambda & 0 & \frac{-r(nb-mb)}{e}\frac{K}{K+B*} \\ \frac{aB^*}{K+B^*} & -r-\lambda & \frac{r(nb-mb)}{e}\frac{K}{K+B*} \\ 0 & e & mb-nb-\lambda \end{vmatrix} = 0$$

$$\Rightarrow (-n - \frac{aB^*}{K+B^*}\lambda)\begin{vmatrix} -r-\lambda & \frac{r(nb-mb)}{e}\frac{K}{K+B*} \\ e & mb-nb-\lambda \end{vmatrix} - 0\begin{vmatrix} \frac{aB^*}{K+B^*} & \frac{r(nb-mb)}{e}\frac{K}{K+B*} \\ 0 & mb-nb-\lambda \end{vmatrix} -$$

$$(\frac{r(nb-mb)}{e}\frac{K}{K+B*})\begin{vmatrix} \frac{aB^*}{K+B^*} & -r-\lambda \\ 0 & e \end{vmatrix} = 0$$

By factorization,

$$\lambda^3 + (nb - mb + r + n + \frac{aB^*}{K+B^*})\lambda^2 + (r(n + \frac{aB^*}{K+B^*})) + (nb-mb)(r+n+\frac{aB^*}{K+B^*}) - (\frac{rK(nb-mb)}{K+B^*})\lambda +$$

$$\Rightarrow (-n - \frac{aB^*}{K+B^*}\lambda)[(-r-\lambda)(mb-nb-\lambda) - \frac{r(nb-mb)}{e}\frac{K}{K+B*}] - (\frac{r(nb-mb)}{e}\frac{K}{K+B*})(\frac{aB^*}{K+B^*}e) = 0$$

$$(r(nb-mb) - \frac{r(nb-mb)K}{K+B^*}) + (\frac{r(nb-mb)K}{K+B^*}) + \frac{r(nb-mb)KaB^*}{K+B^*} = 0$$

With the characteristic equation, $P(\lambda) = \lambda^3 + b_1\lambda^2 + b_2\lambda + b_3 = 0$, using Routh-Hurwitz criteria, Where

$$b_1 = mb - nb + n + r + \frac{aB^*}{K + B^*}$$
$$b_2 = \frac{r(nb - mb)K}{K + B^*} + (nb - mb)(r + n + \frac{aB^*}{K + B^*}) - \frac{rK(nb - mb)}{K + B^*}$$
$$b_3 = (r(nb - mb) - \frac{r(nb - mb)K}{K + B^*}(n + \frac{aB^*}{K + B^*}) + \frac{r(nb - mb)KaB^*}{K + B^*}$$

From observation, it is obvious that $b_1 > 0$. Therefore $b_2, b_3 > 0$. Hence the equilibrium point E_1 is asymptotically stable.

3.6 Method of solution

The Riemann-Liouville fractional integral operator of order $\alpha > 0$, of function $f \in L1(R+)$ is de ned as

$$I_o^\alpha f(t) = \frac{1}{\Gamma(\alpha)} \int_0^t (t - s)^{\alpha - 1} f(s) ds$$

where $\Gamma(.)$ is the Euler gamma function.

Also, the Riemann-Liouville and Caputo fractional derivative of order $\alpha > 0, n - 1 < \alpha < n, n \in N$ for a given continuous function f are de ned by

$$D_t^\alpha f(t) = \frac{1}{\Gamma(n - \alpha)} (\frac{dy}{dx}) n \int_{t_0}^t (t - s)^{n - \alpha - 1} f(s) ds \tag{3.8}$$

$$D_{t_o}^\alpha f(t) = \frac{1}{\Gamma(1 - \alpha)} = \int_a^t (t - s)^{-\alpha} f^1(s) ds \tag{3.9}$$

Where $f^{(1)}$ denote the rst derivative of f(s)

Now from (3.7), by using integration by parts, we obtain

$$D^\alpha f(t) = \frac{1}{\Gamma(2 - \alpha)} [\frac{f^{(1)}(0)}{t^{\alpha - 1}} + \int_0^t (t - s)^{1 - \alpha} f(s)^{(2)} ds] \tag{3.10}$$

From (3.8), by using binomial formula, we have

$$\begin{aligned}(t - s)^{1 - \alpha} &= t^{1 - \alpha} (1 - \frac{s}{t})^{1 - \alpha} \\ &= t^{1 - \alpha} \sum_0^\infty (1 - \alpha)(-1)^p (\frac{s}{t})^p \\ &= t^{1 - \alpha} \sum_{p=0}^\infty \frac{\Gamma(p - 1 + \alpha)}{\Gamma(\alpha - 1) p!} (\frac{s}{t})^p, |\frac{s}{t}| < 1\end{aligned}$$

Substituting into (3.9), we obtain

$$D^{\alpha}f(t)=\frac{1}{\Gamma(2-\alpha)}[\frac{f^{(1)}(0)}{t^{\alpha-1}}+\frac{1}{t^{\alpha-1}}\int_0^t\sum_{p=0}^{\infty}\frac{\Gamma(p-1+\alpha)}{\Gamma(\alpha-1)p!}(\frac{s}{t})^p f^{(2)}(s)ds] \tag{3.11}$$

Rewrite (3.10) as follows

$$D^{\alpha}f(t)=\frac{1}{\Gamma(2-\alpha)}[\frac{f^{(1)}(0)}{t^{\alpha-1}}+\frac{1}{t^{\alpha-1}}\sum_{p=1}^{\infty}\frac{\Gamma(p-1+\alpha)}{\Gamma(\alpha-1)p!t^p}\int_0^t s^p f^{(2)}(s)ds] \tag{3.12}$$

Using integration by part, we get

$$\int_0^t s^p f^{(2)}(s)ds = t^p f^{(1)}(t)-p\int_0^t s^{p-1}f^{(1)}(s)ds = t^p f^{(1)}(t)-pt^{p-1}f(t)+p(p-1)\int_0^t s^{p-2}f(s)ds, p\geq 2 \tag{3.13}$$

By substituting (3.12) into (3.11), we obtain

$$D^{\alpha}f(t)=\{\frac{f^{(1)}(t)}{t^{\alpha-1}}[1+\sum_{p=1}^{\infty}\frac{\Gamma(p-1+\alpha)}{\Gamma(\alpha-1)p!t^p}]-[\frac{\alpha-1}{t^{\alpha}}f(t)+\sum_{p=2}^{\infty}\frac{\Gamma(p-1+\alpha)}{\Gamma(\alpha-1)(p-1)}(\frac{f(t)}{t^{\alpha}}+\frac{V_p(t)}{t^{p-1+\alpha}})]\} \tag{3.14}$$

Where

$$V_p f(t)=-(p-1)\int_0^t \tau^{p-2}f(\tau)d\tau, p=2,3,\dots \tag{3.15}$$

$$\frac{d}{dt}V_p f(t)=-(p-1)t^{p-2}f(t), p=2,3,\dots \tag{3.16}$$

We can approximate $D^{\alpha}f(t)$ by using M terms in sums appearing in (3.13) as follows

$$D^{\alpha}f(t)\approx\{\frac{f^{(1)}(t)}{t^{\alpha-1}}[1+\sum_{p=1}^{M}\frac{\Gamma(p-1+\alpha)}{\Gamma(\alpha-1)p!t^p}]-[\frac{\alpha-1}{t^{\alpha}}f(t)+\sum_{p=2}^{M}\frac{\Gamma(p-1+\alpha)}{\Gamma(\alpha-1)(p-1)}(\frac{f(t)}{t^{\alpha}}+\frac{V_p(t)}{t^{p-1+\alpha}})]\} \tag{3.17}$$

We can rewrite (3.16) as

$$D^{\alpha}f(t)\approx(\alpha,t,M)f^{(1)}t+\Phi(\alpha,t,M)f^{(t)}+\sum_{p=2}^{\infty}A(\alpha,t,p)\frac{V_p(f)(t)}{t^{p-1+\alpha}}$$

Where

$$\Omega(\alpha,t,M)=\frac{1+\sum_{p=1}^{M}\frac{\Gamma(p-1+\alpha)}{\Gamma(\alpha-1)p!t^p}}{\Gamma(2-\alpha)t^{\alpha-1}}$$

$$\Phi(\alpha,t,M)=R(\alpha,t)+\sum_{p=2}^{\infty}\frac{A(\alpha,t,p)}{t^{\alpha}}$$

$$A(\alpha,t,p)=-\frac{\Gamma(p-1+\alpha)}{\Gamma(2-\alpha)\Gamma(\alpha-1)p!}$$

$$R(\alpha,t,)=\frac{1-\alpha}{t^{\alpha}\Gamma(2-\alpha)}$$

We set

$\Theta_1(t) = S(t), \Theta_p(t) = V_p(S)(t)$, For $p = 2,3,\ldots,M$

$\Theta_{M+1}(t) = I(t), \Theta_{M+p}(t) = V_p(I)(t)$, For $p = 2,3,\ldots,M$

$\Theta_{2M+1}(t) = B(t), \Theta_{2M+p}(t) = V_p(B)(t)$, For $p = 2,3,\ldots,M$

We can rewrite system (3.1), (3.2) and (3.3) in the following form

$$\Omega(\alpha,t,M)\Theta_1^l(t)+\Phi(\alpha,t,M)\Theta_1(t)+\sum_{p=2}^{\infty}A(\alpha,t,p)\frac{\Theta_p(t)}{t^{p-1+\alpha}}=n(H-\Theta_1(t))-\frac{\Theta_1(t)\Theta_{2M+1}(t)}{k+\Theta_{2M+1}(t)}$$

$$\Omega(\alpha,t,M)\Theta_{M+1}^l(t)+\Phi(\alpha,t,M)\Theta_{M+1}(t)+\sum_{p=2}^{\infty}A(\alpha,t,p)\frac{\Theta_{M+p}(t)}{t^{p-1+\alpha}}=a\frac{\Theta_1(t)\Theta_{2M+1}(t)}{k+\Theta_{2M+1}(t)}-r\Theta_{M+1}(t) \tag{3.18}$$

$$\Omega(\alpha,t,M)\Theta_{2M+1}^l(t)+\Phi(\alpha,t,M)\Theta_{2M+1}(t)+\sum_{p=2}^{\infty}A(\alpha,t,p)\frac{\Theta_{2M+p}(t)}{t^{p-1+\alpha}}=(nb-mb)\Theta_{2M+1}+e\Theta_{M+1}(t)$$

Where

$$\Theta_p(t)=-(p-1)\int_0^t\tau^{p-2}\Theta_1(\tau)d\tau$$

$$\Theta_{M+p}(t)=-(p-1)\int_0^t\tau^{p-2}\Theta_{M+1}(\tau)d\tau$$

$$\Theta_{2M+p}(t)=-(p-1)\int_0^t\tau^{p-2}\Theta_{2M+1}(\tau)d\tau \tag{3.19}$$

Finally (3.17) and (3.18) can be written as

$$\Theta_1'=\frac{1}{\Omega(\alpha,t,M)}(n(H-\Theta_1(t))-a\frac{\Theta_1(t)\Theta_{2M+1}(t)}{k+\Theta_{2M+1}(t)})-\Phi(\alpha,t,M)\Theta_1(t)-\sum_{p=2}^{\infty}A(\alpha,t,p)\frac{\Theta_p(t)}{t^{p-1+\alpha}}$$

$$\Theta_1'(t) = -(p-1)t^{p-2}\Theta_1(t), p = 2, 3, \ldots, M$$

$$\Theta_{2M+1}'(t) = \frac{1}{\Omega(\alpha,t,M)}(a\frac{\Theta_1(t)\Theta_{2M+1}(t)}{k+\Theta_{2M+1}(t)} - r\Theta_{M+1}(t) - \Phi(\alpha,t,M)\Theta_{M+1}(t) - \sum_{p=2}^{\infty} A(\alpha,t,p)\frac{\Theta_{M+p}(t)}{t^{p-1+\alpha}}) \quad (3.20)$$

$$\Theta_{M+p}'(t) = -(p-1)t^{p-2}\Theta_{M+1}(t), p = 2, 3, \ldots, M$$

$$\Theta_{2M+1}'(t) = \frac{1}{\Omega(\alpha,t,M)}((nb-mb)\Theta_{2M+1} + e\Theta_{M+1}(t) - \Phi(\alpha,t,M)\Theta_{2M+1}(t) - \sum_{p=2}^{\infty} A(\alpha,t,p)\frac{\Theta_{2M+p}(t)}{t^{p-1+\alpha}})$$

$$\Theta_{2M+p}'(t) = -(p-1)t^{p-2}\Theta_{2M+1}(t), p = 2, 3, \ldots, M$$

With the following initial conditions

$$\Theta_1(\delta) = S_o,$$

$$\Theta_p(\delta) = -\frac{p-2}{2}\Delta t^{t-1}S_o, p = 2, 3, \ldots, M$$

$$\Theta_{M+1}(\delta) = I_o,$$

$$\Theta_{M+p}(\delta) = -\frac{p-2}{2}\Delta t^{t-1}I_o, p = 2, 3, \ldots, M$$

$$\Theta_{2M+1}(\delta) = B_o,$$

$$\Theta_{2M+p}(\delta) = -\frac{p-2}{2}\Delta t^{t-1}B_o, p = 2, 3, \ldots, M \quad (3.21)$$

We solve the system (3.19) with the initial conditions (3.20) by using the well-known Runge-Kutta of order fourth.

3.6.1 Runge Kutta method

Runge-Kutta methods are one of the fundamental techniques in scienti c computing. They are used to compute numerical solutions in a step-by-step fashion for ordinary di erential equations (ODEs). Runge-Kutta methods are a class of numerical solutions
to the initial value problem (IVP) consisting of the ordinary di erential equation (ODE)

$$U^0 = F(t, U(t))$$

And the initial conditions

$$U(t_0) = U^0$$

The formula for the fourth order Runge-Kutta method (RK4) is given below. De ne h to be the time step size and $t_i = t_o + ih$. then the following formula

$$w_o = \alpha$$
$$K_1 = hf(t_i, w_i)$$
$$K_2 = hf(t_i + \frac{h}{2}, w_i + \frac{K_1}{2})$$
$$K_3 = hf(t_i + \frac{h}{2}, w_i + \frac{K_2}{2})$$
$$K_4 = hf(t_i + h, w_i + K_3)$$
$$w_{(i+1)} = w_i + \frac{1}{6}(K_1 + 2K_2 + 2K_3 + K_4)$$

Chapter 4

Data Collection and Analysis

This chapter deals with the analysis and numerical simulation of the model. Here, simulation analysis as well as graphical representation of the system of fractional order

at di erent values of α are illustrated.

Region	Cases													Cumulative Attack Rate per 100,000
	1-Jan to 13-Jul	20-Jul	27-Jul	03-Aug	10-Aug	17-Aug	24-Aug	31-Aug	07-Sep	14-Sep	21-Sep	28-Sep	05-Oct	1-Jan to 5 Oct	
	W1-28	W29	W30	W31	W32	W33	W34	W35	W36	W37	W38	W39	W40	W1-40	
Ashanti	0	0	0	0	0	0	30	0	0	130	13	*	*	[illegible]	3.3
Brong Ahafo	0	0	0	1	4	1	4	19	20	17	27	16	67	[illegible]	7.0
Central	0	6	2	22	148	155	160	262	306	487	163	*	*	[illegible]	68.8
Eastern	0	16	50	92	107	154	117	125	180	145	165	180	27	[illegible]	47.5
Greater Accra	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Northern	0	0	0	0	0	0	0	0	0	0	0	0	0	[illegible]	0.0
Upper East	0	0	0	0	0	0	0	0	3	0	2	5	22	[illegible]	2.9
Upper West	0	0	0	0	0	0	0	0	0	1	1	5	*	[illegible]	0.9
Volta	0	0	0	33	6	57	39	69	33	32	16	72	*	[illegible]	15.3
Western	0	0	4	2	8	7	13	17	12	47	28	31	2	[illegible]	6.6
Ghana	99	273	492	1097	2146	2014	2551	2878	2598	2604	1840	1408	955	[illegible]	76.8

Source: WHO, country office, 2014

Table 4.1: Cholera Cases in Ghana by Region by Week, 2014

We attempt to nd numerical solution for a general class of fractional order SI-B deterministic model of the disease below:

$$D^{\alpha}S = n(H - S) - a\frac{BS}{K + B} \tag{4.1}$$

$$D^{\alpha}I = a\frac{SB}{K + B} - rI \tag{4.2}$$

$$D^{\alpha}B = B(nb - mb) + eI, nb > mb \tag{4.3}$$

Let $S(0) = 6500, I(0) = 5 > 0, B(0) = 60 > 0$ be initial conditions as per the data. Also we have $0 < \alpha \leq 1$

At Disease free equilibrium state,

$$H = 6500, a = 0.1, r = 0.4, nb - mb = 0.4, K = 6500, e = 1, n = 0$$

Where

$$R_0 = \frac{aeH}{rk(nb - mb)}$$

$$R_0 = \frac{0.1\text{x}1\text{x}1000}{0.4\text{x}1000\text{x}0.4}$$

$$\Rightarrow R_0 = 0.625$$

Hence $R_0 = 0.625 < 1$

But at the disease Free State (DFE), there are no infections, that is $I = 0$,

$$B(nb - mb) = 0$$

Therefore B=0 provided $(nb - mb)$ 6= 0, $\Rightarrow n = 0$ and $S = H = 6500$. Hence, there exists a disease free equilibrium state given by $E_0(6500,0,0)$.

At the Endemic Equilibrium State,

$$H = 6500, a = 0.6, r = 0.4, nb - mb = 0.02, K = 6500, e = 1, n = 0.2$$

But

$$R_0 = \frac{aeH}{rK(nb - mb}$$

$$R_0 = \frac{0.6 \times 1 \times 6500}{0.4 \times 6500 \times 0.02}$$

$$\Rightarrow R_0 = 75$$

Hence $R_0 = 75 > 1$

But
$$S = \frac{H(a + R_0)}{R_0(a + n)}$$

$$S = \frac{6500(0.6 + 75)}{75(0.6 + 0.01)}$$

$$S = \frac{292500}{45.75}$$

$$S = 6393.44$$

Also,
$$B = \frac{nK(nb - mb)(R_0 - 1)}{e(n + a)}$$

$$B = \frac{0.01\text{x}6500(0.02)(75 - 1)}{1(0.01 + 0.6)}$$

$$B = 1374.29$$

$$I = \frac{nK(nb - mb)^2(R_0 - 1)}{e^2(n + a)}$$

$$I = \frac{0.01\text{x}6500(0.02)^2(75 - 1)}{(0.01 + 0.6)}$$

$$I = 27.49$$

Hence at endemic equilibrium we have the point,

$$(S^*, I^*, B^*) = (6393.44, 27.49, 1374.29)$$

4.0.2 Numerical Results and Discussion

To facilitate the interpretation of our mathematical results developed from the model, we solve the system numerically by using Atanackovic and Stankovic numerical method.

In all numerical runs, the solution has been approximated at;

$$\delta = \Delta t = 0.01$$

$$M = 5$$

$$P = 2,3\ldots,M.$$

In this section, we studied the behavior of cholera at the disease free equilibrium state and at the endemic state described by the fractional order Code o SI-B model using Runge-Kutta of fourth order.

From the results in the presented gures, it is obvious that cholera behave di erently at di erent values of R_0, where R_0 is the basic reproduction number which is estimated as

$$R_0 = \frac{aeH}{rK(nb - mb)}, nb - mb \neq 0$$

If $R_0 < 1$, what this mean is that, the disease free equilibrium state is asymptotically stable. To further explain this, it implies that the disease could be eradicated under this condition in nite time.

Let's consider the rst scenario where;

$$H = 6500, K = 6500, a = 0.1, r = 0.4, nb - mb = 0.4 \text{ and } e = 1,$$

$$R_0 = 0.625 < 1$$

That is, $R_0 = 0.625 < 1$, implies that the disease free equilibrium state is locally asymptotically stable. Hence the disease will die out in the population whereas the size of the susceptible population decreases (See g 4.3) and that of the infectious also decreases (See g 4.4).

Also the concentration of toxigenic vibrio cholerae in water (state variable B) will remain constant. That is, its concentration will not increase for the time period since the rate of exposure to contaminated water (parameter a) is small. (See g 4.5)

In the second scenario, where

$$H = 6500, K = 6500, a = 0.6, r = 0.4, nb - mb = 0.02 \text{ and } e = 1,$$

$$R_0 = 75 > 1,$$

That is, $R_0 = 75 > 1$ implies that the disease at the endemic state is locally asymptotically stable. Hence, the disease will persist in the population (See g 4.6) and (See g 4.7).

Additionally, the concentration of toxigenic vibrio cholerae in water (state variable B) increases and this is because the rate of exposure to contaminated water is relatively high (See g 4.8).

Also, some plots of the numerical solution are used to investigate which of the environmental factors parameters contribute largely to the fast spread of cholera in Ghana; rate of exposure to contaminated water (a) and the rate of contribution of each infected person (e) to the aquatic environment.

Here, the research ndings reveal that the concentration of vibrio cholerae in water depends hugely on the contribution of each infected person (e) to the aquatic environment. This has been illustrated in g4.9, g 4.10, g4.11, g4.12 and g4.13.

In g 4.9, high rate of exposure to contaminated water and high rate of contribution of each infected person to the aquatic environment produces large amount of concentration of toxigenic vibrio cholerae in water. The same result is obtained even when the exposure rate to contaminated water is average (0.5) and the rate of contribution is high (See g4.10)

This further explains the fact that the rate of contribution of each e ected person to the aquatic environment contribute largely to the persistent of cholera in the population.

This paper also reveals that even when the rate of exposure to contaminated water is high or average but the rate of contribution of each infected person to the aquatic environment is low, then the concentration of pathogen in water will be relatively low

(See g4.11 and g 4.12)

Finally, the concentration of pathogen in water will be relatively average if the rate of exposure to contaminated water is high and the rate of contribution of each e ected person to the aquatic reservoir is average (See g.4.13)

Hence the ndings illustrated that, the concentration of toxigenic vibrio cholerae in water (State Variable B) as in the system of equation (1), (2), (3) largely depend on the rate of contribution of each e ected person (parameter e) to the aquatic reservoir or environment.

This paper goes to con rm several reports on Environmental Assessment conducted by NGO's and Research Institutions which reveal that there were generally poor environmental sanitation and inadequate water supply at all the communities where cholera cases reside especially in Greater Accra Region. This explicitly explains why

Greater Accra recorded the highest cases of cholera in the country (See gure 4.2).

4.1 Simulations

The plots below illustrate the graphical representations of the numerical solutions and the behavior of cholera at di erent values of α.

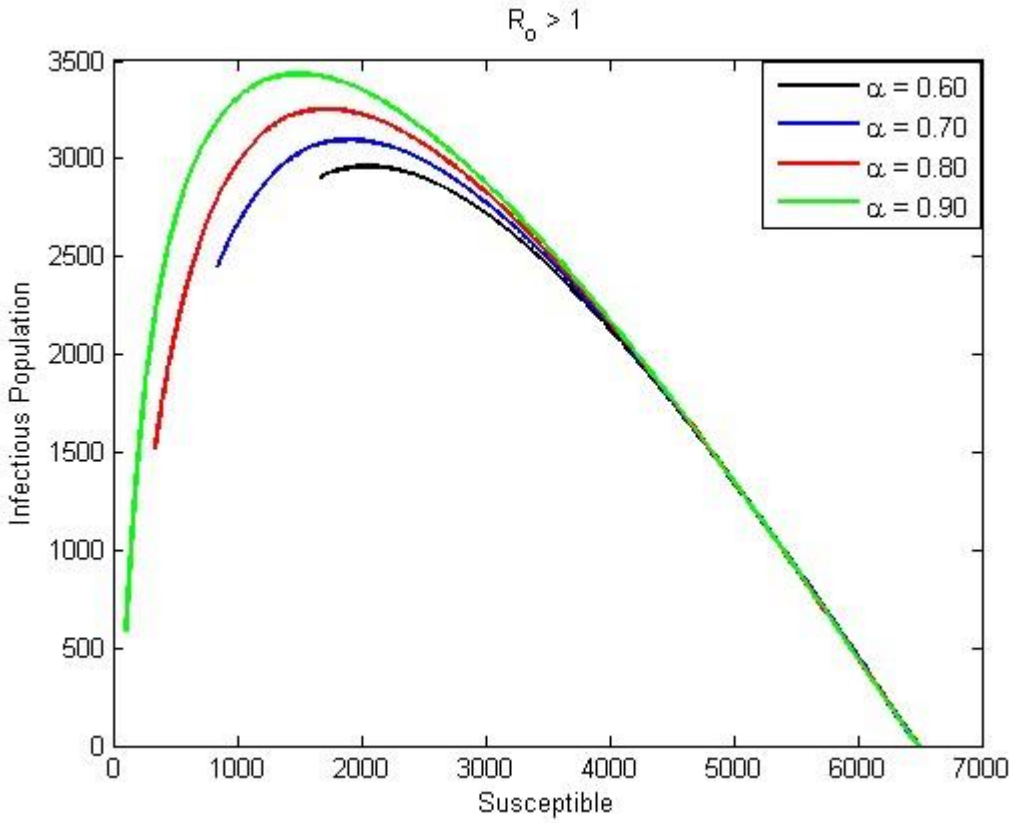


Figure 4.1: Phase diagram at the endemic state showing the size of the infectious population against the susceptible at di erent values of α

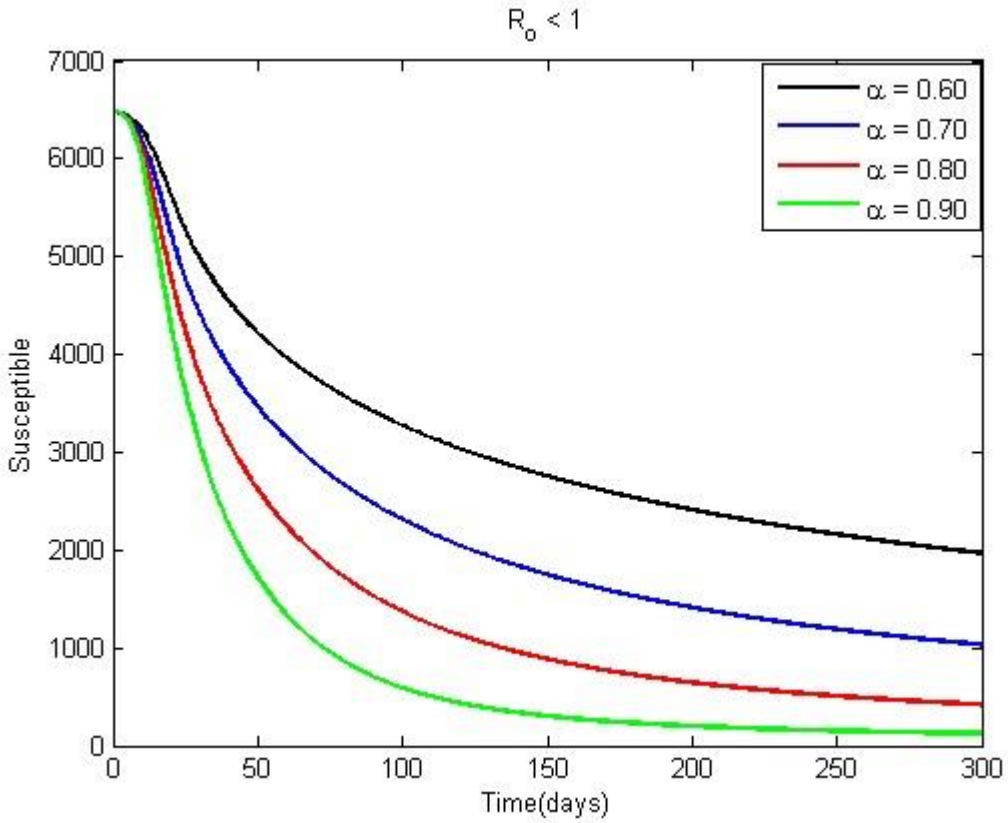


Figure 4.2: Size of the susceptible class over time for the system with di erent values of alpha at the disease free state where $R_0 < 1$

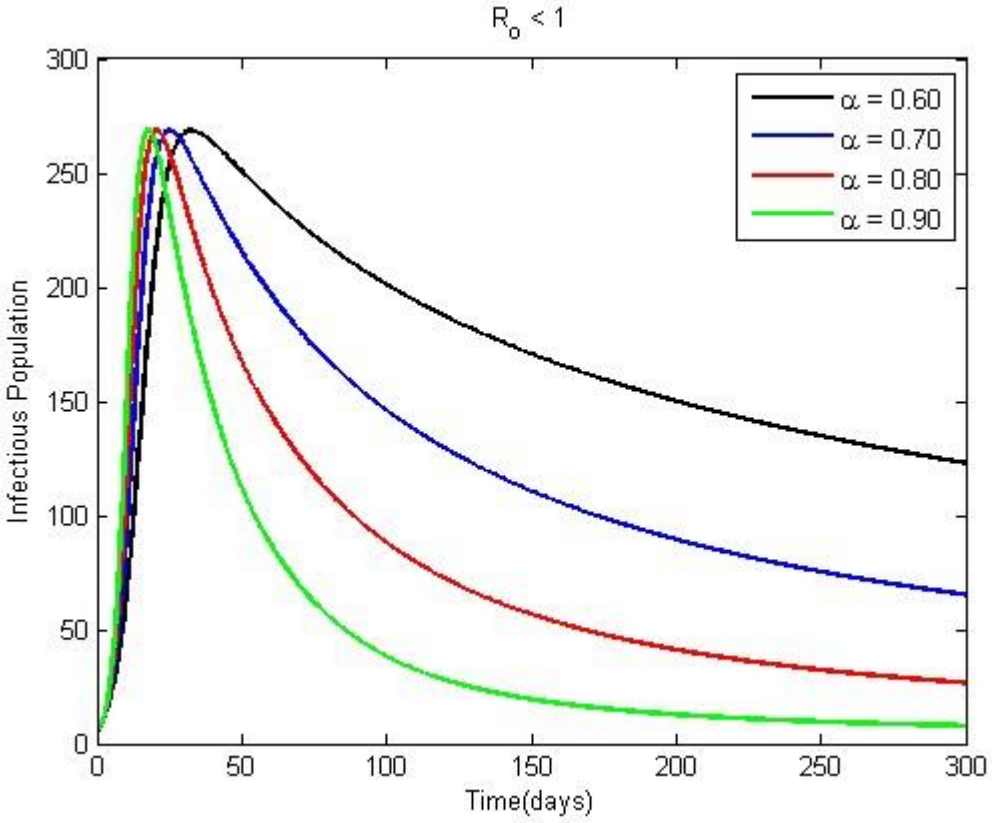


Figure 4.3: Size of the infectious class over time for the system with di erent values of alpha at the disease free state where $R_0 < 1$

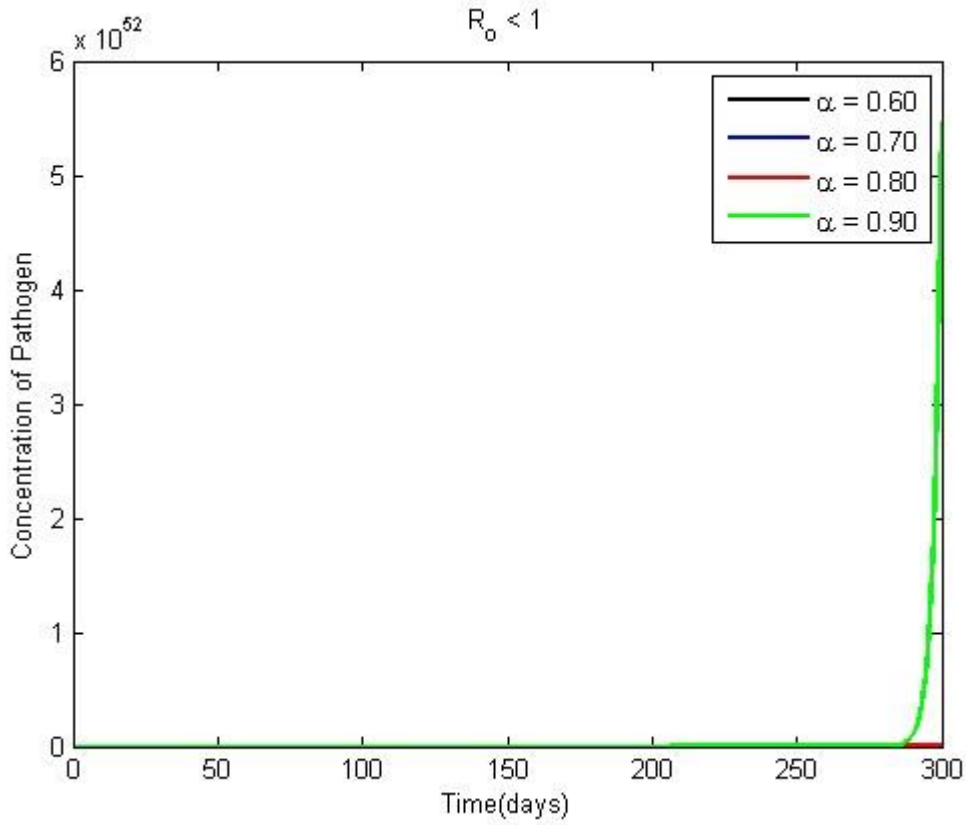


Figure 4.4: Concentration of toxigenic vibrio-cholerae in water over time for the system with di erent values of alpha at the disease free state where $R_0 < 1$

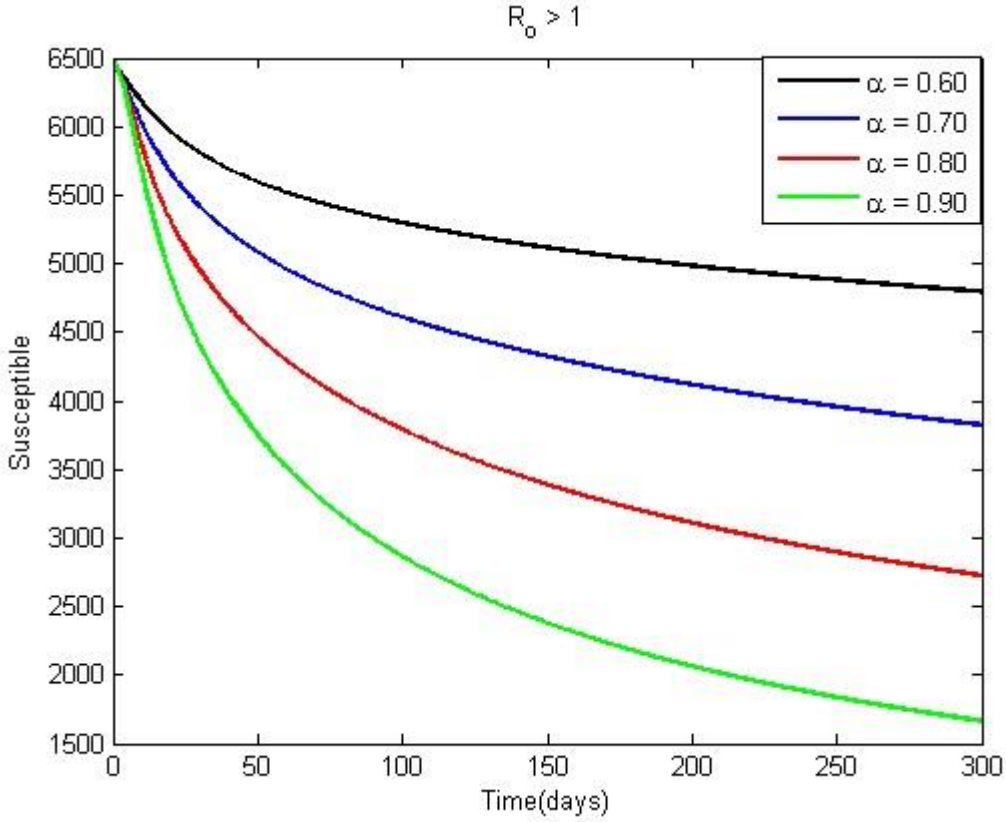


Figure 4.5: Size of the susceptible class over time for the system with di erent values of alpha at the endemic state where $R_0 > 1$

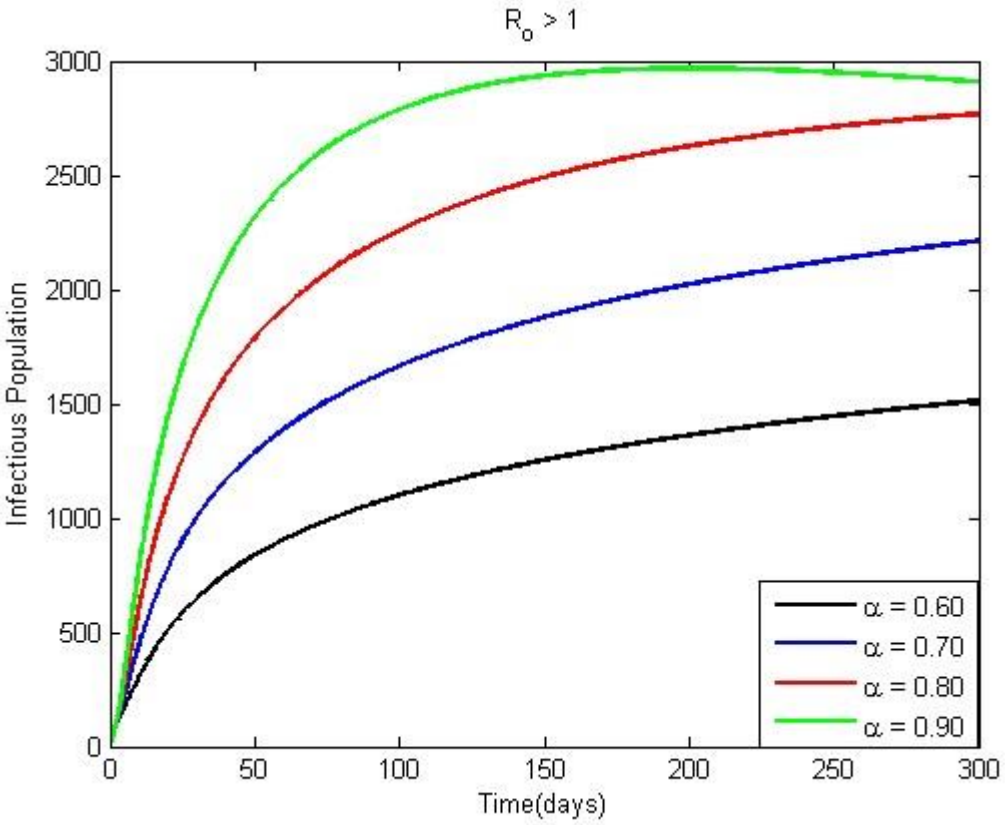


Figure 4.6: Size of the infectious class over time for the system with di erent values of alpha at the endemic state where $R_0 > 1$

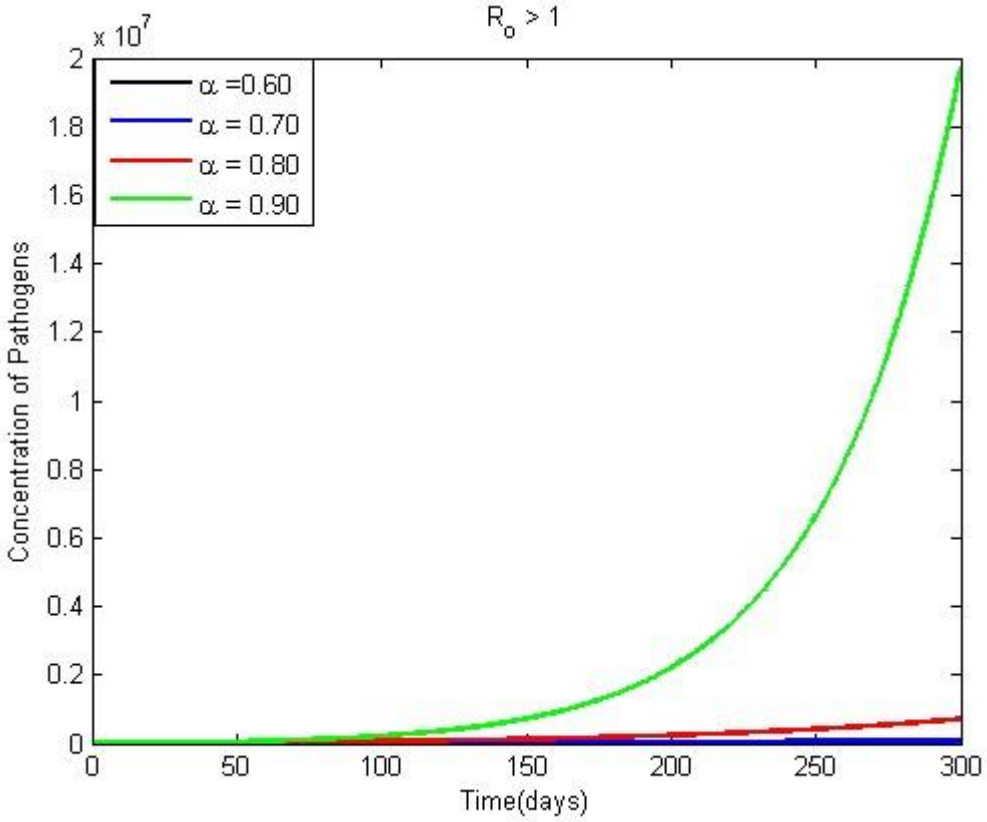


Figure 4.7: Concentration of toxigenic vibrio-cholerae in water over time for the system with di erent values of alpha at the endemic state where $R_0 > 1$

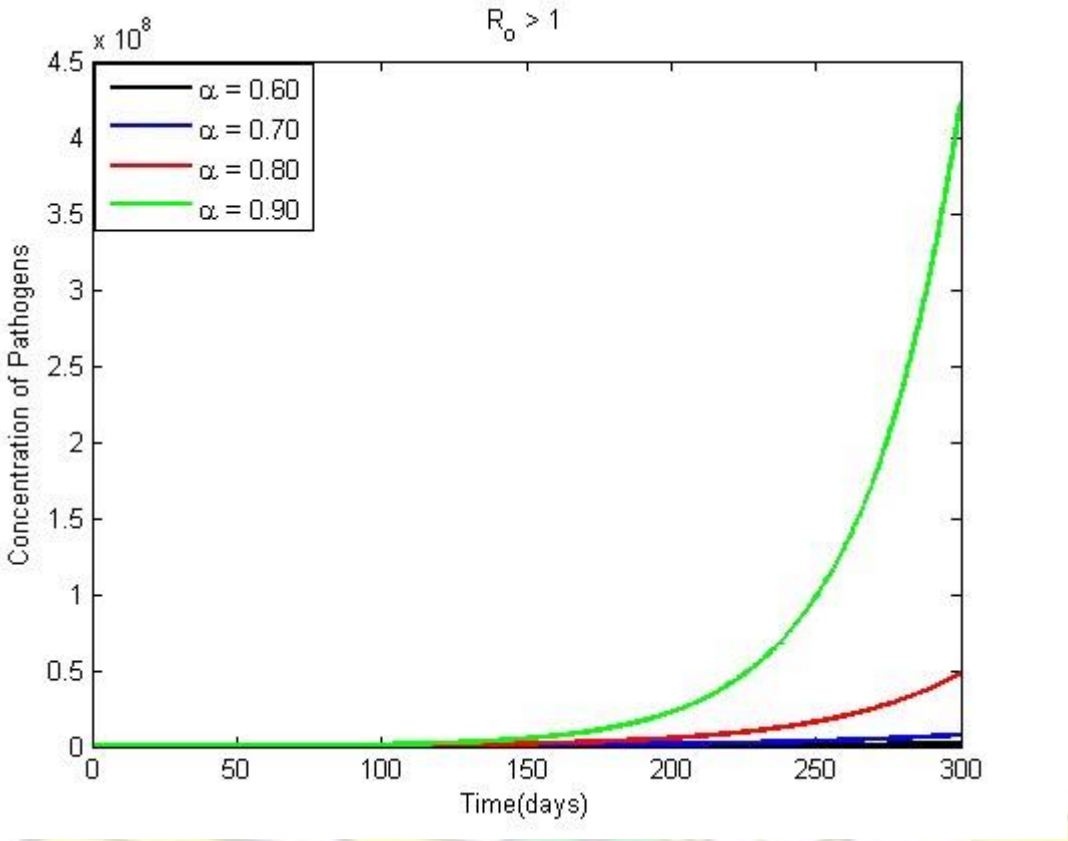


Figure 4.8: Graph of Concentration of toxigenic vibrio-cholerae in water against time with a case of high exposure ($\alpha = 0.80$) to contaminated water and high contribution of each infected person ($e = 0.90$) to the aquatic environment at di erent values of α.

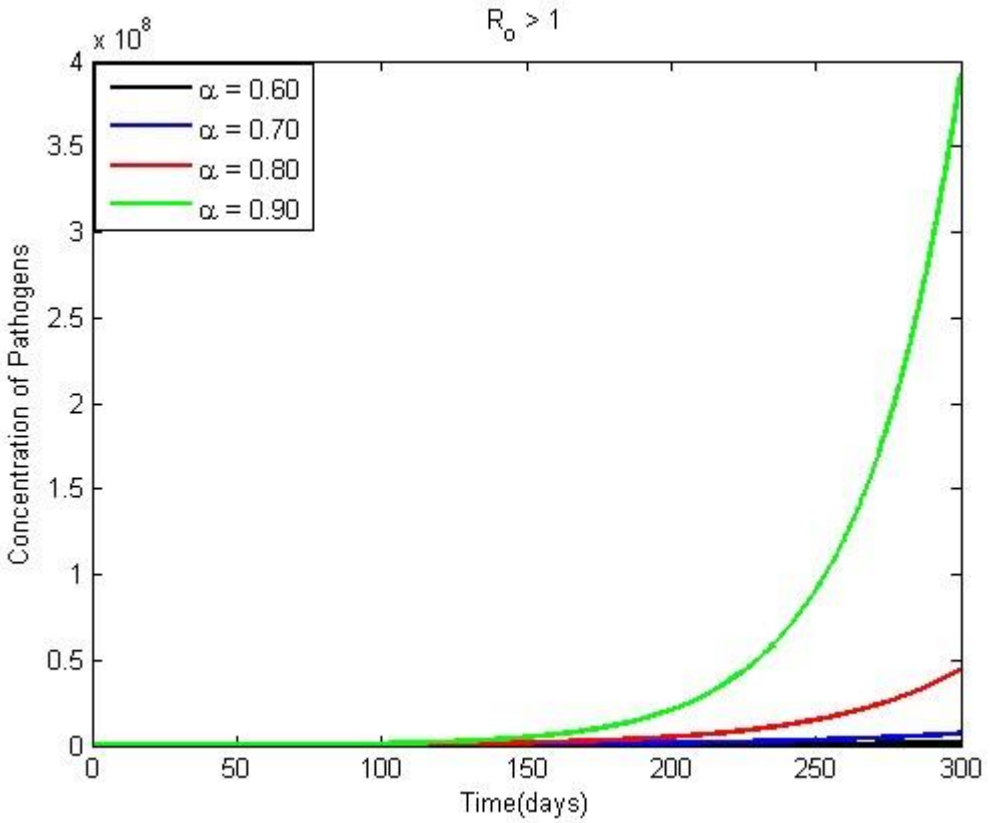


Figure 4.9: Graph of Concentration of toxigenic vibrio-cholerae in water against time with a case of average exposure (α = 0.5)to contaminated water and high contribution of each infected person (e = 0.90) to the aquatic environment at di erent values of α.

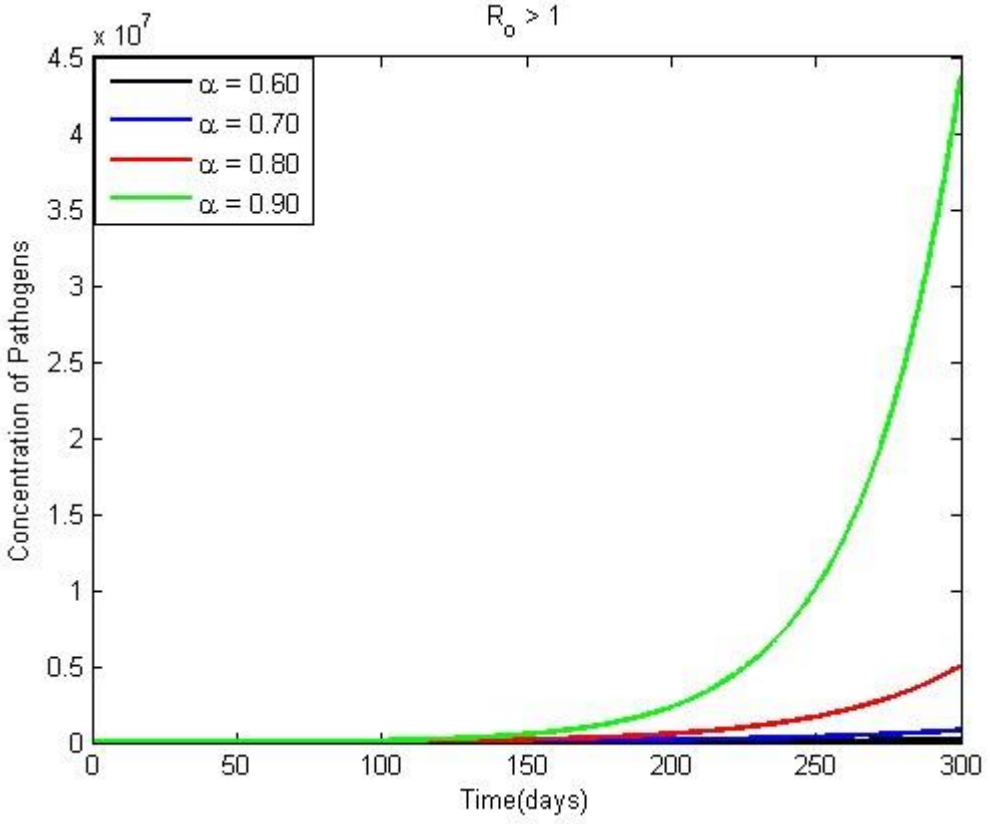


Figure 4.10: Graph of Concentration of toxigenic vibrio-cholerae in water against time with a case of high exposure ($\alpha = 0.8$) to contaminated water and low contribution of each infected person ($e = 0.10$) to the aquatic environment at di erent values of α.

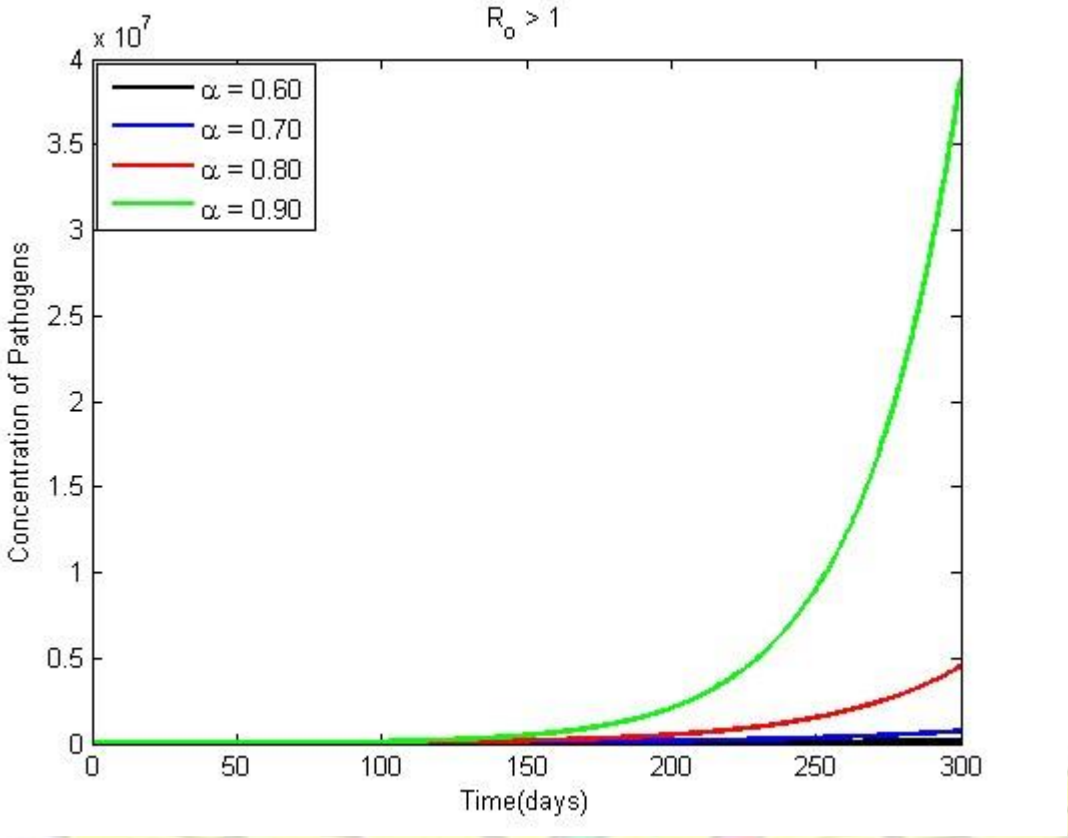


Figure 4.11: Graph of Concentration of toxigenic vibrio-cholerae in water against time with a case of average exposure ($\alpha = 0.5$) to contaminated water and low contribution of each infected person ($e = 0.10$) to the aquatic environment at di erent values of α.

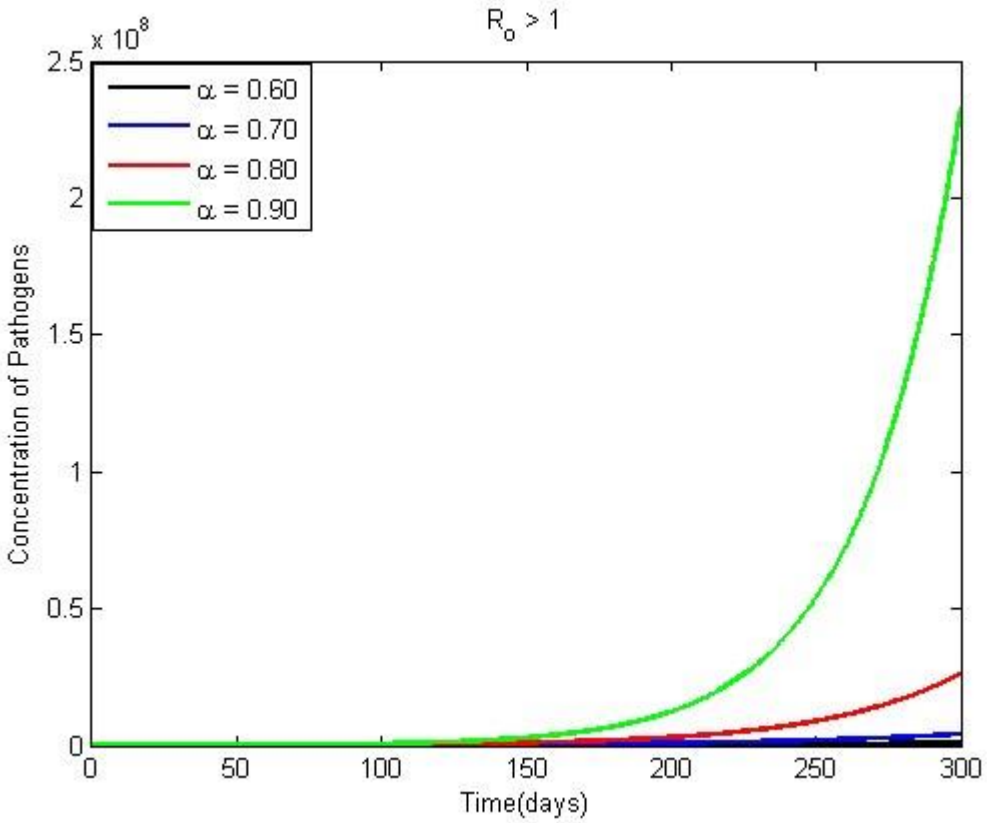


Figure 4.12: Graph of Concentration of toxigenic vibrio-cholerae in water against time with a case of average exposure (α = 0.8) to contaminated water and average contribution of each infected person (e = 0.50) to the aquatic environment at di erent values of α.

Chapter 5

Conclusion, and Recommendation

5.1 Conclusion

In this work, we have studied several features of a fractional order Code o cholera model. We started this work by formulating the SIR-B Code o model. Here, we

present criteria for the existence of disease free equilibrium state and that of the endemic state. Furthermore, the stability of the equilibrium for the system of fractional order Code o cholera model has been discussed in terms of the basic reproduction number

$R_0 = \frac{\alpha \varepsilon H}{rK(nb-mb)}$

Precisely, we have established the following facts:

If $R_0 < 1$, then the diseases free equilibrium state (E_0) is locally asymptotically stable for all $0 < \alpha < 1$. Hence, the disease could be eradicated in nite time.

If $R_0 > 1$, the equilibrium at the endemic state (E_1) is locally asymptotically stable for all $0 < \alpha < 1$. Hence, the disease will persist. Also, the stability analysis for the system is carried out by applying the fractional Routh-Hurwitz criterion.

Going forward, the fractional order Code o cholera model is converted to a system of ordinary di erential equations of integer order by using Atanackovic and Stankovic numerical method and is then solved numerically by using the fourth order well-known Runge-Kutta method.

Also, the graphical numerical solutions are presented to analyze the behavior of the system of equations at each R_0 value. That is, at the diseases free equilibrium state where $R_0 < 1$, the susceptible population and the infectious population decreases while the concentration of toxigenic vibrio cholerae in water remain low since the contribution of the infected person to the aquatic environment or reservoir (parameter e) is small.

At $R_0 > 1$, the disease persist in the susceptible and infectious population whiles the concentration of toxigenic vibrio cholerae in water increases in the population because the contribution of the each infected person to the aquatic environment or reservoir (parameter e) is large.

Finally, the research ndings reveal that the concentration of vibrio cholerae in water depends largely on the rate of exposure to contaminated water (parameter a) and on the contribution of each infected person (parameter e) to the aquatic reservoir or environment.

5.2 Recommendations

Based on our ndings, we recommend that proper education and sensitization be given to the public by relevant authorities and NGO's of the dangers of open defecation and urinating in sources of drinking water. This will reduce the contribution of each infected person to the aquatic reservoir or environment (parameter e).

Also, we recommend that the Government should provide portable water to the populace in order to discourage drinking of untreated water. This will reduce the rate of exposure to contaminated water (parameter a).

Finally, until Government and other stakeholders are able to stop street vending of water and food, poor liquid and solid waste disposal, clean choked drains regularly, complete stoppage of urban slums, then can Ghana and other developing countries
virtually eradicate cholera.

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Appendix

APPENDIX A

Code Title: Numerical solutions to the Fractional Order Differential Equations

```
function result = diff3(t,Y)
% Parameters par.H =
6500; par.n = 0.001;
par.a = 0.5; par.K =
6500; par.r = 0.06;
par.nb_mb = 0.02;
par.e = 1; p = 2; M =
5;
alpha=0.95; sums=0;
t = 1;
```

```
for pp = p:M
sums = sums + A(alpha,p)*(thetaP(p,t)/t^(p-1+alpha)); end


result = zeros(3,1);
result(1) = (1/Omega(alpha,t,M)*(par.n*(par.H-Y(1))) - par.a...
  * (Y(1)*theta2MP(p,t)))- Phi(alpha,t,M)*Y(1) - sums;


sumc  =  0;  for
pp = p:M
sumc = sumc + A(alpha,p)*(thetaMP(p,t)/t^(p-1+alpha)); end result(2) =
(1/Omega(alpha,t,M))* par.a * (Y(1)*Y(2)/(par.K + Y(2))...
-   par.r* Y(2) - Phi(alpha,t,M)*Y(1) - sumc);


sumss = 0; for pp
= p:M
sumss = sumss + A(alpha,p)*(theta2MP(p,t)/t^(p-1+alpha)); end result(3) =
(1/Omega(alpha,t,M)) * (par.nb_mb * Y(3) + par.e * Y(2)...
-   Phi(alpha,t,M)*Y(3) - sumss); end
```

APPENDIX B

Code for fig 4.2-fig4.4

Title: Plots for the Disease Free Equilibrium States

```
S_o = 6500; %65000
I_o = 5;%5 B_o = 15;   %60 h
= 0.25; % 0.1 < h < 1
%the smaller the value of h, the more accurate the result
time = [0 300];
```

```
[a, b]=abmpc3fast1(@eqns_Ro_less1,0,time(2),[S_o; I_o; B_o],h,0.60);
[~, c]=abmpc3fast1(@eqns_Ro_less1,0,time(2),[S_o; I_o; B_o],h,0.70);
[~, d]=abmpc3fast1(@eqns_Ro_less1,0,time(2),[S_o; I_o; B_o],h,0.80); [~,
e]=abmpc3fast1(@eqns_Ro_less1,0,time(2),[S_o; I_o; B_o],h,0.90);
S95 = b(:,1);
I95 = b(:,2);
B95 = b(:,3);
S96 = c(:,1);
I96 = c(:,2);
B96 = c(:,3);
S97 = d(:,1);
I97 = d(:,2);
B97 = d(:,3);
S98 = e(:,1);
I98 = e(:,2);
B98 = e(:,3);

%PLOTS figure plot(a,S95,'k','linewidth',2),hold on plot(a,S96,'b','linewidth',2)
plot(a,S97,'r','linewidth',2) plot(a,S98,'g','linewidth',2)
xlabel('Time(days)'),ylabel('Susceptible') title('R_{o} < 1') legend('\alpha = 0.60','\alpha =
0.70','\alpha = 0.80','\alpha = 0.90')

figure
plot(a,I95,'k','linewidth',2),hold on plot(a,I96,'b','linewidth',2) plot(a,I97,'r','linewidth',2)
plot(a,I98,'g','linewidth',2) xlabel('Time(days)'),ylabel('Infectious Population') title('R_{o} <
1') legend('\alpha = 0.60','\alpha = 0.70','\alpha = 0.80','\alpha = 0.90')

figure plot(a,B95,'k','linewidth',2),hold on plot(a,B96,'b','linewidth',2)
plot(a,B97,'r','linewidth',2) plot(a,B98,'g','linewidth',2)
```

xlabel('Time(days)'),ylabel('Concentration of Pathogen') title('R_{o} < 1') legend('\alpha = 0.60','\alpha = 0.70','\alpha = 0.80','\alpha = 0.90') save less

APPENDIX C

Code for fig 4.5-fig4.7

Title: Plots for the Endemic Equilibrium States

```
S_o = 6500; %000
I_o = 5; %10 B_o = 60;%60 h
= 0.25; % 0.1 < h < 1
%the smaller the value of h, the more accurate the result time = [0 300];
[a, b]=abmpc3fast1(@eqns_Ro_greater1,0,time(2),[S_o; I_o; B_o],h,0.30);
[~, c]=abmpc3fast1(@eqns_Ro_greater1,0,time(2),[S_o; I_o; B_o],h,0.40);
[~, d]=abmpc3fast1(@eqns_Ro_greater1,0,time(2),[S_o; I_o; B_o],h,0.50); [~, e]=abmpc3fast1(@eqns_Ro_greater1,0,time(2),[S_o; I_o; B_o],h,0.60);
S50 = b(:,1);
I50 = b(:,2);
B50 = b(:,3);
S55 = c(:,1);
I55 = c(:,2);
B55 = c(:,3);
S60 = d(:,1);
I60 = d(:,2);
B60 = d(:,3);
S65 = e(:,1);
I65 = e(:,2);
B65 = e(:,3); %PLOTS figure plot(a,S50,'k','linewidth',2),hold on plot(a,S55,'b','linewidth',2) plot(a,S60,'r','linewidth',2) plot(a,S65,'g','linewidth',2)
```

xlabel('Time(days)'),ylabel('Susceptible') title('R_{o} > 1') legend('\alpha = 0.60','\alpha = 0.70','\alpha = 0.80','\alpha = 0.90')

% figure

% plot(a,I50,'k','linewidth',2),hold on

% plot(a,I55,'b','linewidth',2)

% plot(a,I60,'r','linewidth',2)

% plot(a,I65,'g','linewidth',2)

% xlabel('Time(days)'),ylabel('Infectious Population')

% title('R_{o} > 1')

%legend('\alpha = 0.60','\alpha = 0.70','\alpha = 0.80','\alpha = 0.90') figure

plot(a,B50,'k','linewidth',2),hold on plot(a,B55,'b','linewidth',2) plot(a,B60,'r','linewidth',2)

plot(a,B65,'g','linewidth',2) xlabel('Time(days)'),ylabel('Concentration of Pathogens')

title('R_{o} > 1') legend('\alpha =0.60','\alpha = 0.70','\alpha = 0.80','\alpha = 0.90')

save concentration30

APPENDIX D

Code for fig 4.8-fig4.9.4

Title: Plots for the Concentration of toxigenic Vibrio Cholerae in Water

S_o = 6500; %45000

I_o = 5; %10 B_o = 15;%60 h

= 0.25; % 0.1 < h < 1

% the smaller the value of h, the more accurate the result time = [0 300];

[a, b]=abmpc3fast1(@eqns_Ro_greater1,0,time(2),[S_o; I_o; B_o],h,0.60); [~, c]=abmpc3fast1(@eqns_Ro_greater1,0,time(2),[S_o; I_o; B_o],h,0.70);

```
[~, d]=abmpc3fast1(@eqns_Ro_greater1,0,time(2),[S_o; I_o; B_o],h,0.80); [~, e]=abmpc3fast1(@eqns_Ro_greater1,0,time(2),[S_o; I_o; B_o],h,0.90);
S50 = b(:,1);
I50 = b(:,2);
B50 = b(:,3);
S55 = c(:,1);
I55 = c(:,2);
B55 = c(:,3);
S60 = d(:,1);
I60 = d(:,2);
B60 = d(:,3);
S65 = e(:,1);
I65 = e(:,2);
B65 = e(:,3);
%PLOTS
% figure
%                  plot(a,S50,'k','linewidth',2),hold on
%                 plot(a,S55,'b','linewidth',2)
%                 plot(a,S60,'r','linewidth',2)
%                 plot(a,S65,'g','linewidth',2)
%                  xlabel('Time(days)'),ylabel('Susceptible')
%               title('R_{o} > 1')
%legend('\alpha = 0.50','\alpha = 0.55','\alpha = 0.60','\alpha = 0.65')
% figure plot(S50,I50,'k','linewidth',2),hold on
plot(S55,I55,'b','linewidth',2)
plot(S60,I60,'r','linewidth',2)
plot(S65,I65,'g','linewidth',2)
xlabel('Susceptible'),ylabel('Infectious
Population') title('R_{o} > 1') legend('\alpha =
```

```
0.60','\alpha = 0.70','\alpha = 0.80','\alpha =
0.90')
%
% figure
%                  plot(a,B50,'k','linewidth',2),hold on
%                 plot(a,B55,'b','linewidth',2)
%                  plot(a,B60,'r','linewidth',2)
%                  plot(a,B65,'g','linewidth',2)
%                    xlabel('Time(days)'),ylabel('Concentration of Pathogens')
%                  title('R_{o} > 1 Initial conc. @ 30')
%legend('\alpha = 0.50','\alpha = 0.55','\alpha = 0.60','\alpha = 0.65')

save concentration3007
```