DETERMINISTIC SIRB CHOLERA MODEL WITH LOGISTIC APPROACH IN DORMAA-AHENKRO, GHANA

BY

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(BSc. Mechanical Engineering)

A Thesis submitted to the Department of Mathematics, Kwame Nkrumah University of Science and Technology in partial fulfillment of the requirements for the degree of

MASTER OF SCIENCE

Industrial Mathematics

College of Science/Institute of Distance Learning

OCTOBER, 2015

DECLARATION

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

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ACKNOWLEDGEMENT

I thank God for His guidance and protection during my quest for knowledge.

I wish to express my profound gratitude to my supervisor, Dr. F. T. Oduro, lecturer of the Department of Mathematics, College of Science, Kwame Nkrumah University of Science and Technology. His enthusiasm, guidance and useful comments and suggestions enabled me to successfully complete this thesis.

Finally, my sincere appreciation goes to my parents, siblings and other relatives for their love, support and encouragement during my study period. To my fellow postgraduate students, I say, thank you so much for keeping me in company. May the Good Lord bless anybody who contributed to the success of this thesis.

DEDICATION

This thesis is affectionately dedicated to my parents and siblings, whose patience, sacrifices, and encouragement helped in making the thesis possible.

ABSTRACT

In this work, a deterministic differential equation model that incorporates an environmental reservoir of *Vibrio cholerae* was developed for the propagation of cholera using some parameter values from Dormaa-Ahenkro, Ghana. The model was formulated from some modifications of previous cholera models. It looked at *Vibrio cholerae* - the causative agent of cholera -using a logistic approach for its growth in its expected habitat. Analysis was performed on the Jacobian matrix assuming zero *Vibrio cholerae* environments.

The basic reproduction number of the model was derived as $R_o = \frac{\alpha\delta N}{n_B k(\mu + \eta + \gamma)}$ and the critical $n_B k(\mu + \eta + \gamma)$. R_o and S_C are related as $R_o = \frac{N}{S_C}$. population size was also obtained as $S_C = \frac{\alpha\delta}{}$

These two values are used to predict occurrence of cholera outbreak in a community. For $S_C > N$ and $R_o < 1$, cholera-free state is stable and unstable if $S_C > N$ and $R_o > 1$. If $S_C < N$ and $R_o > 1$, then we have a sharp threshold for the transition between cholera-free and endemic situations. The result showed that there would be a cholera-free state if the rates at which people are exposed and are contributing to water and food contaminated by *Vibrio cholerae* are curtailed.

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CHAPTER ONE

INTRODUCTION

1.1 Background of the Study

Cholera has long been, and continues to be, a world health problem. It is a water-borne disease caused by the pathogenic bacterium, *Vibrio cholerae*. It causes a significant suffering and death. Cholera has great effects on public health, social and economic development. Cholera outbreaks cause loss of lives and hinder social and economic development of a country. As a result of this it is studied by many people.

Cholera was first identified in ancient Greece around 470-400 B.C. by Hippocrates and in the Sushrute Samhita, India around 500-400 B.C. Since then seven cholera outbreaks have occured during the 19th and early 20th centuries worldwide (Hays, 2005). The seventh cholera outbreak worldwide began in 1961 and it affected most of the southern hemisphere (WHO, 2001). It continues affecting countries in the southern hemisphere today (Hays, 2005).

John Snow's investigations on cholera outbreaks in London in the 1800s was significant in establishing the germ theory of disease (Yamai et al., 1997; Faruque et al., 1998; Ramamurthy et at., 1993; Felsenfeld, 1996; Glass et al., 1985). Still, severe cholera outbreaks continue to occur. In recent years, there has been a significant trend in cholera outbreaks especially in developing countries, for example cholera outbreak in Haiti in 2010 (WHO, 2010). A large number of people die from cholera annually in the world. More than 3.5 million people are reported from cholera worldwide every year (WHO, 2010). More than 90% of the world's reported cholera cases occur in Africa (Goodgame and Greenough,

1975). Since 1998, cholera outbreaks have been reported consistently from Benin, Ghana, Guinea, and Togo (http://www.cdc.gov_global/cholera). In 1999, the southern African bloc countries accounted for 51% of all cholera cases in Africa and 40% of the resulting deaths (http://en.who.int/cholera/cases).

In 2013, 43% of cases were reported from Africa whereas between 2001-09, 93% to 98% of total cases worldwide were reported from the continent. This proportion changed in 2010 due to the outbreak in the Haiti and Dominican Republic (WHO, 2010). Africa has seen a decrease in the number of reported cases of cholera worldwide since 2012 (en.who.int/cholera/cases).

Cholera reached West Africa and Ghana during the seventh pandemic (WHO, 2001). Cholera has been endemic in Ghana since its introduction in the 1970's (Goodgame and Greenough, 1975). The prevalence of cholera in Ghana dates back to September 1, 1970 when a Togolese in transit at the Kotoka International Airport from Conakry, Guinea, collapsed and was found to have cholera. However, it was not until much later when cholera took root in Ghana. Some Ghanaians went for fishing in waters of Togo, Liberia and Guinea, and one of the fishermen died. His corpse was smuggled to his home town for burial. Since then cholera began to spread along the shores of Ghana and swept through many coastal villages in epidemic proportions. The disease kept on spreading and by July 1971, the Ashanti Region began to report cases indicting that cholera were spreading across the country. Cholera then became endemic in most parts of Ghana over the years with the coastal regions of Ghana: Greater Accra, Central and Western regions boasting of high cases (WHO, 2011).

There have been several major cholera outbreaks over the past three decades (WHO,

2011). In 1982, as many as 15,032 cases were recorded (www.ghanaweb.com/health/artikel.php). Since 1998, cholera outbreaks have been reported consistently in Ghana (Griffith, Kelly-Hope and Miller, 2005). All regions in Ghana except the Northern Region have recorded cases of cholera outbreaks (www.afro.who.int/en/ghana/press). There have been cases of cholera outbreaks in Ghana in recent times.

The current ongoing outbreak which started in early June 2014 in the Accra Metropolis with 6 cases and no death has rapidly escalated reaching alarming magnitude of 16,527 cases including 128 deaths (Case fatality rate of 0.8%) as of 14 September 2014 (www.afro.who.int/en/ghana/press). The epidemic has spread to 91 districts in 8 out of the 10 regions in the country. No cases reported from the Upper West and Northern Regions of Ghana (www.afro.who.int/en/ghana/press). The Greater Accra is the most affected region of the current cholera outbreak in Ghana (Oteng-Ababio, 2014).

In Accra, cholera cases come from overcrowded peri-urban ghettos with poor infrastructures and hygiene conditions, inadequate environmental management and poverty (like Agbogbloshie, James Town and Glife slums) (www.afro.who.int/en/ghana/press).

A total of 304 new cholera cases have been reported in the first 16 days of 2015 in six districts in the Greater Accra and Volta regions of the country (www.afro.who.int/en/ghana/press).The situation is more alarming in the capital, Accra, which has a high infection rate and has claimed many lives (www.theafricareport.com/West-Africa/ghana-cholera-kills-hundreds.html).

The main market centres and slums in Accra are close to refuse dumps, filthy and open gutters with stinking stagnant water which are very dirty but many people queue to buy food sold at these areas. Cases of cholera outbreaks will be persistent because of poor sanitary conditions currently in Accra.

1.1.1 Causes of Cholera

Cholera is a living testimony of poor sanitary conditions**.** It is a severe water-borne infectious disease caused by the bacterium *Vibrio cholerae* (Ryan, 2004; WHO, 2010). *Vibrio cholerae* is a large and very diverse species. It is divided into about 200 sero-groups, of which only serotypes denoted O1 and O139 contain pathogenic members (Alexander, 2008). Cholera has short incubation period, from less than one day to five days. It is characterized by severe watery diarrhoea caused by the production of cholera toxin (an enterotoxin) by *Vibrio cholerae* bacteria in the small intestine. It is caused by eating food or drinking water contaminated with *Vibrio cholerae* (Kaper et al., 1995). The infection occurs in two ways: first, through the introduction of a small, but not very small, number of infected individuals into the population; second, through small, but not very small, fluctuations in the pathogen density in a reservoir (water source).

When an individual takes in food or water containing the bacterium, it releases a toxin in the intestines which causes severe diarrhoea. It has been shown that pathogenic *Vibrio cholerae* can survive refrigeration and freezing in food supplies (Desmarchelier, 1997; Greenough, 1999).

Vibrio Cholerae bacteria live in, and are transmitted by contact with contaminated water or food. Environmental and climatic conditions, such as water and temperature have:

- direct impact on the abundance and/or toxicity of *Vibrio cholerae*.
- indirect impact on other aquatic organisms such as zooplankton, phytoplankton and macrophytes to which we find *Vibrio cholerae* attached. Phytoplankton blooms have a strong effect on the development of zooplankton blooms; they both have impact on the life cycle of *Vibrio cholerae* (Codeço, 2001)

The ability of the bacteria to connect to and live inside aquatic organisms enables them to survive in harsher environments (Codeço, 2001). War also contributes to the disease's ability to invade communities (Faruque et al., 1998).

1.1.2 Symptoms of Cholera

Most people do not get infected with cholera when exposed to *Vibrio cholerae*, yet they can still infect other susceptible individuals via contaminated water because they shed the pathogen in their stool for 7 to14 days. People begin to show symptoms as soon as few hours or as long as five days after infection. Most people exposed often show mild symptoms or are asymptomatic, but sometimes symptoms are grave (Akor, 2007).

About one in every 20 infected individuals develops severe diarrhoea accompanied by vomiting, which can quickly result in dehydration.

- Severe diarrhoea. Cholera causes dangerous fluid loss-as much as 950 cm^3 an hour. The diarrhoea is pale, and milky in appearance which is similar to ricewater stool.
- Nausea and vomiting. Take place in the early and later stages. Vomiting may persist for a number of hours.
- Dehydration. The following are the signs and symptoms of dehydration:

irritability, lethargy, sunken eyes, dry mucous membranes, especially inside of the mouth, throat, nose, and eyelids, extreme thirst, loss of skin elasticity, little or no urine output, low blood pressure, rapid heartbeat and muscle cramps.

Dehydration can result in shock and death if it remains untreated in a matter of hours. Children develop the following symptoms together with the usual symptoms of cholera: extreme drowsiness or even coma, fever and convulsions (en.wikipaedia.org/wiki/cholera_symptoms).

Diagnosis is by finding the bacteria in the stools of people (WHO, 2010). A rapid dipstick test is used to determine the presence of *Vibrio cholerae* (Sack and Chaignat, 2006). Effective sanitation practices, if instituted and adhered to in time, are usually sufficient to stop an epidemic.

1.2 Statement of the Problem

Cholera outbreaks have serious negative effects on public health and social and economic development. It is therefore important to understand how the bacterium which causes cholera survives in an aquatic environment, what the transmission dynamics are, and how this affects cholera as a human disease.

Thus, we formulate a deterministic cholera model to study the spread of cholera in Dormaa-Ahenkro. However, our attention will be focused on indirect SIR (SIRB) differential equation models. We make use of some parameter values from DormaaAhenkro to help us to study the propagation of cholera.

1.3 Objectives of the Study

The following are the objectives of the study:

- To formulate a deterministic SIR differential equations model for the spread of cholera.
- To determine the stability of the equilibrium points of the model.
- To perform numerical simulations of scenarios of the model
- To use these model scenarios to determine how to control the spread of cholera

1.4 Methodology

Mathematical and computer methods will be used for the study. We will also make use of ordinary differential equations and Matlab software to determine of the solutions and stability analysis of the differential equations.

1.4.1 Parameter Values for the Model

Parameter values such as human death rate and recovery rate are obtained from the Dormaa Presbyterian Hospital, Ghana Health Service and CIA World Fact Book. These (Dormaa Presbyterian Hospital and Ghana Health Service) are the two main health facilities in Dormaa-Ahenkro. We also use parameter values, such as *Vibrio cholerae* growth and death rates, shedding rate of pathogens back to the reservoir, semi-saturation concentration and contact rate from Cash et al., 1974, Codeço, 2001, Hartley et al., 206 and Grad et al, 2012 for the study. The population size of Dormaa-Ahenkro is used in the study.

1.4.2 Mathematical Methods

Here, we formulate the deterministic SIRB cholera model and then determine the critical points and hence the stability of these points. We then determine its local stability and by handling plane phase diagrams. We fit parameter values such as death rate, infection rate, recovery or removal rate, *Vibrio cholerae* growth-loss rate and the rate of exposure to contaminated water from the Ghana Health Service, CIA World Factbook (demographic statistics) and other sources into our model.

1.4.3 Computer Methods

Computer methods serve as important tools for the analysis of mathematical models; hence they will be used for our analysis. We will use Matlab software for the analysis of the model for:

- determining the eigenvalues of the equivalent linearized system of the model.
- identifying the type of the stability of the stationary points
- plotting the phase planes and the trajectories of the eigenvalues of the steady states or stationary points.
- the numerical simulations of the deterministic SIRB cholera epidemic model

1.5 Justification of the Study

Cholera outbreaks have tremendous effects on public health and social and economic development. We therefore propose a model to study its transmission dynamism.

We will employ mathematical modelling for the study and predict the dynamics of cholera in order to control it.

1.6 Organization of the Thesis

The thesis is divided into five chapters. Chapter one focuses on the introduction, background to the study, the statement of the problem, methodology, justification of the study and how the thesis is organized. Chapter two reviews the research work that has been carried out on models of cholera. Chapter three is about the methodology used for the study. Here, we review some first order systems of ordinary differential equations and phase portraits of these systems are presented. Also, the deterministic cholera model with the reservoir mediated SIR model called SIRB model is presented. We will derive the basic reproduction number and the critical population size. In chapter four, we will analyze the results by using numerical simulation of the model. All in all, chapter five talks about the conclusion of the thesis and recommendations made for the control of cholera in Dormaa-Ahenkro, Ghana.

CHAPTER TWO

LITERATURE REVIEW

2.1 Background to the Study

Cholera is a waterborne gastroenteric infection that is caused by a heterotrophic bacterium called *Vibrio cholerae.* Cholera has now become a more persistent and global health problem than it was a few decades ago (WHO, 2011). Cholera transmission is closely linked to poor environmental management. It is spread through contact with the pathogen,

by eating food or drinking water containing *Vibrio cholerae*. The growth rate of *Vibrio cholerae* depends on the availability of nutrients and the water temperature of aquatic environments. The growth rate increases with nutrient availability only up to some limiting value (Finkelstein, 1996). The resulting warming of water temperature of aquatic environments increases the incidence of cholera through the faster growth rate of *Vibrio cholerae* (Colwell, 1996; Pascual, 2002; Faruque, 2005; Codeço *et al* 2008). The highest concentrations of *Vibrio cholerae* are known to occur when the water temperature is between 20 ^{o}C and 30 ^{o}C and they can also survive in a variety of foodstuffs and water up to five days in ambient temperatures and up to 10 days at 5-10 degrees Celsius.

The disease in its severest form causes copious diarrhoea lasting from 3 to 7 days. Infected people vomit profusely resulting in loss of large amounts of body fluids and leads to severe electrolyte (chemicals in the bloodstream that regulate important functions of the body) imbalances (especially potassium and sodium) and comas. Thus, they become dehydrated and the dehydration may result in fatality in the absence of treatment. From Akor(2007) only 10% cholera cases comes with diarrhoea and vomiting, but all infected people can contribute to the increase and spread of *Vibrio Cholerae* in the environment. Cholera is treated with rehydration and antibiotics.

Historical accounts of cholera serve as a source of biological information to determine the mechanisms of transmission, persistence, and virulence.

2.2 Ecology of Vibrio cholerae

Vibrio cholerae lives in two distinct habitats: aquatic ecosystems and human intestines.It is a heterotrophic bacterium, which attaches itself to a wide variety of aquatic organisms, especially plankton. *Vibrio cholerae* cannot synthesize its own food and responsible for mineralizing organic matter which forms an important component of aquatic food webs and nutrient cycles (Biddanda and Cotner, 2002).

Human activity and the resulting ecological changes directly affect the bacterium's persistence and spread in aquatic environments (en.wikipaedia.org/wiki/cholera). *Vibrio cholerae* reacts to environmental conditions by increasing or decreasing its rate of metabolism, and can therefore enter a state of dormancy. It can also undergo changes in the quality of its microhabitat by switching between free-living and surface-attached forms and by aggregating into biofilms while attached. In cholera endemic areas, outbreaks start when people get infected with the pathogen from the environment. The outbreaks may be accelerated by faecal contamination (Franco, 1997).

2.3 Life Cycle of *Vibrio Cholerae*

Vibrio cholerae is a gram-negative, slightly curved rod-shaped bacterium whose motility depends on a single polar *flagellum*. *Vibrios* are sensitive to low pH and die rapidly in solutions of pH below 6. However, they are quite tolerant of alkaline conditions. They reach higher population densities in aerated solutions. They can also grow anaerobically.

They have simple nutritional requirements. Fresh isolates are prototrophic. (i.e., they grow in media containing an inorganic nitrogen source, an utilizable carbohydrate, and

appropriate minerals). They grow rapidly with a generation time of less than half an hour in favourable conditions. The growth rate of *Vibrio cholerae* depends on nutrient availability. The rate of growth increases with nutrient availability only up to some limiting value. Thus, the growth of the pathogen follows a logistic dose- response curve (Codeço, 2001; Jensen *et al*, 2006).

Vibrio cholerae is a large and very diverse species. It is divided into 206 serogroups (Shimada *et al*., 1994; Yamai *et al*., 1997), namely O1, O2, etc. Both toxigenic and nontoxigenic strains exist. Non-toxigenic strains can acquire toxicity through a temperate bacteriophage (Albert, Faruque and Mekalanos, 1998). Only O1 and O139 serogroups are pathogenic. (WHO, 1996; Alexander, 2008). This sero-group (O1) is divided into three serotypes, namely Inaba, Ogawa, and Hijokima (Reidl and Klose, June, 2002). Strains from this sero-group were divided into two biotypes, Classical (Koch, 1884) and El Tor.

These two biotypes include members from all of the sero-groups. *Vibrio cholerae* serogroup O1 is been the pathogen which causes cholera (Reidl and Klose, 2002; WHO, 1996).

Some non-O1 strains can cause diarrhoea, but are not epidemic or endemic (Faruque, Albert and Mekalanos, 1998). The non-O1 strains are occasionally isolated from cases of diarrhoea (Ramamurthy, Grag and Sharma, 1993) and from a variety of extra intestinal infections, from wounds, and from the ear, sputum, urine, and cerebrospinal fluid (Morris and Black, 1985). They are ubiquitous in estuarine environments, and infections due to these strains and are commonly of environmental origin (Kaper, Morris and Levine, 1995).

Members of the O139 serotype cause disease clinically indistinguishable from cholera and have caused epidemics. Only toxigenic strains of sero-groups O1 and O139 have caused epidemics (Reidl and Klose, 2002).

Horizontal gene transmission via bacteriophages (viruses that infect bacteria) and other vectors is responsible for creating pathogenic *Vibrio cholerae* by conveying genes involved in the colonization of humans and the production of cholera toxin (Islam et al., 1997). The most critical genes are clustered together in two regions of the bacterial genome (genetic material). The vibrio pathogenicity island (VPI) encodes a number of genes, including those needed to express the toxin coregulated pilus (TCP), which is essential for colonization of the intestines. The lysogenic bacteriophage CTX- , which harbours the genes for cholera toxin, uses the TCP to enter only those strains of *Vibrio cholerae* capable of colonizing humans. It then lysogenizes

invaded cells by integrating its entire genome into that of the host bacterium. Thus, a partnership between CTX- and *Vibrio cholerae* expressing TCP is necessary to cause a cholera epidemic. Observations suggest that the new variant strains detected recently in several parts of Africa and Asia cause more severe cholera with higher fatality rates (WHO, 2010).

2.4 Epidemiology of Cholera

Epidemiology is defined as the study of the transmission dynamics of infectious diseases with the objective of tracing factors that contribute to the dynamics and stability of the disease being considered. (en.wikipedia.org/wiki/cholera/epidemiology). It is the study of

the distribution and determinants of health-related states or events in specified populations, and the application of this study to control of health problems (Last, 2001). Thus, epidemiology describes health and disease in terms of frequencies and distributions of determinants and conditions in a population or in a specific group of a population. Epidemiology also includes the study of associations between specific diseases and factors to which populations are exposed.

The transmission of cholera is closely linked to inadequate environmental management (Rosenberg, 1987). Cholera is an acute intestinal infection caused by the bacterium *Vibrio cholerae.* It has short incubation period from less than one day to five days. *Vibrio cholerae* attaches to and colonizes intestinal lining. The probability of getting sick upon contact with a contaminated reservoir depends on the pathogen density and interactions of the pathogen with the immune system (Cash et al, 1974). An infected individual may die of dehydration in a matter of hours, if he/she is not given prompt treatment (Codeço, 2001). Infected individuals excrete bacteria for between 7 and 14 days. Less than 20% of those infected show typical symptoms of cholera.

Humans are apparently the only natural host for *Vibrio cholerae*. Cholera is acquired by the ingestion of water or food contaminated with the faeces of an infected individual (Epstein, 1995; UN, 2005). It is known that a susceptible individual must ingest approximately$10^3 - 10^6$ *Vibrio cholerae* to become infected with cholera (Grad et al., 2012). During cholera infection, *Vibrio cholerae* secretes cholera toxin. Cholera toxin (enterotoxin) activates adenylate cyclase enzyme in the intestinal wall that is converted into pump that extract water and electrolytes from blood and tissues to intestinal lumen

with shedding of mucous and epithelial cells giving rice water severe diarrhoea. Cells affected by the cholera toxin expel profuse fluids, resulting in electrolyte imbalance.

Cholera exhibits three major epidemiologic patterns: heavily endemic, neo-epidemic (cholera-receptive areas, newly invaded) and in developed countries with good sanitation, occasional limited outbreaks (WHO, 2009). The patterns probably depend largely on environmental factors (including sanitary and cultural aspects), the prior immune status or antigenic experience of the population at risk, and the inherent properties of the vibrios themselves, such as their resistance to gastric acidity, ability to colonize, and toxigenicity.

2.5 History of Cholera

Cholera was first identified by Hippocrates (around 470-400 B.C) and Buddha (around 500-400 B.C). It was made first known in the Indian subcontinent in 1817 (Cook, 1996). Cholera epidemic was first presented in Snow's seminal work in 1855 (Codeço, 2001). Cockburn and Cassanos published an article in 1960 on epidemiology of endemic cholera in 1960 (Cockburn, 1960). Then McCormack et al, (1969) investigated cholera in a rural community in Pakistan (McCormack, 1969).

There have been seven pandemics since 1817 and many lives have been lost worldwide (Hays, 2005; 2010; Lee, 2003). It first spread by trade routes (land and sea) to Russia in 1817, then to the rest of Europe, and from Europe to North America.

The first cholera pandemic occurred in the Bengal region of India starting in 1817 through 1824 (Sack, Nair and Siddique, 2004). The disease dispersed from India to Southeast Asia,

China, Japan, the Middle East, and southern Russia. The second pandemic lasted from 1827 to 1835 and affected the United States and Europe (Byrne, 2008). The third pandemic began in 1839 and ended in 1856, extended to North Africa, and reached South America, for the first time specifically infringing upon Brazil. During the third pandemic 2300 people were killed in England and Wales and even more in Southern European (Drasar and Forrest, 1996). Cholera reached the sub-Saharan African region during the fourth pandemic from 1863 to 1875 (Gaffga et al., 2007). The fifth and sixth pandemics spread from 1881–1896 and 1899-1923 (Hays, 2005). These epidemics were less fatal because of the greater understanding of the cholera bacteria. Egypt, the Arabian Peninsula, Persia, India, and the Philippines were hit hardest during these epidemics, while other areas, like Germany in 1892 and Naples from 1910–1911, experienced severe outbreaks. The current (seventh) pandemic (Albert, Faruque and Mekalanos, 1998; Reidl and Klose, 2002) begun in Indonesia (South Asia) in 1961 and reached Africa and the Americas respectively in 1970 and 1991 (Blake, 1993; Codeço, 2001; Wearing, 2005).

Cholera now affects 3-5 million people globally (Prüss-Üstün et al, 2008) and 100,000-130,000 deaths are recorded every year as of 2010 (WHO, 2010; Lozano, Naghavi, Foreman, Lim, Shibuya, Aboyans, Abraham, Aggarwal And Ahn et al., 2012). Death tolls were believed to be greater than 3 million a year in the early 1980s (Sack, Nair and Siddique, 2004).

Cholera still remains both epidemic and endemic in many areas of the world (Sack, Nair and Siddique, 2004). Regions of the world where Cholera is currently prevalent are Africa, Asia and parts of the Middle East (WHO, 2009). The countries with the highest incidence

rates of cholera are in Africa and southern Asia (WHO, 2008). Most developed countries in North America, Europe and the Western Pacific, primarily have lower cases of cholera (WHO, 2010). Richer countries experience occasional cholera outbreaks due to travelers returning from endemic areas.

In Ghana, high incidence of cholera seems to predominate in the urban communities and that is primary due to high overcrowding and poor sanitary living conditions in urban communities. Intermittent water supply coupled with indiscriminate sanitation practices in these urban communities in Ghana put inhabitants at a greater risk of contracting the disease. The coastal regions of Ghana, Greater Accra, Central and Western regions and Volta Region have high incidence of cholera (Oteng-Ababio, 2014).

2.6 Global and Geographic Distribution of Cholera.

The spatial distribution of cholera comprises the Indian sub-continent, parts of Asia, Africa and Latin America. The geographical distribution of cholera is changing and so is often considered as a re-emerging disease, in part because infections are appearing in novel communities or in communities which have had cases of cholera for many years. This is as a result of the changes in the environment or climate. Cholera has significantly affected most parts of the world. Cholera is endemic in many parts of Africa and Asia, and has more recently become endemic in South and Central America (WHO, 2010).

Cholera was originally endemic to the Indian subcontinent. The Ganges river served as a source (or reservoir) of contamination (Sack, Nair and Siddique, 2004). It spread by the routes (land and sea) to Russia, then Western Europe, Middle East, Africa and the United

States (Sack, Nair and Siddique, 2004). For centuries, cholera has terrorized the world. The distribution of cholera worldwide is alarming. The global trend for increasing travel to endemic regions of the world is likely to produce an increasingly risk for cholera importation (Zuckerman et al, 2007).

There have been seven pandemics since 1817 and many lives have been lost (Hays, 2005). Geographical areas which have experienced cholera epidemics can be characterized into three levels. Cholera-free communities are defined as having no locally acquired infections. In areas of cholera epidemicity, the disease diminishes after an outbreak. In regions of cholera endemicity, the disease does not disappear after an epidemic peak but returns in successive waves.

2.7 Transmission Hypothesis of Cholera

Transmission of cholera occurs through a combination of factors: seasonal bloom of bacteria, contaminated water supply, inadequate sanitation, and contaminated seafood (Sack, Nair, Siddique, 2004). Cholera is transmitted mainly through faecal contamination of food and water caused by poor hygienic conditions (Charles and Rosenberg , 1987). The source of contamination is by other cholera sufferers who shed their bacterium through their untreated diarrhoeal discharge into waterways, groundwater or drinking water supplies. Drinking any contaminated water and eating any foods washed in the water can cause a person to contract the infection. Experiments have shown that *vibrios* consumed with food are more likely to cause infection than those from water alone (Finkelstein, 1996). Other common vehicles of infection include fish and shellfish, leftover cooked grains that have been improperly reheated (Codeço, 2001).

2.8 Susceptibility of Cholera

An individual is said to be susceptible if he/she is unable to withstand foreign materials introduced in the body, especially a drug or disease causing organisms. Susceptible individuals are members of the population who stand the chance of catching a disease or cannot take a certain medicine, antibiotic, etc. if he or she is exposed to the infectious agent. Relatively, little is known of the factors that determine the variability in human susceptibility to cholera infection. Everyone is susceptible to cholera apart from children who are immuned from nursing mothers who have previously got cholera. Children are more susceptible, with two-to-five year olds having the highest rates of infection (Lanata et al, 2002; WHO, 2010).

The following are the factors associated with the risk of contracting cholera:

- Poor sanitary (or unhygienic) conditions: Cholera outbreaks are not uncommon to locations where there are poor hygienic conditions (Emch, 2008; WHO, 2010). These conditions serve as suitable grounds for *Vibrio cholerae.* Such conditions are common to refugee camps, impoverished countries and areas devastated by famine, war or natural disasters. People who reside in these areas stand a greater risk of getting infected with cholera.
- Household exposure: People who live in the same household with an infected person are at a significantly increased risk of contracting cholera.

- Blood group: People with blood group O are more susceptible than people with other blood groups to severe cholera (Sack, Nair, Siddique, 2004; Glass, Holmgren, Haley, 1985)

- Raw or Undercooked food: Eating raw or undercooked contaminated food such as shell fish, one can have increased risk of cholera infection. There is also a significantly high risk of contracting cholera by drinking water polluted with *Vibrio cholerae* (Ryan, 2004; WHO, 2010).

- Hypochlorhydria or Achlorhydria: These are people with reduced or nonexistent stomach acid. Gastric acidity is a major determinant of the size of inoculum required to generate disease, because gastric acid acts as a natural barrier to *Vibrio cholerae. Vibrio cholerae* cannot survive in acidic environments; and the stomach serves as a first-line of defence. People who have low levels of stomach acid-such as children, older adults and those who take antacids, H-2 blockers or proton pump inhibitors lack this protection and stand a high risk of getting infected with cholera (Zuckerman et al., 2007).

- Cystic fibrosis: People who are not affected by cystic fibrosis are more resistant to cholera infection. The genetic deficiency of cystic fibrosis trans-membrane conductance regulator channel proteins, interferes with bacteria binding to the

  gastro intestinal walls thereby reducing the risk of infection (http://www.informahealthcare.com/cholera).

- Malnutrition: Children who are malnourished are more likely to develop severe cases of cholera if they are infected with the disease (WHO, 2010).

2.9 Burden of Cholera

The simple presence of cholera in a community or country has a significantly negative effect on the individual and national prosperity due to its influence on social and economic decisions. Mortality resulting from cholera has significant impacts on national economies. Cholera infection can result in the decrease in the Gross Domestic Productivity (GDP) of a nation, which represents skilled workers who get themselves infected with cholera, and are more likely to be fired by their employers or leave the job as a result of the stigma. There may be costs associated with labour substitution, depending on the value of the activities from which the substituting labour is withdrawn (UNAIDS/WHO, 2004).

Cholera imposes substantive social, political and economic costs (Griffith et al, 2006). It impedes economic development through several channels, including but certainly not limited to, quality of life, fertility, population growth, saving and investment, worker productivity, premature mortality and medical costs. The various effects of cholera are outlined in the sections that follow.

2.9.1 Economic and Social Implication of Cholera

The occurrence of cholera highlights economically and socially determined inequalities in health.

Outbreaks of cholera cause suffering to humans, panic and disrupt the social and economic structure and impede development in the affected communities. Panic causes other countries to curtail or restrict their people from travelling to countries where a cholera

outbreak is occurring, or import restrictions on certain foods. The cholera outbreak in Peru in 1991 cost the country US$ 770 million because of food trade embargoes and adverse effects on tourism (http://en.wikpaedia .org/wiki/cholera/effects/tourism/Peru 1991/.). The costs of cholera are borne by affected communities are as follows:

The first is that of hospital and health centre costs. It comprises the cost of administration, health personnel remunerations, in-service training, per diem and transport for personnel, materials, utilities (i.e. electricity, water, telephone, and postage), maintenance (of vehicles, equipment and buildings), and capital costs (i.e. vehicles, equipment and buildings).

The second component is the cost of medicine used to treat cholera cases. Affected countries spend gargantuan amount of money to import drugs for the treatment of cholera. There is also a huge loss of productivity due to cholera outbreaks resulting from hospitalization time, reduction in function performance for mild/moderate cases; the time family members spend accompanying the affected individuals to a health facility and visiting those that are hospitalized and productive time lost due to premature death.

The third component consists of other losses to the affected countries' economies. Cholera outbreaks impact negatively on both domestic and international demand for tourism industry services of affected countries. There is evidence that when there is cholera outbreak in a country, other (or developed) countries usually discourage their citizens from traveling to this country, which reduces the number of tourists to the affected countries. Consequently, that leads to losses of revenues for the tourism industry, unemployment of

people whose livelihood is dependent directly or indirectly on tourism, and reduction in tax revenues for the governments.

All in all, it is not unusual to have international ban slapped on export of commodities from countries experiencing cholera outbreaks. When the latter happens, it may adversely affect the foreign exchange flows into the affected countries, which is likely to have many other externalities.

2.9.2 Mortality

Cholera has long caused and still causes health problems worldwide. It affects 3-5 million people globally (Prüss-Üstün et al, 2008) and 100,000-130,000 die from cholera every year as of 2010 (WHO, 2010). But the cholera outbreak in Haiti claimed more than 400,000 lives (WHO, 2010). The number of cholera outbreaks continues to increase. A total of 589 854 outbreaks including 7816 deaths were reported to WHO from 58 countries in 2011 (WHO, 2011). Many more cases were unaccounted for due to limitations in surveillance systems and fear of trade and travel sanctions. Cholera continues to be a major problem in several Asian countries as well as in Africa (Albert, Faruque and Mekalanos, 1998).

From 2004 to 2008, over 830,000 cases were notified to WHO, representing a 24% increase in the number of cases reported for this most recent five-year period. Mortality rate in resource poor settings ranges from 5% to 10%, but can be as high as 20% at the time of some epidemics if appropriate rehydration therapy is not available. However, if infected people are given quick and proper treatment, the mortality rate would be less than 1%. A person who is not treated may produce 10 to 20 litres of diarrhoea per day with fatal results.

In 2002, Lanata et al. calculated, using the fraction of diarrhoea cases estimated to be caused by cholera (0.05%), that 11 million cholera cases occur globally every year among children under 5 years of age (Black et al, 2010). However, adults and older children can also get cholera, and mortality can be high in all age groups (WHO, 2010).

Ghana has seen outbreaks of the disease since the 1970s. Ghana officially reported a total of 26,924 cholera cases and 620 deaths to WHO from 1999 to 2005 (WHO, 2005)

The current cholera outbreak which started in June 2014 has protracted, spilling over to 2015. A total of 9,566 cholera cases with 105 deaths were reported in Ghana in 2012, but no deaths were recorded in 2013 despite some reported cases of the disease in the country.

In 2011, 10,628 cholera cases with 105 deaths were reported. Between 1970 and 2012, Ghana recorded a total of 5,498 cholera deaths, according to data compiled by the World Health Organisation (WHO, 2012).

According to the statistics, 1,546 deaths were recorded between 1970 and 1980 while 2,258 deaths were recorded between 1981 and 1990. Between 1991 and 1999, cholera claimed 1,067 lives, and between 2000 and 2012, 627 deaths were recorded.

2.9.3 Interaction of Cholera with other Diseases

Cholera has a significant direct effect in conjunction with other common diseases. People who have their immune system lowered because of infection, such as people with AIDS are more likely to experience a severe case of cholera if they get infected (McGhee et al. 1989; Veazey and Lackner, 2005). AIDS patients who get infected with cholera lose fluids profusely from the body and become dehydrated which results in

death. The typical symptoms of dehydration are low blood pressure, poor skin turgor (or wrinkled hands), sunken eyes and rapid pulse.

2.9.4 Intellectual Development

Children are the most affected by cholera infection, with two-to-four year olds having the highest rates of cholera infection (Lanata et al, 2002). Cholera is an important cause of impairment in intellectual and cognitive development. This disabling cognitive or motor dysfunction interferes with activities of daily living such as school absenteeism although the evidence is less.

Early childhood diarrhoea contributes to under nutrition, stunting and wasting which are associated with malnutrition and in turn with reduced long-term cognitive development.

Variability in reasoning ability, cognitive skills, and years of schooling are considered to be important determinants of future variations in productivity and earnings of individuals (Knight and Sabot, 1990), so the economic impact is likely to be significant.

2.9.5 Effects of Global Climate on Cholera

The dynamics of disease causing organisms in man are closely linked to climate pattern (Pascual et al., 2000) and the typical concentration of these organisms changes greatly with the seasons. In addition, rapid climate change by global warming is altering the ecosystem of microorganisms and regions with an endemic or epidemic might shift drastically (Yoganathan and Rom, 2001).

Cholera outbreaks take place seasonally and are associated with monsoon season, warm temperature, heavy rain fall and increased plankton population. Climate change and weather variability pose threats for cholera. Changes in precipitation, temperature, humidity, salinity and wind have a significant effect on the quality of water used for drinking, recreation and commerce; rainfall causes outbreaks of cholera throughout the world. Temperature also influences the occurrence of bacterial agents and toxic algal blooms. Generally, the numbers of pathogenic vibrios species such as *Vibrio cholerae* are normally low compared with the more abundant non-pathogenic ones, but they always serve as a means of risk of transmission to higher organisms such as man in certain environments. For cholera, a distinct seasonal pattern is evident, particularly in regions of endemicity.

The problem of global warming and inland incursion of sea water covering more and more of the coastal stretches of land could lead us to the brink of a resurgent pandemic. Worldwide, there has been increase in the number of cholera cases and outbreaks in new communities and with changing profiles.

2.9.6 Economic Cost

The economic cost of cholera are divided into two, namely direct cost and indirect cost. The direct costs of cholera are those costs incurred to treat the disease. They include the physician, hospital, or drug costs in the formal medical care system for treating the disease. They also include the costs of community outreach, of community education programs specific to the disease, and of preventive prophylaxis administered to the contacts of sufferers.

Other direct costs include transportation to health care providers, moving expenses, household costs to accommodate the needs of the affected person, and vocational, social and family counselling services.

Two components in estimating the indirect cost of the disease are the total number of days of disability because of morbidity, and the number of years of productive life lost due to premature death during the period being examined. This data, in combination with labour force participation and earning assumptions, permits the estimation of losses to GNP due to the morbidity and mortality under examination (WHO, 2005).

2.9.7 National Economies

It is estimated that cholera causes a decline in economic growth per capita Gross National Product (GNP) in tropical countries, even after accounting for initial endowments, overall life expectancy and geographic location. Cholera has negative effects on the health and wealth of a nation and individuals alike.

For instance, Ghana loses GHC420 million annually due to poor sanitation in order to control, equivalent to US$290 million, according to the Water and Sanitation Program (WSP). This sum is the equivalent of US$12 per person in Ghana per year or 1.6% of the national GDP.

The cholera epidemic in Peru in 1991 cost the country's economy an estimated US$770 million (WHO, 2008). Annually, the economic growth in countries with high incidence of cholera has historically been lower than in countries with lower/no rates of cholera outbreaks (WHO, 2010).

2.10 History of Mathematical Modeling of Infectious Diseases

The study of the emergence of infectious diseases is likely to become increasingly important with increases in human and livestock population (Wolfe et al., 2007) and increasing stress placed on aquatic reservoirs.

An infectious disease is the one in which the causative agent, whether a virus, bacterium, protozoa, or toxin, fungi, etc., can be passed from one host to another through modes of transmission such as direct physical contacts, aerial droplets, water or food, disease vectors, mother to newborns, etc. (http://www.who.org/infectious/diseases)

A model is generally considered to be a representation of (a part of) reality that we aim to study. Mathematical models represent the examined systems in the form of mathematical objects and their relationships, often in the form of various types of (dynamic) equations or in the form of governing rules assembled as computer algorithms.

Mathematical modelling of infectious diseases is a tool for investigating the mechanisms for outbreak and spread of diseases and for predicting the future course in order to control an epidemic. Differential equations are used in mathematical modelling. Mathematical modelling in the field of epidemiology has its roots in the early twentieth century.

Sir Ronald Ross (1857-1932) used mathematical modelling to investigate the effectiveness of various intervention strategies for Malaria (Ross, 1911). In 1766, Daniel Bernoulli published an article where he mathematically analysed the effects of smallpox variolation on life expectancy (Dietz and Heesterbeek, 2000). Some of the earliest mathematical models were developed by Kermack and McKendrick in1927. They examined a series of

models based on healthy, infected, and immune individuals in a constant population (no births or deaths). These are called SIR models without vital dynamics (Hethcote, 1976).

Modern epidemiology has its theoretical roots founded on modelling the spread of a disease and showing that if certain conditions are met, then a disease will go extinct. It still remains a guiding theory that underlies contemporary biomedicine. The study of epidemics has given birth to a varied number of models and explanations for the spread and cause of outbreaks of epidemics. McNeil explained the relation between disease and people (McNeil, 1989). Oldstone work on modelling in disease epidemiology (Oldstone, 1998).

Anderson and May described models to estimate the effects of vaccination programmes on infectious diseases (Anderson and May, 1982, 1985 and 1991).

2.10.1 Compartmental Models in Epidemiology

A compartment in disease epidemiology is defined as a subdivision of a population. Compartmental models are those in which members of a host population are assigned to compartments on the basis of their infection status or other attribute, and the changes in the size of compartments are described as a dynamic system. The individuals in the population are classified as susceptible (S), infected (I) and recovered (R) based on their status of the disease being studied. Thus, these classes are the basic variables identifying the state of population in the epidemiological perspective. The Susceptible -Infected Recovered/Removed models (SIR) are used for modeling the dynamics of diseases that are directly transmitted between humans. Susceptible individuals are healthy and can be infected; infected individuals are those with the disease and are able to transmit the disease; recovered/removed individuals are those individuals who immune or dead because have

been infected and now have recovered. Infected individuals that can transmit the disease are called *infectious*. Infected individuals may not be infectious during the entire duration while being infected.

A compartmental model for infection transmission with an *exposed* (or latent) compartment (explicitly containing those infected but not yet infectious) and lasting immunity is known as an *SEIR* model, and situations where susceptibility can return after infection (or after immunity) would be called an *SIS* (or an *SIRS*) model (Busenberg and Cooke,1993).

An example of an *SEIR* model is given by the following ordinary differential equations:

$$\frac{dS}{dt} = \mu(N - S) - \beta C \frac{SI}{N}$$

$$\frac{dE}{dt} = \beta C \frac{SI}{N} - (\mu + \varepsilon)E$$

$$\frac{dI}{dt} = \varepsilon E - (\mu + \gamma)I$$

Where $N = S + E + I + R$, since N remains constant, the equation for R in the model is included as it can be got once S, E and I are known. Thus, $R = N - (S + E + I)$. The model is an extension of the SIR model, because of the inclusion of the natality and mortality rates, but not the introduction of the exposed class. Compartmental models have provided a clear understanding of the epidemiology of many infectious diseases. An extension of the model

presented here include an additional death rate due to the infection, re-entering the S after recovery or due to loss of immunity, a birth rate directly into the infective class and reduced fertility of infected individuals.

Also, the ways in which births are modeled or transmission is described may influence the dynamic behavior of the model systems (Daley and Gani, 1999). Homogenous mixing within compartments is a very significant assumption made; if it does not apply, heterogeneity becomes an explicit feature of the model. The basic reproduction number R_o is a significant quantity that provides the key to transmission dynamics, the ease by which major epidemics may be prevented and prospects for the eradication of an infection. Thus, it is imperative that it is determined for every model. The concept of the critical community size may apply to the susceptible community in a population where the infection timescale is much faster than the demographic timescale. Here, infections (such as measles) may leave a small susceptible population following an epidemic, but births into the population increase the susceptible pool and effectively increase R_o until another epidemic occurs.

Added to this is that temporal heterogeneity may manifest as seasonal forcing in transmission, and precipitate in infection cycles. Anderson and May (Anderson and May, 1991), added a more disease–specific details in their model such as, the latent period, the vaccinated population, chronic and acute stages of infection.

The refinement of compartmental models to include heterogeneity of the population into the model has been of great help. This is done by distinguishing between population

subgroups with different behaviours. Diekmann (Diekmann, 1990) developed the theory of finding and computing the reproduction number in heterogeneous populations.

Age structure model is a type of compartmental model with several compartments of individuals ranging from one compartment to another, according to aging rates.

2.10.2 Models for Vector-Born Infectious Diseases

Vector-borne diseases are infectious diseases caused by pathogenic microorganisms such as viruses, bacteria or protozoa which are primarily transmitted by disease transmitting biological agents, called vectors, which carry the disease without getting it themselves. Vector-borne diseases have become a major health problem in the developing countries of Africa and Asia usually residing in the tropical and subtropical regions. The spread of the disease in a particular region depends on the adaptability of the vector to survive and grow in that region. Some vector-borne diseases are more prevalent in specific regions due to the vector's ability to adapt in the specific environment and climate. The emergence and reemergence of vector-borne diseases has promoted interest in their mathematical modeling.

Mathematical *modeling* of *vector-borne infectious* diseases originated with Sir Ronald Ross's study of malaria transmission in 1916. It was in his study of the transmission of malaria in 1911 (Ross, 1911), that he introduced the idea of mass action in continuous time. Ross' work qualifies him as the founding father of modern epidemic theory. Anderson McKendrick was partly influenced by Ross. He began studies into mathematical modeling of epidemic processes, at first also in the context of malaria and other tropical infections. The works of Kermack and McKendrick are regarded as the foundation upon which much

of modern theory rests (Anderson and May, 1991). Malaria has long been and continues to be a serious problem for public health worldwide, especially in Africa. One of the distinguishing characteristics of malaria is that the protozoan parasite is indirectly transmitted between humans by blood-feeding mosquitoes. A significant number of human infections depend on similar vectors for their transmission. This gives rise to a new problem in modeling, the need to include the population dynamics of the vector.

2.10.2.1 Modeling Malaria

The following model captures the essential elements of malaria epidemiology:

$$\frac{dU}{dt} = \beta\rho\frac{M}{N}V(1-U) - \gamma U$$

$$\frac{dV}{dt} = \beta\pi U(1-V) - \mu V$$

Where U and V are proportions of infected humans and mosquitoes respectively; M/N is the number of (female) mosquitoes per human host in an infection free steady state; β is the per capita biting rate of mosquitoes on humans; ρ is the probability that an infectious mosquito's bite transmits the parasite; π is the probability that a bite of an infected human by a susceptible mosquito results in transmission of the parasite to the mosquito; γ is the human recovery rate from infection. The basic reproduction number, R_o for this model is given by the expression $R_o = \frac{M}{N}\beta^2\rho\pi\left(\frac{M}{N}\right)^{-1}(\mu+\gamma)^{-1}$

N □□ N □ □

This is defined as the product of the expected time for which a typical infected human remains infectious (1), the expected number of mosquitoes to which the parasite will be □

transmitted (□□), the expected life-span of a mosquito (1/□), the number of mosquitoes

per human host (M/N) and the expected number of humans to which a mosquito will

transmit the parasite (□□). Eradication campaigns have been aimed at controlling the

mosquito population strongly enough to achieve $R < 1$, that is because the threshold value

R_0 = 1 defines a threshold for M/N , the ratio of mosquitoes to humans (Ross, 1911).

2.10.3 Models for Parasite Populations

Epidemiology deals with parasites. Parasites are living organisms that live on other organisms (hosts) and derive nourishment from the hosts and causing harm to them. The effect of parasites on the hosts varies. The most common effect of parasites is an increase in the mortality rate of the affected hosts. Parasitism can lead to a reduction in birth rate, which can even reach the state of parasitic castration. Parasites cause changes in the structure of the host's body in order to increase their transmission efficiency

The two groups of parasites are microparasites and macroparasites. A major difference between microparasites and macroparasites is that the former reproduce rapidly within the

host, whereas the latter reproduce by releasing offsprings into the environment, some of which eventually complete a life-cycle, becoming infective stages, and infect a new host. The infections of the tropical helminth served as the genesis of epidemic theory. Kostitzin's early work in 1934 was followed thirty years later by Macdonald's study of schistosomiasis and a flourishing of activity in the seventies and eighties (Scott and Smith,1994).

The compartmental models that classify a host as susceptible, infectious, etc. are inadequate for infections caused by parasitic helminth. It needs a model that allows multiple infections in a single host. Also, the notion that the number of the susceptibles diminishes during the course of an epidemic does not necessarily hold, differential equation models no longer have a negative feedback mechanism that is automatically incorporated and careful attention must be paid to the mechanisms that regulate the parasite population.

2.10.3.1 The Population Dynamics of Macroparasites

The dynamics of the population of parasitic helminth in a host population of constant size N is modelled as $\frac{dP}{dt} = \square\square P(Q(P)\square 1)P$, where P is the mean number of parasites per host, $\square$ is the mortality rate of parasites from the system and $Q(P)$ is the ratio of parasite transmission rate to the mortality rate. This model is appropriate in a situation where host immunity is a fraction of current mean parasite burden or when the parasite transmission rate is dependent on the parasite population density. Hence Q is a positive non-increasing function of P, at steady state, $Q(P)\square 1$ and the parasite population can persist whenever $Q(P)\square 1$.

The basic reproduction number for the parasite population is given by the numberQ(0). This may be defined as the expected number of offspring of a typical parasite that reaches reproductive maturity, in a completely susceptible host population. For microparasites, the reproduction number is defined in terms of secondary infections of hosts; for macroparasites it is defined in terms of the parasite population dynamics (Grenfell and Dobson, 1995).

2.10.4 Model with Age-Structure

The transmission of childhood infections depends upon the age-structure of the population, with greater contact between those in the same classroom. Models of sexually transmitted infections call for the incorporation of much structure, including age-structure and groups with differences in infectivity or susceptibility (Mollison, 1996). The contact structure of these models must take account of discrete characteristics such as sex, sexual preferences and sexual activity. Two complications are particularly important: varying infectivity as a function of time elapsed since infection and the implications of long lasting partnerships. The first complication is relevant to almost all infections; the second is related to sexual transmission. One of the key notions to come out of HIV modeling is that of a core-group of infected. This is a small group that is very active in making contacts and can keep the epidemic going in a much larger group where the internal contacts alone cannot sustain it (Isham and Medley, 1996).

2.10.4.1 Adding More Classes

Consider an SIR model for the transmission of an infection within a population that may be divided into n classes, for which the contact rate within classes may be different to those

between classes. The classes may be based on, for example, sex or sexual orientation, school attended or college year. Not considering mortality within the population at risk, the model equations for the densities of the susceptible (S_i) and infectious (I_i) populations are

$$\frac{dS_i}{dt} = A_i - (\mu_i + \beta \sum_{j=1}^{n} C_{ij} I_j) S_i$$

$$\frac{dI_i}{dt} = \beta S_i \sum_{j=1}^{n} C_{ij} I_j - (\mu_i + \gamma) I_i$$

For $i = 1 \ldots n$. ($A_i = \mu_i N_i$) and μ_i are the recruitment rates into class i, and the rates at which individuals leave i respectively (Isham and Medley, 1996; Heesterbeek, 2003; Cottingham, 2003)

2.10.5 Mathematical Modeling of Cholera

Mathematical modelling of cholera epidemics follows the usual compartmental-based models (Codeço, 2001). Modelling the dynamics of cholera requires the explicit consideration of the dynamics of pathogens within the reservoir. Cholera is an indirectly transmitted infectious disease. Models of indirectly transmitted diseases are different from vector-based models in that the pathogens can be free-living, or alternatively, the reservoirs are unknown. Alternative hosts are key to the origins and emergence of major human infectious diseases. The free-living bacteria in the aquatic reservoir have long been recognized to determine the endemic–epidemic dynamics of cholera (Codeço, 2001; Pascual et al, 2002).

Capasso and Paveri-Fontana developed the first indirect transmission disease model in 1979 (Capasso and Paveri-Fontana, 1979) to describe the interaction of infected individuals with aquatic populations of pathogenic *Vibrio cholerae*. Codeço (Codeço, 2001) extended

Capasso's model to link SIR dynamics with dynamics of bacteria within reservoirs. These models are termed iSIR models, where the lower case ''i'' denotes indirect transmission dynamics. iSIR models are a family of reservoir meditated SIR models with a threshold pathogen density for infection. Hartley et al (2006) considered a model of cholera transmission that included two types of bacterial states, using the indirect transmission framework. Jensen et al (2006) proposed a model with logistic growth of the pathogen.

A key difference between this iSIR model and other SIR or indirect disease models is the explicit incorporation of a minimal infectious dose (MID). It is known for cholera that a susceptible individual must ingest approximately 10^3–10^6 *Vibrio cholerae* to become infected (Levine et al., 1981; Colwell et al., 1996). The basis for explicitly modeling the MID is that the human innate immune system is capable of eliminating low levels of pathogens and staving off disease (Codeço, 2001).

2.10.6 Use of Mathematical Modeling in Public health

Mathematical modeling has become particularly a useful tool in disease epidemiology. Disease systems are very complex. The spread of a disease can depend on the biology and evolution of the infective agent, the biology and behaviour of a vector population, environmental factors, as well as the biology and behaviour of the host population.

Understanding how these aspects interact is a hallmark to the description and prediction of disease behaviour in a real population.

Mathematical modeling enables us to characterize the general and specific behaviour of these systems analytically and understand which aspects contribute the most to the observed dynamics.

The information obtained from the modeling of a disease is used for analysing data from epidemics, designing experiments, or in making policy decisions for preventive measures. It provides a way to understand primary dynamics of infections. Modeling can also be used to predict which control procedures or treatments could be most effective in stopping (or preventing) the spread of a disease (Kretzschmar, 2001; Ferguson, 2003).

CHAPTER THREE

METHODOLOGY

3.1 Introduction

This chapter focuses on the review of ordinary differential equations (ODE's) and its application to the deterministic SIRB cholera model. SIRB models are a family of reservoir mediated SIR models with a threshold pathogen density for infection. SIR models involve only first-order derivatives of unknown functions of S, I and R. It is called a first order system. For this reason, we will review only first-order systems.

SIRB models are termed iSIR models, where the lower case "i" denotes indirect transmission dynamics. Pathogens are common to environmental sources, including drinking water and can cause infection upon contact with them. The likelihood of getting infected upon contact with a contaminated reservoir depends on the pathogen density and interactions of the pathogen with the immune system.

We will consider the logistic growth model because we will incorporate the logistic equation in our model.

We will also explain the meaning and significance of the basic reproduction number in modeling of cholera; the critical population size and plane phase will be used in our analysis. Since, it is easier to handle two-dimensional system (called planar system), our attention would be focused on two-dimensional systems; we will then link them to the analysis of our model.

3.2 Ordinary Differential Equation (ODE)

An ordinary differential equation (ODE) is an equation containing a function of one independent variable and its derivatives. Any equation of the form:

$$\frac{dy}{dt} = f(t,y) \qquad (3.1)$$

Where $f : R^2 \to R$ is a two- variable or multivariable function and $\frac{dy}{dt}$ represents the derivative y with respect to t is referred to as ordinary differential equation (ODE). Any function say $y = \varphi(t)$, satisfying the differential equation (3.1) is called the solution of the differential equation. If $\varphi(t)$ is the solution of (3.1), then $\varphi'(t) = f(t,\varphi(t))$. For example, show that the pair of functions x(t) = sin(t) and y(t) = cos(t) form a solution of the following system:

$$\frac{dx}{dt} = y(x^2 + y^2) \qquad (3.2.1)$$

$$\frac{dy}{dt} = -x(x^2 + y^2) \qquad (3.2.2)$$

After substitution of x(t) = sin(t) and y(t) = cos(t), the left-hand side of (3.1.1) is

$\frac{dx}{dt} = \cos(t)$, since $x^2 + y^2 = 1$, the right-hand side is $y(x^2 + y^2) = y(t) = \cos t$, Hence

(3.2.1) is satisfied. A similar calculation shows that (3.2.2) is satisfied. Hence the pair x(t) = sin(t) and y(t) = cos(t) forms a solution to the system.

The order of a differential equation is the order of the equation's highest derivative.

Given that F is a function of t, y, and derivatives of y. Then an equation written in terms of t, y, and derivatives of y is of the form $F(t,y,y',...,y_{(n-1)}) = y_n$ (3.2)

Equation (3.2) is called an explicit ordinary differential equation of order n.

An implicit ordinary differential equation of order n takes the form:

$$F(t,y,y',y'',...,y^n) = 0 \quad (3.3)$$

A number of coupled differential equations form a system of equations.

Equation (3.2) can be expressed in a vector form as:

$y = (y_1,y_2,....,y_n)^T \in R^n$, $f : R \times R^n \to R^n$. In column vector form we have:

$$\begin{aligned} y' &= f_1(t,y_1,y_2,...,y_n) \\ &\vdots \\ y' &= f_n(t,y_1,y_2,...,y_n) \end{aligned} \quad (3.4)$$

Where f_1,…, and f_n are functions of n+ 1 variable $t, y_1,y_2,...., \text{ and } y_n$.

The system of equations (3.4) is a first order system of differential equations. This system has n equations with n unknowns. That is the number of equations is equal to the number of unknowns, and this number is called the dimension. These first order systems of equations are used in the study of dynamical systems such as modeling of infectious diseases.

Further classifications of ordinary differential equations are:

- Autonomous: A differential equation not depending on t. The dependent variable is explicitly expressed. All autonomous differential equations are separable. An example of autonomous differential equation is given below:

$$\frac{dy}{dt} = ky \text{ , } k \text{ is a constant} \qquad (3.5)$$

- Linear: A differential equation is said to be linear if F can be written as a linear combination of the derivatives of y:

$$\frac{dy(t)}{dt} = Ay(t) + f(t) \qquad (3.6)$$

OR

$$a_n \frac{dy^n}{dt^n} + a_{n-1} \frac{dy^{n-1}}{dt^{n-1}} + \ldots + a_2 \frac{dy^2}{dt^2} + a_1 \frac{dy}{dt} + a_0 y = f(t) \text{ , } a_n, a_{n-1}, a_2, a_1, a_0, \text{ are constants}$$

- If $f(t) \neq 0$, then equation (3.5.1) is called homogeneous and consequently has one automatic solution, the trivial solution, y = 0. The solution of a linear homogeneous equation is a complementary function, y_c.

- If $f(t) \neq 0$ then equation (3.5) is called non-homogeneous and its solution is called the particular integral, y_p.

- The general solution to a linear equation can be written as $y = y_c + y_p$

- Any equation that cannot be written in the form of (3.6) is called non-linear. The following are examples of non-linear equations:

(a) $2y\frac{d^2y}{dt^2} + y = t^2$ (b) $\left(\frac{dy}{dt}\right)^2 + 4y = 0$

3.3 Eigenvalues of a matrix

Consider the $n \times n$ matrix $A = [a_{ij}]$ and a scalar λ (a real or complex number). λ is an eigenvalue of A if there exists a non-zero vector x in R^n such that $(Ax = \lambda x)$. The vector x is called eigenvector.

Now, $Ax = \lambda x$

$Ax - \lambda x = 0$

$(A - \lambda I)x = 0$ (3.7)

Equation (3.2) has n linear algebraic equations in the n unknowns $x = x_1, x_2, \ldots, x_n$. These equations have a solution $x \neq 0$, if and only if the determinant of the co-efficient matrix $(A - \lambda I)$

zero. Thus, $|A - \lambda I| = 0$. Let us consider the 2×2 matrix A below:

$$A = \begin{bmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{bmatrix} \text{ and } I = \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}$$

Now, $(A - \lambda I)x = 0$

$$\begin{bmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{bmatrix} - \lambda \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix} \begin{bmatrix} x_1 \\ x_2 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \end{bmatrix}$$

$$\begin{bmatrix} a_{11} - \lambda & a_{12} \\ a_{21} & a_{22} - \lambda \end{bmatrix} \begin{bmatrix} x_1 \\ x_2 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \end{bmatrix}$$

$$\begin{bmatrix} a_{11} - \lambda & a_{12} \\ a_{21} & a_{22} - \lambda \end{bmatrix} x = \begin{bmatrix} 0 \\ 0 \end{bmatrix}$$

The matrix $(A - \lambda I)$ is not invertible (singular) if and only if its determinant, $|A - \lambda I| = 0$, since $x \neq 0$.

The eigenvalues of A are defined as the roots of: determinant$(A - \lambda I) = |A - \lambda I| = 0$

$$\begin{vmatrix} a_{11} - \lambda & a_{12} \\ a_{21} & a_{22} - \lambda \end{vmatrix} = 0$$

$$(a_{11} - \lambda)(a_{22} - \lambda) - a_{12}a_{21} = 0$$

$$\lambda^2 - (a_{11} + a_{22})\lambda + a_{11}a_{22} - a_{12}a_{21} = 0$$

$$\lambda^2 - tr(A)\lambda + |A| = 0$$

Where tr(A) called trace of matrix A, is the sum of the diagonal entries of A,

$Det(A) = |A| = a_{11}\, a_{22} - a_{12}\, a_{21}$ is the determinant of matrix A. The expression or equation above is called the characteristic polynomial of degree two. The zeros of this polynomial are λ_1 and λ_2 called the eigenvalues of matrix, A.

The behavior of the solution depends on the eigenvalues. If the eigenvalues are negative, i.e. $\lambda < 0$, then the solution of the system is stable; if the eigenvalues are positive, the system is unstable.

Example 3.1

Consider the linear system below:

$$\frac{dx}{dt} = -2x$$

$$\frac{dy}{dt} = -3y$$

□x□□ □□ 2 0 □ □x□

□y□□□ □ □□ 0□3□□ □ □□y□□

□

x□ □ A**x**

□x□□ □□ 2 0 □ □x□

x□ □ □□y□□□ ; A □ □□ 0□ 3□□ ; **x** □ □□y□□

The system has eigenvalues satisfying |A□λI |□ λ² □tr(A)λ□ |A|□ 0

tr(A)□ □2□(□3) □ □5; A □ ¦ ¦ 6

λ² □5λ□6 □0 □(λ□2)(λ□3) □0

□ λ □ □2 or λ □ □3

Therefore, the eigenvalues of Aare □₁□ □2and λ₂ □□3. Since the eigenvalues of the system

are negative and distinct, the system is (stable) sink.

Example 3.1.1

Consider the linear system below:

□*x*□ □ 2x

□y□ □ 3y

□

□x□□ □2 0□ □x□

□□y□□□ □ □□0 3□□□□□y□□

□x□□ □2 0□ □x□

x□ □ □y□□□ ; A □ □□0 3□□ ;

x □ □□y□□ □

The system has eigenvalues satisfying $|A - \lambda I| = \lambda^2 - tr(A)\lambda + |A| = 0$

$tr(A) = 2 + 3 = 5$; $A = \begin{vmatrix} & \\ & 6 \end{vmatrix}$ $\lambda^2 - 5\lambda + 6 = 0$

$(\lambda - 2)(\lambda - 3) = 0$

$\lambda = 2$ or $\lambda = 3$

Therefore, the eigenvalues of A are $\lambda_1 = 2$ and $\lambda_2 = 3$. Since the eigenvalues of the system are positive and distinct, hence the solution of the system with this type of qualitative behaviour in its neighbourhood is an (unstable) source.

3.4 Nature of Solutions of Non-linear Systems and Linearization

The stability of typical equilibria of smooth ODEs is determined by the sign of real part of eigenvalues of the Jacobian matrix. These eigenvalues are often referred to as the eigenvalues of the equilibrium points. The Jacobian matrix of a system of smooth ODEs is the matrix of the partial derivatives of the right-hand side with respect to state variables,

where all derivatives are evaluated at the equilibrium point. Its eigenvalues determine linear stability properties of the equilibrium.

The Hartman-Grobman Theorem is an important theorem in ODE systems theory. It is about the local behavior of an autonomous dynamical system in the neighborhood of a hyperbolic equilibrium, stating that the behavior of the dynamical system near the hyperbolic equilibrium (non-zero eigenvalue) is qualitatively the same as (i.e., topologically equivalent to) the behavior of its linearization near this equilibrium point.

Consider the two-dimensional system below:

$$\frac{dx}{dt} = u(x, y)$$

$$\frac{dy}{dt} = v(x, y) \quad (3.8)$$

Let $x = x_0 + p$ and $y = y_0 + q$, where p and q are small perturbations. Now, for the small perturbations we make use of the linear Taylor polynomial functions to approximate each of $u(x, y)$ near the equilibrium (x_0, y_0):

$$u(x_0 + p, y_0 + q) \approx u(x_0, y_0) + p\frac{\partial u(x_0, y_0)}{\partial x} + q\frac{\partial V(x_0, y_0)}{\partial y} + \ldots$$

$$v(x_0 + p, y_0 + q) = v(x_0, y_0) + p\left(\frac{\partial u(x^0, y^0)}{\partial x}\right) + q\left(\frac{\partial V(x^0, y^0)}{\partial y}\right) + \ldots$$

At the equilibrium point (x_0, y_0), we have $u(x_0, y_0) = 0$ and $v(x_0, y_0) = 0$.

$$u(x_0 + p, y_0 + q) = p\left(\frac{\partial u(x_0, y_0)}{\partial x}\right) + q\left(\frac{\partial V(x_0, y_0)}{\partial y}\right)$$

$$v(x_0 + p, y_0 + q) = p\left(\frac{\partial u(x_0, y_0)}{\partial x}\right) + q\left(\frac{\partial V(x_0, y_0)}{\partial y}\right)$$

Since p and q, are so small, higher order terms can be neglected.

The above equations are expressed succinctly in the matrix form as:

$$\begin{bmatrix} u(x, y) \\ v(x, y) \end{bmatrix} = \begin{bmatrix} \frac{\partial u}{\partial x} & \frac{\partial u}{\partial y} \\ \frac{\partial v}{\partial x} & \frac{\partial v}{\partial y} \end{bmatrix} \begin{bmatrix} p \\ q \end{bmatrix} \quad (3.9)$$

Since $x(t) = x_0 + p(t)$ and $y(t) = y_0 + q(t)$, we also have $\dot{x} = \dot{p}$; $\dot{y} = \dot{q}$. Substituting the pieces together and $\dot{X} = U(x, y)$ into (3.8), give a system of linear differential equations for the perturbations p and q below:

□□u □u□
— —

□□□qp□□□□ □□□□xv□□yv□□ □□□qp□□ P□ □ J(x0 , y0) □ P , where P□ □ □□qp□□□□□ , P □ □□□qp□□□

□ □ □ □

□□□x □y□□ —

J(x0 □□□ u^x (x0,y0) □□ u^y (x0,y0)□□ is called the Jacobian matrix. It is calculated once

,y0) □ □□v □v □□

□(x0,y0)(x0,y0)

□□□x □y □□

for each non-linear system. The linear system for u and v has a trivial steady state

(u, v) □ (0,0). The Jacobian matrix is evaluated for each equilibrium or critical point of the linearized system and the eigenvalues are used to determine the nature of the solution of the original nonlinear system.

The behaviour of the original non-linear system near an equilibrium point is the same as that of the linear approximation, except when the linear system has a centre. If the linear system has a centre, the equilibrium point of the original non-linear system may be a stable centre, a stable spiral sink or an unstable spiral source.

Example 3.2

Consider the following non-linear system of differential equations:

□x□ □ (1□ x □ 2y)x

□

□y□ □ (x □1)y

We first determine the critical points of the system by setting $(\dot{x}, \dot{y}) = 0$ as follows:

When x□ □ 0 □ (1□ x -2y)□ 0 (1)

y□ □ 0 □ (x □1)y □ 0 (2)

The second equation gives x □1 or y □ 0

When x □ 1, substituting into (1) gives 2□2y □ 0 ,which leads to y □ 1. So (1 , 1) is an equilibrium point. When y □ 0,substituting into (1) gives(1□ x)x □ 0, hence

x □ 0 or x □ -1. So the equilibrium points are (0 , 0) (□1 , 0) is an equilibrium point.

Next, we determine the Jacobian matrix and evaluate it for each critical point.

We make the following notation:

x□ □ u(x, y)□ (1□ *x* □ 2y)x

y□ □ v(x, y)□ (x □1)y

The Jacobian matrix for the system is given by:

□□u □u□

□— —

J(x, y)□ □□□xv□□yv□□□ □ □□□1□ 2xy□ 2y □x 2□x1□□□

□□□x □y□□

$$\begin{bmatrix} -1 & 0 \end{bmatrix}$$

At the point$(0, 0)$, $J(0,0) = \begin{bmatrix} 0 & -1 \end{bmatrix}$

$$\begin{bmatrix} \end{bmatrix}$$

The eigenvalues, λ of the Jacobian matrix are given by $|J - \lambda I| = 0$ if and if $|J| = 0$ We now determine the eigenvalues as follows:

$$|J - \lambda I| = 0$$

$$\begin{vmatrix} -1-\lambda & 0 \\ \\ 0 & -1-\lambda \end{vmatrix} = 0$$

$$(-1-\lambda)(-1-\lambda) = 0$$

$\lambda = -1$ or $\lambda = -1$

The eigenvalues of the Jacobian matrix are $\lambda_1 = -1$ and $\lambda_2 = -1$

At the point$(-1, 0)$,

$$\begin{bmatrix} -1 & 2 \end{bmatrix}$$

At the point$(-1, 0)$, $J(-1,0) = \begin{bmatrix} 0 & 2 \end{bmatrix}$

$$\begin{bmatrix} \end{bmatrix}$$

The system has eigenvalues satisfying $|J - \lambda I| = \lambda^2 - \text{tr}(J)\lambda + |J| = 0$

tr(J)□ □1□2 □ □3; J □ $\begin{vmatrix} 2 \end{vmatrix}$ λ² □3λ □ 2 □

0 □(λ □1)(λ □ 2) □ 0

□ λ □ -1 or λ □ -2

□1 □ 2□

At the point(1 , 1) , J(1 ,1) □ □1 0 □□

□

The system has eigenvalues satisfying$\left|J \square \lambda I\right| \square \lambda^2 \square \text{tr}(J)\, \lambda \square \left|J\right| \square 0$

tr(J)□1□0 □1; J □ $\begin{vmatrix} 2 \end{vmatrix}$

λ2 □λ □ 2 □ 0 The roots of the equation are found using the quadratic formula:

$\frac{-b \square \sqrt{b^2 \square 4ac}}{2a}$, a □1; b □ -1; c □ 2

λ □

$\square \lambda \square \frac{1 \square \sqrt{(\square 1)^2 \square 4(1)(2)}}{2(1)} \square \frac{1 \square \sqrt{1 \square 8}}{2} \square \frac{1 \square \sqrt{\square 7}}{2} \square \frac{1 \square i\sqrt{7}}{2}$

Hence the eigenvalues are $\frac{-1 \pm i\sqrt{7}}{2}$. All the eigenvalues of are negative, hence the linearized system is a stable at the critical point. Therefore the nonlinear system behaves in a similar way.

3.5 The Phase Plane (Phase Portrait) Analysis

Phase plane analysis is one of the most important techniques for studying the behavior of nonlinear systems, since there is usually no analytical solution for a nonlinear system. Phase portrait is a graphical representation of the nature of the solution of a given system of differential equations.

3.6 The Critical Point

An equilibrium solution of the system of differential equations, $\mathbf{x}' = \mathbf{Ax}$ is a point (x, y) where, $\mathbf{x}' = \mathbf{0}$ that is, where $x'(t) = y'(t) = 0$. An equilibrium solution is a constant solution of the system, and is usually called a critical point. For a linear system $\mathbf{x}' = \mathbf{Ax}$, an equilibrium solution occurs at each solution of the system (of homogeneous algebraic equations) $A\mathbf{x} = 0$. As we have seen, such a system has exactly one solution, located at the origin, if determinant $(\mathbf{A}) \neq 0$. If determinant $(\mathbf{A}) = 0$, then there are infinitely many solutions. An equilibrium is asymptotically stable if all eigenvalues have negative real parts; it is unstable if at least one eigenvalue has positive real part.

An equilibrium point is said to be stable when all points in the neighbourhood of the point remain in the neighbourhood of the equilibrium point as time increases; otherwise it is

unstable. The equilibrium is said to be hyperbolic if all eigenvalues of the Jacobian matrix have non-zero real parts (Hartman-Grobman Theorem).

3.6.1 Classification of Critical Points

A two dimensional system has two eigenvalues, which are either both real or complexconjugate.

Depending on the types and signs of the eigenvalues, a hyperbolic equilibrium (or critical point) can be any one of the following:

- Node
- Saddle
- Focus (Spiral point)
- Centre

3.6.2 Node

A critical point X_o is a node if every trajectory approaches X_o as $t \to \infty$ or every trajectory recedes from X_o as $t \to \infty$, and each trajectory approaches (or recedes) from X_o in a fixed direction. (That is, every trajectory is tangent to a line through X_o). A critical point is called a node when both eigenvalues are real and have the same sign. The node is stable when the eigenvalues are negative and unstable when they are positive. A node can be proper or improper.

Example 3.3.1

Consider the system of differential equations below:

□*x*□ □ □x

□

□y□ □ □2y

□x□□ □□1 0 □ □x□

□y□□□ □ □□ 0□ 2□□□□□y□□

□

□ **x**□ □ A**x**

□□1 0 □

□ A □ □□ 0 □2□□ Has eigenvalues satisfying the characteristic equation

λ^2 □ tr(A) λ □ |A □ 0

λ^2 □3λ □ 2 □ 0 □ (λ □1) (λ □ 2) □ 0

□ λ □ □1 or λ □ □ 2

Since both eigenvalues are real and negative, we have a stable node. The only straight-line paths are the two axes, which correspond to the eigenvectors of the matrix A.

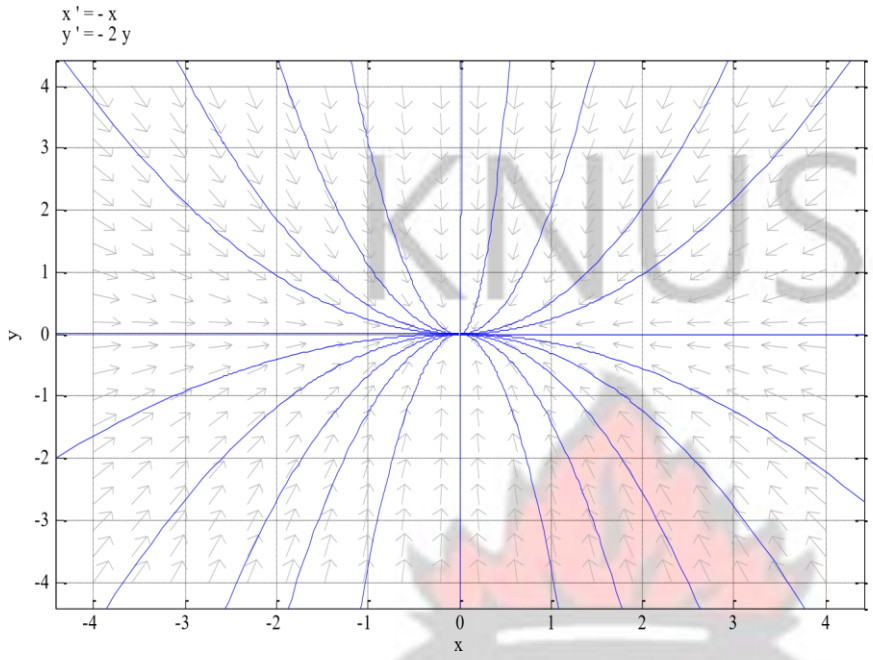


Figure 3.1: Phase Portraits of a stable node generated using d field8 and pplane8 from Matlab with the x-axis, □4 □ x □ 4and the y-axis,□4 □ y □ 4 and the x□ □ □x and y□ □ □2y

Example 3.3.2

Consider the system of differential equations below:

□*x*□ □ x
□

□y□ □ 2y

□x□□ □1 0□ □x□

□□y□□□ □ □□0 2□□□□□y□□

□ **x**□ □ A**x**

□1 0□

□ A □ □0 2□□ Has eigenvalues satisfying the characteristic equation

□

$\lambda^2 \square \text{tr}(A)\,\lambda \square \det A \square 0$

$\lambda^2 \square 3\lambda \square 2 \square 0 \square (\lambda \square 2)(\lambda \square 1) \square 0 \;\square\; \lambda \square 2$

or $\lambda \square 1$

Since both eigenvalues are real and positive, we have an unstable node. The only straightline paths are the two axes, which correspond to the eigenvectors of the matrix A. The phase portrait is as displayed below:

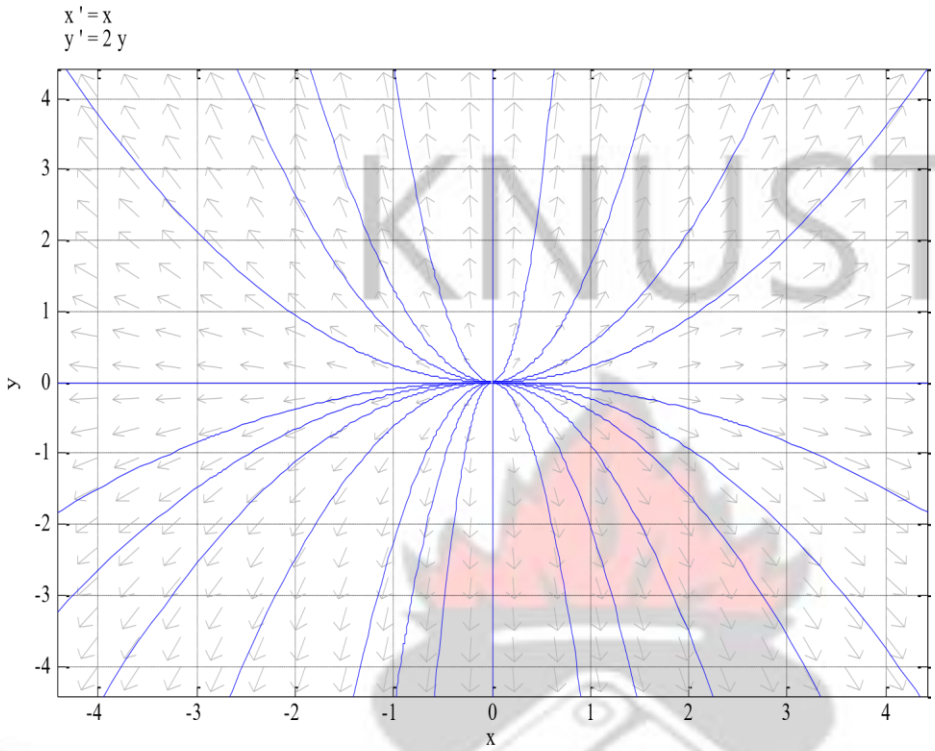


Figure 3.2: Phase Portraits of an unstable node generated using dfield8 and pplane8 from Matlab with the x-axis, □4 □ x □ 4and the y-axis,□4 □ y □ 4 and the x□ □ x and y□ □ 2y

3.6.2.1 Improper (Degenerate) Node

When the coefficient matrix of a system has distinct real eigenvalues and only one linearly independent eigenvector, then the critical point is called an improper node. Improper nodes are asymptotically stable if the eigenvalues are negative. They are unstable if the eigenvalues are positive.

Example 3.3.1.1

Consider the following system: $\begin{cases} \dot{x} = x + y \\ \dot{y} = y \end{cases}$

The system can be written as:

$\dot{x} = Ax$

$A = \begin{pmatrix} 1 & 1 \\ 0 & 1 \end{pmatrix}$ Has eigenvalues satisfying the characteristic equation $\lambda^2 - tr(A)\lambda + |A| = 0$

$\lambda^2 - 2\lambda + 1 = 0 \Rightarrow (\lambda - 1)(\lambda - 1) = 0$

$\lambda = 1$
(Multiplicity two)

The eigenvalues of the matrix are $\lambda = 1$(twice). Since both the eigenvalues are real, repeated and positive with only one eigenvector, we have an unstable improper node.

However, if the eigenvalues are negative, i.e.$\lambda < 0$, then the equilibrium point is a (stable) improper node (sink). The phase paths are obtained by reversing the arrows of the (unstable) improper source. The only straight line path is in the direction of the eigenvector of the coefficient matrix, A.

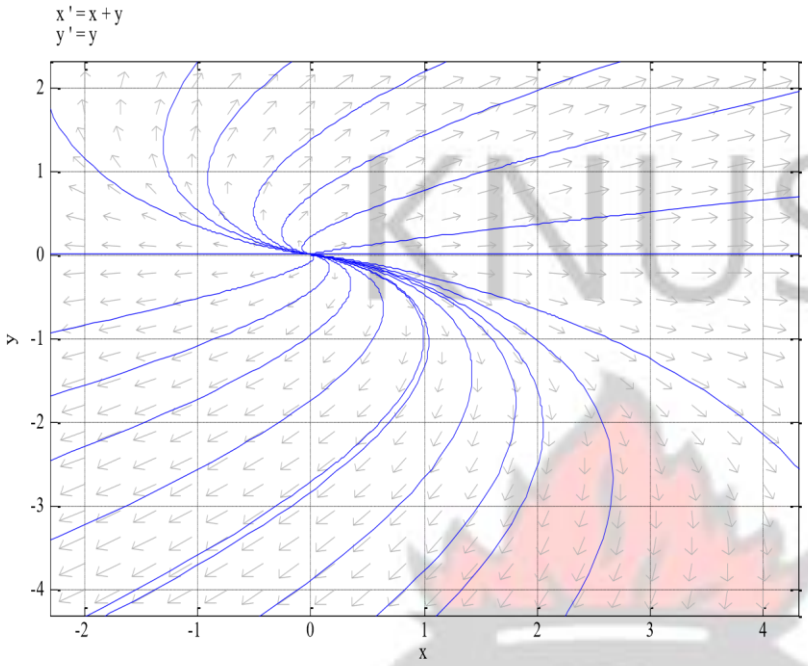


Figure 3.3: Phase Portraits of an unstable improper node generated using dfield8 and pplane8 from Matlab with the x-axis, □2 □ x □ 4and the y-axis,□4 □ y □ 2 and the x□ □ x □ yand y□ □ y

3.6.2.2 Proper Node

A node is called proper when both eigenvalues of the systems are real, equal and repeated with two eigenvectors. Proper nodes are unstable if both eigenvalues are positive; asymptotically stable if eigenvalues are negative.

Example 3.3.1.2

Consider the following system:

□x□ □ x

□

□y□ □ y

□ x□ □ Ax

□1 0□ ^{2} tr(A)λ □|A| □ 0

□ A □ □0 1□□ Has eigenvalues satisfying the characteristic equation λ □

□

λ^2 □2λ □1□ 0 □(λ□1) (λ□1) □ 0

□1□λ □ 0 □ λ □1 (Has multiplicity **two**).

□ λ$_1$ □ λ$_2$ □^{1}

Here, we have repeated eigenvalue of multiplicity two, both of the same positive sign; hence we have an unstable proper node. A proper node is asymptotically when both eigenvalues are negative i.e. λ □ 0. All trajectories are tangent to the line spanned by the first eigenvector.

The coefficient matrix has identical positive eigenvalues and two linearly independent eigenvectors, all the paths are straight lines radiating away from the origin as shown in the figure below.

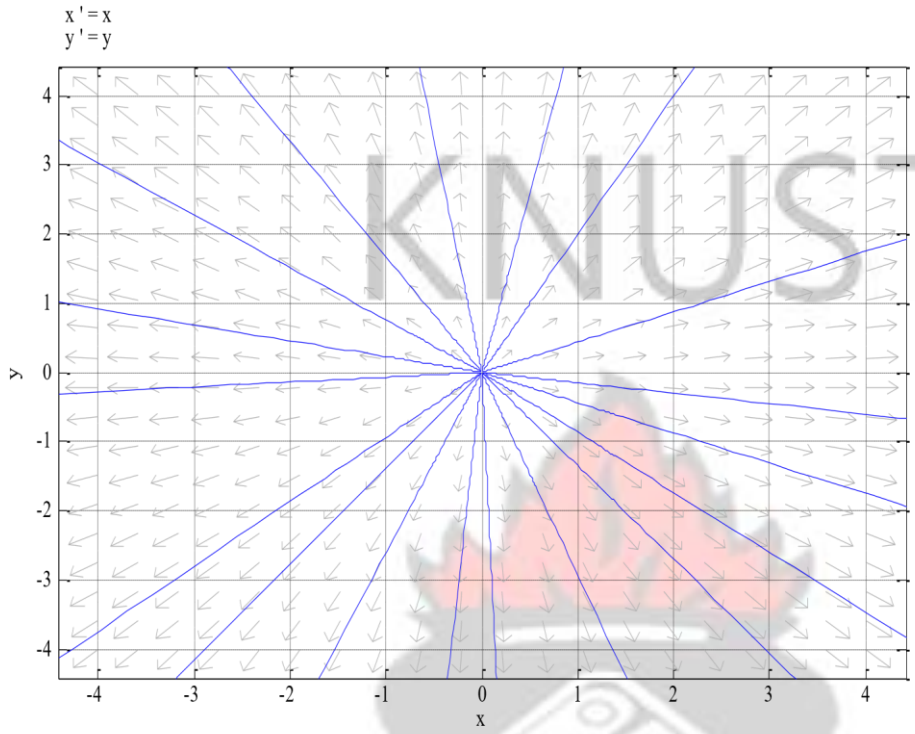


Figure 3.4: Phase Portraits of an unstable proper node generated using dfield8 and pplane8 from Matlab with the x-axis, □2 □ x □ 4and the y-axis,□4 □ y □ 2 and the x□ □ x and y□ □ y

3.6.3 Saddle Point

A saddle point is a critical point, X_o at which there are two incoming trajectories, two outgoing trajectories, and all the other trajectories in a neighborhood of X_o by passX_o.

Saddle points occur when both eigenvalues are real and one of them is positive and the other is negative. Saddles are always unstable.

Example 3.4

Let us consider the system below:

$$\frac{dx}{dt} = 2x$$

$$\frac{dy}{dt} = -2y$$

$$\frac{dx}{dt} = Ax$$

$$A = \begin{pmatrix} 2 & 0 \\ 0 & -2 \end{pmatrix}$$ Has eigenvalues satisfying the characteristic equation

$$\lambda^2 - tr(A)\lambda + |A| = 0 \quad \lambda^2 - 4 = 0$$

$$(\lambda - 2)(2+\lambda) = 0$$

$$\lambda = -2 \text{ or } \lambda = 2$$

Hence, we have two distinct eigenvalues, one positive and the other negative. The only straight-line paths are the two axes, which correspond to the eigenvectors of the matrix A.

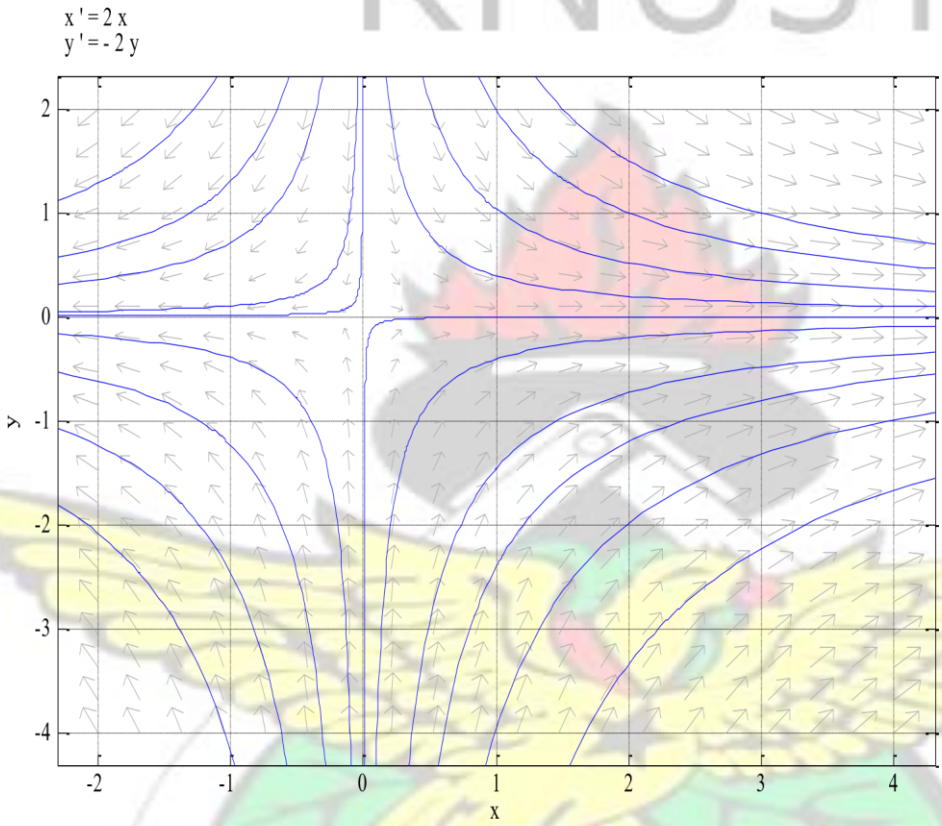


Figure 3.5: Phase Portraits of an (unstable) saddle generated using dfield8 and pplane8 from Matlab with the x-axis, □2 □ x □ 4and the y-axis,□4 □ y □ 2 and the x□ □ 2xand y□ □ □2y

3.6.4 Focus (Spiral Point)

A spiral point is a critical point X_o about which the trajectories spiral, approaching X_o as t $\rightarrow \infty$ (or tracing these spirals in the opposite sense away from X_o). This occurs when the coefficient matrix has a pair of complex-conjugate eigenvalues with real parts. The focus is stable when the eigenvalues have negative real part and unstable when they have positive real part.

Example 3.5

Consider the following system:

$$\frac{dx}{dt} = 2x - 3y$$

$$\frac{dy}{dt} = 3x - 2y$$

$$\frac{dx}{dt} = Ax$$

$$A = \begin{pmatrix} 2 & -3 \\ 3 & -2 \end{pmatrix}$$ Has eigenvalues satisfying the characteristic equation

$$\lambda^2 - tr(A)\lambda + |A| = 0$$

$$tr(A) = 4$$

$$; \quad |A| = 13$$

$$\lambda^2 - 4\lambda + 13 = 0$$

Using the quadratic formula;

$$\lambda = \frac{-b \pm \sqrt{b^2 - 4ac}}{2a}, \quad a = 1; \; b = 4; \; c = 13$$

$$\lambda = \frac{-4 \pm \sqrt{(-4)^2 - 4(1)(13)}}{2(1)} = \frac{-4 \pm \sqrt{-36}}{2} = \frac{-4 \pm 6i}{2} = -2 \pm 3i$$

The eigenvalues of the system are $\lambda_1 = -2 + 3i$ and $\lambda_2 = -2 - 3i$. The eigenvalues have negative real part and hence the equilibrium point is a stable spiral sink. The corresponding eigenvectors are $[1 \quad -i]^T$ and $[1 \quad i]^T$. The paths spiral towards the origin, so the origin is a sink and therefore we have a stable equilibrium point. The phase portrait is shown in figure 3.6 below.

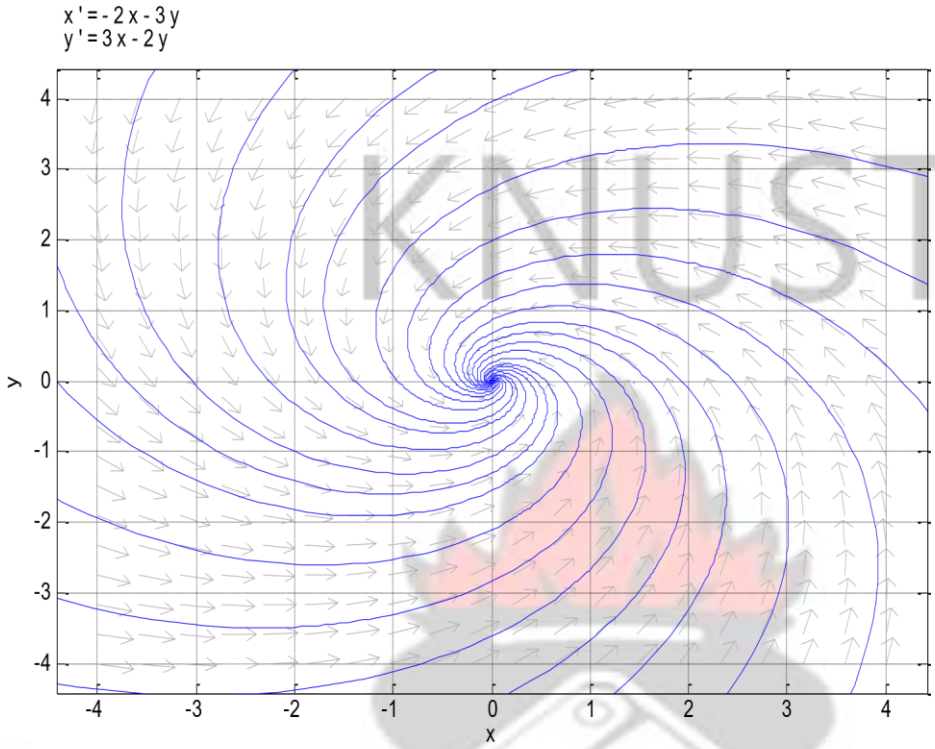


Figure 3.6: Phase Portraits of a stable spiral (spiral sink) generated using dfield8 and pplane8 from Matlab with the x-axis, □4 □ x □ 4and the y-axis,□4 □ y □ 4 and the x□ □ □2x □3y and y□ □ 3*x* □2y

3.6.5 Centre

A centre is a critical point that is enclosed by infinitely many closed trajectories. The trajectories neither converge to the critical point nor move to infinite distant away. They rather stay in a constant circular shape. A centre, which is a closed orbit (e.g. a circle) is neutrally stable. A centre equilibrium point occurs when the coefficient matrix has a pair of purely complex-conjugate eigenvalues.

Example 3.6

Let us consider the following system of ordinary differential equations:

$$\begin{cases} x' = y \\ y' = -4x \end{cases}$$

The system can be written as $\mathbf{x}' = A\mathbf{x}$

$$A = \begin{bmatrix} 0 & 1 \\ -4 & 0 \end{bmatrix}$$ Has eigenvalues satisfying the characteristic equation

$$\lambda^2 - \text{tr}(A)\lambda + |A| = 0$$

$\lambda^2 + 4 = 0 \Rightarrow \lambda = \pm 2i$.The system has a pair of purely complex-conjugate eigenvalues $\lambda_1 = 2i$ and $\lambda_2 = -2i$, hence the critical point of this system is a centre. The portrait for this system is displayed in the figure below.

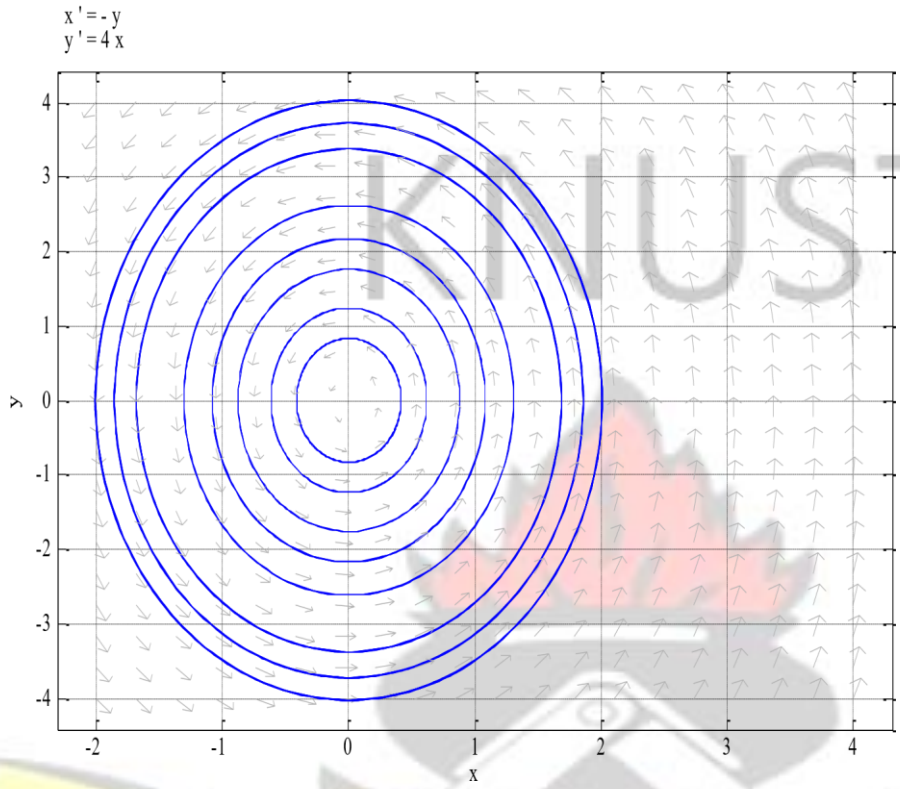


Figure 3.7: Phase Portraits of a (stable) centre generated using dfield8 and pplane8 from Matlab with the x-axis, □4 □ x □ 4and the y-axis,□4 □ y □ 4 and the x□ □ □y and y□ □

4*x* **3.7 Deterministic Models**

These are mathematical models in which no randomness or noise is involved in the development of future states of the system. They are normally represented in the form of ordinary differential equations (ODE's). They always produce output from given sets of initial conditions or initial states.

3.8 The Basic Reproduction Number or Ratio, R_0

The basic reproduction number is one of the most important threshold parameters for many epidemiological models which—in the deterministic limit—dictates whether a newly invading pathogen will cause a disease outbreak (Anderson, May, 1991). It is defined as the average number of new infections produced when a single infected individual is introduced into a completely susceptible host population of individuals (Frazer et al, 2011).

The parameter provides significant insight into the transmission dynamics of a disease and can guide strategies to control its spread (Dietz, 1993). Thus, the basic reproduction number is considered as the threshold quantity that determines the initial spread and persistence of a disease in a new host population.

If $R_0<1$, then one infected individual introduced into the population will die, without not being able to replace themselves by new infection. On the other hand, if $R_0 > 1$, there will be cholera outbreak.

For one infected subdivision of the population, R_0 is simply the product of the infection rate and the mean duration of the infection. However, for more complicated models with several infected compartments, this parameter is found by investigating the stability of the disease free equilibrium.

3.9 Exponential Population Growth Model

This is a simple continuous model of growth of a single population. It is most often suitable for modeling populations of organisms with many more resources available to them than they are able to use. In this model, we make the following assumptions:

- The rate of growth of the population is proportional the size of the population, P.
- The population is closed, that is, it ignores immigration and emigration and therefore we focus only on births (B) and deaths (D).
- The population increases if birth rate is higher than death rate.
- The population decreases if death rate is higher than birth rate.

The population size changes therefore changes according to:

$$\frac{dP}{dt} \propto P$$

$$\frac{dP}{dt} = rP$$, where r is the per capita growth rate.

$$\frac{dP}{dt} = rP$$

$$\frac{dP}{P} = r\,dt$$

Integrating both sides of the equation, we get:

$$\int \frac{dP}{P}$$

$\int \frac{1}{P}\,dP = \int r\,dt$

$\ln P = rt + C$

$P = e^{rt + C} \qquad P = e^{rt} e^{C}$

$P = A e^{rt}$, where $A = e^{C}$ conatant Initial conditions: $P(0) = P_o$, substituting this into the equation, yields $A = P_o$

$$P = P_o e^{rt} \tag{3.10}$$

Now, as $t \to \infty$, populations experiencing exponential growth increase without bound if $r > 0$ and will decay if $r < 0$.

3.10 Logistic Population Growth Model

This growth model considers that birth and birth rates are density dependent, resulting in a maximum population size called carrying capacity (K), instead of a constant per capita growth rate. Because of the density dependence, this type growth is a more suitable model than the exponential growth for many populations, since no population experiences unlimited resources or space. We write the net birth and death rates r_b and r_d in terms of a linear combination density

dependent birth and death rates, denoted by B_o and D_o, and density dependent rates, bP and dP. That is:

$r_b = B_o - bP$; $r_d = D_o - dP$

As the population increases, the birth rate decreases while the death rate increase. For the population to exist, it required that $B_o > D_o$. From the exponential growth model,

$$\frac{dP}{dt} = rP, \quad r = r_b - r_d$$

$$\frac{dP}{dt} = (r_b - r_d)P = r_b P - r_d P$$

$$\frac{dP}{dt} = (B_o - bP)P - (D_o - dP)P$$

$$\frac{dP}{dt} = (B_o - D_o)P - (bP - dP)P$$

$$\frac{dP}{dt} = (B_o - D_o)P\left[1 - \frac{(b_o - d)P}{B_o - D_o}\right]$$

Setting $\sigma = B_o - D_o$, $K = \frac{B_o - D_o}{b - d}$ and setting $b = d$, we obtain:

$$\frac{dP}{dt} = \sigma P\left[1 - \frac{P}{K}\right] \qquad (3.11)$$

Equation (3.11) is called **logistic equation.**

3.11 Deterministic SIRB Cholera Model

These models are different from vector-borne models (Ross, 1908; Macdonald, 1952) in that the pathogen can stably persist in reservoirs, leading to distinct mechanisms of disease emergence. These are models in which transmission occurs through contact with reservoirs containing human pathogens, and not through direct person-to-person contact. Mathematical modeling of cholera epidemics follows the usual compartmental-based models (Codeço, 2001; Coelho, 2006). We make the following assumptions:

- The total human population, denoted as N, is conserved
- Transmission occurs through contact with reservoirs containing human pathogens, and not through direct person-to-person contact.
- Susceptible individuals are disease free and assumed to have no immunity.
- The recruitment rate into the susceptible class is given by, $A = \mu N$, which could include immigrants and /or new borns that are unaffected. μ (day^{-1}) is the per capita human death rate, $\frac{1}{\mu}$ is the average lifespan of individuals in the total population. η is the per capita cholera related death rate (day^{-1})
- Once susceptible individuals become infected, they immediately become symptomatic and infectious.

- The contact rate,α to the reservoir is identical for every individual; the minimum infectious dose (MID) can be re-scaled as a threshold pathogen density for infection.
- If the in-reservoir pathogen density is above the MID, susceptible individuals contact more pathogens than the infectious dose and become infected.
- Infected individuals shed the pathogens back to the reservoir at a fixed rate,

  δ (day^{-1}) $= \frac{\phi}{W}$, ϕ is the rate at which bacteria produced by infected person reach and terminate in a water reservoir of volume W, increasing the possibility of susceptible individuals contracting the disease.

- The incidence, which determines the rate of new infection, is represented by:

  $\frac{\alpha\theta(B)}{k + B}$, where $\theta(B)$ (cell litre^{-1} day^{-1}) is logistic dose response, α (day^{-1}) is the contact rate with contaminated food and water and k is the halfsaturation concentration(cell litre^{-1}) (i.e.,MID50, the minimum infectious dose in water sufficient to produce disease in 50% of those exposed).

- Free-living vibrios reproduce in water/food, the natality rate isσ (day^{-1}) and mortality rate is ν (day^{-1}), so the net loss rate of vibrios is$n_B = \nu - \sigma$
- The rate at which infected individuals recover from cholera is γ (day^{-1})
- The growth of pathogen is excellently fitted using logistic equation (Britton, 2003).

μ μ

η μ

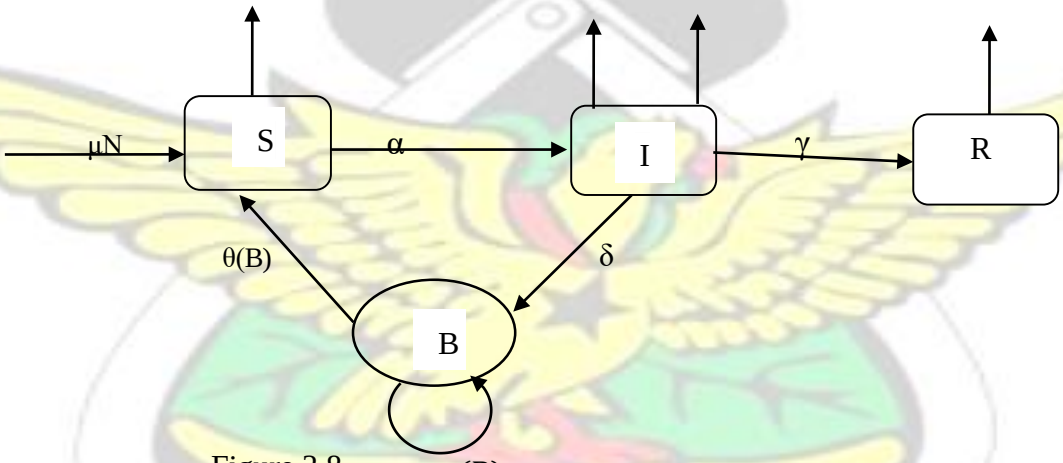


Figure 3.8

Figure 3.8 shows the schematic representation of the influx between the four compartments of population denoted as the susceptible (S), the infected (I), and the recovered (R) and the pathogen density in the reservoir is denoted as B. The model is called SIRB-Susceptible, Infected and Pathogen density. The model is represented by the following sets of differential equations:

dS

dt μN αθ(B)S μS

$$\frac{dI}{dt} = \alpha\theta(B)S - \mu I - \eta I - \gamma I$$

$$\frac{dR}{dt} = \gamma R - \mu R \qquad (3.12)$$

$$\frac{dB}{dt} = \pi(B) - \delta I$$

$$S(0) = S_0 > 0 \quad ; \quad I(0) = I_0 > 0 \quad ; \quad R(0) = R_0 > 0 \quad ; \quad B(0) = B_0 > 0$$

$$S + I + R = N \quad ; \quad \pi(B) = \sigma B\left(1 - \frac{B}{K}\right) - \nu B,$$

where $\pi(B)$ is the growth dynamics of pathogen), is the natural in-reservoir growth rate of pathogens in the absence of human hosts. Since $\frac{dS}{dt} + \frac{dI}{dt} + \frac{dR}{dt} = 0$, the total human population denoted as N, is conserved. An equation for R is superfluous here since N = S + I + R is constant, thus, $R = N - S - I$, and we now focus on S, I and B model.

Substituting and simplifying equation (3.12) becomes:

$$\frac{dS}{dt} = \mu(N - S) - \alpha\frac{B}{k + B}S \qquad (1)$$

$$\frac{dI}{dt} = \alpha\frac{B}{k + B}S$$

$$\frac{dI}{dt} = \alpha \frac{B}{k+B} S - (\mu + \eta + \gamma) I \qquad (2) \qquad (3.13)$$

$$\frac{dB}{dt} = \sigma B\left(1 - \frac{B}{K}\right) - \nu B + \delta I \qquad (3)$$

$S(0) = S_0 \geq 0$; $I(0) = I_0 \geq 0$; $B(0) = B_0 \geq 0$

Equation 1 of (3.13) describes the dynamics of the susceptible individuals in the community with size N. Equation 2 of (3.13) describes the dynamics of the infected people in the community. Infected people increase as the susceptible individuals increase and their number decrease as they recover or die as of cholera disease. Also, measures to curtail the disease such as hygiene and total sanitation indirectly affect infections.

Equation 3 of (3.13) talks about the dynamics of the toxigenic bacteria in the environment comprising, the contaminated food or water consumed by people.

3.12 Equilibrium Points and Stability Analysis

Equilibrium analysis gives the fixed points, or equilibrium solutions, the values or state variables for which the system remains unchanged. At that time the rates of change are equated to zero. On the other hand, local equilibrium analysis is useful in determining the equilibrium solutions. To analyze the stability of the system around the equilibrium, we linearize the system around equilibrium points, which we obtained from the Jacobian matrix of the system and determine the eigenvalues of the system. We make the following notation:

B

$$X(S,I,B) = \mu(N - S) - \alpha \frac{S}{k + B}$$

$$Y(S, I,B) = \alpha \frac{B}{k + B} S - (\mu + \eta + \gamma)I$$

$$Z(S,I,B) = \sigma B\left(1 - \frac{}{K}\right) - \nu B - \delta I$$

The Jacobean matrix of the system is computed as follows:

$$J(S, I ,B) = \begin{bmatrix} \frac{\partial X}{\partial S} & \frac{\partial X}{\partial I} & \frac{\partial X}{\partial B} \\ \frac{\partial Y}{\partial S} & \frac{\partial Y}{\partial I} & \frac{\partial Y}{\partial B} \\ \frac{\partial Z}{\partial S} & \frac{\partial Z}{\partial I} & \frac{\partial Z}{\partial B} \end{bmatrix}$$

$$J(S, I, B) = \begin{bmatrix} -\mu - k\alpha B - B & 0 & -\frac{(k\alpha BS - B)_2}{} - \frac{k\alpha S - B}{} \\ k\alpha B - B & -(\mu + \eta + \gamma) & \frac{(k\alpha BS - B)_2}{} - \frac{k\alpha S - B}{} \\ \alpha B & 0 & \delta \quad \sigma - \frac{2}{K} - \nu \end{bmatrix}$$

When there are no *Vibrio cholerae* bacteria in the community, B = 0, nobody is infected, I = 0 and the population remains S = N. The community matrix becomes cholera-free at the point E_o (S_0,I_0,B_0) = (N,0,0). This point is referred to as the Disease-Free Equilibrium (DFE). All the individuals are susceptible. There are neither infective nor immune individuals nor toxigenic bacteria in the reservoir.

At the disease free equilibrium, S = N, I = B = 0, equation 1of (3.13) becomes linear

differential equation: $\frac{dS}{dt} = \mu(N - S) - \alpha \frac{BS}{k + B} \Rightarrow \frac{dS}{dt} = \mu(N - S)$

The expected population size at this state is given by the solution of:

$$\frac{dS}{dt} = \mu(N - S)$$

$$\Rightarrow \int \frac{dS}{(N - S)} = \int \mu dt$$

$$\Rightarrow -\ln(N - S) = \mu t + C$$

$$\Rightarrow N - S = e^{-\mu t - C}$$

$$\Rightarrow S = N - Ae^{-\mu t}$$

Initial condition: $S(0) = S_0$, putting this into the above equation yields:

$$S_0 = N - A \Rightarrow A = N - S_0$$

$$\Rightarrow S(t) = N + (S_0 - N)e^{-\mu t} \tag{3.14}$$

Where S_0 is the initial number of susceptible individuals. Now as t □□, S □ N, which is the asymptotic population size. Thus, the population will consist of only susceptible individuals.

We now compute the Jacobian matrix at the DFE, E_o (S_0, I_0, B_0) = (N, 0, 0)

□□□μ —0— □ αN□□ □□□μ 0 □ αNk □□ k —

$_0$□ □ □ μ □ η□ γ) —□ □ □ μ □ η□ γ) —□ k

□ δ δ □

□ 0 k □ ^{0}□ □□ □(ν □σ)□

□□ σ □ ν□ □ 0 □□

□□ □□

□ αN □ □ αN □ J 0 (J 0 (

J_o a block matrix with a down-left zero block, the first eigenvalue of J_o is given by λ_1 □□μ and because the parameter μ is positive,λ_1 is negative. Now we focus on the down right block from J_o which we denote as J_{dr}. This block is a two dimensional system so we apply the corresponding Routh-Hurwitz criteria.

Theorem: Let A be a 2 × 2 matrix with real eigenvalues λ_1 and λ_2.The eigenvalues are negative if the following conditions are held.

(a) det(A) > 0 (b) tr(A) < 0

Now

$$J_{dr} = \begin{bmatrix} -(\mu+\eta+\gamma) & \alpha N \\ k & -n_B \end{bmatrix} \quad \text{Applying the above Theorem on } J_{dr} \text{ we obtain the following inequalities:}$$

$$\det(J_{dr}) = n_B(\mu+\eta+\gamma) - \frac{\alpha\delta N}{k} > 0 \qquad (3.15)$$

$$tr(J_{dr}) = -n_B(\mu+\eta+\gamma) < 0 \qquad (3.16)$$

Remember that μ, η, γ and k are all positive parameters and n_B is positive; (3.15) is always true.

We now consider (3.16)

$$n_B(\mu+\eta+\gamma) - \frac{\alpha\delta N}{k} > 0$$

$$n_B(\mu+\eta+\gamma) < \frac{\alpha\delta N}{k}$$

$$\frac{n_B k(\mu+\eta+\gamma)}{\alpha\delta} < N$$

$$\frac{n^B k(\mu+\eta+\gamma)}{} \qquad (3.17)$$

Let $S_C = \alpha\delta$

$$-S_C < N \qquad N > S_C \qquad (3.18)$$

This then gives the condition for a transition between the systems being in a disease free state to an endemic or epidemic state. This implies that the human population must have a minimum size for an endemic state to persist. This minimum size is determined by the biological parameters for the survival of the bacteria, contact between humans and bacteria, as well those determining the infectiousness and virulence of the disease. Conversely, we can use this information to determine if a population of a given size could support endemic cholera, given these parameters.

The DFE, (N, 0, 0) is asymptotically stable if $N > S_C$. S_C is the critical population size of *Vibrio* cholerae which will lead to an epidemic outbreak if the population size is greater than the threshold. I does not appear in the expression for S_C so the danger of an outbreak is not influenced by the number of infected individuals arriving in a new locality, but only the population size in relation to various attributes of the food or water supply. It controls the process of the dynamics in the system. If the population size is less than the critical threshold, the infected population will decrease to zero. This may seem counterintuitive, but it is the direct consequence of the way the models are constructed.

$$n_B(\mu + \eta + \gamma) > \frac{\alpha\delta N}{0\ k}$$

If the above inequality is satisfied, then the DFE will be asymptotically stable. The disease dies out with time. That is, if the rate of exposure of people to contaminated water or food and the rate of contribution of infested *Vibrio cholerae* is less than the concentration of *Vibrio cholerae* in the reservoir that yields 50% chance of catching cholera, then the DFE becomes asymptotically stable.

The basic reproduction number,R_o can be deduced from (3.15) as follows:

$$n_B(\mu + \eta + \gamma) \geq \frac{\alpha\delta N}{k} \geq 0$$

$$n_B k(\mu + \eta + \gamma) \geq \alpha\delta N \geq 0$$

$$n_B k(\mu + \eta + \gamma) \geq 1 \geq 0 \quad \alpha\delta N$$

We define $R_o \geq \frac{\alpha\delta N}{n_B k(\mu + \eta + \gamma)} \geq \frac{1}{R_o} \geq 1 \geq 0 \quad \geq R_o \geq 1$ (3.19)

Hence $R_0 < 1$, the DFE is locally asymptotically stable. If the rate at which people are exposed to contaminated food and water, and the shedding of *Vibrio cholerae* to the aquatic environment are checked, *Vibrio cholerae* population becomes asymptotically stable. Thus, if R_0 is less than unity, *Vibrio cholerae* dies out and the DFE will be locally asymptotically stable. It is crystal clear to establish that when$R_0 \geq 1$, all the three eigenvalues are negative; DFE is asymptotically stable; when $R_0 \geq 1$, we have threshold condition. But cholera becomes endemic whenever$R_0 \geq 1$, over a long period of time.

The DFE becomes unstable, and there is a unique positive endemic equilibrium X^* which is locally asymptotically stable.

3.12.1 Critical Population Size (S_C) and Basic Reproduction Number (R_o) We can also deduce the relationship between S_C and R_o as follows:

$$S_C = \frac{n_B k(\mu + \eta + \gamma)}{\alpha\delta N}; \quad R_o = \frac{\alpha\delta N}{n_B k(\mu + \eta + \gamma)}$$

$$R_o = \frac{\alpha\delta N}{n_B k(\mu + \eta + \gamma)} \qquad S_C$$

3.12.2 Existence of Endemic Equilibrium

This is the state under which all three epidemiological classes coexist in equilibrium. The endemic equilibrium is obtained by setting the right-hand side of the system of equations (3.13) to zero as follows:

$$\begin{cases} \frac{dS}{dt} = \mu(N - S) - \alpha\frac{B}{k + B}BS \\ \frac{dI}{dt} = \alpha\frac{B}{k + B}S - (\mu + \eta + \gamma)I \\ \frac{dB}{dt} = \sigma B\left(1 - \frac{B}{K}\right) - \nu BI - \delta I \end{cases} \tag{3.13}$$

$$\frac{dS}{dt} = \mu(N - S) - \alpha\frac{B}{k + B}BS = 0 \Rightarrow (\mu + \alpha\frac{B}{k + B})S = \mu N$$

$$\square S \square \mu N \frac{(k \square B)}{\mu(k \square B)\square \alpha B} \quad (1a)$$

$$S^{\square}\square \frac{\mu N(k_{\square} \square B_{\square})_{\square}}{\mu(k \square B)\square \alpha B} \quad (1b)$$

$$\frac{dI}{} \square \alpha S\square(\mu \square \eta\square \gamma)I \square 0\square I \square \frac{B}{B\square H(k \square B)(\mu \square \eta\square \gamma)} \quad (2a)$$

$$\text{Hence } I^{\square}\square \frac{\alpha B_{\square}\square S\square}{(k \square B)(\mu \square \eta\square \gamma)} \quad (2b)$$

Combining (1) and (2), we obtain:

$$I \square \frac{(k \square B)\alpha B\mu N}{\mu(k \square B)\square \alpha B \square \mu B \square \alpha N} \quad (3a) \quad \frac{(k \square B)(\mu \square \eta\square \gamma)}{(\mu(k \square B)\square \alpha B)(\mu \square \eta\square \gamma)}$$

$$\frac{dB}{dt} \square \sigma B(1\square \frac{B}{K})\square \nu B\square \delta I \square 0 \quad (3a \text{ of } 3.13)$$

Substituting (3) into this, we have;

$$\sigma B(1\square \frac{B}{K})\square \nu B\square \delta\square \frac{\alpha\mu BN}{(\mu(k \square B)\square \alpha B)\square(\mu \square \eta\square \gamma)} \square 0$$

$$\square \sigma(1\square \frac{B}{K}) \square \nu \square \frac{\mu}{(\mu(k \square B) \square \alpha B)} \square \frac{\alpha\delta N}{(\mu \square \eta\square \gamma)} \square 0$$

□ σ(K □ B) □ νK□ $\frac{\mu K}{(\mu(k \square B) \square \alpha B)} \square \frac{\alpha\delta N}{(\mu \square \eta \square \gamma)} \square 0$

□ (σ□ ν)K□σB□ $\frac{\mu K}{(\mu(k \square B) \square \alpha B)} \square \frac{\alpha\delta N}{(\mu \square \eta \square \gamma)} \square 0$

But $R_o \square \frac{\alpha\delta N}{n_B k(\mu \square \eta \square \gamma)}$ and $n_B \square \nu \square \sigma$

□□n_BK□σB□ $\frac{\mu n_B R_o kK}{(\mu(k \square B) \square \alpha B)} \square 0$ □$(n_B K \square \sigma B)(\mu(k \square B) \square \alpha B) \square \mu n_B R_o kK \square 0$

Expanding and simplifying, we obtain:

$\sigma(\mu \square \alpha)B^2 \square((\mu \square \alpha)n_B K \square \sigma\mu k)B \square \mu n_B k R_o K \square 0$

$\square B_2 \square \frac{((\mu \square \alpha)n_B K \square \sigma\mu k)B}{\sigma(\mu \square \alpha)} \square \frac{\mu n_B k R_o K}{\sigma(\mu \square \alpha)} \square 0 \quad \square B^{*2} \square bB^* \square c \square 0$ (3b)

a □1 ; b □ $\frac{((\mu \square \alpha)n_B K \square \sigma\mu k)}{\sigma(\mu \square \alpha)}$; $c \square\square \frac{\mu n_B k R_o K}{\sigma(\mu \square \alpha)}$

For endemic equilibrium, I > 0. Thus,

□ αB□S□ □□ □ □

I □ ________________ □ 0 □ αB S □ 0 □ B □ 0 or S □ 0 (k □
B)(μ □ η□ γ)

Hence the endemic equilibrium is given as $E(S^*, I^*, B^*)$.

The solution to the quadratic equation (3.13 of 4) gives the endemic equilibrium of the pathogen of the system. If the natality rate of *Vibrio cholerae* is greater than the mortality rate, then cholera will be endemic. But if the loss rate or mortality rate is perpetually greater than its production rate, then as t tends to infinity *Vibrio cholerae* population will eventually reduce to an asymptotic size and there will not be a threat (epidemic). Thus, the endemic equilibrium is represented by the pathogen density in the reservoir.

CHAPTER FOUR

MODELING AND SIMULATION

4.1 Introduction

In this chapter, we will fit the parameter values into the model and then determine the stability of the equilibrium points. Also, we will implement numerical simulations of the models to explore the behavior of the models.

4.2 The Cholera Deterministic Model Formulation

The parameter values such as mortality and recovery rates were taken from CIA World Factbook (demographic statistics) and Ghana Health Service; other parameter values, such as contact(exposure) rate, mortality rate (*Vibrio cholerae*), shedding rate, net growth rate (*Vibrio cholerae*), semi-saturation concentration and carrying capacity of *Vibrio cholerae*

were obtained from Codeço, 2001 and Grad et al, 2012. Some were estimated as shown in table (4.1) below. These parameter values were fitted into our model in order to determine the equilibrium points.

Table 4.1: Table of parameter values

Description	Symbol	Parameter Value	Source
Population Size	N	27002	(Demographics, 2011) (Dormaa-Ahenkro, Ghana)
Birth and death rate	μ	$5\square10^{\square5}$	CIA World Factbook (Estimated)
Contact rate	α	Variable($10^{\square5}$ - 1)	(Grad et al., 2012)
Cholera related death rate	η	0.033	(Hartley, 2006) (Estimated)
Recovery rate	γ	0.17	Presby Hospital (Estimated) (Dormaa-Ahenkro)
Shedding rate	δ	Variable(0.01-10)	(Grad et al., 2012)
Growth rate(*Vibrio cholerae*)	σ	0.30	(Codeço, 2001)
Loss rate(*Vibrio cholerae*)	ν	0.63	(Codeço, 2001)
Semi-saturation concentration	k	10_6	(Grad et al., 2012)
Carrying capacity (*Vibrio cholerae*)	K	10_8	(Cash et al., 1974; Levine et al., 1988)

4.2.1 Estimation of some Parameter Values

Infected individuals have a mean lifetime of 30 days, hence, the per capita cholera related death rate, $\eta = \frac{1}{30} = 0.033 \text{ day}^{-1}$. The actual mean lifetime for the disease throughout the population varies from 3 to 6 days. Hence, the rate at which infected individuals recover from cholera is given as $\gamma = \frac{1}{3} = 0.33 \text{ day}^{-1}$ to $\frac{1}{6} = 0.17 \text{ day}^{-1}$ (Grad et al., 2012).

The average lifespan of individuals in the total population is 55 years or 20075 days (Ghana Statistical Service, 2011, Dormaa-Ahenkro). Hence the natural mortality rate of individuals in the population is $\mu = \frac{1}{20075} = 5 \times 10^{-5} \text{ day}^{-1}$.

4.2.2 Evaluation of the Critical Population Size, S_C and the basic Reproduction Number, R_o

Suppose that we take $\alpha = 1$ and $\delta = 10$, we obtain the following:

$$S_C = \frac{n_B k(\mu + \eta + \gamma)}{\alpha\delta}$$

$$S_C = \frac{(0.33)(1\times10^{6})(5\times10^{-5} + 0.033 + 0.17)}{(1)(10)} = 6700.65 = 6701 = 27002$$

Also, $R_o = \frac{\alpha\delta N}{n_B k(\mu + \eta + \gamma)} = \frac{N}{S_C}$

$$R_o = \frac{27002}{6701} = 4.03 > 1$$

Since the critical population size, $S_C = 6701$ is less than the population size, N =27002 and the basic reproduction number $R_o = 4.03$ is greater than unity, then the disease-free equilibrium (DFE) is unstable, and there exists a unique positive endemic equilibrium which is locally asymptotically stable. Hence, if $\alpha = 1$ and $\delta = 10$, there will be cholera outbreak in the community.

Assuming $\alpha = 0.5$ and $\delta = 10$

$$S_C = \frac{n_B k(\mu + \eta + \gamma)}{\alpha\delta}$$

$$S_C = \frac{(0.33)(1\times10^6)(5\times10^{-5} + 0.033 + 0.17)}{(0.5)(10)} = 13401.1 \approx 13401 < 27002$$

Also, $R_o = \frac{\alpha\delta N}{S_C} = \frac{N}{13401} = \frac{27002}{13401} = 2.01 = \frac{n_B k(\mu + \eta + \gamma)}{}$

Also, the estimated critical population size, $S_C = 13401$ is less than the population size, N =27002 and the basic reproduction number $R_o = 2.01$ is greater than unity, therefore, the disease-free equilibrium (DFE) is unstable, and there exists a unique positive endemic equilibrium which is locally asymptotically stable. Hence, if $\alpha = 0.5$ and $\delta = 10$, there will be cholera outbreak in the community.

If we further reduce the contact rate, $\alpha = 0.24$, and take $\delta = 0.01$, we obtain

$S_C \approx 279200$ and $R_o \approx 0.097$, which is less than unity. Therefore, the disease-free equilibrium (DFE) becomes stable, which is locally asymptotically stable. Hence, if $\alpha \approx 0.24$ and $\delta \approx 0.01$, the community will be cholera-free. It can be noticed that if we reduce the contact rate to its lowest level, the system becomes globally asymptotically stable

4.2.3 Equilibrium Points of the Deterministic Model

In order to determine the equilibrium points of the deterministic cholera model, we fit the parameter values into the deterministic cholera model equations (3.13). Thus, we substitute the parameter values into the following equations for S^*, I^* and B^* to determine critical points.

$$S^* = \frac{\mu N (k + B^*)}{\mu(k + B^*) + \alpha B^*}$$

$$I^* = \frac{(k + B)\alpha B^* S^*}{(\mu + \eta + \gamma)}$$

$$B^{*2} + bB^* + c = 0$$

$$a = 1 \; ; \; b = \frac{((\mu+\alpha)n_B K+\sigma\mu k)}{\sigma(\mu+\alpha)} \; ; \; c = \frac{\mu n_B k K + \mu n_B k R_o K}{\sigma(\mu+\alpha)}$$

For endemic equilibrium, $I^* > 0$. Thus,

$$I^* = \frac{(k \quad B\alpha B^*)(\mu^* S^* \eta \gamma)}{} = 0 \quad \alpha B^* S^* = 0 \quad B^* = 0 \text{ or } S^* = 0$$

Substituting the parameter values in table (1), for $\alpha = 1$, we obtain:

$$b = \frac{((5\times10^{-5}+1)(0.33)(1\times10^{8})+(0.30)(5\times10^{-5}))(1\times10^{6})}{(0.30)(5\times10^{-5}+1)} = 1.1\times10^{8}$$

$$c = \frac{\mu n_B kK - \mu n_B kR_o K}{\sigma(\mu + \alpha)} = \frac{(5\times10^{-5}\times0.33\times10^{6}\times10^{8})(1-4.03)}{0.30(5\times10^{-5}+1)} = -1.67\times10^{10}$$

$$B^* = \frac{-b \pm \sqrt{b^2 - 4ac}}{2a}$$

$$\Rightarrow B^* = \frac{-1.1\times10^{8} \pm \sqrt{(1.1\times10^{8})^2 - 4(1)(-1.67\times10^{10})}}{2(1)}$$

$$\Rightarrow B^* = \frac{-1.1\times10^{8} \pm 1.1\times10^{8}}{2} \Rightarrow B^* = 0 \text{ or } B^* = -1.0\times10^{8}$$

Substituting $B^* = 0$ into (1) and (3) yield:

$S^* = 27002$ and $I^* = 0$; $B^* = -1.1\times10^{8}$ is not biologically feasible. Hence the endemic equilibrium condition is given by $E^*(S^*, I^*, B^*) = E^*(27002,0,0)$. This is analogous to the disease-free equilibrium which means there is a disease-free state. We will now focus our attention to the stability analysis of the disease free-state.

4.2.4 Stability Analysis of the Deterministic Cholera Model at the Disease-Free State The

Jacobian Matrix of the system is given by:

$$J(S, I, B) = \begin{bmatrix} -\mu - k - \alpha B & -\frac{\alpha BS}{(k+B)^2} - \alpha S \\ 0 & \frac{\alpha BS}{(k+B)^2} - (\mu + \eta + \gamma) - \frac{\alpha S}{k+B} \\ 0 & \delta \end{bmatrix}$$

$$J(E_o) = \begin{bmatrix} -5\times10^{-5} & -0.027002 \\ 0 & -0.20305 \end{bmatrix}$$

$$J_{dr} = \begin{bmatrix} -0.20305 & -0.027002 \\ 10 & -0.33 \end{bmatrix}$$

Since $J(E_o)$ is a block matrix with a down-left zero block, the first eigenvalue is $\lambda_1 = -5\times10^{-5}$. We now focus on the down-right block, J_{dr} and determine the other eigenvalues as follows:

The above system has eigenvalues satisfying $|J_{dr} - \lambda I| = \lambda^2 - tr(J_{dr})\lambda + |J_{dr}| = 0$

$\lambda^2 - 0.53305\lambda - 0.2030135 = 0$

The eigenvalues are given as $\lambda_2 = 0.25697168$ and $\lambda_3 = -0.79002197$. Since one of the three eigenvalues of the disease-free equilibrium (DFE) is positive, then DFE (27002, 0, 0) is unstable. This means that *Vibrio cholerae* exists and the disease-free state becomes unstable.

4.3 Analysis of the Logistic Cholera Model

Let $f(B) = \frac{dB}{dt} = \sigma B\left(1 - \frac{B}{K}\right) - \nu B$, then $f'(B) = \frac{d}{dB}\left(\frac{dB}{dt}\right) = \sigma - 2\left(\frac{\sigma B}{K}\right) - \nu$. The logistic model for the pathogen density B is given as $\frac{dB}{dt} = \sigma B\left(1 - \frac{B}{K}\right) - \nu B$. This equation can be solved by separation of variables, but it is not necessary to do so in order to understand the behaviour of its solution. The steady states or equilibrium solutions are obtained by setting $\frac{dB}{dt} = 0$ and solving for B: $0 = \sigma B\left(1 - \frac{B}{K}\right) - \nu B \quad \Rightarrow \quad \left(1 - \frac{B}{K}\right) - \frac{\nu}{\sigma} = 0 \quad \Rightarrow \quad B = 0$ or $\left(1 - \frac{B}{K}\right) - \frac{\nu}{\sigma} = 0 \quad \Rightarrow \quad B = K - \frac{\nu K}{\sigma} = K\left(1 - \frac{\nu}{\sigma}\right) = 10^8\left(1 - \frac{0.63}{3.7}\right) = 3.7 \times 10^7$

Now we evaluate the derivative at each equilibrium point. This gives the eigenvalue(s) at each equilibrium point. For $B = 0$: $f'(0) = \sigma - 2\left(\frac{\sigma(0)}{K}\right) - \nu = (\nu - \sigma) = n_B = -0.33 < 0$

The eigenvalue is negative and the model is stable. Also, for $B \square K(1\square \nu)$:

$$f\square(K(1\square \nu))\square \sigma \square 2\square \frac{\sigma K(1\square \nu)}{K} \square \nu \square \square(\sigma \square \nu)\square 2\sigma\nu \square \square(0.30\square 0.63) \square 2(0.30)(0.63) \square -1.308\square 0$$

The eigenvalue is negative this time too. Hence the system is stable.

The solution of the logistic cholera equation gives two negative eigenvalues, $\square 0.33$ and $\square 1.308$. This means that the logistic cholera model is stable. Hence *Vibrio cholerae* exists in the environment. The analysis (figure 4.1) of the logistic cholera equation indicates that the growth of *Vibrio cholerae* is not constant. The pathogen density decreases 450 for about 44 days and remains constant from there until 200 days as shown in the figure below.

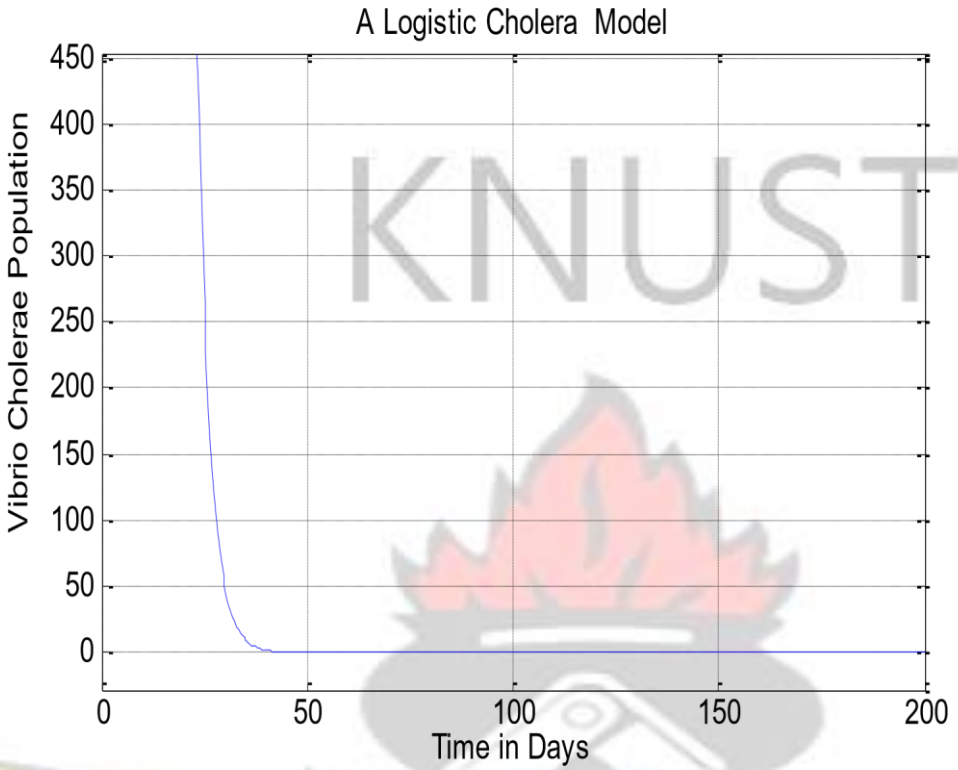


Figure 4.1: Numerical Simulation of the Logistic Equation

4.4 Numerical Simulations

Numerical simulations are very important tools for analyzing the disease progression patterns. We will obtain numerical results using MATLAB, by means of some epidemiological parameter values from table (4.1). Since outbreak of cholera epidemics depends on the exposure rate to the pathogen, it was varied while the other parameters remained unchanged for the purpose of our simulation. Hence we perform numerical simulation of the deterministic cholera model.

4.4.1 Simulations of the Deterministic Cholera Model

A numerical simulation of the deterministic cholera model (equation 3.13) was performed with parameter values,α □ 1; ν □ 0.63; σ □ 0.30; δ □ 10; k □10^6. The corresponding

critical population size, $S_C \approx 6701$and the basic reproduction number,$R_o \approx 4.03$. A plot of S, I, B against time yielded by the simulation is displayed in Figure 4.2(a). We observe from the figure that infection lasted for about 118 days. It started after about 40 days and ended after about 158 days. The number of infected individuals reach a peak value of about 3300 (representing approximately 12 percent). The bacteria population increased steadily from zero (0) to about 51000 and declined to zero (0). The number of susceptible individuals declined gradually from 27002 to constant value of about 5000 and remained at this value for a very long period of time.

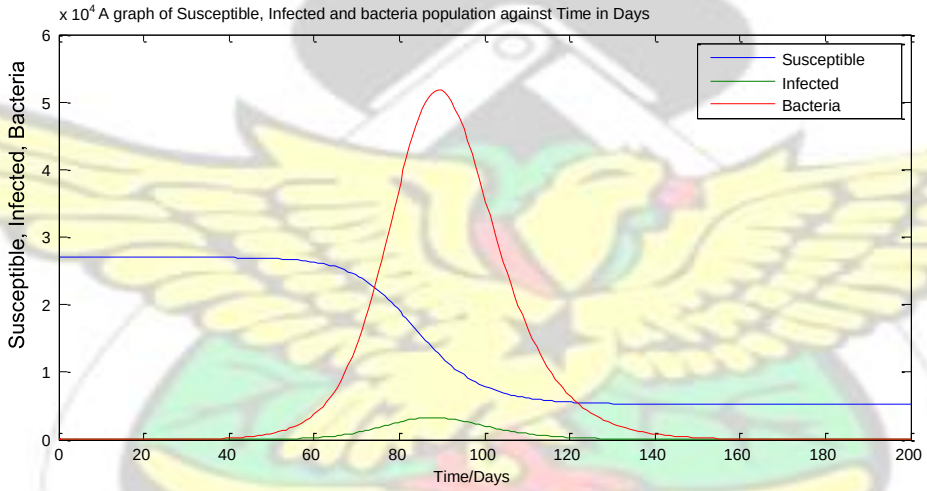


Figure 4.2(a): Indicates the numerical simulation of the susceptible, infected and bacteria density with initial conditions S(0) = 27002, I(0) = 0; B(0) = 0 and $R_o = 4.03$

The system behaved much in the same way as in figure 4.2(a), except that in figure 4.2(b), the infection started at an earlier time and ended at a time frame of about 105 days. The infection was at its peak value when the time was 40 days when the bacteria concentration

was 51000 and declined to zero and remained at zero of over a long period of time. Number of susceptible decreases and stays constant. This was as a result of the introduction of more infected individuals into the community. Other susceptible individuals were infected via contaminated water or food because they (infected people) shed the pathogen in their stool and triggered the rate of infection.

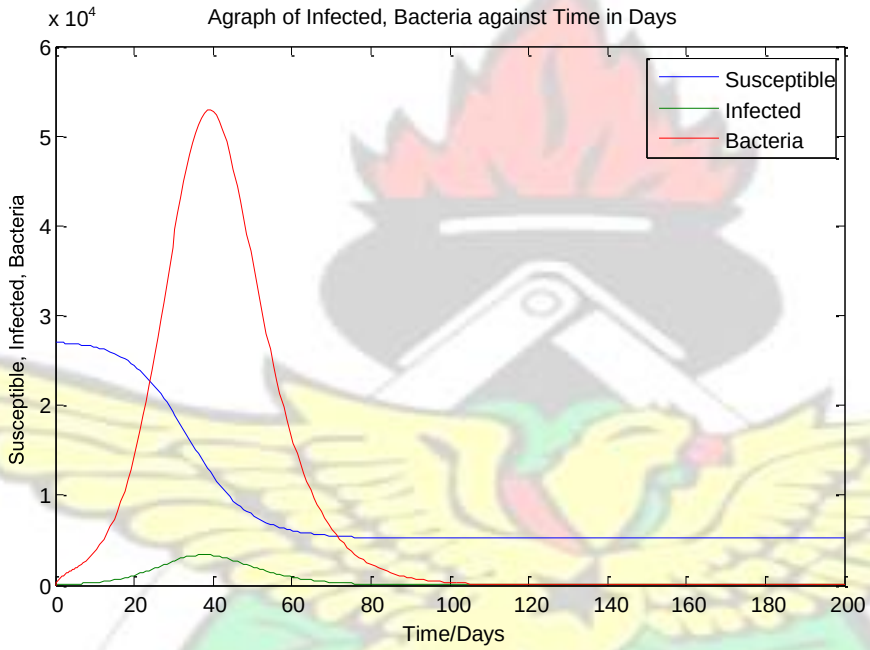


Figure 4.2(b): The numerical simulation of the susceptible, infected and bacteria density with initial conditions S(0) = 27002, I(0) = 1000; B(0) = 0 and R_o = 4.03

In figure 4.2(c), the bacteria population started decreasing from about 780 000 when the time was about zero day. It remained constant after about 35 days for a longer period of time. This suggests that the disease cholera is endemic in the environment, varying remarkably with time.

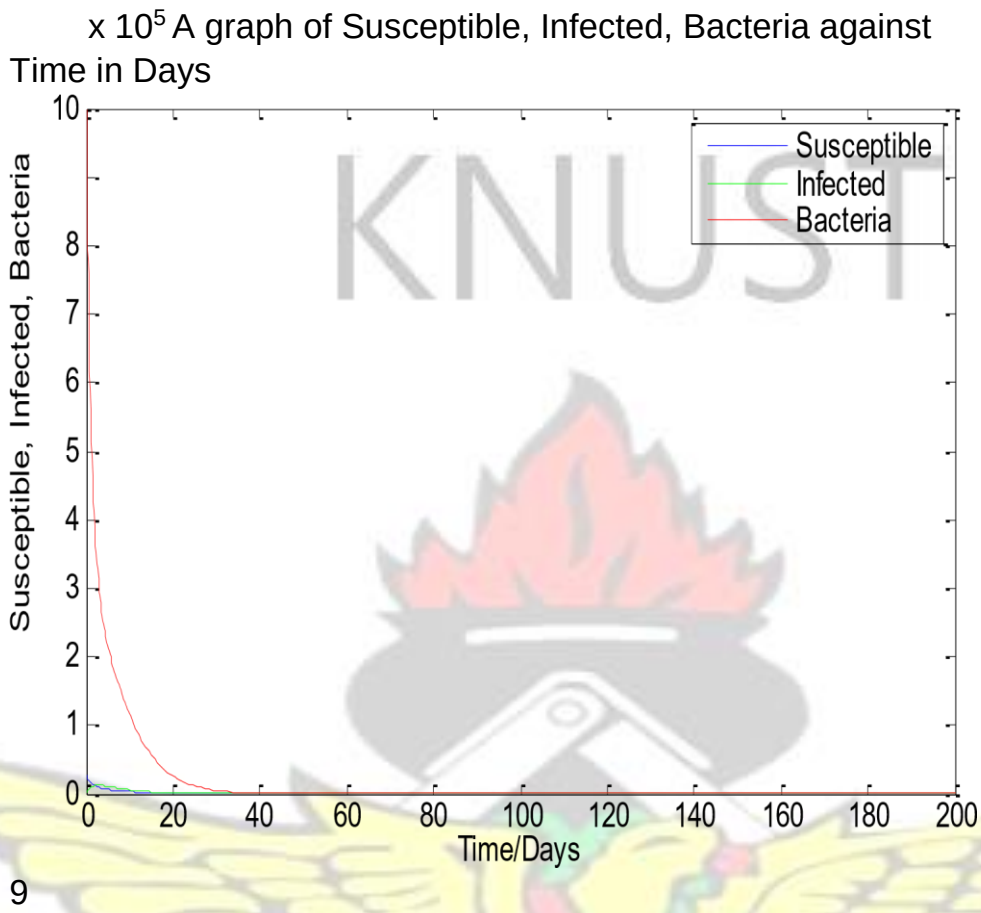


Figure 4.2(c): The numerical simulation of the susceptible, infected and bacteria density with initial conditions S(0) = 27002; I(0) = 10^3; B(0) = 10^6 and R_o = 4.03

Here (Figure 4.2(c)), the bacteria population at the start of the infection and stays constant. However, the infected population at the beginning of the epidemic, then decreases and remains constant. The susceptible population also decreases at the start of the outbreak and stays constant.

4.4.2 Simulations of the Deterministic Cholera Model with Reduced Contact Rate

A numerical simulation of the deterministic cholera model performed using different initial conditions with parameter values kept the same except for reduced contact rate α = 0.5; the corresponding critical population size, S_C = 13401 and the basic reproduction number, R_o = 2.01.

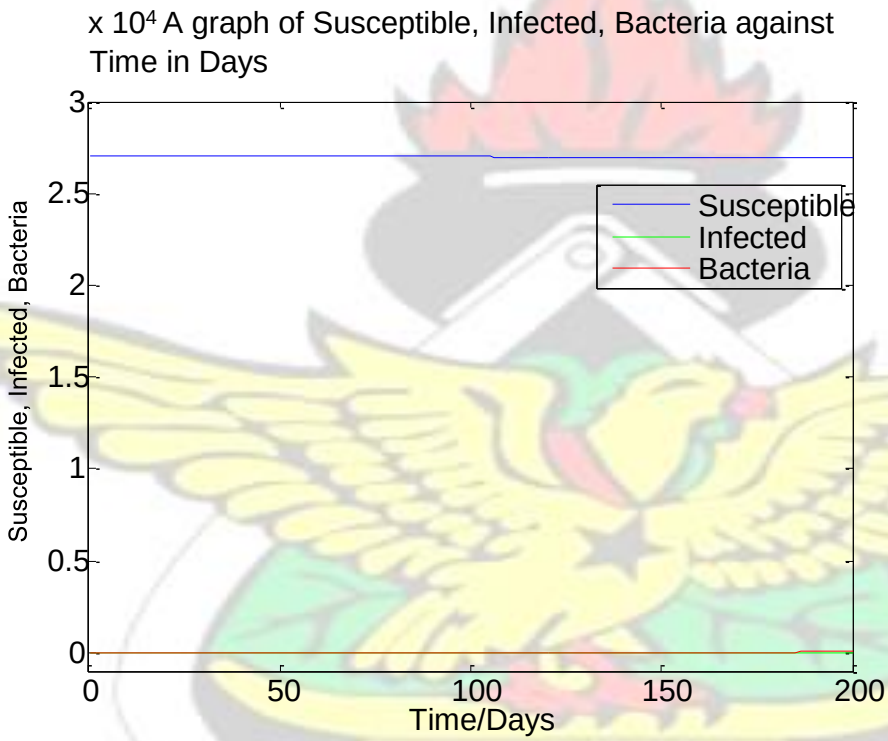


Figure 4.3(a): The numerical simulation of the susceptible, infected and bacteria density with initial conditions S(0) = 27002; I(0) = 0; B(0) = 0 and R_o = 2.01

Figure 4.3(a) show that the susceptible population remained constant for longer period of time even though there were some cases of cholera which started from about 175 days. The incidence of cholera means that *Vibrio cholerae* exists in the environment.

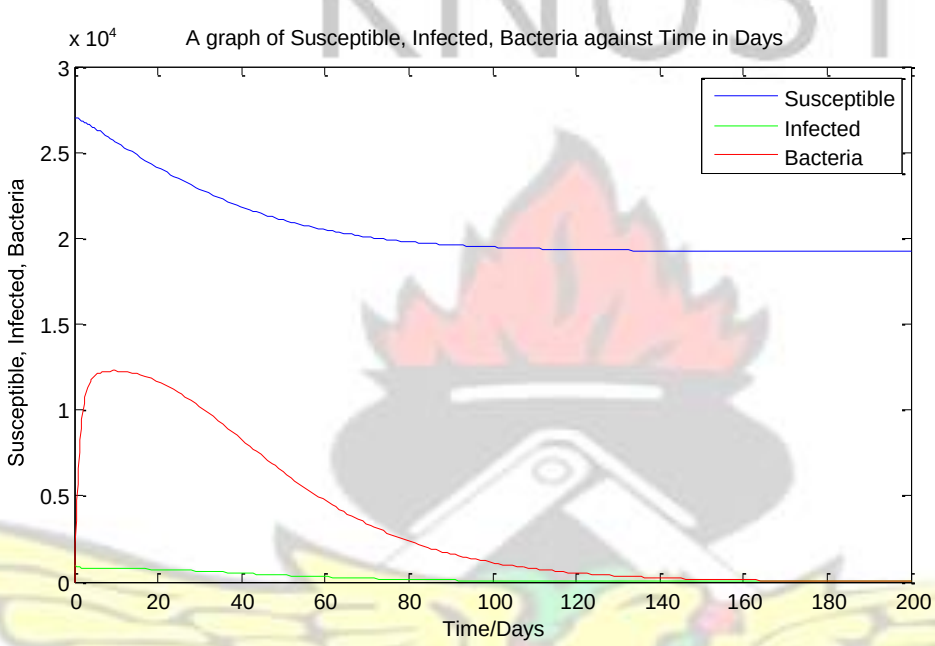


Figure 4.3(b): Numerical Simulation of SIB with reduced contact rate and initial conditions; S(0) = 27002; I(0) = 10^3; B(0) = 0.

In figure 4.3(b), the number of susceptible individuals decreased gradually and remained constant from about 100 days. The bacteria population increased from zero(0) to a peak value of about 12000. It then decreased from this value to and remained constant from about 165 days.

x 10^5 A graph of Susceptible, Infected, Bacteria against Time in Days

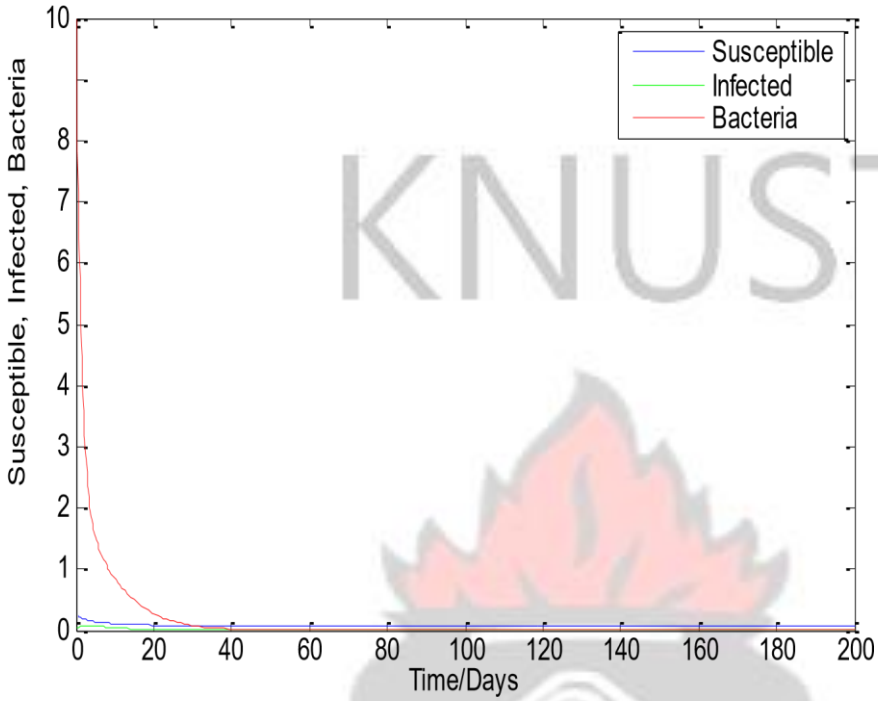


Figure 4.3(c): The numerical simulation of the susceptible, infected and bacteria density with initial conditions S(0) = 27002; I(0) = 10^3; B(0) = 10^6 and R_o = 2.01

In figure 4.3(c), the susceptible population started to decrease at the start of the infection and remained constant for a long time. It decreased for a shorter period of time. The number of the infected increased and then decreased and then stayed for 20 days and died out. The concentration of the bacteria started to decrease at the beginning and remained at a constant value after 40 days. This is due to the reduction in the contact rate and the maintenance of proper sanitary environmental conditions.

4.4.3 Simulations of the Deterministic Cholera Model with further Reduced Contact

Rate

A numerical simulation of the deterministic cholera model performed using different initial conditions with parameter values kept the same except for further reduced contact rate α = 0.20; the corresponding critical population size, S_C = 335030 and the basic reproduction number, R_o = 0.081.

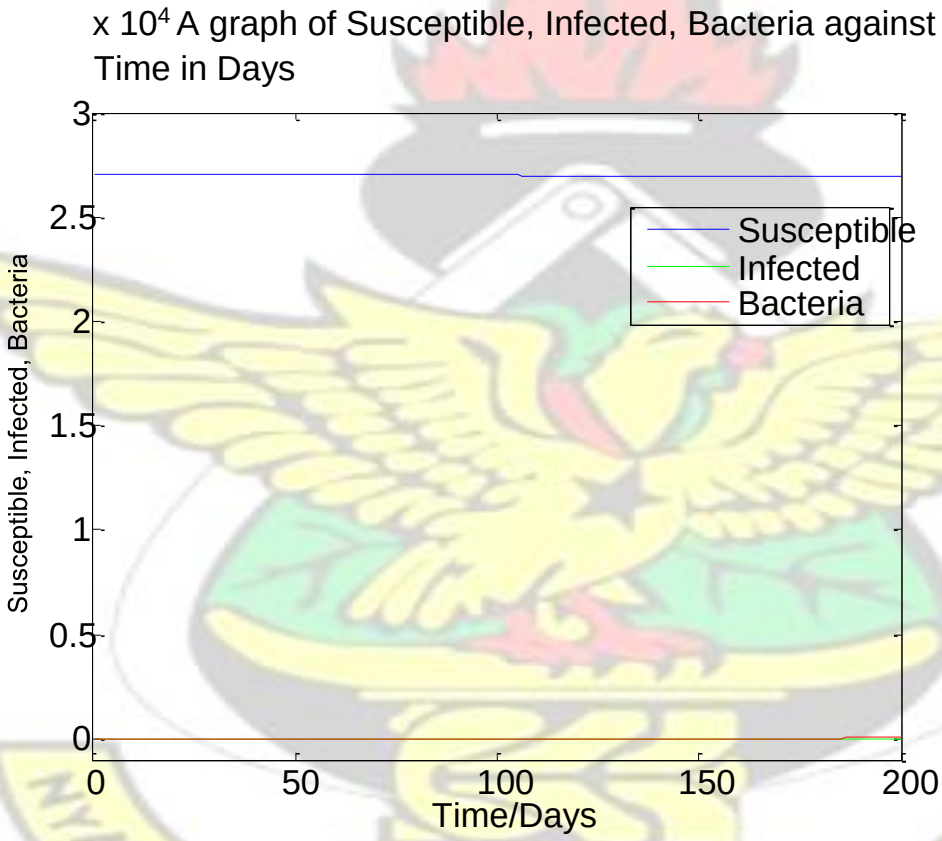


Figure 4.4(a): The numerical simulation of the susceptible, infected and bacteria density with initial conditions S(0) = 27002; I(0) = 0; B(0) = 0 and R_o = 0.81

Here, the number of the susceptible stayed at a constnt value. The bacteria and the infected populations remained at zero until after 180 days after which there were few cases of cholera. Cholera remained endemic for quite a long period of time.

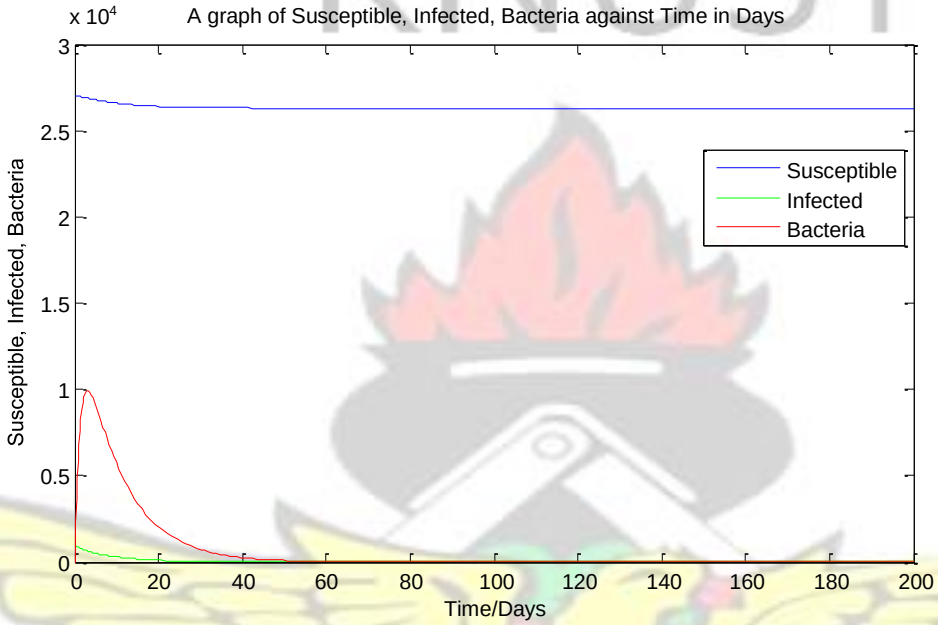


Figure 4.4(b): The numerical simulation of the susceptible, infected and bacteria density with initial conditions S(0) = 27002; I(0) = 10^3; B(0) = 0 and R_o = 0.081

In figure 4.4(b), the number of the susceptible individuals decreased for about 40 days and remained constant for a long time. The number of the infected decreased as the population of bacteria decreased and remained constant until after about 52 days and then the number disappeared. The bacteria population remained constant after 52 days for a long period of time.

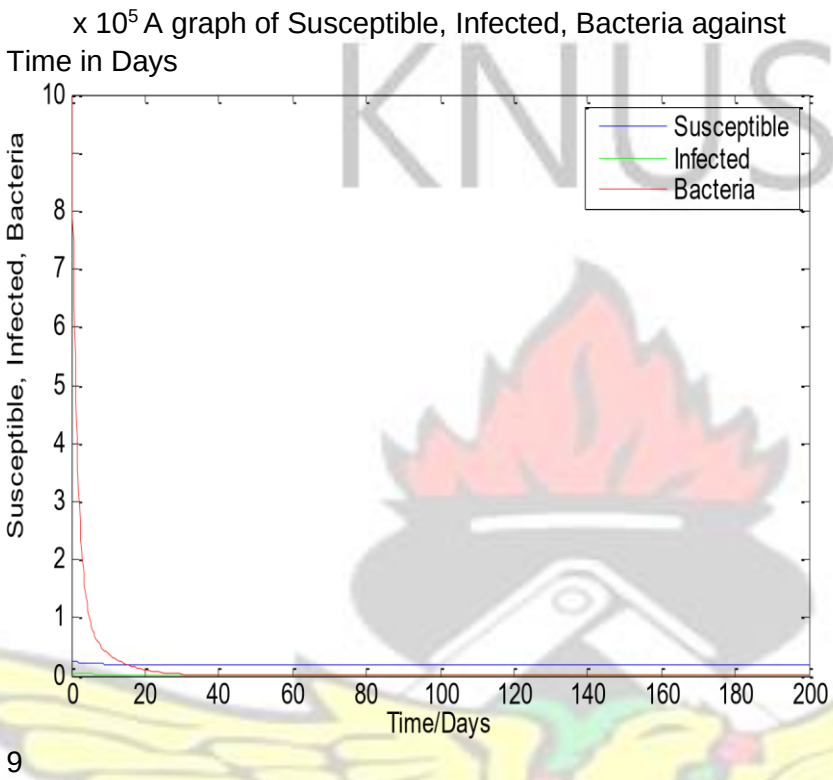
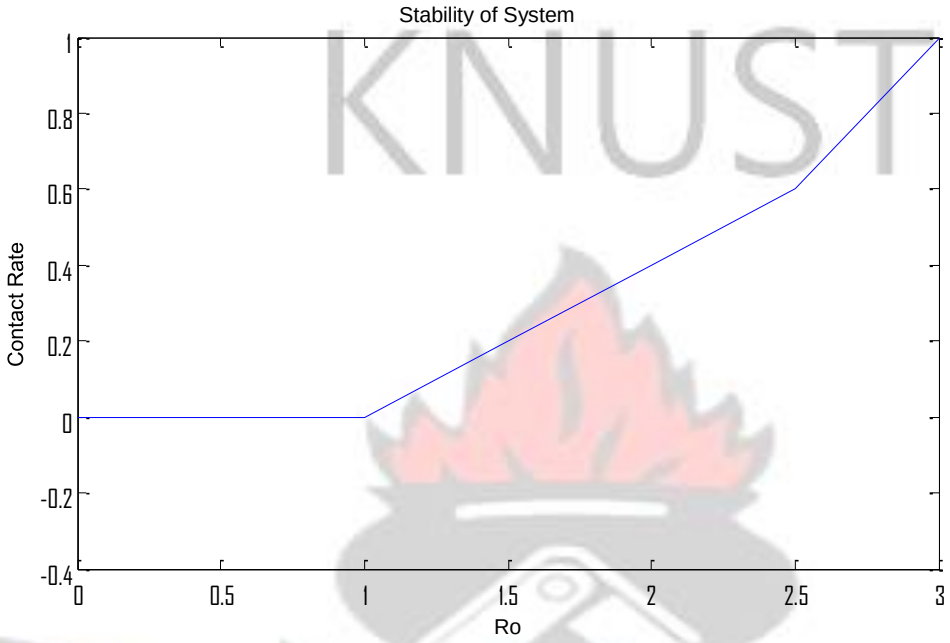


Figure 4.4(c): The numerical simulation of the susceptible, infected and bacteria density with initial conditions S(0) = 27002; I(0) = 10^3; B(0) = 10^6 and R_o = 0.081

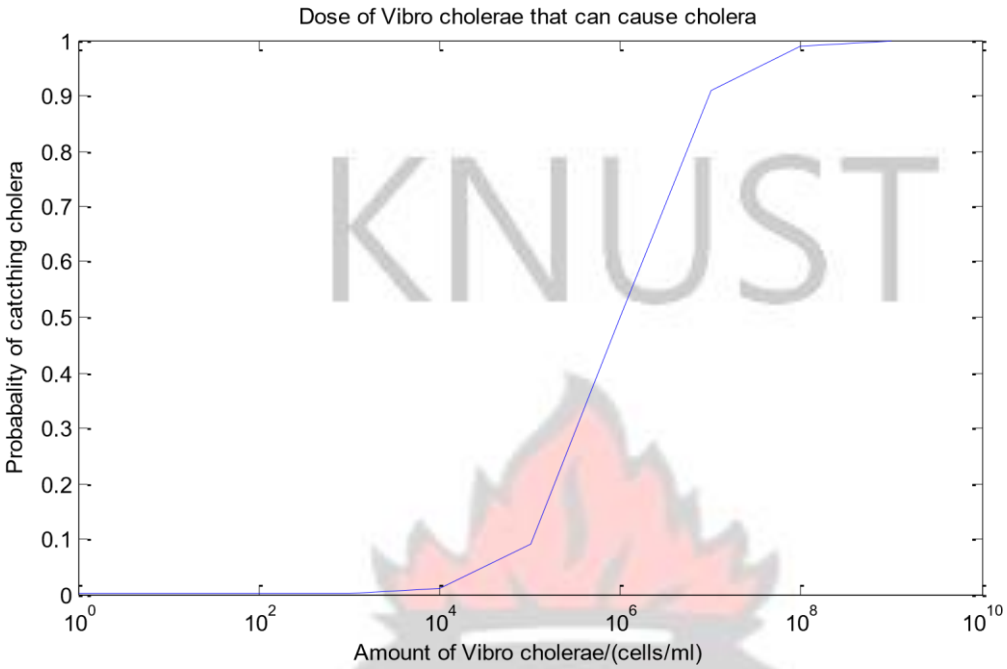
In figure 4.4(c), the infected population increased and decreased for a period of about 7 days and stayed constant for about 23 days and disappeared. The number of bacteria decreased and remained at a constant value after about 30 days. The number of susceptible also decreased and stayed constant after about 10 days.

4.5 Numerical Simulation of the Stability of the System



Ro < 1, Ro = 1 and Ro > 1.

Figure 4.5: Numerical Simulation of Contact Rate against Basic Reproduction Number, R_o. The figure above shows that when $R_o < 1$, the infection is zero, $R_o = 1$, turning point, $R_o > 1$, there will be outbreak. From the figure, we can establish $R_0 = 1$ as a sharp threshold for stability exchange between the DFE and the endemic equilibrium.



4.5.1 Numerical Simulation of Probability of Catching Cholera

Figure 4.6: Numerical Simulation of Probability of catching Cholera against Amount of Vibrio cholerae. Figure 4.6 describes amount of *Vibrio cholerae* that when ingested can cause the corresponding probability of catching cholera disease. It can be deduced from the figure above that as the number of bacteria in the reservoir increases, the probability of catching cholera also increases.

4.6 Summary of Discussion on Simulations

It can be noticed from the numerical simulation diagrams that when the basic reproduction number of cholera is less than one, the number of infected individuals and bacteria remains at zero for a long period of time before we experienced few cases of cholera. However, we can see from the simulation diagrams that if the basic reproduction

number is more than unity, the disease free-state becomes unstable and cholera becomes endemic for a long period of time.

4.7 Conclusion

It is observed that solutions with various different initial conditions converge to the same endemic equilibrium, a verification of the global asymptotical stability of cholera. A numerical simulation of the cholera free equilibrium showed that cholera is asymptotically stable. From the numerical simulations, if we keep the contact and shedding rates at most 0.24 and 0.01 respectively, cholera free-state will remain asymptotically stable. This can be done by promoting adequate sanitary environmental management and observing proper personal hygiene.

CHAPTER FIVE

CONCLUSION AND RECOMMENDATIONS

5.1 INTRODUCTION

This chapter focuses on the conclusion and recommendations of the thesis. The work began with a study of the epidemiology of cholera disease. We then reviewed ordinary differential equations and applied them to mathematical models of infectious diseases. The dynamics of dynamical systems of differential equations were then discussed, with the interest in equilibrium points, phase portrait and solution paths, since these are important tools in describing solutions of differential equations analytically. This was then applied to our model, the deterministic cholera model.

5.2 CONCLUSION

In our findings, we were made to know that *Vibrio cholerae* bacteria, is not only ingested from drinking water, but also in food poorly handled in terms of hygienic and sanitary conditions. Rate of growth of *Vibrio cholerae* in the environment will increase, if sanitary and hygienic measures decrease. In the analysis, the stability of zero equilibrium state is obtained. Disease-free equilibrium is achieved at zero infectives and zero toxigenic bacteria number. Critical number (threshold) S_c is obtained, which is one of the yardstick of predicting cholera outbreak. If the number of susceptibles in the population is greater than the critical number (S_c), cholera outbreak will occur. Otherwise, the cases of cholera will decrease and return to zero.

Another important means for predicting cholera outbreak in this work is the basic reproduction number (R_o). If R_o is greater than one, cholera outbreak will occur in the

concern community, if it is less than one the case(s) reduce(s) and die(s) out. If $R_o = 1$, the case is undetermined.

From this work if α andδ are high, R_o will be greater than one and the S_c will be less than the susceptible population, which means cholera outbreak will occur. If α and$\delta$are low, $R_o < 1$ and S_c will be higher than the number of susceptible individuals. Which implies no cholera outbreak. There is need to ascertain the minimum rates of α andδwhich must be maintained to assure hindrance of cholera outbreak. It should be noted that cholera outbreak can occur in a region where it had never occurred before, the chance of this happening is higher when $R_o > 1$.

Hence, we see the importance of the mathematical model as they can be used to explore and identify the types of data that needs to be collected and the parameter values that need to be accessed.

Cholera, caused by *Vibrio cholerae*, lends itself to analyses of the role of climate in infectious disease, coupled to population dynamics of pathogenic microorganisms, for several reasons. Cholera has a historical context linking it to specific seasons and biogeographical zones. In addition, the population dynamics of *Vibrio 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. Hence, the role of the environment and climate in disease dynamics has become a subject of increasing interest to microbiologists, clinicians, epidemiologists, and ecologists in recent times.

The cholera model provides a template for future research on climate-sensitive diseases, allowing definition of critical parameters and offering a means of developing more sophisticated methods for prediction of disease outbreaks.

All in all, from our findings, we say that the standard advice with regards to the prevention of cholera is to abstain from potentially contaminated food and water. Control of cholera requires proper sewage disposal and adequate water sanitation, as well as the detection and treatment of carriers or reservoirs. Classical control efforts encompass improvements of sanitation system, safer water treatment and improved food/personal hygiene. Water sanitation leads to the death of vibrios at a rate of ν .

5.3 RECOMMENDATIONS

- The model did not include the stochastic model since it was a bit complicated. We therefore recommend that further research is to be extended to include the stochastic cholera model
- The model assumed a homogenous constant population. We recommend that further research would be extended to include a heterogeneous mixing pattern in the population.
- We recommend the promotion of public health education aimed at behaviour change e.g. the washing of hands with soap: after using toilets and latrines, before preparing food and before eating in order to reduce the contact rate as low as

  $\alpha \square 0.24 \text{and} \delta \square 0.01$. This is due to the fact that as the contact and shedding rates increase, more percent of the population get infected, while a reduction in these

rates result in a decreased percentage of the infected class. Hence the need for a reduction in this parameter value.

- We recommend that the Local Municipal assembly provide the people with adequate sewage and sanitary infrastructure for collection and sanitary disposal of wastes including solid waste, liquid waste, human excreta, industrial wastes, clinical and other hazardous wastes. This will lead to a decreased number in the exposure or contact rate and hence a reduction in the number of people who get infected.

- We recommend the promotion of effective communication strategies, training and environmental education to sustain public awareness. For example people should be educated to buy food from a hygienic environment and to wash their hands with soap before eating and after visiting toilet.

- We recommend that sanitary laws be promulgated, inspected and enforced. People who violate these sanitary regulations should be brought to book.

- We recommend that intensive educational program and proper policy decisions be carried out which may include the promotion of the widespread availability of prophylactics and the increased availability of drugs such as ORS in order to replace the lost electrolytes through better medical treatment of the infected individuals.

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