Modelling Cholera Transmission with Delayed Bacterial Shedding and Disinfection Control

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Abstract

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This study focuses on the world dynamics of a cholera model that includes delayed bacterial shedding and water disinfection. From the method of the next generation matrix, a basic reproduction number is found that sets a threshold of disease persistence. It is shown that the disease disappears if $R_0 < 1$, which means that the disease-free equilibrium is globally asymptotically stable. The system is not destabilized by the delay, which leads to periodic oscillations. The numerical simulations validate the theoretical analysis, which illustrates the importance of delay and disinfection in cholera prevention and control.

Key Words: Cholera, delay differential equations, basic reproduction number, disinfection, stability analysis, Lyapunov function.

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Chapter 1

Introduction

Cholera, a diarrheal disease that can be fatal and is caused by the bacteria Vibrio cholerae is still a big public health problem around the world, especially in places where people don't have access to clean water and sanitation [23]. The disease is spread mainly by consuming contaminated water or food, and if treatment is not received, it can result in severe dehydration and high mortality. In many regions of Africa, Asia, and Latin America, cholera is still common despite improvements in medical care and public health initiatives [23]. Outbreaks frequently occur after natural disasters and humanitarian crises [3].

Understanding the dynamics of cholera transmission and analyzing intervention methods has been made possible in large part by mathematical modelling [2, 24]. Capasso and Paveri-Fontana [3] created the first mathematical model for cholera by analyzing the cholera outbreak in the Mediterranean region of Europe in 1973. Their

analysis showed how mathematical frameworks may be used to forecast epidemics and evaluate management strategies. This basis has been built upon by subsequent models that have included the function of environmental reservoirs, bacterial persistence in water, and human reactions to epidemics [2, 24].

Cholera modelling focuses significantly on the basic reproduction number R_0, which predicts the likelihood of an epidemic [19, 25]. The population will eventually be cholera-free if the disease-free equilibrium remains stable. On the other hand, the endemic equilibrium will remain stable if the disease continues [4]. Using mathematical methods such as bifurcation analysis and Lyapunov functions, the stability of these equilibria has been thoroughly investigated [1, 19, 21].

Recent research has highlighted the significance of including temporal delays to account for incubation periods, delayed bacterial shedding, and intervention lags, even if traditional cholera models have offered insightful information [5, 26]. The global stability of a cholera model with temporal delays was examined by Wang & Wei [1], who showed how delays can have a major impact on the disease's long-term behavior. A delay differential equation model that included vaccination controls was also created by Singh et al. [5], demonstrating the importance of prompt action in lowering the disease burden. According to these studies, delay factors are essential in determining the course of cholera epidemics and need to be considered in epidemiological models.

The effect of the press on the spread of the disease is another field of cholera modelling. Public awareness campaigns can change individual behavior and lower

transmission rates, as proposed by Liao and Yang's [6] cholera model with numerous delays and media effects [20, 27, 28]. According to their findings, outbreak dynamics can be greatly impacted by the quick and exact distribution of information. A mathematical model for cholera epidemics was also created by Chin and Kimbir [7], who included public health messages as a control variable.

The function of disinfection techniques in containing cholera outbreaks has gotten less attention despite these developments. It turns out that one of the best ways to reduce the number of bacteria in the environment and stop the spread of disease is to disinfect water [29, 30]. Research has shown that while timely interventions can stabilize the system, postponing the use of disinfectants can result in uncontrollable outbreaks [5, 30]. This study adds to earlier ones by including disinfection methods and time delays. This gives us more understanding of how cholera spreads and how to stop it.

Chapter 2 covers the mathematical concepts required to understand infectious disease dynamics, starting with ordinary differential equations and progressing to delay differential equations. Introduces basic concepts such as existence and uniqueness, equilibrium points, and linearization techniques, which serve as the theoretical foundation for evaluating time-delayed systems.

Chapter 3 presents a new cholera model that includes both delayed bacterial shedding and disinfection. The four interacting populations that are taken into account by the model are susceptible persons, infected individuals, the concentration of bacteria

in water, and the concentration of disinfectant. We use non-linear delay differential equations to develop the system and figure out the basic reproduction number R_0. We investigate the possibility of endemic and disease-free equilibria and determine algebraic requirements for their feasibility.

In Chapter 4, we do a detailed stability study on the equilibria under both delayed and non-delayed circumstances. Four scenarios are discussed: (i) disease-free equilibrium without delay, (ii) endemic equilibrium without delay, (iii) disease-free equilibrium with delay, and (iv) endemic equilibrium with delay. Local stability is examined in each situation using linearization, eigenvalue methods, the Routh-Hurwitz criterion, and transcendental characteristic equations when appropriate. We use Lyapunov functions to show that the disease-free equilibrium is globally asymptotically stable when the basic reproduction number R_0 is less than 1. The analysis demonstrates how the delay parameter may affect the system's long-term behavior and threshold conditions, possibly resulting in endemicity or persistent oscillations.

Chapter 5 provides a computational study of the model using **MATLAB** simulations. The numerical results support the theoretical findings and indicate the impact of the delay parameter on infection dynamics. Simulations verify that delays can cause transient oscillations, slow down convergence to equilibrium, and in some cases, sustain breakouts even when other factors are under control. The four simulation situations provide quantitative and visual confirmation of the theoretical results and match the analytical cases examined in Chapter 4.

Chapter 2

Preliminaries

2.1 Theorems in Dynamical Systems

Differential equations in mathematical Modelling are fundamental for understanding and forecasting the dynamics of biological systems. Dynamical systems are used in epidemiology to learn more about how infectious diseases change over time, how actions impact their distribution, and how a disease can either become endemic or be eradicated.

This chapter discusses the necessary mathematical framework for understanding and analyzing the behavior of such systems, starting with ordinary differential equations (ODEs) and continuing to delay differential equations (DDEs). We provide definitions, theorems, and examples to introduce the reader to basic theoretical concepts and provide a foundation for the more complex models covered in the following

chapters.

A dynamical system shows how a point in space changes over time. A dynamical system can be expressed as:

$$\frac{dx(t)}{dt} = f(x(t), t); \quad x(t_0) = x_0$$

where $x(t) \in \mathbb{R}^n$ is the state vector at time t, and $f : \mathbb{R}^n \times \mathbb{R} \to \mathbb{R}^n$ is a function that governs the system's behavior.

Existence and Uniqueness Theorem: The Picard-Lindelöf Theorem (also known as the Cauchy-Lipschitz Theorem) is essential for providing the existence and uniqueness of solutions to differential equations under specified initial conditions.

Theorem (Picard-Lindelöf): If $f(x, t)$ is continuous on t and Lipschitz continuous in x in some neighborhood of (x_0, t_0), the there exits a unique solution $x(t)$ defined in some interval around t_0. This theorem assures that our system will always behave the same way, no matter the starting conditions [8].

Equilibrium and stability analysis: An equilibrium point (or steady-state) x^* of a system satisfies:

$$f(x^*) = 0.$$

We need to linearize the nonlinear system to analyze the behavior near an equilibrium:

$$\frac{dx}{dt} = f(x) \quad \Rightarrow \frac{d\bar{x}}{dt} = Df(x^*)\bar{x}$$

Here, $Df(x^*)$ is the Jacobian matrix evaluated at the equilibrium point, and $\bar{x} = x - x^*$ is a small perturbation from equilibrium. The eigenvalues of the Jacobian determine

the local stability.

The equilibrium is asymptotically stable if all the eigenvalues have negative real parts. If at least one eigenvalue has a positive real part, the equilibrium is unstable.

If eigenvalues have zero real parts, higher-order analysis is needed to determine stability.

Hartman-Grobman Theorem: This theorem justifies the linearization of nonlinear systems.

Theorem: Let x^* be a hyperbolic equilibrium (i.e., all eigenvalues of $Df(x^*)$ have nonzero real parts.) Then the behavior of the nonlinear system near x^* is qualitatively the same as the linearized system.

The theorem states that the local phase portrait of a nonlinear system close to a hyperbolic equilibrium is topologically equivalent to its linear approximation [9].

Consider two species with populations $x(t)$ and $y(t)$ at time t, which compete with each other for resources. We assume that in the absence of either species, the other would have a logistic population growth as in the prey-predator model. We assume that their competition affects the rate of decline in each population, which is proportional to their product xy

$$\frac{dx}{dt} = x(a_1 - b_1x - c_1y),$$
$$\frac{dy}{dt} = y(a_2 - b_2y - c_2x).$$

To find out the equilibrium points we need to set $\frac{dx}{dt} = 0$ and $\frac{dy}{dt} = 0$. From this we get the conditions, $x = 0$ or $a_1 - b_1x - c_1y = 0$ and $y = 0$ or $a_2 - b_2y - c_2x = 0$.

Solving these, we get four critical points:

$E_1 = (0, 0)$ (both species die out),

$E_2 = (\frac{a_1}{b_1}, 0)$ (only the second species die out),

$E_3 = (0, \frac{a_2}{b_2})$ (only the first species die out),

$E_4 = (\frac{a_1 b_2 - a_2 c_1}{b_1 b_2 - c_1 c_2}, \frac{a_2 b_1 - a_1 c_2}{b_1 b_2 - c_1 c_2})$ (both species co-exist).

To analyze the stability, we linearized the system using the Jacobian matrix at each equilibrium point

$$J = \begin{pmatrix} \frac{\partial f}{\partial x} & \frac{\partial f}{\partial y} \\ \\ \frac{\partial g}{\partial x} & \frac{\partial g}{\partial y} \end{pmatrix}$$

$$= \begin{pmatrix} a_1 - 2b_1 x - c_1 y & -c_1 x \\ \\ -c_2 y & a_2 - 2b_2 y - c_2 x \end{pmatrix}.$$

Then we have to determine the stability at each equilibrium point. At $E_1 = (0, 0)$, the Jacobian becomes,

$$J = \begin{pmatrix} a_1 & 0 \\ \\ 0 & a_2 \end{pmatrix}.$$

The eigenvalues are $\lambda_1 = a_1$ and $\lambda_2 = a_2$. If both eigenvalues are positive, then we can say this equilibrium point is an unstable node.

At $E_2 = (\frac{a_1}{b_1}, 0)$, the Jacobian becomes,

$$J = \begin{pmatrix} -a_1 & -\frac{c_1 a_1}{b_1} \\ \\ 0 & a_2 - \frac{c_2 a_1}{b_1} \end{pmatrix}.$$

We get two eigenvalues $\lambda_1 = -a_1$ and $\lambda_2 = a_2 - \frac{a_1 c_2}{b_1}$. If $\lambda_2 < 0$, it will be locally stable, and if $\lambda_2 > 0$, it will be a saddle point (unstable).

At $E_3 = (0, \frac{a_2}{b_2})$,

$$J = \begin{pmatrix} a_1 - \frac{c_1 a_2}{b_2} & 0 \\ -\frac{c_2 a_2}{b_2} & -a_2 \end{pmatrix},$$

$\lambda_1 = a_1 - \frac{c_1 a_2}{b_2}$ and $\lambda_2 = -a_2$ are the eigenvalues of this Jacobian. If $\lambda_1 < 0$, it will be locally stable, and if $\lambda_1 > 0$, it will be a saddle point (unstable).

At the coexistence point $E_4 = (x^*, y^*) = (\frac{a_1 b_2 - a_2 c_1}{b_1 b_2 - c_1 c_2}, \frac{a_2 b_1 - a_1 c_2}{b_1 b_2 - c_1 c_2})$, the Jacobian is,

$$J = \begin{pmatrix} a_1 - 2b_1 x^* - c_1 y^* & -c_1 x^* \\ -c_2 y^* & a_2 - 2b_2 y^* - c_2 x^* \end{pmatrix}.$$

After solving this we get the eigenvalues $\lambda_{1,2} = \frac{-(b_1 x^* + b_2 y^*) \pm \sqrt{(b_1 x^* + b_2 y^*)^2 - 4(b_1 b_2 - c_1 c_2) x^* y^*}}{2}$.

Hence, E_4 is unstable if $b_1 b_2 - c_1 c_2 < 0$, then the discriminant is positive and greater than $(b_1 x^* + b_2 y^*)^2$. Thus, the eigenvalues are real and have a positive sign. On the other hand, if $b_1 b_2 - c_1 c_2 > 0$, then the discriminant is positive and less than $(b_1 x^* + b_2 y^*)^2$. Thus, the eigenvalues are real, negative, and unequal or complex with a negative real part. Thus, the critical point E_4 is asymptotically stable. Hence, coexistence is possible if $b_1 b_2 > c_1 c_2$ [15].

Consider a Lotka-Voltera Model,

$$\frac{dx}{dt} = x(60 - 4x - 3y),$$

$$\frac{dy}{dt} = y(42 - 3x - 2y).$$

At first, we need to set the derivatives equal to zero

$$x(60 - 4x - 3y) = 0,$$

$$y(42 - 3x - 2y) = 0.$$

After solving this we get four critical points $(0, 0)$, $(0, 21)$, $(15, 0)$ and $(6, 12)$. Evaluate stability using the Jacobian:

$$f(x, y) = x(60 - 4x - 3y),$$

$$g(x, y) = y(42 - 3x - 2y),$$

$$J = \begin{pmatrix} \frac{\partial f}{\partial x} & \frac{\partial f}{\partial y} \\ \\ \frac{\partial g}{\partial x} & \frac{\partial g}{\partial y} \end{pmatrix},$$

$$= \begin{pmatrix} 60 - 8x - 3y & -3x \\ \\ -2y & 42 - 6y - 2x \end{pmatrix},$$

At critical point $(0, 0)$

$$J = \begin{pmatrix} 60 & 0 \\ \\ 0 & 42 \end{pmatrix},$$

we get two eigenvalues $\lambda_1 = 60$ and $\lambda_2 = 42$ from this Jacobian matrix. As both of the eigenvalues have positive real parts, we can say $(0, 0)$ is an unstable improper node.

Similarly, for the second and third critical points $(0, 21)$ and $(15, 0)$, we get the eigenvalues $\lambda_1 = -3$, $\lambda_2 = -42$ and $\lambda_1 = -60$, $\lambda_2 = -3$. For both of the critical

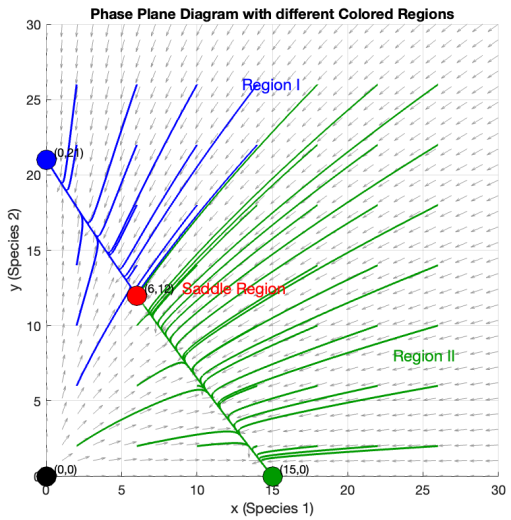

Figure 2.1: Phase plane of Lotka Voltera Model

points, we get negative real parts means that $(0, 21)$ and $(15, 0)$ both are asymptotically stable improper nodes.

And for the fourth critical point, we get this equation from the Jacobian matrix, $\lambda^2 + 48\lambda - 72 = 0$. We get $\lambda_1 = -24 + 18\sqrt{2}$ and $\lambda_2 = -24 - 18\sqrt{2}$, where one is a positive value and the other one is negative. So, we can say $(6, 12)$ is an unstable saddle point.

This phase plane diagram shows three regions. In region I (blue), species 2 survives as it outcompetes species 1. Species 1 outcompetes species 2 in region II (green), allowing it to exist alone. The saddle region (red) is a delicate equilibrium close to the saddle point $(6, 12)$, where species dominance is determined by small changes in initial conditions. The figure shows competitive exclusion, a situation in which living together is unstable and only one species survives based on the starting populations

[15].

Routh-Hurwitz Criterion: The Routh-Hurwitz criterion is a mathematical method for determining the stability of a linear time-invariant (LTI) system. It examines the system's characteristic equation without directly computing its roots. The criterion assures the stability of the system by establishing the necessary and sufficient conditions for all roots of a polynomial to have negative real parts [13].

It is especially important as determining the roots of higher-order polynomials can be difficult or complex. Instead, stability can be examined simply and quickly by looking at the signs and magnitudes of the coefficients that are arranged in a Routh array.

For first and second-order polynomials, all the coefficients must be positive,

$$P(x) = c_1 x + c_0 = 0, \text{ where } c_i > 0 \text{ for } i = 0, 1,$$

$$P(x) = c_2 x^2 + c_1 x + c_0 = 0, \text{ where } c_i > 0 \text{ for } i = 0, 1, 2.$$

For a third-order polynomial, $P(x) = c_3 x^3 + c_2 x^2 + c_1 x + c_0 = 0$. All the coefficients must be positive, where $c_i > 0$, for $i = 0, 1, 2, 3$ and $c_2 c_1 - c_3 c_0 > 0$.

For a fourth-order polynomial, $P(x) = c_4 x^4 + c_3 x^3 + c_2 x^2 + c_1 x + c_0 = 0$. All the coefficients must be positive, where

(i) $c_i > 0$, for $i = 0, 1, 2, 3$,

(ii) $c_2 c_1 - c_3 c_0 > 0$,

(iii) $c_3 c_2 c_1 - c_4 c_1^2 - c_3^2 c_0 > 0$.

Consider a third-order polynomial, $P(x) = x^3 + 4x^2 + 5x + 2$. The coefficients are

$c_3 = 1, c_2 = 4, c_1 = 5, c_0 = 2$. Here, all the coefficients are positive $c_i > 0$ for $i = 0, 1, 2, 3$ means the first condition of Routh-Hurwitz is satisfied.

Now, the second condition is $c_2c_1 - c_3c_0 = 4 \times 5 - 1 \times 2 = 20 - 2 = 18 > 0$. We can say that the system is stable by Routh-Hurwitz criterion.

2.2 Differential Equations in Modelling and Disease Dynamics:

Differential equations are often used to model biological processes, such as population growth, disease spread, and the evolution of treatments over time. The SIR (Susceptible-Infected-Recovered) model is a fundamental example in epidemiology:

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI, \\ \frac{dI}{dt} &= \beta SI - \gamma I, \\ \frac{dR}{dt} &= \gamma I, \end{aligned}$$

where $S(t)$ denotes the number of susceptible individuals, $I(t)$ denotes the number of infected individuals, and $R(t)$ denotes the number of recovered individuals. β and γ represent the transmission and recovery rates. This model represents the growth of individuals through various disease states. The basic reproduction number $R_0 = \frac{\beta}{\gamma}$ shows how many secondary infections one infected person typically causes. On the SIR model graph, you can see how a disease spreads over time. Initially, most of

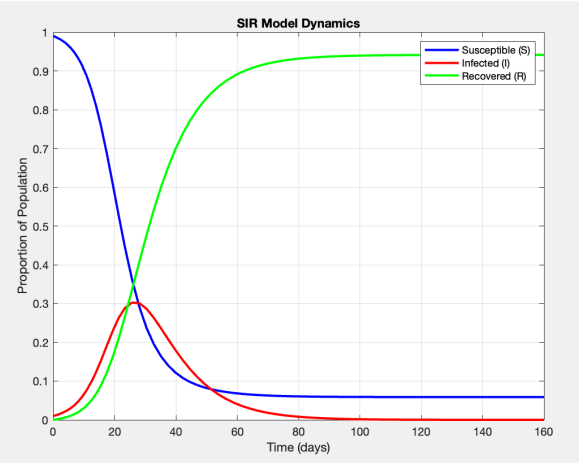

Figure 2.2: SIR Model

the population is susceptible, with a minor percentage infected. The infection rate increases rapidly, reaches a peak, and then decreases as people recover. Ultimately, most people recover, a smaller number of individuals stay susceptible, and the disease dies [12].

The differential equations of the basic HIV model are:

$$\begin{aligned}
\frac{dT}{dt} &= \lambda - dT - \beta TV, \\
\frac{dI}{dt} &= \beta TV - \delta I, \\
\frac{dV}{dt} &= pI - cV,
\end{aligned}$$

where $T(t)$ is the concentration of healthy CD4+ T-cells. $I(t)$ is the concentration of infected CD4+ T-cells . $V(t)$ is the concentration of free HIV virions, and the parameter λ is the rate of production of new uninfected T-cells. d is the natural death rate of an uninfected T-cell. β is the rate at which the virus infects T-cells. δ

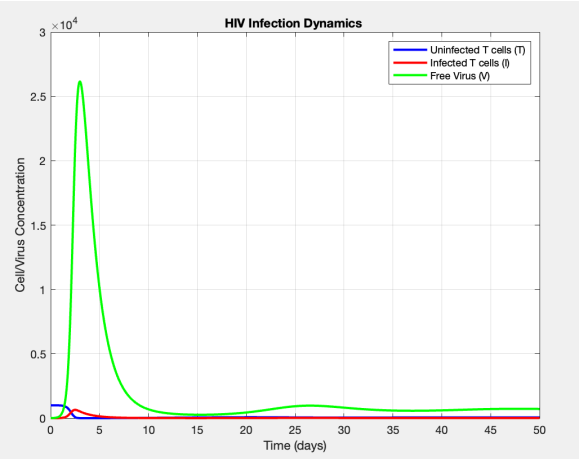

Figure 2.3: HIV Model

denotes the death rate of infected T-cells. p is the number of new virions produced per infected cell, and c is the clearance rate of free virus. From the figure, we can see that at first the virus spreads quickly and infects a lot of T-cells. As a result, uninfected T-cells decrease while infected T-cells increase. After several days, the immune system responds, reducing the virus and infected cells. Finally, every value levels out, indicating a chronic infection in which the virus remains in the body at a low, steady level [11].

2.3 Delay Differential Equations:

Changes in real-world systems do not always happen instantly. Delays are often natural, such as incubation periods in infectious conditions or latency in population reactions. We use delay parameters to capture the incubation period (time between

infection and symptoms), delayed bacterial shedding in water (as in cholera), immune response lag, and reaction time for public health interventions [10]. Ignoring these delays can result in incorrect projections and a simplified interpretation of the dynamics. Consider the Lotka-Voltera competition system,

$$x'(t) = x(t)[2 - ax(t) - by(t - r)],$$

$$y'(t) = y(t)[2 - cx(t - r) - dy(t)].$$

We are going to determine the stability of the positive steady state when $a = d = 2$ and $b = c = 1$ [10]. We need to set the right-hand sides equal to zero to determine the positive steady state:

$$2 - ax^* - by^* = 0,$$

$$2 - cx^* - dy^* = 0.$$

When $a = d = 2$ and $b = c = 1$, we get,

$$2 - 2x^* - y^* = 0,$$

$$2 - x^* - 2y^* = 0.$$

Solving these above two equations we get the steady state $(x^*, y^*) = (\frac{2}{3}, \frac{2}{3})$

For linearization let, $u(t) = x(t) - x^*$ and $v(t) = y(t) - y^*$.

The linearized system becomes,

$$\begin{aligned} u'(t) &= x^*[-au(t) - bv(t-r)], \\ v'(t) &= y^*[-cu(t-r) - dv(t)], \\ \Rightarrow \quad u'(t) &= \frac{2}{3}[-2u(t) - v(t-r)], \\ v'(t) &= \frac{2}{3}[-u(t-r) - 2v(t)]. \end{aligned}$$

Let, exponential solutions $u(t) = Ue^{\lambda t},\ v(t) = Ve^{\lambda t}$. Then we get the characteristic matrix,

$$A = \begin{pmatrix} -\frac{4}{3} & -\frac{2}{3}e^{-\lambda r} \\ -\frac{2}{3}e^{-\lambda r} & -\frac{4}{3} \end{pmatrix}.$$

We need to find out the determinant of the above matrix.

$$det(A - \lambda I) = \begin{vmatrix} -\frac{4}{3} - \lambda & -\frac{2}{3}e^{-\lambda r} \\ -\frac{2}{3}e^{-\lambda r} & -\frac{4}{3} - \lambda \end{vmatrix} = 0,$$

$$\begin{aligned} \Rightarrow \quad & (\frac{4}{3} + \lambda)^2 - (\frac{2}{3}e^{-\lambda r})^2 = 0, \\ \Rightarrow \quad & (\frac{4}{3} + \lambda)^2 = (\frac{2}{3}e^{-\lambda r})^2, \\ \Rightarrow \quad & \frac{4}{3} + \lambda = \pm\frac{2}{3}e^{-\lambda r}, \\ \Rightarrow \quad & \lambda = -\frac{4}{3} \pm \frac{2}{3}e^{-\lambda r}. \end{aligned}$$

This gives two transcendental equations:

$$\lambda = -\frac{4}{3} + \frac{2}{3}e^{-\lambda r}, \tag{2.1}$$

$$\lambda = -\frac{4}{3} - \frac{2}{3}e^{-\lambda r}. \tag{2.2}$$

If the delay $r = 0$, then we get from (2.1) and (2.2) $\lambda = -\frac{2}{3}$ and $\lambda = -2$. As both roots are real and negative, we can say the equilibrium is locally asymptotically stable for $r = 0$.

When $r \neq 0$, substitute $\lambda = i\omega$ (purely imaginary root) in (2.1), we get,

$$\begin{aligned} i\omega &= -\frac{4}{3} + \frac{2}{3}e^{-i\omega r}, \\ i\omega &= -\frac{4}{3} + \frac{2}{3}(\cos\omega r - i\sin\omega r), \\ i\omega &= -\frac{4}{3} + \frac{2}{3}\cos\omega r - \frac{2}{3}i\sin\omega r. \end{aligned}$$

Separating the real and imaginary parts, we get

real part: $\frac{4}{3} = \frac{2}{3}\cos\omega r \Rightarrow \cos\omega r = 2$,

imaginary part: $\omega = -\frac{2}{3}\sin\omega r$.

Here $\cos\omega r = 2$ has no real solution, since $|\cos\omega r| \leq 1$ for all real ω. The characteristic equation has no purely imaginary roots, and hence no Hopf bifurcation occurs as r increases. Also, the roots depend continuously on r. This means the steady state stays locally asymptotically stable for all $r > 0$.

2.4 Lyapunov Function

A Lyapunov function is a scalar function $V : \mathbb{R}^n \to \mathbb{R}$ that determines the stability of an equilibrium point around the origin of a dynamical system. Consider a system defined as follows:

$$\frac{dx}{dt} = f(x),\ x \in \mathbb{R}^n$$

A continuously differentiable function $V(x)$ is called a Lyapunov function in a region $D \subset \mathbb{R}^n$ of the origin if it satisfies the following conditions:

1. Positive definiteness: $V(0) = 0,\ V(x) > 0\ \forall\ x \in D - \{0\}$

2. Negative semi-definiteness of the derivative (along trajectories of the system): $\dot{V(x)} = \nabla V(x).f(x)\ \forall\ x \in D$ [16].

A Lyapunov function is like a tool that helps us check if a system will remain constant and reach a steady state over time. It's like how energy decreases in a machine due to friction. The system is stable if this function decreases over time or remains constant. And we don't need to solve the entire equation to know this; simply selecting the correct function is sufficient.

For systems with delay, we apply Lyapunov function that considers the system's history [17]. These are particularly helpful in biological models. Hal Smith [10] explains that if this function continues to decrease and reaches its lowest value in steady state, the system is globally stable. McCluskey et al. developed a Lyapunov function for a cholera model with age structure and delay. This showed that the world situation could stay stable even if recovery was slow [22].

We look at a model of microbial growth with a medium to show how a delay differential equation can be used in biology. This example is taken from Hal Smith's [10] work on dynamical systems with delay. The model represents the interaction of a microbial population with a nutrient substrate, including a time delay that represents the lag between nutrient absorption and microbial reproduction. The system is given

by

$$S'(t) = 1 - S(t) - f(S(t))x(t),$$

$$x'(t) = e^{-r} f(S(t-r))x(t-r) - x(t),$$

where $S(t)$ represents the substrate concentration at time t, $x(t)$ denotes the microbial population density at time t, $r > 0$ is the time delay associated with microbial reproduction. The function $f(S)$ for the growth of bacteria is given by $f(S) = \frac{mS}{a+S}$. The constants $m > 0$ and $a > 0$ indicate the maximum specific growth rate and half-saturation constant, respectively.

The first equation describes substrate dynamics, with $1 - S(t)$ accounting for intake and decay and $f(S(t))x(t)$ representing substrate consumption by microorganisms. The second equation includes a delay term $f(S(t-r))$ showing that microbe development at time t is dependent on the availability of substrate at time $t-r$. The exponential term e^{-r} indicates that the effectiveness of delayed growth declines with increasing delay and substrate consumption rate.

This model is a good example of how delays occur naturally in biological systems and can have a considerable impact on the system's dynamics, especially in terms of stability, oscillations, and extinction thresholds. Figure 2.4 shows the time evaluation of substrate concentration $S(t)$ and microbial population $x(t)$ based on the delayed microbial growth model.

At the beginning, the substrate $S(t)$ is entirely accessible, and the microbial population $x(t)$ is at an average level. The microorganisms consume the substrate over

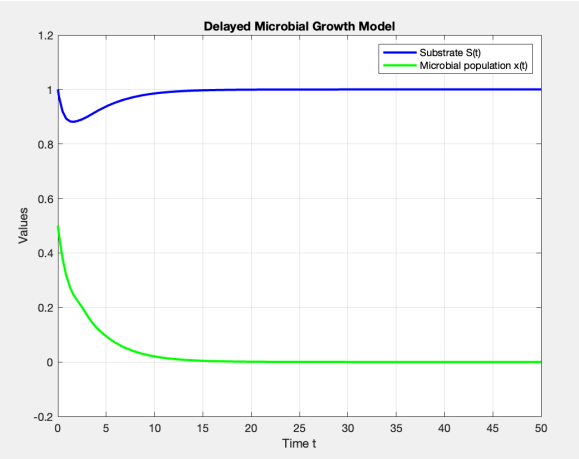

Figure 2.4: Delayed Microbial Growth

time, which lowers $S(t)$. But because of the delay $r = 2$, the microbial population does not respond quickly to the current substrate supply. Instead, its growth is dependent on the substrate concentration from a previous period.

The delay causes damped oscillations in both $S(t)$ and $x(t)$, with each variable fluctuating before settling in a stable state. The delay creates short-term instability but not permanent oscillations or instability in this parameter domain. This emphasizes the importance of delay in shaping transient dynamics, even if long-term behavior is consistent [10].

Chapter 3

Mathematical Modelling

3.1 Mathematical Model

This chapter discusses how a mathematical model was developed and how it can be used to explain why cholera spreads. The model takes into account several important factors, including how infections can spread through contaminated water, what happens when bacteria shed later than expected, and how cleaning can lower the number of bacteria in water. The compartmental model structure incorporates delay differential equations to describe the incubation and shedding times, and it represents both environmental and human aspects. The system of differential equations that governs

our model is given by:

$$\begin{aligned}
\frac{dS}{dt} &= nH - nS(t) - a\Lambda(B(t))S(t), \\
\frac{dI}{dt} &= a\Lambda(B(t))S(t) - rI(t), \\
\frac{dB}{dt} &= \mu I(t-\tau) - mB(t) - \alpha D(t)B(t), \\
\frac{dR}{dt} &= \gamma I(t) - nR(t), \\
\frac{dD}{dt} &= \beta B(t) - \psi D(t) - \theta B(t)D(t).
\end{aligned} \tag{3.1}$$

where $H = S+I+R$ denotes the total human population, $S(t)$ describes the number of susceptible humans, $I(t)$ means the number of infected humans, $R(t)$ defines the individuals that achieve a permanent immunity after recovery. $B(t)$ denotes the bacterial concentration of cholera in water, $D(t)$ is the concentration of disinfectant in the water at time t. Here a is the contact rate with contaminated water, μ defines the average contribution of each infected person to the aquatic population of Vibrio cholerae, m represents the net death rate of vibrios, Λ is the probability of a person being infected with cholera, $r = n+\gamma$ where n denotes the natural human birth/death rate, γ means the recovery rate, α represents how strongly the disinfectant impacts the bacterial decay rate in the water, β denotes the constant proportionality to the bacteria concentration, ψ is the natural decay rate of the disinfectant, θ represents the amount that is consumed by the bacteria, τ is the delay parameter that describes the time between the infected person and when he gives off the pathogenic bacteria of Vibrio cholerae to the aquatic environment. The nonlinear incidence function is

represented by

$$a\Lambda(B) = a\frac{B}{K+B}, \tag{3.2}$$

where a denotes the contact rate with contaminated water and K represents the half saturation rate [1]. When $B = K$, the chance of getting an illness is half what it normally is. This form shows that the risk of infection goes up less sharply when there are a lot of bacteria around.[4][32]

Since the $R(t)$ equation has no connection to any other equation and has no direct impact on infection or bacteria dynamics, we can consider the following reduced four-dimensional system

$$\begin{aligned}
\frac{dS}{dt} &= nH - nS(t) - a\Lambda(B(t))S(t), \\
\frac{dI}{dt} &= a\Lambda(B(t))S(t) - rI(t), \\
\frac{dB}{dt} &= \mu I(t-\tau) - mB(t) - \alpha D(t)B(t), \\
\frac{dD}{dt} &= \beta B(t) - \psi D(t) - \theta B(t)D(t).
\end{aligned} \tag{3.3}$$

This reduced system is easier to analyze and focuses on infection and the environment.

3.2 Equilibrium Points and Basic Reproduction Numbers

We examine the system's equilibrium points to understand long-term behavior. An equilibrium point is a state where the system remains constant over time, which means that all of its derivatives are equal to zero.

We can easily get the disease-free equilibrium (DFE) in a population that is healthy and free of bacterial contamination $E_0 = (H, 0, 0, 0)$, which means the uninfected individuals stabilize at E_0. For a disease-free equilibrium, we consider the equations corresponding to the disease-related classes $I(t)$ and $B(t)$.

$$\frac{dI}{dt} = a\frac{B}{K+B}S - rI,$$
$$\frac{dB}{dt} = \mu I - mB - \alpha DB.$$

We need to define the new infection and transition terms from these two differential equations. At DFE $S = H$ and $B \to 0$, the new infection term for I is $\frac{aB}{K}H$ and the transition terms are rI and $(\mu I - mB)$ respectively.[33] Jacobian of the new infection in terms of DFE is

$$J_i = \begin{pmatrix} \frac{\partial}{\partial I}(\frac{aB}{K}H) & \frac{\partial}{\partial B}(\frac{aB}{K}H) \\ \\ \frac{\partial}{\partial I}(0) & \frac{\partial}{\partial B}(0) \end{pmatrix}$$
$$= \begin{pmatrix} 0 & \frac{aH}{K} \\ \\ 0 & 0 \end{pmatrix},$$

and the Jacobian of the transition term is

$$J_t = \begin{pmatrix} \frac{\partial}{\partial I}(rI) & \frac{\partial}{\partial B}(rI) \\ \\ \frac{\partial}{\partial I}(-\mu I + mB) & \frac{\partial}{\partial B}(-\mu I + mB) \end{pmatrix}$$
$$= \begin{pmatrix} r & 0 \\ \\ -\mu & m \end{pmatrix}.$$

Now, we get,

$$J_i.J_t^{-1} = \begin{pmatrix} \frac{aH\mu}{Kmr} & \frac{aH}{Km} \\ 0 & 0 \end{pmatrix}.$$

The eigenvalues of the above matrix are $\lambda_1 = 0$ and $\lambda_2 = \frac{aH\mu}{Kmr}$. The basic reproduction number is given by the spectral radius of this matrix [19]. From these eigenvalues, we can say the basic reproduction number of this cholera model is

$$R_0 = \frac{aH\mu}{Kmr}. \tag{3.4}$$

The biological meaning of R_0 is that it indicates the average amount of secondary infections that one diseased individual causes in a completely susceptible population. The square root form means the two-step infection pathway (humans infect water, and water infects humans). If $R_0 < 1$, the DFE is locally stable and the infection will ultimately die out. When $R_0 \leq 1$, there is a unique disease-free equilibrium $E_0 = (H, 0, 0, 0)$. If $R_0 > 1$, the DFE becomes unstable and the infection may continue, resulting in an endemic equilibrium. When $R_0 > 1$, besides E_0, there also exists a unique positive equilibrium given by,

$$\begin{aligned} S^* &= \frac{nH(K + B^*)}{nK + nB^* + aB^*}, \\ I^* &= \frac{anHB^*}{r(nK + nB^* + aB^*)}, \\ B^* &= \frac{\mu anB^*H(\psi + \theta B^*)}{r(nK + nB^* + aB^*)(m\psi + m\theta B^* + \alpha\beta B^*)}, \\ D^* &= \frac{\beta B^*}{\psi + \theta B^*}. \end{aligned} \tag{3.5}$$

If we compare the equation of B^* with $C_1 B^{*2} + C_2 B^* + C_3 = 0$, we get

$$B^* = \frac{-C_2 \pm \sqrt{C_2^2 - 4C_1 C_3}}{2C_1},$$

where

$$C_1 = \frac{r}{\mu anH}(n+a)(m\theta + \alpha\beta),$$

$$C_2 = \frac{r}{\mu anH}(m\psi(n+a) + nK\alpha\beta) + \theta(\eta - 1),$$

$$C_3 = \psi(\eta - 1).$$

Here $\eta = \frac{Kmr}{aH\mu}$, and we can write $R_0 = \frac{aH\mu}{Kmr} = \frac{1}{\eta}$.

If $R_0 > 1$, i.e. $\eta < 1$, then the positive equilibrium $E = (S^*, I^*, B^*, D^*)$ exists.

Case I: If $\eta > 1$, then $C_1, C_2, C_3 > 0$; no positive root for B^*.

Case II: If $\eta < 1$, then $C_1 > 0, C_2$ might be positive or negative and $C_3 < 0$.

The two roots of B^* are $B_1^* = \frac{-C_2 + \sqrt{C_2^2 - 4C_1C_2}}{2C_1}$ and $\frac{-C_2 - \sqrt{C_2^2 - 4C_1C_2}}{2C_1}$.

We can verify that $B_1^* - B_2^* = \frac{\sqrt{C_2^2 - 4C_1C_2}}{C_1} > 0$, which leads to $B_1^* > B_2^*$. Therefore, B_1^* is the largest root of B^*. It follows that $B_1^* > 0$ and $B_2^* < 0$, and we need to reject the negative root. Therefore, $B^* = B_1^*$.

By substituting $B = B^*$ back to (3.5), we find expressions for $S^*, I^*, B^*,$ and D^*. In terms of the variable B^*, the expressions are algebraically complex and involve quadratic or higher-order equations.

3.3 Positivity and Boundedness

Under the above initial conditions, all solutions of the system are positive and ultimately bounded in $(R_+ \times C^+ \times R_+ \times R_+)$.

Proof: We divide the proof into two sections: first, we show that the solutions remain positive, and second, we prove that they are ultimately bounded in $(R_+ \times C^+ \times R_+ \times R_+)$.

(i) Positivity of the Solutions:

The system's initial conditions $S(0) \geq 0$, $I(\theta) \geq 0$, $B(0) \geq 0$ and $D(0) \geq 0$ for all $\theta \in [-\tau, 0]$ are chosen to ensure that the solutions are nonnegative.

The first equation of the system (3.3) is

$$\frac{dS}{dt} = nH - nS(t) - a\Lambda(B(t))S(t).$$

If $S(t) = 0$, then $\frac{dS}{dt} = nH \geq 0$. So, $S(t)$ cannot be negative.

The second equation of the system (3.3) is,

$$\frac{dI}{dt} = a\Lambda(B(t))S(t) - rI(t).$$

If $I(t) = 0$, then $\frac{dI}{dt} = a\Lambda(B(t))S(t) \geq 0$. So, $I(t)$ stays nonnegative.

The third equation of the system (3.3) is

$$\frac{dB}{dt} = \mu I(t-\tau) - mB(t) - \alpha D(t)B(t).$$

If $B(t) = 0$, then $\frac{dB}{dt} = \mu I(t-\tau) \geq 0$. So, $B(t)$ cannot become negative.

The fourth equation of the system (3.3) is,

$$\frac{dD}{dt} = \beta B(t) - \psi D(t) - \theta B(t) D(t).$$

If $D(t) = 0$, then $\frac{dD}{dt} = \beta B(t) \geq 0$. So, $D(t)$ remains nonnegative.

Hence, we can say all the model variables $S(t), I(t), B(t), D(t)$ remain positive for all $t \geq 0$.

(ii) Boundedness of the Solutions:

We can rewrite the first equation of (3.3) as,

$$\frac{dS}{dt} + \left(n + a\frac{B(t)}{B(t)+K}\right) S(t) = nH.$$

This is a linear ODE with a positive integrating factor $e^{\int_0^t \left(n + a\frac{B(s)}{B(s)+K}\right) ds}$.

If we multiply the above equation by the integrating factor, we get

$$e^{\int_0^t \left(n + a\frac{B(s)}{B(s)+K}\right) ds} \frac{dS}{dt} + e^{\int_0^t \left(n + a\frac{B(s)}{B(s)+K}\right) ds} \left(n + a\frac{B(t)}{B(t)+K}\right) S(t) = e^{\int_0^t \left(n + a\frac{B(s)}{B(s)+K}\right) ds} nH,$$

$$S(t) = e^{-\int_0^t \left(n + a\frac{B(s)}{B(s)+K}\right) ds} \left[S(0) + \int_0^t e^{\int_0^s \left(n + a\frac{B(u)}{B(u)+K}\right) du} nH ds\right].$$

Using $\frac{B}{K+B} \leq 1$, we get

$$\begin{aligned} S(t) &\leq e^{-\int_0^t (n+a) ds} \left[S(0) + \int_0^t e^{\int_0^s (n+a) du} nH ds\right] \\ &= e^{-(n+a)t} \left[S(0) + nH \int_0^t e^{(n+a)s} ds\right] \\ &= e^{-(n+a)t} \left[S(0) + \frac{nH}{n+a}(e^{(n+a)t} - 1)\right] \\ &= \left(S(0) - \frac{nH}{n+a}\right) e^{-(n+a)t} + \frac{nH}{n+a}. \end{aligned}$$

So, as $t \to \infty, S(t) \to \frac{nH}{n+a} < H$. The solution satisfies $\limsup_{t\to\infty} S(t) \leq H,\ \forall t \geq 0$.

We can rewrite the second equation of (3.3) as,

$$\frac{dI}{dt} + rI(t) = a\frac{B(t)}{B(t)+K}S(t).$$

The integrating factor is $e^{\int_0^t r ds} = e^{rt}$. If we multiply the above equation by the integrating factor, we get

$$e^{rt}\frac{dI}{dt} + e^{rt}rI(t) = e^{rt}a\frac{B(t)}{B(t)+K}S(t)$$

$$\Rightarrow \frac{d}{dt}\left(I(t)e^{rt}\right) = a\frac{B(t)}{B(t)+K}S(t)e^{rt}$$

$$I(t) = e^{-rt}\left[I(0) + \int_0^t a\frac{B(s)}{B(s)+K}S(s)e^{rs}ds\right].$$

Using $\frac{B}{K+B} \leq 1$ and $S(t) \leq H$, we get

$$I(t) \leq e^{-rt}\left[I(0) + aH\int_0^t e^{rs}ds\right] = e^{-rt}\left[I(0) + \frac{aH}{r}(e^{rt}-1)\right].$$

Thus

$$I(t) \leq \frac{aH}{r} + e^{-rt}\left[I(0) - \frac{aH}{r}\right] \Rightarrow \limsup_{t\to\infty} I(t) \leq \frac{aH}{r}.$$

The third equation of (3.3) becomes

$$\frac{dB}{dt} + (m + \alpha D(t))B(t) = \mu I(t-\tau).$$

Since the integrating factor is $e^{\int_0^t (m+\alpha D(s))ds}$, we have

$$\frac{d}{dt}\left(B(t)e^{\int_0^t (m+\alpha D(s))ds}\right) = \mu I(t-\tau)e^{\int_0^t (m+\alpha D(s))ds},$$

$$B(t) = e^{-\int_0^t (m+\alpha D(s))ds}\left[B(0) + \int_0^t \mu I(s-\tau)e^{\int_0^s (m+\alpha D(u))du}ds\right].$$

By combining the boundedness of $I(t-\tau) \leq \frac{aH}{r}$ and $D(t) \geq 0$ (ensures exponential decay), we get

$$B(t) \leq e^{-\int_0^t (m+\alpha D(s))ds}\left[B(0) + \mu\frac{aH}{r}\int_0^t e^{\int_0^s (m+\alpha D(u))du}ds\right].$$

This implies

$$\limsup_{t\to\infty} B(t) \leq \frac{aH\mu}{mr}, \forall\ t \geq 0.$$

Rewriting the fourth equation of (3.3) becomes

$$\frac{dD}{dt} + (\psi + \theta B(t))D(t) = \beta B(t).$$

The integrating factor is $e^{\int_0^t (\psi+\theta B(s))ds}$, so we get

$$\frac{d}{dt}\left(D(t)e^{\int_0^t (\psi+\theta B(s))ds}\right) = \beta B(t)e^{\int_0^t (\psi+\theta B(s))ds},$$

$$D(t) = e^{-\int_0^t (\psi+\theta B(s))ds}\left[D(0) + \int_0^t \beta B(s)e^{\int_0^s (\psi+\theta B(u))du}ds\right].$$

Using the boundedness of $B(t) \leq \frac{aH\mu}{mr}$, we get

$$\limsup_{t\to\infty} D(t) \leq \frac{\beta aH\mu}{\psi mr},\ \forall t \geq 0.$$

Therefore, $S(t), I(t), B(t)$ and $D(t)$ are ultimately bounded in $R_+ \times C^+ \times R_+ \times R_+$.

$$\Gamma = \left\{(S, I, B, D) \in R_+ \times C^+ \times R_+ \times R_+ : |S| \leq H, |I| \leq \frac{aH}{r}, |B| \leq \frac{aH\mu}{mr}, |D| \leq \frac{\beta aH\mu}{\psi mr}\right\}.$$

We ensured that the model is biologically well-posed, and we showed that all solutions are non-negative and bound over time. This indicates that population compartments remain non-negative and concentrations do not escalate to infinity.

Chapter 4

Stability Analysis

Stability analysis is a crucial method in the study of infectious disease dynamics. It enables us to determine if the population will return to equilibrium after slight impacts. When it comes to cholera, understanding the conditions under which the disease persists or resolves can directly impact public health policies.

The local stability of the endemic equilibrium and the disease-free equilibrium (DFE) under both non-delayed and delayed bacterial shedding scenarios is analyzed in these sections. This results in four basic cases.

The Jacobian of the system (3.3) is

$$J = \begin{pmatrix} -n - a\frac{B^*}{B^*+K} & 0 & -\frac{aS^*K}{(B^*+K)^2} & 0 \\ a\frac{B^*}{B^*+K} & -r & \frac{aS^*K}{(B^*+K)^2} & 0 \\ 0 & \mu e^{-\lambda\tau} & -m - \alpha D^* & -\alpha B^* \\ 0 & 0 & \beta - \theta D^* & -\psi - \theta B^* \end{pmatrix}. \tag{4.1}$$

4.1 The Disease-Free Equilibrium and The Endemic Equilibrium Without Delay

Case I: The Disease-Free Equilibrium $E_0 = (H, 0, 0, 0)$ when $\tau = 0$: In this scenario, we assume that infected individuals release bacteria into the environment right away, implying that there is no delay between infection and transmission to the aquatic reservoir of Vibrio. We analyze the DFE, which represents a state where everyone is susceptible and there are no infections or contaminated environments. The Jacobian matrix for $\tau = 0$ at $(H, 0, 0, 0)$ is

$$J_i = \begin{pmatrix} -n & 0 & -\frac{aH}{K} & 0 \\ 0 & -r & \frac{aH}{K} & 0 \\ 0 & \mu & -m & 0 \\ 0 & 0 & \beta & -\psi \end{pmatrix}.$$

When the model is linearized around the equilibrium, the infected and bacterial compartments' Jacobian matrix becomes block-diagonal. And we get, $\lambda_1 = -n, \lambda_2 = -\psi$

and the simplified characteristic equation of this matrix J_i is

$$\lambda^2 + (m+r)\lambda + (mr - \frac{aH\mu}{K}) = 0.$$

If we compare this polynomial equation to $x^2 + a_1 x + a_0 = 0$, we get,

$a_1 = m + r$ and $a_0 = mr - \frac{aH\mu}{K}$.

If $a_0, a_1 > 0$, then all the real roots will be negative.

Here, $a_1 = m + r > 0$ as the parameters m and r are positive.

The Routh-Hurwitz conditions say that all coefficients must be positive to ensure all eigenvalues have negative real parts.

If $a_0 = mr - \frac{aH\mu}{K} > 0$, then, $mr > \frac{aH\mu}{K}$. The basic reproduction number R_0, which is determined in chapter 3, can be used to rewrite this condition: $\frac{aH\mu}{Kmr} < 1 \Rightarrow R_0 < 1$.

Therefore, if $R_0 < 1$, then the DFE is locally asymptotically stable and unstable if $R_0 > 1$ [31]. The result confirms typical epidemiological intuition that a disease dies out in a completely susceptible population if each infected person causes fewer than one secondary infection.

The importance of this finding lies in the positive effects of preventative strategies. For instance, lowering bacterial shedding μ (improving sanitation), increasing bacterial death m, or reducing exposure to contaminated water a can bring R_0 below 1, guaranteeing that the illness cannot persist in the community.

Case II: The Endemic Equilibrium $E = (S^*, I^*, B^*, D^*)$ when $\tau = 0$: When $R_0 > 1$, all compartments obtain non-zero stable states, indicating a unique endemic

equilibrium. In this scenario, cholera becomes a permanent part of the population environment system. The Jacobian matrix for $\tau = 0$ is

$$J_{ii} = \begin{pmatrix} -n - a\frac{B^*}{B^*+K} & 0 & -\frac{aS^*K}{(B^*+K)^2} & 0 \\ a\frac{B^*}{B^*+K} & -r & \frac{aS^*K}{(B^*+K)^2} & 0 \\ 0 & \mu & -m - \alpha D^* & -\alpha B^* \\ 0 & 0 & \beta - \theta D^* & -\psi - \theta B^* \end{pmatrix}.$$

The determinant of the above Jacobian matrix is,

$$\det(J_{ii} - \lambda I) = \begin{vmatrix} -n - a\frac{B^*}{B^*+K} - \lambda & 0 & -\frac{aS^*K}{(B^*+K)^2} & 0 \\ a\frac{B^*}{B^*+K} & -r - \lambda & \frac{aS^*K}{(B^*+K)^2} & 0 \\ 0 & \mu & -m - \alpha D^* - \lambda & -\alpha B^* \\ 0 & 0 & \beta - \theta D^* & -\psi - \theta B^* - \lambda \end{vmatrix} = 0$$

$$\Rightarrow \quad (-n - \frac{aB^*}{B^*+K} - \lambda)[(-r-\lambda)\{(m + \alpha D^* + \lambda)(\psi + \theta B^* + \lambda) + \alpha\beta B^* - \alpha\theta B^* D^*\}$$
$$+ \frac{a\mu S^* K}{(B^*+K)^2}(\psi + \theta B^* + \lambda)] + \frac{a\mu S^* K}{(B^*+K)^2}\frac{aB^*}{B^*+K}(\psi + \theta B^* + \lambda) = 0$$

$$\Rightarrow \quad (n + \frac{aB^*}{B^*+K} + \lambda)[(r+\lambda)\{\lambda^2 + \lambda(m + \alpha D^* + \psi + \theta B^*) + (m\psi + \theta m B^* + \alpha\psi D^*$$
$$+ \alpha\beta B^*)\} - \frac{a\mu S^* K}{(B^*+K)^2}(\psi + \theta B^* + \lambda)] + \frac{a\mu S^* K}{(B^*+K)^2}\frac{aB^*}{B^*+K}(\psi + \theta B^* + \lambda) = 0$$

$$\Rightarrow \quad (n + \frac{aB^*}{B^*+K} + \lambda)\Big[\lambda^3 + \lambda^2(m + r + \psi + \alpha D^* + \theta B^*) + \lambda\{r(m + \alpha D^* + \psi + \theta B^*)$$
$$+ (m\psi + \theta m B^* + \alpha\psi D^* + \alpha\beta B^*) - \frac{a\mu S^* K}{(B^*+K)^2}\} + \{r(m\psi + \theta m B^* + \alpha\psi D^* + \alpha\beta B^*)$$
$$- \frac{a\mu S^* K}{(B^*+K)^2}(\psi + \theta B^*)\}\Big] + \frac{a\mu S^* K}{(B^*+K)^2}\frac{aB^*}{B^*+K}(\psi + \theta B^* + \lambda) = 0$$

$$\Rightarrow \quad \lambda^4 + \lambda^3(m+n+r+\psi+\alpha D^*+\theta B^*+\frac{aB^*}{B^*+K}) + \lambda^2\{(n+\frac{aB^*}{B^*+K})(m+r+\psi$$

$$+\alpha D^*+\theta B^*)+r(m+\alpha D^*+\psi+\theta B^*)+(m\psi+\theta mB^*+\alpha\psi D^*+\alpha\beta B^*)$$

$$-\frac{a\mu S^*K}{(B^*+K)^2}\} + \lambda\Bigg[(n+\frac{aB^*}{B^*+K})\{r(m+\alpha D^*+\psi+\theta B^*)+(m\psi+\theta mB^*+\alpha\psi D^*$$

$$+\alpha\beta B^*)-\frac{a\mu S^*K}{(B^*+K)^2}\}+r(m\psi+\theta mB^*+\alpha\psi D^*+\alpha\beta B^*)-\frac{a\mu S^*K}{(B^*+K)^2}(\psi+\theta B^*)$$

$$+\frac{a\mu S^*K}{(B^*+K)^2}\frac{aB^*}{B^*+K}\Bigg] + [(n+\frac{aB^*}{B^*+K})\{r(m\psi+\theta mB^*+\alpha\psi D^*+\alpha\beta B^*)$$

$$-\frac{a\mu S^*K}{(B^*+K)^2}(\psi+\theta B^*)\}+\frac{a\mu S^*K}{(B^*+K)^2}\frac{aB^*}{B^*+K}(\psi+\theta B^*)] = 0.$$

Comparing this equation to this fourth-degree characteristic polynomial $a_4\lambda^4+a_3\lambda^3+a_2\lambda^2+a_1\lambda+a_0=0$ we get,

$$a_4 = 1,$$

$$a_3 = m+n+r+\psi+\alpha D^*+\theta B^*+\frac{aB^*}{B^*+K},$$

$$a_2 = (n+\frac{aB^*}{B^*+K})(m+r+\psi+\alpha D^*+\theta B^*)+r(m+\alpha D^*+\psi+\theta B^*)$$
$$+(m\psi+\theta mB^*+\alpha\psi D^*+\alpha\beta B^*)-\frac{a\mu S^*K}{(B^*+K)^2},$$

$$a_1 = (n+\frac{aB^*}{B^*+K})\{r(m+\alpha D^*+\psi+\theta B^*)+(m\psi+\theta mB^*+\alpha\psi D^*+\alpha\beta B^*)$$
$$-\frac{a\mu S^*K}{(B^*+K)^2}\}+r(m\psi+\theta mB^*+\alpha\psi D^*+\alpha\beta B^*)-\frac{a\mu S^*K}{(B^*+K)^2}(\psi+\theta B^*)$$
$$+\frac{a\mu S^*K}{(B^*+K)^2}\frac{aB^*}{B^*+K},$$

$$a_0 = (n+\frac{aB^*}{B^*+K})\{r(m\psi+\theta mB^*+\alpha\psi D^*+\alpha\beta B^*)-\frac{a\mu S^*K}{(B^*+K)^2}(\psi+\theta B^*)\}$$
$$+\frac{a\mu S^*K}{(B^*+K)^2}\frac{aB^*}{B^*+K}(\psi+\theta B^*).$$

The Routh–Hurwitz criterion for fourth-order polynomials

$i) a_i > 0,$ for all $i = 0, 1, 2, 3, 4,$

$ii) a_2 a_1 - a_3 a_0 > 0,$

$iii) a_3 a_2 a_1 - a_4 a_1^2 - a_3^2 a_0 > 0.$

The Routh-Hurwitz stability criterion explains what conditions must be satisfied for the eigenvalues to have negative real parts. These criteria can be proven algebraically or numerically [1]. When they hold, the endemic equilibrium is locally asymptotically stable, meaning that the disease remains constant in the population if no changes are taken. This means that in real-world circumstances where cholera is endemic (for example, in areas of Sub-Saharan Africa and South Asia), the illness stabilizes until strong interventions are implemented.

4.2 The Disease-Free Equilibrium and The Endemic Equilibrium With Delay

Case III: The Disease-Free Equilibrium $E_0 = (H, 0, 0, 0)$ when $\tau \neq 0$: In real life, there is a delay between an individual's infection and the bacterial discharge into the environment. The biological incubation period or behavioral issues, like a delay in seeking care or poor sanitation, could be represented by this delay τ. The exponential term $e^{-\lambda\tau}$ in the linearized bacterial equation made the Jacobian matrix

more complicated:

$$J_{iii} = \begin{pmatrix} -n & 0 & -\frac{aH}{K} & 0 \\ 0 & -r & \frac{aH}{K} & 0 \\ 0 & \mu e^{-\lambda\tau} & -m & 0 \\ 0 & 0 & \beta & -\psi \end{pmatrix}.$$

Here, $\lambda_1 = -n, \lambda_2 = -\psi$ and the characteristic polynomial of the matrix J_{iii} becomes transcendental

$$\lambda^2 + (m+r)\lambda + (mr - \frac{aH\mu}{K}e^{-\lambda\tau}) = 0.$$

Now we will use the method of imaginary roots and separating real and imaginary parts [17]. Assume, $\lambda = i\omega$ (purely imaginary root). Substitute $\lambda = i\omega$ in the characteristic equation, we get,

$$\begin{aligned} &(i\omega)^2 + i(m+r)\omega + (mr - \frac{aH\mu}{K}e^{-i\omega\tau}) = 0 \\ \Rightarrow \quad &-\omega^2 + i(m+r)\omega + mr - \frac{aH\mu}{K}(\cos\omega\tau - i\sin\omega\tau) = 0 \\ \Rightarrow\ &-\omega^2 + i(m+r)\omega + mr - \frac{aH\mu}{K}\cos\omega\tau + i\frac{aH\mu}{K}\sin\omega\tau = 0. \end{aligned} \tag{4.2}$$

The real part of the equation (4.2) is

$$\begin{aligned} &-\omega^2 + mr - \frac{aH\mu}{K}\cos\omega\tau = 0 \\ \Rightarrow \quad &(-\omega^2 + mr)^2 = (\frac{aH\mu}{K}\cos\omega\tau)^2 \\ \Rightarrow\ &\omega^4 - 2\omega^2 mr + m^2r^2 = \frac{a^2H^2\mu^2}{K^2}\cos^2\omega\tau. \end{aligned} \tag{4.3}$$

The imaginary part is

$$(m+r)\omega + \frac{aH\mu}{K}\sin\omega\tau = 0$$
$$\Rightarrow \{(m+r)\omega\}^2 = (-\frac{aH\mu}{K}\sin\omega\tau)^2$$
$$\Rightarrow (m^2+2mr+r^2)^2\omega^2 = \frac{a^2H^2\mu^2}{K^2}\sin^2\omega\tau. \tag{4.4}$$

After adding (4.3) and (4.4) , we have

$$\omega^4 - 2\omega^2 mr + m^2r^2 + (m^2+2mr+r^2)^2\omega^2 = \frac{a^2H^2\mu^2}{K^2}(\cos^2\omega\tau + \sin^2\omega\tau)$$
$$\Rightarrow \quad \omega^4 + (m^2+r^2)\omega^2 + m^2r^2 - \frac{a^2H^2\mu^2}{K^2} = 0.$$

Comparing the above equation to the quadratic equation $\omega^2 + a_1\omega + a_0 = 0$ we get

$a_1 = m^2 + r^2 > 0$ as the parameters m and r are positive.

If $a_0 = m^2r^2 - \frac{a^2H^2\mu^2}{K^2} > 0$, then $m^2r^2 > \frac{a^2H^2\mu^2}{K^2}$, $\frac{a^2H^2\mu^2}{K^2m^2r^2} < 1$ or, $R_0^2 < 1$.

For $a_0 > 0$, we get $R_0^2 < 1$ and the equation has no positive real roots or purely imaginary roots, ensuring the local stability of the DFE.

Case IV: The Endemic Equilibrium $E = (S^*, I^*, B^*, D^*)$ when $\tau \neq 0$: In this case, we investigate the endemic equilibrium when a time-based delay is present. The system dynamics of this case involve both long-term infection and bacteria's delayed contribution to the environment. The linearized system gives a transcendental characteristic equation containing exponential delay components. The characteristic

equation of the matrix (4.1) is given by,

$$\det(J-\lambda I)=\begin{vmatrix} -n-a\frac{B^*}{B^*+K}-\lambda & 0 & -\frac{aS^*K}{(B^*+K)^2} & 0 \\ a\frac{B^*}{B^*+K} & -r-\lambda & \frac{aS^*K}{(B^*+K)^2} & 0 \\ 0 & \mu e^{-\lambda\tau} & -m-\alpha D^*-\lambda & -\alpha B^* \\ 0 & 0 & \beta-\theta D^* & -\psi-\theta B^*-\lambda \end{vmatrix}=0$$

$$\begin{aligned}
\Rightarrow\quad & (-n-\frac{aB^*}{B^*+K}-\lambda)[(-r-\lambda)\{(m+\alpha D^*+\lambda)(\psi+\theta B^*+\lambda)+(\alpha\beta B^* \\
& -\alpha\theta B^*D^*)\}+\frac{a\mu S^*K}{(B^*+K)^2}(\psi+\theta B^*+\lambda)e^{-\lambda\tau}]+\frac{a\mu S^*K}{(B^*+K)^2}\frac{aB^*}{B^*+K}(\psi \\
& +\theta B^*+\lambda)e^{-\lambda\tau}=0 \\
\Rightarrow\quad & (n+\frac{aB^*}{B^*+K}+\lambda)[(r+\lambda)\{\lambda^2+\lambda(m+\alpha D^*+\psi+\theta B^*)+(m\psi+\theta mB^* \\
& +\alpha\psi D^*+\alpha\beta B^*)\}-\frac{a\mu S^*K}{(B^*+K)^2}(\psi+\theta B^*+\lambda)e^{-\lambda\tau}]+\frac{a\mu S^*K}{(B^*+K)^2}\frac{aB^*}{B^*+K}(\psi \\
& +\theta B^*+\lambda)e^{-\lambda\tau}=0 \\
\Rightarrow\quad & (n+\frac{aB^*}{B^*+K}+\lambda)\Big[\lambda^3+\lambda^2(m+r+\psi+\alpha D^*+\theta B^*)+\lambda\{r(m+\alpha D^* \\
& +\psi+\theta B^*)+(m\psi+\theta mB^*+\alpha\psi D^*+\alpha\beta B^*)-\frac{a\mu S^*K}{(B^*+K)^2}e^{-\lambda\tau}\} \\
& +\{r(m\psi+\theta mB^*+\alpha\psi D^*+\alpha\beta B^*)-\frac{a\mu S^*K}{(B^*+K)^2}(\psi+\theta B^*)e^{-\lambda\tau}\}\Big] \\
& +\frac{a\mu S^*K}{(B^*+K)^2}\frac{aB^*}{B^*+K}(\psi+\theta B^*+\lambda)e^{-\lambda\tau}=0
\end{aligned}$$

$$\Rightarrow \quad \lambda^4 + \lambda^3\left(m+n+r+\psi+\alpha D^*+\theta B^*+\frac{aB^*}{B^*+K}\right)+\lambda^2\{(n+\frac{aB^*}{B^*+K})(m+$$

$$+r+\psi+\alpha D^*+\theta B^*)+r(m+\alpha D^*+\psi+\theta B^*)+(m\psi+\theta mB^*+\alpha\psi D^*+\alpha\beta B^*)$$

$$-\frac{a\mu S^*K}{(B^*+K)^2}e^{-\lambda\tau}\}+\lambda\Bigg[(n+\frac{aB^*}{B^*+K})\{r(m+\alpha D^*+\psi+\theta B^*)+(m\psi+\theta mB^*$$

$$+\alpha\psi D^*+\alpha\beta B^*)-\frac{a\mu S^*K}{(B^*+K)^2}e^{-\lambda\tau}\}+r(m\psi+\theta mB^*+\alpha\psi D^*+\alpha\beta B^*)$$

$$-\frac{a\mu S^*K}{(B^*+K)^2}(\psi+\theta B^*)e^{-\lambda\tau}+\frac{a\mu S^*K}{(B^*+K)^2}\frac{aB^*}{B^*+K}e^{-\lambda\tau}\Bigg]+\Bigg[(n+\frac{aB^*}{B^*+K})\{r(m\psi$$

$$+\theta mB^*+\alpha\psi D^*+\alpha\beta B^*)-\frac{a\mu S^*K}{(B^*+K)^2}(\psi+\theta B^*)e^{-\lambda\tau}\}$$

$$+\frac{a\mu S^*K}{(B^*+K)^2}\frac{aB^*}{B^*+K}(\psi+\theta B^*)e^{-\lambda\tau}\Bigg]=0$$

Expanding this yields a transcendental equation which can be expressed as

$$A_0(\lambda)+A_1(\lambda)e^{-\lambda\tau}=0, \tag{4.5}$$

where,

$$A_0(\lambda)=a_{01}\lambda^4+a_{02}\lambda^3+a_{03}\lambda^2+a_{04}\lambda+a_{05},$$

$$A_1(\lambda)=a_{11}\lambda^2+a_{12}\lambda+a_{13},$$

$$a_{01}=1,$$

$$a_{02}=m+n+r+\psi+\alpha D^*+\theta B^*+\frac{aB^*}{B^*+K},$$

$$a_{03}=(n+\frac{aB^*}{B^*+K})(m+r+\psi+\alpha D^*+\theta B^*)+r(m+\alpha D^*+\psi+\theta B^*)$$

$$+(m\psi+\theta mB^*+\alpha\psi D^*+\alpha\beta B^*),$$

$$a_{04} = (n + \frac{aB^*}{B^* + K})\{(r(m + \alpha D^* + \psi + \theta B^*) + (m\psi + \theta m B^* + \alpha\psi D^* + \alpha\beta B^*)\}$$

$$+ r(m\psi + \theta m B^* + \alpha\psi D^* + \alpha\beta B^*),$$

$$a_{05} = r(n + \frac{aB^*}{B^* + K})(m\psi + \theta m B^* + \alpha\psi D^* + \alpha\beta B^*),$$

$$a_{11} = -\frac{a\mu S^* K}{(B^* + K)^2},$$

$$a_{12} = -\frac{a\mu S^* K}{(B^* + K)^2}(n + \psi + \theta B^*),$$

$$a_{13} = -n\frac{a\mu S^* K}{(B^* + K)^2}(\psi + \theta B^*).$$

We again substitute $\lambda = i\omega$ (purely imaginary root) in the equation (4.5), and we get

$A_0(i\omega) + A_1(i\omega)e^{-i\omega\tau} = 0$

$\Rightarrow A_0(i\omega) + A_1(i\omega)(\cos\omega\tau - i\sin\omega\tau) = 0$

$\Rightarrow a_{01}(i\omega)^4 + a_{02}(i\omega)^3 + a_{03}(i\omega)^2 + a_{04}(i\omega) + a_{05} + (a_{11}(i\omega)^2 + a_{12}(i\omega) + a_{13})(\cos\omega\tau -$

$i\sin\omega\tau) = 0$

$\Rightarrow a_{01}\omega^4 - ia_{02}\omega^3 - a_{03}\omega^2 + ia_{04}\omega + a_{05} + (-a_{11}\omega^2 + ia_{12}\omega + a_{13})(\cos\omega\tau - i\sin\omega\tau) = 0.$

Separating the real and imaginary parts, we get

$$a_{01}\omega^4 - a_{03}\omega^2 + a_{05} = (a_{11}\omega^2 - a_{13})\cos\omega\tau - a_{12}\omega\sin\omega\tau$$

$$a_{02}\omega^3 - a_{04}\omega = a_{12}\omega\cos\omega\tau - (a_{11}\omega^2 - a_{13})\sin\omega\tau.$$

After squaring and adding both equations, we have

$$(a_{01}\omega^4 - a_{03}\omega^2 + a_{05})^2 + (a_{02}\omega^3 - a_{04}\omega)^2 = (a_{11}\omega^2 - a_{13})^2 + (a_{12}\omega)^2.$$

Manipulate the above equation into a quadratic polynomial in $\theta = \omega^2$:

$$(a_{01}\theta^2 - a_{03}\theta + a_{05})^2 + (a_{02}\theta\sqrt{\theta} - a_{04}\sqrt{\theta})^2 = (a_{11}\theta - a_{13})^2 + (a_{12}\sqrt{\theta})^2$$

$$\Rightarrow a_{01}\theta^4 + \theta^3(a_{02}^2 - 2a_{01}a_{03}) + \theta^2(a_{03}^2 + 2a_{01}a_{05} - 2a_{02}a_{04} - a_{11}^2)$$

$$+ \theta(-2a_{03}a_{05} + a_{04}^2 + 2a_{11}a_{13} - a_{12}^2) + (a_{05}^2 - a_{13}^2) = 0.$$

The characteristic polynomial for θ is $P(\theta) = c_4\theta^4 + c_3\theta^3 + c_2\theta^2 + c_1\theta + c_0$.

If this polynomial has no positive real roots, then the endemic equilibrium is locally asymptotically stable for all $\tau \neq 0$. If any of the roots are positive, the system may oscillate or diverge from equilibrium [10]. By extensive numerical experiments, we find that there is no positive root of the polynomial, indicating that there is no stability switch when τ increases [18].

However, if the delay τ exceeds a certain threshold, a Hopf Bifurcation can occur, leading to oscillatory solutions. In epidemiological terms, this implies recurrent outbreaks. According to Singh et al. [5], these oscillations simulate recurrent cholera outbreaks, where unexpected surges occur due to exposure variations or delays in control actions. This behavior is consistent with cholera dynamics in areas with irregular surveillance or changing access to clean water. Even when the average infection rate and disinfection efforts are proper, delayed interventions might result in reappearance cycles, which the model detects naturally.

4.3 Global Stability

Theorem 4.3.1: If $R_0 < 1$, then the disease-free equilibrium E_0 of the model is globally asymptotically stable on Γ.

Proof: Consider the Lyapunov function $V : \Gamma \to \mathbb{R}$ defined by:

$$V(S(t), I_t, B(t), D(t)) = \mu\left(S - H\ln\frac{S}{H}\right) + \mu I_t(0) + rB(t) + K_1 D(t) + r\mu\int_{-\tau}^{0} I_t(z)dz,$$

where, $K_1 = \frac{rm}{\beta}(1 - R_0) > 0$ for $R_0 < 1$, and $I_t(z) = I(t + z)$ for $z \in [-\tau, 0]$. Thus, for $R_0 < 1, V$ is positive definite in Γ with respect to the disease-free equilibrium E_0.

Now compute the derivative of V of the system,

$$\begin{aligned}
\dot{V} &= \mu\left(1 - \frac{H}{S}\right)\frac{dS}{dt} + \mu\frac{dI}{dt} + r\frac{dB}{dt} + K_1\frac{dD}{dt} + r\mu(I(t) - I(t-\tau)) \\
&= \mu\left(1 - \frac{H}{S}\right)(nH - nS - a\Lambda S) + \mu(a\Lambda S - rI) + r(\mu I(t-\tau) - mB - aDB) \\
&\quad + K_1(\beta B - \psi D - \theta BD) + r\mu I(t) - r\mu I(t-\tau) \\
&= \mu\left(\frac{S-H}{S}\right)(n(H-S)) - \mu a\Lambda S + \mu a\Lambda H + \mu a\Lambda S - \mu rI + \mu rI(t-\tau) - rmB \\
&\quad - \alpha rDB + K_1\beta B - K_1(\psi D + \theta BD) + \mu rI(t) - \mu rI(t-\tau) \\
&= -n\mu\frac{(H-S)^2}{S} + \mu a\Lambda H + (K_1\beta - rm)B - (\alpha rDB + K_1\psi D + K_1\theta BD) \\
&= -n\mu\frac{(H-S)^2}{S} + \mu\frac{aB}{B+K}H + \left(\frac{rm}{\beta}(1-R_0)\beta - rm\right)B - (\alpha rDB + K_1\psi D \\
&\quad + K_1\theta BD)
\end{aligned}$$

$$= -n\mu\frac{(H-S)^2}{S} + \mu\frac{aB}{B+K}H - \frac{aH\mu B}{K} - (\alpha rDB + K_1\psi D + K_1\theta BD)$$
$$= -n\mu\frac{(H-S)^2}{S} - \frac{aH\mu B}{K}\left(1 - \frac{K}{B+K}\right) - (\alpha rDB + K_1\psi D + K_1\theta BD).$$

Hence, $\dot{V} \leq 0$ on Γ and $\dot{V} = 0$ if and only if $S(t) = H$ and $B(t) = D(t) = 0$. Moreover from the third equation of (3.3), $I(t) = 0$ when $B(t) = 0$. Hence $\dot{V} < 0$ for all $(S, I, B, D) \neq E_0$ in Γ whereas $\dot{V} = 0$ if and only if $(S, I, B, D) = E_0$. This implies that E_0 is the largest invariant subset contained in the set $F = \{(S, I, B, D) \in \Gamma : \dot{V} = 0\}$. Thus, by LaSalle's invariance principle [14], we conclude that E_0 is globally asymptotically stable on Γ.

We can see from the figure 4.1 that for different initial conditions, the curve of $I(t), B(t)$, and $D(t)$ begins above zero and steadily goes down, eventually approaching zero from above, indicating that the Lyapunov function became constant as the system stabilized. Since $\dot{V} \leq 0$, the system will naturally go back to E_0 over time and

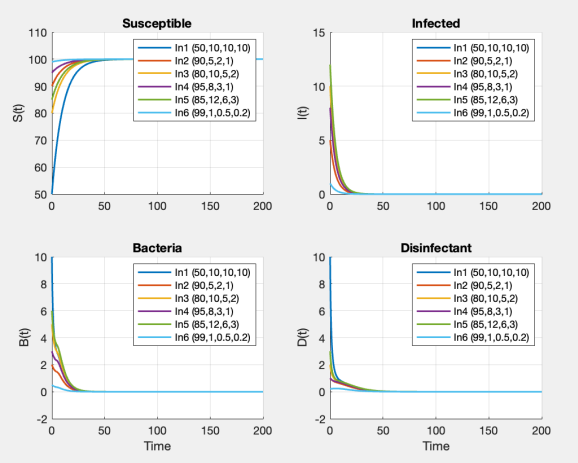

Figure 4.1: Global Stability of disease-free equilibrium

approach zero only at the disease-free equilibrium. This confirms global stability as the infection decreases and the bacterial concentration converges to the disease-free equilibrium [17].

Chapter 5

Numerical Simulations

This chapter includes a numerical analysis of the cholera model defined in Chapter 3 and analyzed mathematically in Chapter 4. Our goal is to find out how different values of the delay parameter τ, which measures the time between infection and bacterial release, change the basic reproduction number and the way infections spread. The simulations verify the theoretical results for each case and show how delay affects how the disease acts in the long run.

Four coupled differential equations are part of the complete model used in the simulations

$$\begin{aligned}
\frac{dS}{dt} &= nH - nS - a\Lambda(B)S, \\
\frac{dI}{dt} &= a\Lambda(B)S - rI, \\
\frac{dB}{dt} &= \mu e^{-n\tau} I(t-\tau) - mB - \alpha DB, \\
\frac{dD}{dt} &= \beta B - \psi D - \theta BD.
\end{aligned} \tag{5.1}$$

This system is simulated for different values of τ to see how it affects the development and control of disease.

5.1 Numerical Simulations for the model 3.3:

Simulations were performed using MATLAB for solving the ODE and DDE system over the interval $t \in [0, 50]$. Biologically feasible parameter values were chosen, and the initial conditions were picked to show a low bacterial load and infection. Now we see simulation figures for each of the four cases from Chapter 4. We use the following parameter values:

$$H = 100, n = 0.1, a = 0.05, K = 300, m = 0.33$$

$$\alpha = 0.05, \gamma = 0.1, \beta = 0.1, \psi = 0.1, \theta = 0.1$$

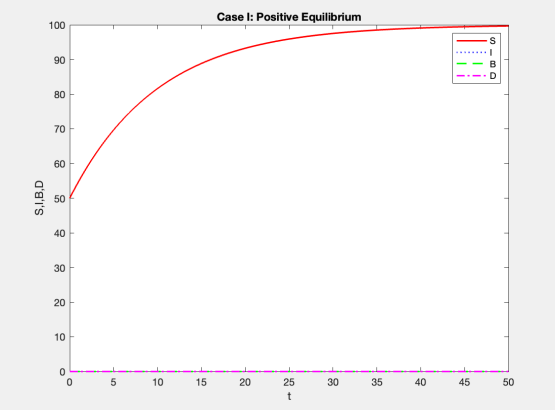

Figure 5.1: Disease-free equilibrium without delay

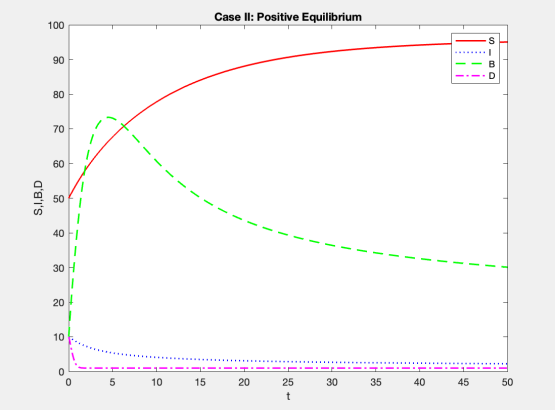

Figure 5.2: Non-disease free equilibrium without delay

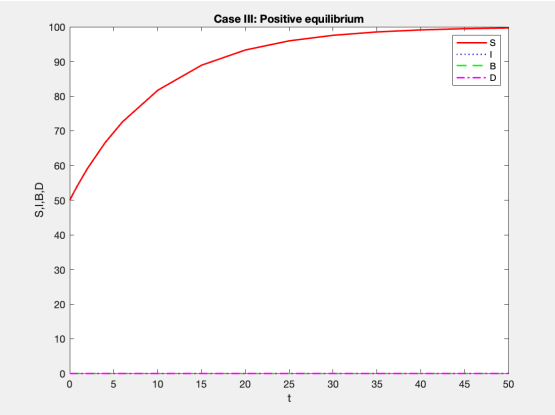

Figure 5.3: Disease-free equilibrium with delay

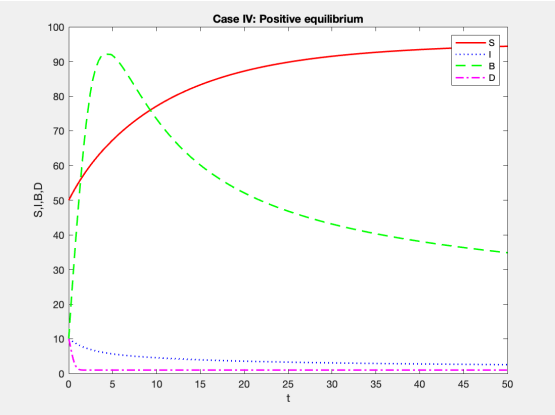

Figure 5.4: Non-disease free equilibrium with delay

For case-I and case-III, the value of μ is 0.1, and for case-II and case-IV, the $\mu = 5$. And we considered $(S^*, I^*, B^*, D^*) = (50, 10, 10, 10)$ for non-disease free equilibrium.

5.2 Numerical Simulations for the model 5.1:

To investigate the effects of the delay τ on disease transmission, we consider a modified basic reproduction number $R_0(\tau) = \frac{aH\mu}{kmr}e^{-n\tau} = R_0 e^{-n\tau}$ which is an exponentially decreasing function of τ and R_0 is the no-delay $R_0(\tau)$ value. In terms of biology, this delay is the time duration between infection and bacterial release into the environment. As τ increases, the probability of infected individuals surviving long enough to contribute to bacterial contamination decreases, reducing the possibility of constant transmission.

Simulations were showed for different τ values, and the corresponding $R_0(\tau)$ values

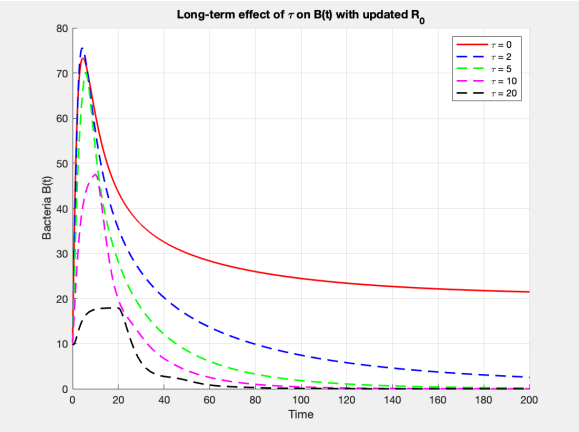

Figure 5.5: The effect of τ on $B(t)$

were calculated as follows:

For these different delay values, the bacteria concentration $B(t)$ was simulated over a large time horizon (up to $t = 200$). The figure displays the temporal evolution of $B(t)$ for each delay and provides a summary of the findings.

When $\tau = 0$ and $\tau = 2$, the modified basic reproduction number $R_0(\tau) > 1$ indicates that the disease may remain in the population. In this situation, the bacterial population reaches a non-zero endemic stable state.

At $\tau = 5$, $R_0(\tau)$ goes below 1 and the bacteria concentration eventually decreases.

At τ increases (for example $\tau = 10$ and $\tau = 20$), $R_0(\tau)$ reduces significantly, causing a faster reduction of $B(t)$ to zero.

These results imply that the time delay τ is an important factor in preventing infections. A significantly large delay can force the system towards a disease-free equilibrium by lowering $R_0(\tau)$ below the threshold value 1.

τ	$R_0(\tau)$
0	1.2626
2	1.0338
5	0.7658
10	0.4645
20	0.1709

Table 5.1: For different τ values the corresponding $R_0(\tau)$ values

It means that methods that effectively hold off the time between infection and environmental contamination (for example, early treatment or isolation) may significantly decrease the spread of cholera.

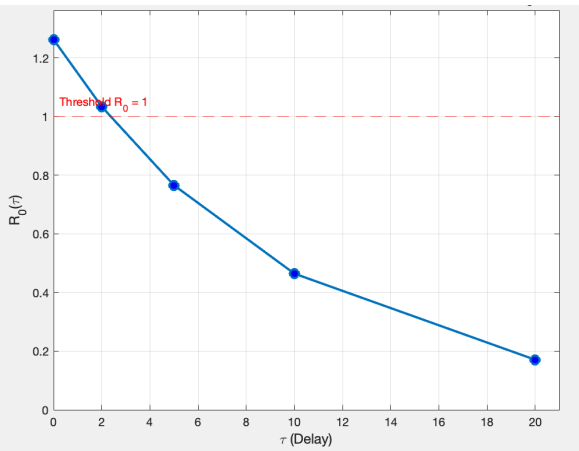

Figure 5.6: Effect of Delay τ on Modified Basic Reproduction Number $R_0(\tau)$

Chapter 6

Conclusion and Future Work

The dynamics of cholera transmission have been examined in this thesis using a delay differential equation model, with a focus on the consequences of delayed bacterial shedding and the use of disinfection as a control measure. The inspiration came from real-world observations of cholera outbreaks continuing in areas with poor sanitation, postponed treatments, and low awareness. Existing models in the literature have mostly focused on conventional transmission dynamics, sometimes missing the critical importance of time-based delays and environmental interventions such as water purification. This work fills that gap by combining delay and disinfection processes into a single mathematical framework.

Our model builds on the work of Codeco [2], Capasso and Paveri-Fontana [3], and Mukandavire [4] and extends their concepts by explicitly incorporating a disinfection compartment as well as a delay in pathogen release. This work is similarly comparable

to Wang and Wei's [1] delay-based modelling, which showed how delays are crucial in defining global dynamics even though they don't always result in oscillations. The basic reproduction number R_0 is an important threshold in our model. If $R_0 < 1$, the disease-free equilibrium is locally and numerically stable, suggesting cholera extinction. If $R_0 > 1$, the model supports an endemic equilibrium that can become persistent.

We used the Routh-Hurwitz criterion and transcendental characteristic equations to look at local stability and then used **MATLAB** simulations to show how delay and disinfecting rates affect how long an outbreak lasts or how quickly it goes away. Although some results support Wang and Wei's [1] finding that delay by itself might not cause periodic behavior, our numerical simulations show susceptibility to delay and temporary oscillations, particularly in situations when disinfection is insufficient or delayed to respond.

Wang and Wei [1] used Lyapunov functions to show global asymptotic stability. Our study, on the other hand, focused on local stability and numerical verification because it was more complicated to include a disinfection term and non-linear saturation. However, our results suggest that structures behave similarly. Stability and long-term results depend mostly on whether R_0 crosses unity and how quickly disinfection measures are applied.

We studied and established a cholera model with a one-time delay to show the time between when a person gets infected and when they start releasing bacteria

into the environment. However, early on in this project, we thought about a more general model with two delays, one for bacteria shedding and another for the effect of disinfection or other reactions.

We had a positivity issue when we tried to use both delays in the model. This means that some of the answers went negative, which doesn't make sense for real populations. Therefore, to ensure the appropriate operation of the system, we eliminated one of the delays.

In the future, we intend to return to the two-delay model and thoroughly investigate it. Our goal is to discover a solution to the positivity problem, either by modifying the model structure or creating better conditions so that we can maintain both delays without producing implausible outcomes.

Another interesting aspect of future research is determining whether the delays produce any changes in stability. We found no stability switches in this project where the system flips from stable to unstable based on the length of the delay. However, in more complicated models with two delays, this type of behavior can be observed. We want to see if different combinations of delays can result in oscillations or outbreaks that come and go over time.

In addition to making the model more realistic, resolving these issues in the future may help us better understand how time impacts cholera outbreaks and help us create more accurate simulations.

Chapter 7

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Appendix A

MATLAB Codes

```
%Case I: mu =0.1 Case II: mu=5

t=linspace(0,50,1000);

in1=[50,10,10,10]';


H = 100;       % Total human population

n = 0.1;      % Natural removal rate

a = 0.05;         % Contact rate

K = 300;         % Half-saturation constant

r = 0.2;     % Recovery rate

mu = 0.1;          % Shedding rate

m = 0.33;        % Bacteria removal rate

alpha = 0.05;    % Disinfectant effect

beta = 0.1;      % Bacteria growth from contamination
```

```
psi = 0.1;      % Disinfectant decay rate

theta = 0.1;    % Interaction effect


[tt,yy]=ode45(@(t,y) choleraODE(t,y,n,H, a, K, r, mu, m, alpha, beta, psi, theta),t,in1)


figure

plot(tt,yy(:,1),'r-','LineWidth',1.5)

hold on

plot(tt,yy(:,2),'b:','LineWidth',1.5)

hold on

plot(tt,yy(:,3),'g--','LineWidth',1.5)

hold on

plot(tt,yy(:,4),'m-.','LineWidth',1.5)

hold off

xlabel('t')

ylabel('S,I,B,D')

legend('S','I','B','D')

title('Case I: Positive Equilibrium')


function dydt=choleraODE(t,y,n,H, a, K, r, mu, m, alpha, beta, psi, theta)


dydt=[n*H - n*y(1) - a * (y(3) / (y(3) + K)) * y(1)
```

```
    a * (y(3) / (y(3) + K)) * y(1) - r*y(2)

    mu*y(2) - m*y(3) - alpha*y(4)*y(3)

    beta*y(3) - psi*y(4) - theta*y(3)*y(4)];

end
```

```
%Case III: mu =0.1 Case IV: mu=5


lags = [2];

tspan = [0 50];

sol = dde23(@choleraDDE, lags, @history, tspan);


figure

plot(sol.x,sol.y(1,:),'r-','LineWidth',1.5)

hold on

plot(sol.x,sol.y(2,:),'b:','LineWidth',1.5)

hold on

plot(sol.x,sol.y(3,:),'g--','LineWidth',1.5)

hold on

plot(sol.x,sol.y(4,:),'m-.','LineWidth',1.5)

hold off

xlabel('t')

ylabel('S,I,B,D')

legend('S','I','B','D')

title('Case III: Positive equilibrium')


function dydt=choleraDDE(t,y,Z)
```

```
H = 100; n = 0.1; a = 0.05;  K = 300;  r = 0.2; mu = 0.1;  m = 0.33;

alpha = 0.05;   beta = 0.1;   psi = 0.1;   theta = 0.1;


ylag1=Z(:,1);

dydt=[n*H - n*y(1) - a * (y(3) / (y(3) + K)) * y(1)

    a * (y(3) / (y(3) + K)) * y(1) - r*y(2)

    mu*ylag1(2) - m*y(3) - alpha*y(4)*y(3)

    beta*y(3) - psi*y(4) - theta*y(3)*y(4)];

end


function s = history(t)

  s = [50,10,10,10]';

end
```