People's Democratic Republic of Algeria
Higher Education and Research Scientifique
Larbi Tebessi University - Tebessa
Faculty of Exact Sciences and Natural and LIfe Sciences
Departement: Mathematics and Computer Sciences

DOCTORAL THESIS
Field : Mathematics and Computer Sciences
Option : Mathematics
Specialty : Applied Mathematics

Theme :

Control and applications of dynamical systems

Presented by:
Nouar Chorfi

Supervising Commitee:

- Abderrahmane Zarai	*Prof*	*Larbi Tebessi, Tebessa University*	*President*
- Salem AbdelMalek	*Prof*	*Larbi Tebessi, Tebessa University*	*Supervisor*
- Samir Bendoukha	*Prof*	*Taibah University, Saudi Arabia*	*Co- Supervisor*
- Salim Mesbahi	*Prof*	*Ferhat Abbas, Sétif 1 University*	*Examiner*
-Abdelhak Hafdallah	*MCA*	*Larbi Tebessi, Tebessa University*	*Examiner*
- Lamia Djebara	*MCA*	*Abbes Laghrour, Khenchela University*	*Examiner*

Academic year : 2024 /2025


بسم الله الرحمن الرحيم

Dedicace

I dedicate this thesis to the following individuals:

To my beloved mother and father, whose unwavering love and endless support have been my foundation and inspiration.

To my wonderful wife and children, Ayham and Norsin, whose boundless love and sacrifices have been my strength.
To my dear siblings, who have shared in both my joys and challenges, offering me constant encouragement and support.

To my friends and colleagues at Chorfi Taib High School, for their support and moral backing throughout my academic journey.

To all who have supported me, with kind words, advice, or assistance, and helped me reach this milestone.

Acknowledgements

First and foremost, I thank God the Almighty for granting me the patience, the will and energy to pursue and complete this humble work.

I would like to express my sincere appreciation and profound thanks to supervisor **Prof. Salem Abdelmalek** and co-supervisor **Prof. Samir Bendoukha** for their continuous and unwavering support throughout my thesis study and related research. Their patience, constant encouragement, and vast knowledge have had a significant impact on guiding my steps during all stages of the research and writing process. Their generous mentorship and consistent attention allowed me to overcome the challenges I faced and played a pivotal role in the successful completion of this work.

I hope that my sincere gratitude is conveyed here. I would also like to express my thanks to **Prof. Zarai Abderrahmane** for the honor of chairing the committee. It is also an honor to have **Prof. Hafidh Allah Abdelhak** from Tébessa University present. I am privileged to have **Prof. Salim Mesbahi** from Sétif 1 University, and I warmly thank them for kindly accepting to be members of my jury. I would also like to thank **Prof. Djebara Lamia** from Khenchela University for agreeing to be part of the committee.

Abstract

The work presented in this thesis is a study two types of problems associated with the HIV/AIDS epidemic model: the equilibrium model's stability analysis and the optimal control problem within the frameworks of ODE and PDE senses. We analyzed the local and global stability using the theory of Volterra-Lyapunov stable matrices combined with the classical Lyapunov function method. For the optimal control problem, an optimal control strategy was proposed that incorporates three key measures to combat the spread of HIV/AIDS: promoting condom use, screening individuals unaware of their infection status, and providing treatment to those infected. The objective functional was designed to minimize the total number of both susceptible and infected individuals. Then an optimal control is obtained which minimizes the objective functional. Numerical simulations were carried out to illustrate and validate the analytical findings.

Keywords: HIV/AIDS, Epidemic model, Local and global asymptotic stability, Reaction-diffusion, Optimal control.

Résumé

Le travail présenté dans cette thèse porte sur l'étude de deux types de problèmes liés au modèle épidémiologique du VIH/SIDA : l'analyse de la stabilité du modèle d'équilibre et le problème de contrôle optimal dans les cas des équations différentielles ordinaires (ODE) et des équations aux dérivées partielles (PDE). Nous avons étudié la stabilité locale et globale en utilisant la théorie des matrices stables de Volterra-Lyapunov ainsi que la méthode classique des fonctions de Lyapunov, appliquées au système dans le cadre des ODE et des PDE. Concernant le problème de contrôle optimal, nous avons proposé un contrôleur optimal prenant en compte trois mesures différentes pour lutter contre la propagation du VIH/SIDA : l'utilisation de préservatifs, le dépistage des individus ignorants leur statut sérologique, et le traitement des personnes infectées. Une fonctionnelle objectif a été définie, visant à minimiser une combinaison du nombre d'individus susceptibles et du nombre d'individus infectés. Un contrôle optimal a ensuite été obtenu pour minimiser cette fonctionnelle. Des simulations numériques ont été réalisées pour illustrer les résultats analytiques.

Mots-clés : VIH/SIDA, Modèle épidémiologique, Stabilité asymptotique locale et globale, Réaction-diffusion, Contrôle optimal.

الملخص

يتناول العمل المقدّم في هذه الأطروحة دراسة نوعين من المسائل المرتبطة بنموذج فيروس نقص المناعة البشرية HIV/AIDS: تحليل استقرار النظام عند نقاط التوازن، ومشكلة التحكم الأمثل في حالتي ODE و PDE. تم تحليل الاستقرار المحلي والكلي للنظام باستخدام نظريات المصفوفات المستقرة لفولترا – ليابونوف، مع دمج دالة ليابونوف الكلاسيكية. بالنسبة لمشكلة التحكم الأمثل، تم اقتراح استراتيجية تحكم أمثل تشمل ثلاث تدابير رئيسية لمكافحة انتشار فيروس نقص المناعة البشرية: تعزيز استخدام الواقي الذكري، فحص الأفراد الذين لا يعلمون بحالة إصابتهم، وتوفير العلاج للمصابين. تم تصميم دالة الهدف للتقليل من العدد الإجمالي للأفراد القابلين للإصابة والمصابين، ثم تم الحصول على تحكم أمثل يقلل من دالة الهدف. قمنا أيضًا بإجراء محاكاة عددية للتوضيح والتحقق من صحة النتائج التحليلية.

الكلمات المفتاحية : فيروس نقص المناعة البشرية HIV/AIDS، نظام وبائي، الاستقرار المقارب المحلي و الكلي، التفاعل و الانتشار ، التحكم الأمثل .

Publications and Conferences

Publications

- N. Chorfi, S. Bendoukha and S. Abdelmalek, The optimal control of an HIV/AIDS reaction-diffusion epidemic model, *Discrete and Continuous Dynamical Systems-S*, (2024).
- N. Chorfi, S. Abdelmalek and S. Bendoukha, Stability analysis and optimal control of an HIV/AIDS epidemic model, preprint, 2023, 2304.08251.

Participation in National and International Conferences

- N. Chorfi, S. Bendoukha and S. Abdelmalek, An optimal control problem for a reaction-diffusion HIV/AIDS system, *IEEE International Conference on Recent Advances in Mathematics and Informatics(ICRAMI' 2021)*, September 21-22, 2021 at Tebessa, Algeria.
- N. Chorfi, S. Abdelmalek and S. Bendoukha, Stability analysis and an optimal control applied to the spread of HIV/AIDS model, *African Conference on Dynamical Systems and Ordinary Differential Equations (ACDSODE'21), March 20-23, 2021, Bejaia university, Algeria.*
- N. Chorfi, S. Abdelmalek and S. Bendoukha, Stability analysis and an optimal control of fractional-Order modified HIV/AIDS model, *International on Pure and Applied Mathematical (IC-PAM'21)*, May 26-27, 2021, Ourgla, Algeria.

- N. Chorfi, S. Abdelmalek and S. Bendoukha, Stability analysis for reaction-diffusion HIV/AIDS system, *National Conference on Pure and Applied Mathematics (CNMPA'2021)*, April 15, 2021 at Tebessa university, Algeria.

Contents

Contents x

Introduction 1

1 Preliminary notions 8

1.1 Some useful theorem 8

1.2 Fundamental ODE stability theory 10

1.2.1 Stability for nonlinear autonomous systems 11

1.2.2 Stability of equilibria via linearization 13

1.2.3 Global stability via Lyapunov functions 14

1.2.4 The Volterra-Lyapunov matrix theory for global stability 15

1.2.5 Basic theorem of Algebra 17

1.2.6 Technique for computing $\mathscr{R}_0$ in disease models 18

1.3 Reaction-Diffusion systems 21

1.3.1 Positivity of solutions 22

1.3.2 Some results on the existence of solutions for evolution equations . . 23

1.4 Stability theory for reaction-diffusion systems 24

1.4.1 Properties of the eigenvalues of the Laplace operator 24

1.4.2 The method of eigenfunction expansions 25

1.5 Optimal control for ODE case 27

1.5.1 Formulating the optimal control problem 27

1.5.2 Solving the optimal control problem 29

1.5.3 Forward-backward sweep method 30

1.6 Optimal control for PDE case 34

1.6.1 Existence of an optimal control 35

1.6.2 Sensitivities and necessary conditions 36

2 Stability analysis and optimal control of an HIV/AIDS epidemic model 38

2.1 Mathematical HIV/AIDS model 38

2.2 Positivity and well-posedness of solutions 41

2.2.1 Positivity of solutions 41

2.2.2 Well-Posedness of solutions in a feasible region 42

2.3 Existence of equilibrium points and calculation of $\mathscr{R}_0$ 43

2.4 Stability analysis of equilibria 45

2.4.1 The local and global asymptotic stability when $\mathscr{R}_0 < 1$ 45

2.4.2 The local and global asymptotic stability when $\mathscr{R}_0 > 1$ 49

2.5 Optimal control of the HIV/AIDS model 57

2.5.1 Existence of an optimal control 58

2.5.2 Characterization of the optimal control 60

2.6 Numerical simulations 63

2.6.1 Simulation of stability analysis 63

2.6.2 Optimal control simulation 65

3 The optimal control of an HIV/AIDS reaction-diffusion epidemic model 69

3.1 Reaction-Diffusion HIV/AIDS model 70

3.2 Local stability of the equilibria 71

3.3 Global stability of the equilibria 77

3.3.1 Global asymptotic stability of the disease-free equilibrium 77

3.3.2 Global asymptotic stability of the endemic equilibrium model 79

3.4 Mathematical model and optimal control 81

3.4.1 Existence and uniqueness of a strong nonnegative solution. 82

3.4.2 Existence of the optimal solution 86

3.4.3 Derivation of optimal control 90

3.5 Numerical simulations 97

Conclusion 99

Bibliographie 102

Introduction

The Human Immunodeficiency Virus (HIV) is an infection that attacks the body's immune system and can progress to an advanced stage known as Acquired Immunodeficiency Syndrome (AIDS) if left untreated. The virus primarily targets white blood cells, weakening the immune system and making the body more vulnerable to diseases such as tuberculosis, infections, and certain types of cancer. The fluids of the body from an infected person, such as blood, breast milk, semen, and vaginal fluids. However, it is not spread through kissing, hugging, or sharing food. It can also be transmitted from mother to fetus. While there is no definitive cure for HIV, antiretroviral therapy (ART) is an effective method for controlling the virus. If left untreated, the virus may progress to AIDS after many years. According to the UNAIDS 2023 report, approximately 39.9 million people worldwide were living with HIV, including 38.6 million adults (over 15 years old) and 1.4 million children (under 15 years old). Additionally, 53 % of those living with HIV were women and girls.n the same year, 1.3 million new HIV infections were reported, and 630,000 people died from AIDS-related illnesses. Nowadays, the disease can be controlled through the use of condoms, abstinence, infection treatment, and blood testing. Keep in mind that in order to effectively prevent the spread of HIV, both those who are susceptible and those who are already infected must be well-informed about the many defenses against the disease. It is essential to examine various strategies for managing HIV/AIDS to help reduce its transmission, as there is currently no cure. The increasing number of unexpected infectious diseases recorded globally, which have become a major concern worldwide, has motivated our focus on prevention. In 2023, it is estimated that approximately 86% of individuals living with HIV were

aware of their status. However, around 5.4 million people remain unaware of their infection, highlighting the urgent need to improve testing and awareness initiatives.

The challenge of unaware infected individuals calls for an urgent need to better understand the key factors in disease transmission and to develop effective and optimal strategies for the prevention and control of the HIV/AIDS epidemic.

For decades, mathematical models have been utilized to analyze and comprehend the dynamics of various infectious disease epidemics, such as HIV/AIDS, tuberculosis, malaria, and others. These models have also been applied to develop control strategies and evaluate their effects on disease transmission. For instance, a basic model was introduced in [3] to study the spread of AIDS and its response to various influencing factors. In [44], the author proposed a framework for the transmission of HIV/AIDS in India.

Various control strategies have been developed for HIV/AIDS models. Recently, the application of optimal control theory has shown to be an effective method in disease modeling, offering a more detailed understanding of disease dynamics and enabling the formulation of precise preventive measures. In this context, the authors in [41] proposed and improved model by incorporating time-dependent control functions such as condom use, screening of unaware infectives, and treatment of infectives.

Most disease models in the literature are of the ODE type, as they focus solely on the concentration of various population groups while neglecting their spatial diffusion. Epidemiologically, spatial diffusion cannot be ignored in epidemic models. Recently, reaction-diffusion equations have been used by many authors in epidemiology [1, 5, 29, 31]. For instance, a model featuring a vaccinated group was analyzed in [1]. The authors examined the asymptotic stability of the spatially diffusive SVIR model, which accounts for the continuous immigration of all population groups. Along with considering spatial diffusion, it is also essential to incorporate optimal control in this work. In fact, optimal control theory has been effectively applied to various reaction-diffusion epidemiological and population

models, such as the general SIS model [54], SIR model [57], prey-predator model [56], and cancer invasion model [25]. However, to the best of our knowledge, there are only a few HIV/AIDS epidemic models within the reaction-diffusion framework that have been developed to analyze asymptotic stability and implement optimal control strategies for reducing HIV infection.

In this work, we focus on two main topics: the asymptotic stability of a reaction-diffusion HIV/AIDS system and applying optimal control theory. Our work began with the study of the fourth-order ODE system that describes the dynamics of HIV/AIDS transmission proposed in [41], where we investigated its stability and designed optimal control strategies. This part of the study was submitted as a draft [14] and is currently under review for publication in a scientific journal. Subsequently, we extended this ODE system into a reaction-diffusion system , allowing for a more in-depth stability analysis and the development of more comprehensive optimal control strategies. This extended work has been accepted and published as a research article [13]. The details of these studies and contributions will be presented in Chapters 2 and 3 of this thesis.

This thesis is structured into three chapters, as outlined below:

Chapter 1 : In this chapter, we review some of the necessary notion, and some preliminary denfinitions concerning stability and optimal control theory in ODE and PDE cases that will be useful in the following chapters.

Chapter 2 : In this chapter, we propose a continuous mathematical ODE model that describes the dynamics of a population infected with HIV/AIDS and present some basic properties of the model. Next, we determine the equilibria of the system and analyze their local and global asymptotic stability. After understanding the dynamics of the uncontrolled system, we incorporate three control measures into the model and demonstrate the existence of optimal controls. Pontryagin's Maximum Principle is utilized to characterize these optimal controls. Lastly, numerical simulations are conducted to validate the theoretical findings.

Chapter 3 : We propose a reaction-diffusion HIV/AIDS system with homogeneous Neumann boundary conditions, which extends the ODE model discussed in Chapter 2. We examine the local and global asymptotic stability of the system's equilibria. The model and optimal control formulation are introduced, the existence of a global positive strong solution is established. The existence of an optimal control is established through a minimizing sequence argument and the continuous dependence of the states on the control. Using standard optimality techniques, we analyze the objective functional and leverage the relationships between the state, sensitivity and adjoint equations to formulate a characterization of the control.

Notations

The following are some notations that are used in this work.

- $\mathbb{N}$: The set of natural numbers
- $\mathbb{R}$: The set of real numbers
- Ω: Open bounded subset of $\mathbb{R}^n$
- $\mathbb{R}^n$: Denotes the set of all n-tuples $x = (x_1, x_2, ..., x_n)$
- $D(A)$: Domain of A.
- M^{-1}: The inverse of matrix M
- $\det(M)$: Denotes the determinant of a matrix M
- M^T: The transpose of matrix M
- $M > 0$ (< 0) : The matrix M is symmetric positive (negative) definite
- $\widetilde{M}$: denote the $(n-1) \times (n-1)$ matrix obtained from any $n \times n$ matrix M by deleting its last row and last column
- $\mathscr{R}_0$: The basic reproduction number
- $\mathscr{U}$: The set of optimal controls
- $u_t = \dfrac{\partial u}{\partial t}$: partial derivative of u with respect to time t.
- $\nabla u = \left(\dfrac{\partial u}{\partial x_1}(x), \ldots, \dfrac{\partial u}{\partial x_n}(x) \right)$: gradient operator
- $\Delta u = \nabla \cdot \nabla u = \sum_{i=1}^{n} \dfrac{\partial^2 u}{\partial x_i^2}$: Laplace operator of u.

- $\dfrac{\partial u}{\partial \eta}(x) = \nabla u(x) \cdot \overrightarrow{\eta}(x)$: outward normal derivative on $\partial\Omega$
- $C([0,T];X) = \{u\colon [0,T] \to X \mid u \text{ is continuous } \}$
- $\langle u, v\rangle$: is the inner product or the scalar product of u and v
- $L^p(\Omega) = \left\{u : \Omega \to \mathbb{R}, \text{ mesurable and } \int_\Omega |u(x)|^p dx < \infty\right\}$, $1 \leq p < \infty$
- $\|u\|_{L^p(\Omega)} = \left(\int_\Omega |u(x)|^p dx\right)^{\frac{1}{p}}$
- $\langle u, v\rangle_{L^2(\Omega)} = \int_\Omega uv\, dx$ is the inner product in $L^2(\Omega)$
- $L^\infty(\Omega) = \{u : \Omega \to \mathbb{R}, \text{ mesurable and } \exists C \in \mathbb{R}_+ : |u| \leq C, \text{ p.p. } \}$
- $\|u\|_{L^\infty(\Omega)} = \inf\{C, |u(x)| \leq C, \text{ p.p. } \}$
- $\mathrm{L^p(0,\ T; X)} = \left\{u : [0,\ \mathrm{T}] \longrightarrow \mathrm{X};\ \text{mesurable and } \int_0^{\mathrm{T}} \|u(t)\|_{\mathrm{X}}^p dt < \infty\right\}$
- $\|u\|^p_{L^p(0,T,X)} dt = \int_0^T \|u\|^p_X dt$
- $L^p(0,T;L^p(\Omega)) = L^p(Q) = L^p([0,T]\times\Omega)$
- $L^\infty(0,T;X) = \left\{u : [0,T] \to X \text{ mesurable and } ess \sup_{t\in[0,T]} \|u\|_X\, dt < \infty\right\}$
- $\|u\|_{\mathbb{L}^\infty(0,T;X)} = ess \sup_{t\in[0,T]} \|u\|_X < \infty$
- $H^1(\Omega) = \left\{u \in L^2(\Omega), \dfrac{\partial u}{\partial x_i} \in L^2(\Omega)\right\}$
- $H^1_0(\Omega) = \{u \in H^1(\Omega) \setminus u = 0 \text{ in } \partial\Omega\}$
- $H^m(\Omega) = \{u \in L^2(\Omega) / D^\alpha u \in L^2(\Omega) \text{ for all } \alpha \in \mathbb{N}^n, |\alpha| \leq m, m \in \mathbb{N}^*\}$: Sobolev space
- $W^{n,p}(\Omega) = \{u \in L^p(\Omega), D^\alpha u \in L^p(\Omega), |\alpha| \leq m\ \}$
- $H^m(\Omega) = W^{n,2}(\Omega)$
- ODE : Ordinary Differential Equation
- PDE : Partial Differential Equation

- OC: Optimal control
- IC : Initial conditions
- BC : Boundary conditions

Chapter 1

Preliminary notions

In this chapter, we introduce the preliminary notions used throughout this thesis, highlighting some useful theorem and the fundamental stability theory in the context of ODE and PDE cases. Additionally, we explore the theory of optimal control as applied to ODE and PDE models.

1.1 Some useful theorem

Weak convergence

Let H be a real Hilbert space endowed with the scalar product (inner product) $(\cdot,\cdot)$ and the corresponding norm $\|\cdot\|$ defined by $\|x\| = (x,x)^{\frac{1}{2}}$.

Definition 1 ***(Weak convergence)*** *. We say that the sequence $\{u_n\} \subset H$ is weakly convergent to $u \in H$ if*

$$\lim_{n\to+\infty} \langle u_n, v\rangle = \langle u, v\rangle \quad \textit{for any } v \in H.$$

Theorem 1 *[4, page 212] Let $\{u_n\}$ be a sequence in the Hilbert space H and $u \in H$.*

1. *If* $\{u_n\}$ *is strongly convergent to* u*, that is,* $\lim_{n\to+\infty} \|u_n - u\| = 0$*, then* $\{f_n\}$ *is weakly convergent to* u*.*

2. *If* $\{u_n\}$ *is weakly convergent to* u*, then the sequence* $\|u_n\|$ *is bounded and*

$$\|u\| \leq \liminf \|u_n\|.$$

3. *If* $\{u_n\}$ *is weakly convergent to* u *and* $\{v_n\} \subset H$ *is strongly convergent to* $v \in H$*, then* $\{\langle u_n, v_n\rangle\}$ *is convergent to* $\langle u, v\rangle$ *in* $\mathbb{R}$*.*

For a finite-dimensional space, the weak and strong convergence are equivalent to the usual convergence.

Definition 2 *We say that a subset* $\mathcal{A} \subset H$ *is sequentially weakly compact if every sequence* $\{x_n\} \in \mathcal{A}$ *contains a weakly convergent subsequence.*

For finite-dimensional spaces, the sequentially weakly compact sets are the relatively compact sets, and the weak convergence is the usual one. A very important property of Hilbert spaces, and more generally of reflexive Banach spaces, is that every bounded subset is sequentially weakly compact. Namely, we have the following result .

Theorem 2 *Let* $\{u_n\} \subset H$ *be a bounded sequence. Then there exists a subsequence* $\{u_{n_k}\} \subset \{u_n\}$ *that is weakly convergent to an element of* H*.*

If we apply Theorem (2) to the Hilbert space $H = L^2(\Omega)$ is a nonempty bounded open subset), it follows that every bounded subset of $L^2(\Omega)$ is sequentially weakly compact.

If $\{f_n\} \subset L^2(\Omega)$ is a bounded sequence of functions, that is, there exists $M > 0$ such that

$$\|f_n\|_{L^2(\Omega)} \leq M \quad \text{for any } n,$$

then there exists the subsequence $\{f_{n_k}\} \subset \{f_n\}$ and $f \in L^2(\Omega)$ such that

$$\lim_{k\to+\infty} \int_\Omega f_{n_k}(x)\varphi(x)\,dx = \int_\Omega f(x)\varphi(x)\,dx \quad \text{for any } \varphi \in L^2(\Omega).$$

Green's formula

We now recall Green's formula, which generalize the integration by parts formula in one dimension, it is presented as follows:

Theorem 3 *[2] In dimension n. For any $u \in H^2(\Omega)$, and $v \in H^1(\Omega)$ we have*

$$\int_\Omega (\Delta u) v dx = \int_{\partial\Omega} \frac{\partial u}{\partial \eta} v ds - \int_\Omega \nabla u \nabla v dx,$$

where s is the surface mesure of $\partial\Omega$. Note that in the case when $u \in \mathbb{H}^2(\Omega)$, and $v \in \mathbb{H}_0^1(\Omega)$ Green's identity reads

$$\int_\Omega (\Delta u) v dx = -\int_\Omega \nabla u \nabla v dx.$$

Remarque 1 *If we write this formula in dimension one, Ω becomes a segment (a, b) in $\mathbb{R}$ and we nd the integration by parts formula: So let $u, v \in \mathbb{C}^1[a, b]$ we have a special case of the Green's formula.*

$$\int_a^b u'(x) v(x) dx = -\int_a^b u(x) v'(x) dx + u(b)v(b) - u(a)v(a).$$

Gronwall Lemma

Now we recall a basic inequality that is used in the study of elliptic and parabolic problems.

Lemma 1 *[27, page 8] Let $\varphi : [0, T] \to \mathbb{R}^+$ satisfy*

$$0 \leq \varphi(t) \leq a + b \int_0^t \varphi(s) ds, \quad \text{for all } 0 \leq t \leqslant T.$$

Gronwall showed that, if a and b are nonnegative constants, then

$$0 \leq \varphi(t) \leq a e^{bt}, \quad \text{for } 0 \leq t \leqslant T.$$

1.2 Fundamental ODE stability theory

In this section, we present the tools of Lyapunov stability theory, which will be used to analyze and study the stability of the epidemic model.

1.2.1 Stability for nonlinear autonomous systems

Consider a nonlinear autonomous dynamical system

$$\begin{cases} \dfrac{dw(t)}{dt} = F(w(t)), \\ w(0) = w_0, \end{cases} \tag{1.1}$$

where $w \in \Omega \subset \mathbb{R}^n$ and $F : \Omega \to \mathbb{R}^n$ is a locally Lipschitz continuous function defined on an open domain $\Omega \subset \mathbb{R}^n$ to $\mathbb{R}^n$. Equilibrium points are fundamental in analyzing the dynamics of any physical system in biology, economics, physics, etc. They are used in the study of stability theory, which is a topic of great importance to scientists.

Definition 3 ***(Equilibrium points)*** *A point $w_{eq} \in \mathbb{R}^n$ within the state space is defined as an equilibrium point of system (1.1) if it satisfies $\dfrac{dw}{dt} = 0$, which is equivalent to $F(w_{eq}) = 0$. This implies that if the system starts in state , it will remain in that state indefinitely. A dynamical system may have zero, one, or several equilibrium points. When multiple equilibrium points exist, it is necessary to examine the stability of each one.*

Definition 4 *[28]* ***(Invariant set)*** *A subset $\Upsilon \subseteq \mathbb{R}^n$ is an invariant set relative to system (1.1) if Υ contains the orbits of all its points.*

Definition 5 *[22]****(A positively invariant set)*** *A positively invariant set is a set with the following properties: Given a dynamical system (1.1) and trajectory $w(t; u_0)$ where w_0 is the initial point. Let $\Upsilon = \{w \in \mathbb{R}^n \mid \varphi(w) = 0\}$ where φ is a real-valued function. The set Υ is said to be positively invariant if $w_0 \in \Upsilon$ implies that $w(t; w_0) \in \Upsilon$ for all times $t \geq 0$. In other words, a solution that starts in Υ remains in Υ for all times $t \geq 0$.*

Definition 6 *[22]****(The region of attraction of the equilibrium)*** *Assume that $w = w_{eq}$ is an equilibrium point of (1.1) and let φ be the solution of the system. The set*

$$\Upsilon = \left\{ \zeta \in \Omega \mid \limsup_{t \to \infty} \varphi(t, \zeta) = w_{eq} \right\}$$

is called the region of attraction of the equilibrium w_{eq}.

The following definitions are presented to understand different types of stability of equilibrium points .

Definition 7 *[30, 49] **(Locally stable)** An equilibrium point is locally stable if all solutions which start near w_{eq} remain near w_{eq} for all time. This means that an equilibrium point w_{eq} for system (1.1) is called stable (in the sense of Lyapunov) if, given any $\epsilon > 0$, there exists $\delta(\epsilon) > 0$ (meaning that the initial conditions are in a neighborhood of w_{eq}) such that*

$$\|w(0) - w_{eq}\| < \delta(\epsilon) \implies \|w(t) - w_{eq}\| < \epsilon, \quad \text{for all} \quad t > 0.$$

Otherwise, it is unstable. In other words, stability in the sense of Lyapunov means that solution trajectories starting within the δ-neighbourhood of the equilibrium point w_{eq} remain forever in some ϵ-neighbourhood. Asymptotic stability, on the other hand, means that solution trajectories that start close enough to equilibrium points not only stay close enough but eventually converge to it. More precisely, we have the following definition:

Definition 8 *[20] **(Locally and globally asymptotically stable)** An equilibrium point w_{eq} is said to be locally asymptotically stable if, in addition, for any initial condition $\|w(0) - w_{eq}\| < \epsilon$, it holds that*

$$\lim_{t\to\infty} \|w(t) - w_{eq}\| = 0.$$

In other words, an equilibrium point is locally asymptotically stable if it is locally stable and if all solutions starting near w_{eq} converge to w_{eq} as $t \to \infty$. This corresponds to the situation where all trajectories close to the equilibrium point eventually converge to it as time increases. If the system is asymptotically stable regardless of the initial state vector $w(0)$, then the equilibrium point is globally asymptotically stable.

Local stability can be extended to a stability in a global sense.

Definition 9 ***(Global stability)**: Global stability means that the system will come to the equilibrium point from any possible starting point (i.e., there is no "nearby" condition).*

1.2.2 Stability of equilibria via linearization

In Lyapunov's first method, the linearization techniques is applied to study the stability. The study of stability in the case of nonlinear systems poses a very difficult problem, however, Lyapunov and others have noticed by studying the trajectories of integral curves in the neighborhood of equilibrium that, in the majority of cases, the equilibrium points of nonlinear systems can be brought back to the same types of equilibrium points of linear systems. So the study of a linear system is easy since it is solved in a purely algebraic criterion and the determination of the nonlinear stability of the equilibrium point is reduced to the linearization of the system (1.1) at this equilibrium point then, to answer the questions of stability, we must consider the linearization of the system (1.1) around the point of equilibrium gives the following linear system:

$$\begin{aligned}\frac{dw(t)}{dt} &= \left.\frac{\partial F(w(t))}{\partial w}\right|_{w=w_{eq}} w(t),\\ &= \mathscr{A} w(t).\end{aligned}$$

It can be obtained by constructing the Jacobian matrix, where $a_{ij} = \left[\dfrac{\partial f_i(w)}{\partial w_j}\right]_{w=w_{eq}}$ with $i, j = 1, 2, \ldots, n$ and $\mathscr{A} = (a_{ij})$. In the case a 2-species in system (1.1) (i.e. $m = 2$):

$$\frac{\partial v}{\partial t} = f_1(v, w), \quad \frac{\partial w}{\partial t} = f_2(v, w). \tag{1.2}$$

Assume there exists a quilibrium point $\mathscr{E}_{eq} = (v_{eq}, w_{eq})$, such that

$$f_1(v_{eq}, w_{eq}) = f_2(v_{eq}, w_{eq}) = 0.$$

The Jacobian of the system (1.2) at $\mathscr{E}_{eq}$ is defined by:

$$\mathscr{A} = \begin{pmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{pmatrix} = \begin{pmatrix} \left.\dfrac{\partial f_1}{\partial v}\right|_{\mathscr{E}_{eq}} & \left.\dfrac{\partial f_1}{\partial w}\right|_{\mathscr{E}_{eq}} \\ \left.\dfrac{\partial f_2}{\partial v}\right|_{\mathscr{E}_{eq}} & \left.\dfrac{\partial f_2}{\partial w}\right|_{\mathscr{E}_{eq}} \end{pmatrix}.$$

Theorem 4 *Let $\mathscr{A}$ be the Jacobian matrix of the nonlinear system (1.1). Then:*

1. *If all the eigenvalues of the Jacobian matrix $\mathscr{A}$ have strictly negative real parts, the nonlinear system (1.1) is asymptotically stable.*

2. *If all the eigenvalues of the Jacobian matrix $\mathscr{A}$ have negative real parts, the nonlinear system (1.1) is stable.*

3. *If at least one eigenvalue of $\mathscr{A}$ has a real part strictly greater than zero, the nonlinear system is unstable.*

1.2.3 Global stability via Lyapunov functions

For higher-dimensional systems, there are several techniques that could establish the global stability of an equilibrium. One of the most commonly used is the Lyapunov function. Lyapunov functions are used to prove the global stability of an equilibrium. They are named after the Russian mathematician Aleksandr Mikhailovich Lyapunov, who proposed the theory in his doctoral dissertation [38].

Theorem 5 *[30] Let $w = w_{eq}$ be an equilibrium point for system (1.1), and let $\Omega \subset \mathbb{R}^n$, be a domain containing w_{eq}. Let $\mathcal{V} : \Omega \to \mathbb{R}$ be a continuously differentiable function such that*

- $\mathcal{V}(w_{eq}) = 0$ *and* $\mathcal{V}(w) > 0$ *for* $w \in \Omega - \{w_{eq}\}$.
- $\mathcal{V}'(w) = \nabla\mathcal{V} \cdot F$, *given by*

$$\begin{aligned}\mathcal{V}'(w(t)) &= \frac{d}{dt}\mathcal{V}(w)(t) = \sum_{i=1}^{n} \frac{\partial \mathcal{V}}{\partial w_i} w_i' = \sum_{i=1}^{n} \frac{\partial \mathcal{V}}{\partial w_i} f_i = \langle \nabla\mathcal{V}, F(w) \rangle \\ &= \left[\frac{\partial \mathcal{V}}{\partial w_1}, \ldots, \frac{\partial \mathcal{V}}{\partial w_n} \right] [f_1, \ldots, f_n]^T = \frac{\partial \mathcal{V}}{\partial w} F(w) \leq 0, \ \text{in } \Omega.\end{aligned}$$

Then, $\mathcal{V}(u)$ is called a Lyapunov function and when we use direct Lyapunov method, we can get from the system if it is stable, asymptotic or unstable, but in some cases this method fails to prove stability, in this case we apply Lasalle invariance principle to get asymptotic stability.

Theorem 6 *[30] **(LaSalle's Theorem)** Let $w = w_{eq}$ be an equilibrium point for system (1.1), and $\Omega \subset \mathbb{R}^n$ be a domain containing w_{eq}. Let $\mathcal{V} : \Omega \to \mathbb{R}$ be a continuously differentiable function such that $\mathcal{V}'(w) \leq 0$ in Ω. Let $\Gamma = \{w \in \Omega : \mathcal{V}'(w) = 0\} = \{w_{eq}\}$. Then, w_{eq} is asymptotically stable.*

Remark 4: *If $\Omega = \mathbb{R}^n$ in the previous theorem, then w_{eq} is globally asymptotically stable.*

1.2.4 The Volterra-Lyapunov matrix theory for global stability

Here, we will introduce the necessary concepts that will facilitate our global stability analysis of equilibria system. The following fundamental result on matrix stability was originally proved by Lyapunov.

Lemma 2 *Let A be an $n \times n$ real matrix. Then all the eigenvalues of A have negative (positive) real parts if and only if there exists a matrix $H > 0$ such that $HA + A^T H^T < 0 (> 0)$.*

Definition 10 *We say a nonsingular $n \times n$ matrix A is Volterra-Lyapunov stable if there exists a positive diagonal $n \times n$ matrix M such that $MA + A^T M^T < 0$.*

The following lemma determines all 2×2 Volterra-Lyapunov stable matrices.

Lemma 3 *[55] Let $D = \begin{bmatrix} d_{11} & d_{12} \\ d_{21} & d_{22} \end{bmatrix}$ be a 2×2 matrix. Then D is Volterra-Lyapunov stable if and only if $d_{11} < 0, d_{22} < 0$ and $\det(D) = d_{11}d_{22} - d_{12}d_{21} > 0$.*

The characterization of Volterra-Lyapunov stable matrices of higher dimensions, however, is much more difficult. We need the following definition.

Definition 11 *We say a nonsingular $n \times n$ matrix A is diagonally stable (or positive stable) if there exists a positive diagonal $n \times n$ matrix M such that $MA + A^T M^T > 0$.*

From Definitions 10 and 11, it is clear that a matrix A is Volterra-Lyapunov stable if and only if its negative matrix, $-A$, is diagonally stable.

Lemma 4 *[55] Let $P = (p_{ij})$ be a 3×3 real matrix and $\hat{Q} = (\hat{q}_{ij}) = \det(P)Q$ be the adjoint of P, where $Q = (q_{1j})$ is the inverse of P. Then P is diagonally stable if and only if all the signed principal minors of $-P$ are positive, and the inequalities:*

$$(P_{31} + ZP_{13})^2 < 4P_{11}P_{33}Z,$$

$$(\widehat{q}_{31} + Z\widehat{q}_{13})^2 < 4\widehat{q}_{11}\widehat{q}_{33}Z$$

are satisfied simultaneously.

Based on Lemma 4, the following generalized result was obtained by Redheffer [45, 46] which will be frequently used in our global stability analysis. For simplicity, we only state the sufficient condition below.

Lemma 5 *[55] Let $D = [d_{ij}]$ be a nonsingular $n \times n$ matrix $(n \geq 2)$ and $M = \operatorname{diag}(m_1, \ldots, m_n)$ be a positive diagonal $n \times n$ matrix. Let $E = D^{-1}$. Then, $d_{nn} > 0, \widetilde{ME} + (\widetilde{ME})^T > 0$, and $\widetilde{MD} + (\widetilde{MD})^T > 0$, it is possible to choose $m_n > 0$ such that $MD + D^T M^T > 0$.*

Lemma 6 *[19] Let consider a disease model system written in the form*

$$\begin{cases} \dfrac{dv}{dt} = F(v, w), \\ \\ \dfrac{dw}{dt} = G(v, w), \end{cases} \tag{1.3}$$

and

$$G(v, 0) = 0, \tag{1.4}$$

where $v \in \mathbb{R}^m$ denotes (by its components) the uninfected populations and $w \in \mathbb{R}^n$ denotes (by its components) the infectious populations, $\mathscr{E}_0 = (v_{eq}, 0)$ denotes the DFE of the system.

Also assume the following conditions:

$(\mathbf{C_1})$ *For $\dfrac{dv}{dt} = F(v, 0)$. v_{eq} is globally asymptotically stable.*

($\mathbf{C_2}$) $G(v,w) = Aw - \hat{G}(v,w)$, *with* $\hat{G}(v,w) \geq 0$ *for* $(v,w) \in \Upsilon$,

where the jacobian matrix $A = \dfrac{\partial G}{\partial w}(v_{eq}, 0)$ *has all non-negative off-diagonal elements,*

and Υ *is the region where the model makes biological sense.*

Then the DFE $\mathscr{E}_0 = (v_{eq}, 0)$ *is globally asymptotically stable provided that* $\mathscr{R}_0 < 1$.

1.2.5 Basic theorem of Algebra

Theorem 7 ***(Routh–Hurwitz Criteria).*** *Consider the nth-degree polynomial with real constant coefficients*

$$p(\lambda) = \lambda^n + a_1\lambda^{n-1} + ... + a_{n-1}\lambda + a_n = 0.$$

Define n Hurwitz matrices using the coefficients a_i *of the characteristic polynomial:*

$$H_1 = a_1, H_2 = \begin{pmatrix} a_1 & 1 \\ a_3 & a_2 \end{pmatrix}, \; H_3 = \begin{pmatrix} a_1 & 1 & 0 \\ a_3 & a_2 & a_1 \\ a_5 & a_4 & a_3 \end{pmatrix}$$

and

$$H_n = \begin{pmatrix} a_1 & 1 & 0 & 0 & ... & 0 \\ a_3 & a_2 & a_1 & 1 & ... & 0 \\ a_5 & a_4 & a_3 & a_2 & ... & 1 \\ \vdots & \vdots & \vdots & \vdots & ... & \vdots \\ 0 & 0 & 0 & 0 & ... & a_n \end{pmatrix},$$

where $a_j = 0$ *if* $j > n$. *All roots of the polynomial* $P(\lambda)$ *are negative or have negative real part if and only if the determinants of all Hurwitz matrices are positive:*

$$\det H_j > 0, \qquad j = 1, ..., n.$$

The Routh–Hurwitz criteria for polynomials of degree n = 2, 3, 4 are given in

Table 1.1: **Routh-Hurwitz criteria**

n	Coefficient signs	Additional conditions
2	$a_1 > 0, a_2 > 0$	-
3	$a_1 > 0, a_2 > 0, a_3 > 0$	$a_1 a_2 > a_3$
4	$a_1 > 0, a_2 > 0, a_3 > 0, a_4 > 0$	$a_1 a_2 a_3 > a_3^2 + a_1^2 a_4$

Lemma 7 *[53] **(Descartes' Rule of Signs)** Consider a polynomial with real coefficient of the form*

$$p(\lambda) = a_0\lambda^n + a_1\lambda^{n-1} + ... + a_{n-1}\lambda + a_n = 0, a_0 \neq 0. \tag{1.5}$$

The sequence of coefficients of (1.5) is given by

$$a_n, a_{n-1}, ..., a_1, a_0.$$

Let k be the total number of sign changes from one coefficient to the next in the sequence. Then, the number of positive real roots of the polynomial is either equal to k, or k minus a positive even integer. (Note: if $k = 1$, then there exists exactly one positive real root).

1.2.6 Technique for computing $\mathscr{R}_0$ in disease models

To determine the epidemiological threshold $\mathscr{R}_0$, we employ an efficient method for calculating the basic reproduction number $\mathscr{R}_0$. This method, introduced by **P. Van Den Driessche** and **J. Watmough** [23], is designed to compute the principal eigenvalues of the "next-generation operator" associated with epidemiological ordinary differential equations (ODEs). Called to as the *Next Generation Matrix* method, this approach is particularly applicable when the population is divided into distinct and mutually exclusive categories. Assume there are $n > 0$ compartments representing disease states and $m > 0$ compartments representing non-disease states. The method below was introduced in [24, 39]. We then proceed with the following steps:

1. First, we arrange the equations so that the first n components of the ODE system correspond to the infected compartments. Thus, we write the original ODE system as

$$\begin{aligned} v_j' &= f_j(v,w), \quad j = 1,\dots m \\ w_i' &= g_i(v,w), \quad i = 1,\dots,n \end{aligned}$$

where $v = (v_1,\dots,v_m)^T \in \mathbb{R}^m$ represent the population in the non-disease compartment and $w = (w_1,\dots,w_n)^T \in \mathbb{R}^n$ represent the population in the disease compartment.

2. Second, we split the right-hand side in the infected compartments in the following way:

$$\begin{aligned} v_j' &= f_j(v,w), && j = 1,\dots,m \\ w_i' &= \mathscr{F}_i(v,w) - \mathscr{V}_i(v,w), && i = 1,\dots,n \end{aligned}$$

where

- $\mathscr{F}_i(v,w)$ is the rate of appearance of new infections in compartment i,
- $\mathscr{V}_i(v,w)$ incorporates the remaining transitional terms, namely births, deaths, disease progression, and recovery.

We note that this decomposition in infected and noninfected compartments as well as the decomposition into $\mathscr{F}$ and $\mathscr{V}$ may not be unique. Different decompositions may correspond to different interpretations of the disease process and may lead to somewhat different expressions of the reproduction number. The decomposition should satisfy the following properties:

- $\mathscr{F}_i(v,0) = 0$ and $\mathscr{V}_i(v,0) = 0$ for $v \geq 0$ and $i = 1,\dots,n$. The first condition says that all new infections are secondary infections arising from infected hosts. The second condition says that there is no immigration of susceptible individuals into the disease compartments.
- $\mathscr{F}_i(v,w) \geq 0$ for all $v, w \geq 0$.

- $\mathscr{V}_i(v, w) \leq 0$ whenever $w_i = 0$, for $i = 1, \ldots, n$. Each component $\mathscr{V}_i$ represents the net outflow of a compartment and must give inflow only (that is, be negative) if the compartment is empty.
- $\sum_{i=1}^{n} \mathscr{V}_i(v, w) \geq 0$ for all $v, w \geq 0$. The total outflow of all infected compartments is positive.

3. Assume that the disease-free system

$$v' = f(v, 0)$$

has a unique disease-free equilibrium $\mathscr{E}_0 = (v_{eq}, 0)$ such that all solutions with initial conditions of the form $(v_{eq}, 0)$ approach $(v_{eq}, 0)$ as $t \to \infty$. Determine the disease-free equilibrium $\mathscr{E}_0$.

4. Determine the matrices F and V with components

$$F = \left[\frac{\partial \mathscr{F}_i\left(v_{eq}, 0\right)}{\partial w_j}\right] \quad \text{and} \quad V = \left[\frac{\partial \mathscr{V}_i\left(v_{eq}, 0\right)}{\partial w_j}\right].$$

These matrices appear from the linearization of the system (2) around the disease-free equilibrium.

5. The Next-Generation Matrix, $\mathscr{K}$, is defined as:

$$\mathscr{K} = FV^{-1},$$

and the basic reproduction number, $\mathscr{R}_0$, is defined as:

$$\mathscr{R}_0 = \rho(FV^{-1}),$$

where $\rho(A)$ denotes the spectral radius of A.

Definition 12 *The spectral radius of a matrix A is defined as the maximum of the absolute values of the eigenvalues of A:*

$$\rho(A) = \sup\{|\lambda| : \lambda \in \sigma(A)\}$$

where $\sigma(A)$ denotes the set of eigenvalues of A.

It can be shown that V is a nonsingular M-matrix.

Definition 13 *A matrix A is called an M-matrix if:*

- *A has the Z-pattern, that is, the off-diagonal elements of A are nonpositive.*
- *The inverse of A exists and has nonnegative elements: $A^{-1} \geq 0$.*

Theorem 8 *[6] **(Perron-Frobenius theorem)** Let K be a matrix whose elements are nonnegative, and such that for some positive integer l, every element of the matrix K^l is positive. Then K has a simple positive eigenvalue λ_0 with a corresponding eigenvector having all positive components, and $|\lambda_j| < \lambda_0$ for every other eigenvalue λ_j.*

Since V is an M-matrix, $V^{-1} \geq 0$, that is, V^{-1} has only nonnegative entries. Since F also has only nonnegative entries, the next-generation matrix $\mathscr{K} = FV^{-1}$ is alsononnegative. That implies that the next-generation matrix has its spectral radius as an eigenvalue by the Perron-Frobenius theorem (8), and there are no other eigenvalues with larger modulus. This largest positive eigenvalue gives $\mathscr{R}_0$. Hence, The reproduction number $\mathscr{R}_0$ is computed as the largest positive eigenvalue of the next-generation matrix.

1.3 Reaction-Diffusion systems

Mathematically, by combining the two reaction f and diffusion processes $\mathscr{D}$, we obtain an equation of reaction-diffusion type. These are evolution equations which take the form of semi-linear parabolic partial differential equations. They can be represented by the general form:

$$\frac{\partial w}{\partial t} = \mathscr{D}\Delta w + f(w), \quad t \geq 0 \text{ and } x \in \Omega \subset \mathbb{R}^n, \tag{1.6}$$

where $w = w(t, x) \in \mathbb{R}^m$ represents the unknown vector function defined on $\mathbb{R}^+ \times \Omega$ with values in $\mathbb{R}^m$. Here, $f : \mathbb{R}^m \to \mathbb{R}^m$ describes all local reactions and is a nonlinear function

that represents the reaction phenomenon in question (e.g., human interaction or chemical reaction). $\mathscr{D}$ denotes a diagonal diffusion coefficient matrix for the kinetics. Note that we assume this system to be isotropic and uniform, so $\mathscr{D}$ is represented by a scalar matrix, independent of coordinates. The simplest reaction-diffusion equation in one spatial dimension and plane geometry (one-component reaction-diffusion equations) is:

$$\frac{\partial w}{\partial t} = \mathscr{D}\frac{\partial^2 w}{\partial x^2} + f(w), \quad t \geq 0 \text{ and } x \in \mathbb{R}. \tag{1.7}$$

For a general two-component system, the equation can be represented in the form:

$$\begin{pmatrix} \dfrac{\partial v}{\partial t} \\ \dfrac{\partial w}{\partial t} \end{pmatrix} = \begin{pmatrix} D_v & 0 \\ 0 & D_w \end{pmatrix} \begin{pmatrix} v \\ w \end{pmatrix} + \begin{pmatrix} F(v,w) \\ G(v,w) \end{pmatrix}, \tag{1.8}$$

where D_u and D_v are the diffusion coefficients for the components u and v, respectively, and F and G are nonlinear functions describing the reaction terms.

Reaction-diffusion systems are used to model a variety of phenomena in the natural sciences such as biology, chemistry, population dynamics, thermics, and also in physics, crystallization, medicine, etc. For example:

- In chemistry, the individuals represent chemicals.
- In biochemistry, they can represent molecules.
- In population dynamics, they represent humans.
- In the environment, they can represent animals or plants in a forest.

1.3.1 Positivity of solutions

Let us introduce the general system

$$\begin{cases} \dfrac{\partial w_i}{\partial t} - d_i \Delta w_i = f_i(w_1, w_2, \ldots, w_m) & \text{on } \mathbb{R}^+ \times \Omega, \\ \dfrac{\partial w_i}{\partial \nu} = 0 & \text{on } \mathbb{R}^+ \times \partial\Omega, \\ w_i(0,x) = w_{0i}(x) \geq 0, & i = 1, \ldots, m, \end{cases} \tag{1.9}$$

where $\Omega \subset \mathbb{R}^n$ is a bounded domain in $\mathbb{R}^n$ with smooth boundary $\partial\Omega$, and $d_i > 0$ for all $i = 1, \ldots, m$.

Definition 14 *[42]* ***(Quasi-positive function)*** *. The nonlinearity $F = (f_i)_{i=1,\ldots,m}$ (in system (1.9)), where $f_i : \mathbb{R}^m \to \mathbb{R}^m$, is called quasi-positive if satisfies:*

$$\forall w = (w_1, \ldots, w_m) \in \mathbb{R}^m_+, \quad \forall i = 1, \ldots, m, \quad f_i(w_1, \ldots, w_{i-1}, 0, w_{i+1}, \ldots, w_m) \geq 0. \quad (1.10)$$

Lemma 8 ***[42].*** *If in (1.9), moreover, the nonlinearity $(f_i)_{i=1,\ldots,m}$ is quasi-positive and $w_{0i}(x) \geq 0$ for all $i = 1, \ldots, m$ and $x \in \Omega$, then the solutions of system (1.9) satisfy*

$$w_i(t, x) \geq 0, \text{ for all } x \in \Omega \text{ and } t \in [0, T).$$

1.3.2 Some results on the existence of solutions for evolution equations

First recall a general existence result which we use in the chapter 3 (Proposition 1.2, p. 175, [12]; see also [51, 43]). Consider the initial value problem

$$\begin{cases} \dfrac{\partial z}{\partial t} = Az + f(t, z(t)), \quad t \in [0, T] \\ z(0) = z_0, \end{cases} \quad (1.11)$$

where A is a linear operator defined on a Banach space X, with the domain $D(A)$ and $f : [0, T] \times X \to X$ is a given function. If X is a Hilbert space endowed with the scalar product $(.,.)$, then the linear operator A is called dissipative if $(Az, z) \leq 0$, $(\forall z \in D(A))$.

Theorem 9 *X be a real Banach space, $A : D(A) \subseteq X \to X$ be the infinitesimal generator of a C0- semigroup of linear contractions $S(t), t \geq 0$ on X, and $f : [0, T] \times X \to X$ be a function measurable in t and Lipschitz continuous in $x \in X$, uniformly with respect to $t \in [0, T]$.*

(i) *If $z_0 \in X$, then problem (1.11) admits a unique mild solution, i.e. a function $z \in C([0, T]; X)$ which verifies the equality $z(t) = S(t)z_0 + \int_0^t S(t-s)f(s, z(s))ds \quad (\forall t \in [0, T])$.*

(ii) *If X is a Hilbert space, A is self-adjoint and dissipative on X and $z_0 \in D(A)$, then the mild solution is in fact a strong solution and $z \in W^{1,2}([0,T];X) \cap L^2(0,T;D(A))$.*

1.4 Stability theory for reaction-diffusion systems

Throughout this section, we will present our most important results about asymptotic stability for reaction-diffusion systems . We consider the system of reaction-diffusion equations (1.9) which can be written as follows:

$$\frac{\partial w(t,x)}{\partial t} = \mathscr{D}\Delta w(t,x) + F(w(t,x)), \quad t \geq 0,\ x \in \Omega, \tag{1.12}$$

where $F = (f_1, \ldots, f_n)$, $\mathscr{D} = \operatorname{diag}(d_1, \ldots, d_n)$, $\Delta w = (\Delta w_1, \ldots, \Delta w_n)$, and $w_0 = (w_{01}, \ldots, w_{0n})$, subject to initial conditions

$$w(0,x) = w_0(x), \quad x \in \Omega, \tag{1.13}$$

and Neumann boundary conditions

$$\frac{\partial w(t,x)}{\partial \eta} = 0,\ t > 0,\ x \in \partial\Omega. \tag{1.14}$$

Definition 15 *The constant vector w_{eq} is said to be a equilibrium solution of equation (1.12) subject to the initial data (1.13) and homogeneous Neumann boundary conditions (1.14) if $F(w_{eq}) = 0$.*

1.4.1 Properties of the eigenvalues of the Laplace operator

The Laplacian is an unbounded operator. To apply the Local Stability analysis in the context of partial differential equations from the previous chapter, we use the Neumann Laplacians (see [36]):

$$\begin{cases} -\Delta w_j = \lambda_j w_j, & \text{in } \Omega, \\ \dfrac{\partial w_j}{\partial \eta} = 0, & \text{on } \partial\Omega. \end{cases}$$

We denote the eigenvalues of the Laplacian with Neumann boundary conditions by

$$0 = \lambda_0 < \lambda_1 \leq \lambda_2 \leq \lambda_3 \leq \cdots \nearrow +\infty.$$

1.4.2 The method of eigenfunction expansions

The eigenfunction expansion method is an analytical approach that converts a partial differential equation (PDE) involving both space and time variables into a system of ordinary differential equations (ODEs) with respect to time only.

Let us denote by $\{\lambda_i; \{\Phi_{ij}\}_{j=1}^{m_i}\}_{i=0}^{\infty}$ the set of eigenvalues λ_i and the associated normalized eigenfunctions $\{\Phi_{ij}\}$ for an elliptic operator $-\Delta$ subject to a homogeneous Neumann boundary condition on Ω. Here, the eigenvalues satisfy $0 = \lambda_0 < \lambda_1 \leq \lambda_2 \leq \ldots$, and each λ_i has an algebraic multiplicity $m_i \geq 1$. Note that Φ_0 is constant, and $\lambda_i \to \infty$ as $i \to \infty$.

Thus, $d_1, \ldots, d_n$ and λ_i satisfy the following: $-\Delta\Phi_{ij} = \lambda_i \Phi_{ij}$ in Ω, with the boundary condition $\dfrac{\partial \Phi_{ij}}{\partial \eta} = 0$ on $\partial\Omega$, and the normalization condition $\int_\Omega \Phi_{ij}^2(x)\, dx = 1$. To define the linearization of system (1.12) around its equilibrium point, we obtain the following linear system:

$$\frac{\partial w}{\partial t} = \mathscr{D}\Delta w + \mathscr{A} w, \tag{1.15}$$

with the same initial and boundary conditions as specified in (1.12). The solution to the linear system (1.15) can be expressed in the form

$$w(t, x) = \sum_{i=0}^{\infty} \Phi_{ij}(x) e^{\mathscr{A}_i t} w_{0i}.$$

Let us denote the linearizing operator by $\mathcal{L} = \mathscr{D}\Delta + \mathscr{A}$. Similar to the ordinary differential equation (ODE) case, the asymptotic stability of the equilibrium point can be determined by examining the eigenvalues of the operator $\mathcal{L}$. Specifically, the solution is asymptotically stable if all eigenvalues of $\mathcal{L}$ have negative real parts. For example, in the case where $n = 4$, to achieve this, suppose $(\phi(x), \psi(x), \chi(x), \omega(x))^t$ is an eigenfunction of $\mathcal{L}$ corresponding to

an eigenvalue λ. By definition, the characteristic equation can be given by

$$\mathcal{L}\left(\phi(x),\psi(x),\chi(x),\omega(x)\right)^T = \xi\left(\phi(x),\psi(x),\chi(x),\omega(x)\right)^T,$$

leading to

$$(\mathcal{L}-\xi I)\begin{pmatrix}\phi\\ \psi\\ \chi\\ \omega\end{pmatrix} = \begin{pmatrix}0\\ 0\\ 0\\ 0\end{pmatrix}.$$

Let $(\phi(x),\psi(x),\chi(x),\omega(x))^T$ form a complete orthonormal basis in $L^2(\Omega)$ space, for this we can write $\phi = \sum_{0\le i\le\infty,1\le j\le m_i} a_{ij}\Phi_{ij}$, $\psi = \sum_{0\le i\le\infty,1\le j\le m_i} b_{ij}\Phi_{ij}$, $\chi = \sum_{0\le i\le\infty,1\le j\le m_i} c_{ij}\Phi_{ij}$, $\omega = \sum_{0\le i\le\infty,1\le j\le m_i} d_{ij}\Phi_{ij}$. This can be rearranged to the form

$$\sum_{0\le i\le\infty,1\le j\le m_i}(\mathscr{A}-\lambda_i\mathscr{D}-\xi I)\begin{pmatrix}a_{ij}\\ b_{ij}\\ c_{ij}\\ d_{ij}\end{pmatrix}\Phi_{ij} = \begin{pmatrix}0\\ 0\\ 0\\ 0\end{pmatrix}.$$

Theorem 10 *[22, 20]*

(i) The equilibrium point of the nonlinear problem (1.12) is (locally) asymptotically stable if the equilibrium point of the linearized problem (1.15) is asymptotically stable.

(ii) The equilibrium point w_{eq} of the system (1.12) is globally asymptotically stable if, for each nonnegative integer i, the eigenvalues of $(\mathscr{A}-\lambda_i\mathscr{D})$ have negative real parts.

(iii) The equilibrium point w_{eq} is unstable if, for some n, there exists an eigenvalue of $(\mathscr{A}-\lambda_i\mathscr{D})$ with either a positive real part or a zero real part with a non-simple elementary divisor.

Definition 16 ***(Lyapunov Functional)*** *We call*

$$\mathscr{L}:\mathbb{R}^+\to\mathbb{R}^+,$$

a functional Lyapunov associated with a system (1.9) *if* $\mathscr{L}$ *satisfying:*

$$\frac{d}{dt}\mathscr{L}(w(t,.)) \leq 0,$$

for all $t > 0$ *and any solution* $w(t,.) = (w_1(t,.), .w_2(t,.), \ldots, w_m(t,.))$ *of system* (1.9).

1.5 Optimal control for ODE case

This section presents the fundamental results in Optimal control Theory applied to biological models for systems with continuous-time Ordinary Differential Equations (ODEs). The conditions for the existence of optimal control are discussed, and Pontryagin's Maximum Principle is introduced. Additionally, a numerical method for solving optimal control problems is described.

1.5.1 Formulating the optimal control problem

An optimal control problem must be formulated to create an optimal control strategy for a disease outbreak. An important part of the optimal control problem is the function to be optimized, also called the objective function. This is a cost function that must be minimized and can be described as:

$$\mathscr{J}(u) = \int_{t_0}^{t_1} f(t, w(t), u(t))dt, \tag{1.16}$$

subject to the dynamic constraint

$$w'(t) = g(t, w(t), u(t)), \tag{1.17}$$

with initial condition

$$w(0) = w_0, \tag{1.18}$$

where $w(t)$ and $u(t)$ are the state and control variables, respectively, f and g will always represent continuously differentiable functions in all three arguments. Therefore, the control(s)

will always be piecewise continuous and the related states will be piecewise differentiable.. Ultimately, the goal is to find a function u^* that satisfies :

$$\mathscr{J}(u^*) = \min_{u \in \mathscr{U}} \mathscr{J}(u), \tag{1.19}$$

where our control set $\mathscr{U}$ to be Lebesgue measurable functions.

The existence of the optimal control can be obtained using a result by Fleming and Rishel [26]. First, we introduce definitions and an existence theorem that is helpful in proving the existence of optimal control.

Definition 17 ***(Convex Sets)*** *A set C is* convex *if the line segment between any two points in C lies in C, i.e.,*

$$\forall x, y \in C, \forall \vartheta \in [0,1], \quad \vartheta x + (1-\vartheta)y \in C.$$

Definition 18 ***(Convex function)*** *Let $f : I \to \mathbb{R}$ be a continuous function where I is an interval of $\mathbb{R}$. We say that f is a convex function if:*

$$\forall (x,y) \in I^2, \forall \vartheta \in [0,1],\ f(\vartheta x + (1-\vartheta)y) \leq \vartheta f(x) + (1-\vartheta) f(y).$$

This inequality is called the convexity inequality.

Theorem 11 *[8]* ***(Existence theorem)*** *Let $w'(t) = F_i(t, w_1, w_2, .., w_n)$, for $i = 1, 2, ..., n$ be a system of n differential equations with initial conditions $w_i(t_0) = w_{0i}$, for $i = 1, 2, ..., n$. If each of the functions $F_1, ...F_n$ and the partial derivatives $\frac{\partial F_1}{\partial w_1}, ..., \frac{\partial F_1}{\partial w_n}, ..., \frac{\partial F_n}{\partial w_1}, ..., \frac{\partial F_n}{\partial w_n}$ be continuous in a region R of $t, w_1, w_2, ..., w_n$ space defined by $\alpha < t < \beta, \alpha_1 < w_1 < \beta_1, ..., \alpha_n < w_n < \beta_n$,. Let the point $(t, w_{01}, w_{02}, \ldots, w_{0n})$ be in $\mathbb{R}$. Then, there exists an interval $|t - t_0| < h$ in which there is a unique solution $w_1 = \phi_1(t), \ldots, w_n = \phi_n(t)$ to the system of differential equations that satisfies the initial conditions.*

Theorem 12 *[26]. Consider the control problem with system (1.17)-(1.18). There exists an optimal control $u^* \in \mathscr{U}$ such that*

$$\mathscr{J}(u^*) = \min_{u \in \mathscr{U}} \mathscr{J}(u).$$

If the following conditions are met:

(i) *The set of controls and associated state variables is not empty.*

(ii) *The control set $\mathscr{U}$ should be closed and convex.*

(iii) *The right-hand side of the state system $g(t, w(t), u(t))$ is bounded by a linear function of the state and control variables.*

(iv) *The integrand $f(t, w(t), u(t))$ of the objective functional is convex on $\mathscr{U}$ and is bounded below by $C_1 |u|^\gamma - C_2$, with $C_1 > 0$, $C_2 > 0$ and $\gamma > 1$.*

1.5.2 Solving the optimal control problem

The optimal control $u(t)$ can be derived using Pontryagin's maximum principle. Pontryagin's maximum principle is a tool that generates a system of ordinary differential equations (ODEs) in terms of state and adjoint variables (with their respective initial and boundary conditions) that are satisfied at the optimum. This resulting system can then be solved numerically. The optimal control can be denoted as $u^*(t)$, and the state and adjoint variables evaluated at the optimum can be denoted as $w^*(t)$ and $\lambda^*(t)$, respectively. According to Pontryagin's maximum principle, it is is necessary to derive the Hamiltonian function.

Definition 19 ***(Hamiltonian)*** *Consider the OC problem (1.16)-(1.18). The Hamiltonian H is given by:*

$$\mathscr{H}(t, w(t), u(t), \lambda(t)) = f(t, w(t), u(t)) + \lambda(t) g(t, w(t), u(t)).$$

The first-order necessary condition for optimality in solving the optimal control problem can be derived by applying Pontryagin's maximum principle, and it is expressed as follows:

Theorem 13 *[32]If $u^*(t)$ and $w^*(t)$ with $t \in [t_0, t_1]$, are optimal for problem (1.16)-(1.18), then there exists a piecewise differentiable adjoint function $\lambda(t)$, such that :*

$$w'(t) = \frac{\partial \mathscr{H}}{\partial \lambda}(w(t), u(t), \lambda(t)), \tag{1.20}$$

$$\lambda'(t) = -\frac{\partial \mathscr{H}}{\partial w}(w(t), u(t), \lambda(t)), \tag{1.21}$$

so that

$$H(w^*(t), u^*(t), \lambda^*(t)) \leq H(w^*(t), u(t), \lambda^*(t)), u \in \mathscr{U} \tag{1.22}$$

and the corresponding boundary conditions are satisfied

$$w(t_0) = w_0, \tag{1.23}$$

$$\lambda(t_1) = 0. \tag{1.24}$$

The equation (1.21) is called the adjoint equation and equation (1.24) is termed the transversallity condition. From equation (1.22) the optimality equation can be derived,

$$\frac{\partial \mathscr{H}}{\partial u}(w(t), u(t), \lambda(t)) = 0, \text{ at } u^* \text{ for each } t \in [t_0, t_1]\,. \tag{1.25}$$

Proof. The proof can be found in Lenhart and Workman [32]. Furthermore, for the minimization of the control problem the following equation at u^* must hold:

$$\frac{\partial^2 \mathscr{H}}{\partial u^2} \geq 0. \tag{2.2.10}$$

■

1.5.3 Forward-backward sweep method

Forward-backward sweep method, is outlined in a recent book by Lenhart and Workman [32]. The method starts with an initial guess for the control variable. Next, the state equations are solved forward in time, while the adjoint equations are solved backward. The control is updated by incorporating the new values of the states and adjoint variables into its definition, and the process continues iteratively until convergence is achieved. Consider the optimal control problem:

$$\min_u \int_{t_0}^{t_1} f(t, w, u)dt,$$

$$\text{subject to } w'(t) = g(t, w(t), u(t)), w(t_0) = w_0.$$

We present a numerical algorithm to determine the optimal control u^*. The time interval $[t_0, t_1]$ is divided into subintervals with specific points of interest $t_0 = b_1, b_2, \ldots, b_N, b_{N+1} = t_1$, where these points are typically equally spaced. The approximation is represented by the vector $\vec{u} = (u_1, \ldots, u_{N+1})$, where $u_i \approx u(b_i)$. There are multiple methods available to solve the optimal control problem.

Let $\vec{w} = (w_1, \ldots, w_{N+1})$ and $\vec{\lambda} = (\lambda_1, \ldots, \lambda_{N+1})$ represent the vector approximations for the state and adjoint variables, respectively. According to Lenhart and Workman [32], the steps for implementing the forward-backward sweep method are as follows:

Step 1. Begin with an initial guess for $\vec{u}$ over the interval (typically, $\vec{u} \equiv 0$ suffices).

Step 2. Using the initial condition $w(t_0) = w_0$ and the current values of $\vec{u}$, solve for $\vec{w}$ forward in time based on the corresponding differential equation from the optimality system.

Step 3. Apply the transversality condition $\lambda_{N+1} = \lambda(t_1) = 0$, and using the values for $\vec{u}$ and $\vec{w}$, solve for $\vec{\lambda}$ backward in time according to its differential equation from the optimality system.

Step 4. Update $\vec{u}$ by incorporating the new values of $\vec{w}$ and $\vec{\lambda}$ into the characterization of the optimal control.

Step 5. Check for convergence. If the values of the variables in the current iteration are sufficiently close to those from the previous iteration, output the current values as the solution. If not, return to **Step 2**.

For **Steps 2** and **3**, any standard ODE solver can be applied. For instance, Wang [52] applied the same approach, solving the differential equations using the `ode45` solver in Matlab. In this context, a Runge-Kutta 4 routine is employed.

Let $w'(t) = f(t, w(t))$, then the 4th order Runge-Kutta method is given by:

$$w_{i+1} = w_i + \frac{h}{6}(k_1 + 2k_2 + 2k_3 + k_4), \tag{1.26}$$

where

$$\begin{aligned} k_1 &= f(t_i, w_i), \\ k_2 &= f(t_i + \frac{h}{2}, w_i + \frac{h}{2}k_1), \\ k_3 &= f(t_i + \frac{h}{2}, w_i + \frac{h}{2}k_2), \\ k_4 &= f(t_i + h, w_i + hk_3). \end{aligned} \tag{1.27}$$

The parameter h is the time step. Notice not only that w_{i+1} is the approximation of $w(t_i+h)$, but also that the values of k_1, k_2, k_3 and k_4 are computed for each i and used in $i+1$.. Additionally, this method has an error of $O(h^4)$. More details on the stability and accuracy of the 4th-order Runge-Kutta method can be found in Butcher [9, 10]. For the control u, there are various approaches to approximate its value. For instance, an interpolating polynomial or spline for u could be constructed. In most cases, it is sufficient to approximate u as follows:

$$u_{new} * (1 - c^k) + oldu * c^k, \tag{1.28}$$

where k is the current iteration and $0 < c < 1$. The terms u_{new} and $oldu$ represent the control estimates obtained from the current characterization and the previous sweep, respectively. This is a weighted average, where the weight shifts towards the current iteration with each step. In our numerical experiments, we utilize the average.

$$\frac{u_i + u_{i+1}}{2}.$$

We use the 4th-order Runge-Kutta method with 3 input variables, allowing us to solve the state equations forward in time.

$$\begin{aligned} k_1 &= f(t_i, w_i, u_i), \\ k_2 &= f(t_i + \frac{h}{2}, w_i + \frac{h}{2}k_1, \frac{1}{2}(u_i + u_{i+1})), \\ k_3 &= f(t_i + \frac{h}{2}, w_i + \frac{h}{2}k_2, \frac{1}{2}(u_i + u_{i+1})), \\ k_4 &= f(t_i + h, w_i + hk_3, u_{i+1}), \\ w_{i+1} &= w_i + \frac{h}{6}(k_1 + 2k_2 + 2k_3 + k_4). \end{aligned}$$

To solve the adjoints backward in time

$$
\begin{aligned}
&j = N + 2 - i \\
&k_1 = f(t_j, \lambda_j, w_j, u_j), \\
&k_2 = f(t_j - \frac{h}{2}, \lambda_j - \frac{h}{2}k_1, \frac{1}{2}\left(w_j + w_{j-1}\right), \frac{1}{2}\left(u_j + u_{j-1}\right)), \\
&k_3 = f(t_j - \frac{h}{2}, \lambda_j - \frac{h}{2}k_2, \frac{1}{2}\left(w_j + w_{j-1}\right), \frac{1}{2}\left(u_j + u_{j-1}\right)), \\
&k_4 = f(t_j - h, \lambda_j - hk_3, w_{j-1}, u_{j-1}), \\
&\lambda_{j-1} = \lambda_j - \frac{h}{6}(k_1 + 2k_2 + 2k_3 + k_4),
\end{aligned}
$$

where N represents the total number of time steps, with $i = 1, 2, 3, \ldots, N$.

Various convergence tests are available for **Step 5**. Often, it is sufficient to require that $\|u - oldu\| = \sum_{i=1}^{N+1} |u_i - oldu_i|$ is small, where $\vec{u}$ is the vector of estimated control values for the current iteration, and $\vec{oldu}$ is the vector of estimated values from the previous iteration. Here, $\|.\|$ denotes the ℓ^1 norm for vectors, meaning the sum of the absolute values of the components. Both vectors have a length of $N+1$. Specifically, the stopping criterion used is explained in Lenhart and Workman [32], which requires the relative errors to be negligibly small, i.e.,

$$
\begin{aligned}
&\frac{\left\|\vec{u} - \vec{oldu}\right\|}{\left\|\vec{u}\right\|} \leq \delta, \\
&\frac{\left\|\vec{w} - \vec{oldw}\right\|}{\left\|\vec{w}\right\|} \leq \delta \\
&\frac{\left\|\vec{\lambda} - \vec{old\lambda}\right\|}{\left\|\vec{\lambda}\right\|} \leq \delta,
\end{aligned}
$$

where δ is the accepted tolerance. A small adjustment is necessary to account for the possibility of zero controls. Therefore, we multiply both sides by $\left\|\vec{u}\right\|$ to eliminate it from the denominator. Hence, our condition becomes:

$$
\delta \left\|\vec{u}\right\| - \left\|\vec{u} - \vec{oldu}\right\| \geq 0,
$$

or

$$\delta \sum_{i=1}^{N+1} |u_i| - \sum_{i=1}^{N+1} |u_i - oldu_i| \geq 0.$$

By the same reason, we can deduce that

$$\delta \left\| \vec{w} \right\| - \left\| \vec{w} - \vec{oldw} \right\| \geq 0,$$
$$\delta \left\| \vec{\lambda} \right\| - \left\| \vec{\lambda} - \vec{old\lambda} \right\| \geq 0.$$

The convergence and stability of the forward-backward sweep algorithm are discussed in McAsey et al. [40].

1.6 Optimal control for PDE case

The concept of optimal control for partial differential equations (PDEs) typically involves a PDE with a state variable $w(t, x)$ and a control function $u(t, x)$, both of which depend on space and time. The objective functional defines the goal of the problem, and in this context, we express our functional in integral form. Let us now consider the following optimal control problem:

$$\mathscr{J}(u) = \int_0^T \int_\Omega f(t, x, w(t, x), u(t, x)) dx dt,$$

subject to

$$Aw(t, x) = g(w(t, x), u(t, x)) \text{ in } [0, T] \times \Omega, \text{ along with } IC, BC,$$

Let Ω be an open, connected subset of $\mathbb{R}^n$, and let A be a partial differential operator with the corresponding initial conditions (IC) and boundary conditions (BC). The functions f and g are continuous in terms of the state variable w and the control function u. We focus on problems that involve both spatial and temporal variables, though steady-state problems, which depend solely on spatial variables, can also be addressed [21, 35, 37]. Our objective is to determine the optimal control u^* from an appropriate control set such that

$$\mathscr{J}(u^*) = \inf_{u \in \mathscr{U}} \mathscr{J}(u).$$

After defining a control set $\mathscr{U}$ and a solution space for the states, one can typically demonstrate the existence of a state solution for a given control. In particular, for each control u, there exists a state solution $w = w(u)$, showing the dependence of w on u.

1.6.1 Existence of an optimal control

Proving the existence of an optimal control in the context of partial differential equations (PDEs) is more challenging than in the case of ordinary differential equations (ODEs). To justify convergence, it is essential to have a priori estimates of the norms of the states within the solution space. When the controls are bounded above and below, corresponding bounds for the states in the solution space can generally be derived. This boundedness ensures the existence of a minimizing sequence u_n where

$$\lim_{n \to \infty} \mathscr{J}(u_n) = \inf_{u \in \mathscr{U}} \mathscr{J}(u).$$

In the suitable weak sense, this typically leads to

$$u_n \to u^* \text{ in } L^2([0,T] \times \Omega),$$
$$w_n = w(u_n) \to w^* \text{ in the solution space,}$$

for some u^* and w^*, it is essential to show that $w^* = w(u^*)$, which indicates that the solution depends continuously on the controls. Furthermore, it is necessary to prove that u^* is an optimal control, i.e.,

$$\mathscr{J}(u^*) = \inf_{u \in \mathscr{U}} \mathscr{J}(u).$$

To obtain the necessary conditions, it is required to differentiate the objective functional with respect to the control. More specifically, we must differentiate the mapping

$$u \to \mathscr{J}(u).$$

Observe that $w = w(u)$ typically contributes to $\mathscr{J}(u)$, so we also need to differentiate the mapping

$$u \to w(u).$$

In a typical well-posed PDE problem, the continuous dependence of the solution on the control ensures the continuity of this mapping. However, in this case, differentiable dependence is required.

1.6.2 Sensitivities and necessary conditions

The map $u \mapsto w(u)$ is weakly differentiable in the directional derivatives sense (Gâteaux):

$$\lim_{\varepsilon \to 0} \frac{w(u + \varepsilon k) - w(u)}{\varepsilon} = \psi \ .$$

The function ψ represents the sensitivity of the state to the control. In the case of ordinary differential equations, the adjoint is chosen to cancel the sensitivity terms. However, in this context, we need the sensitivity partial differential equation in order to derive the adjoint partial differential equation. A priori estimates of the difference quotients in the norm of the solution space ensure the existence of the limit function ψ and demonstrate that it satisfies a partial differential equation, which is the linearized version of the state PDE.

$$\mathcal{L}\psi = F(w, k, u) \text{ with appropriate BC, IC} \ .$$

It is important to note that the linear operator $\mathcal{L}$ comes from linearizing the state PDE operator A. Typically, ψ will have zero boundary conditions and initial conditions since $w(u+\epsilon k)$ and $w(u)$ have the same boundary and initial conditions. The objective functional $\mathscr{J}(u)$ is differentiated with respect to u at u^*,

$$0 \leq \lim_{\varepsilon \to 0^+} \frac{\mathscr{J}(u^* + \varepsilon k) - \mathscr{J}(u^*)}{\varepsilon}.$$

We use the adjoint problem λ and ψ to simplify and derive an explicit characterization of the optimal control.

$$u^* = G(w^*, \lambda)$$

The purpose of λ and ψ is to simplify the difference quotient of $\mathscr{J}$ and to derive the characterization of the optimal control. In the adjoint equation, the operator acts as the adjoint operator corresponding to the one applied to ψ in the sensitivity equation. The boundary conditions for the adjoint system are determined by both the boundary conditions of the sensitivity equations and the properties of the adjoint operator. Formally, the operator $\mathcal{L}$ and its adjoint operator $\mathcal{L}^*$ are related by

$$\langle \mathcal{L}\psi, \lambda \rangle = \langle \mathcal{L}^*\lambda, \psi \rangle,$$

where $\langle \cdot, \cdot \rangle$ represents the L^2 inner product. A key technique is integration by parts in multiple dimensions, which enables us to transfer the derivatives on ψ from the operator $\mathcal{L}$ to the derivatives of λ in the adjoint operator $\mathcal{L}^*$.

In a time-dependent problem, the adjoint problem generally includes conditions at the final time, which are similar to the transversality conditions discussed so far. The nonhomogeneous term in the adjoint equation originates from differentiating the integrand of the objective functional $\mathscr{J}$ with respect to the state. In informal terms, we have:

$$\mathcal{L}^*\lambda = \frac{\partial(\text{integrand of } \mathscr{J})}{\partial w},$$

where $\mathcal{L}$ represents the operator from the ψ PDE. We will define the optimal control based on the solutions of both the state and adjoint equations. The collection of the state and adjoint equations, together with the characterization of the control, is known as the optimality system.

Chapter 2

Stability analysis and optimal control of an HIV/AIDS epidemic model

This chapter explores an HIV/AIDS epidemic model that divides the population into four distinct groups. A thorough stability analysis shows that the system achieves both local and global asymptotic stability at its equilibrium point. To manage the spread of the disease, an optimal control strategy is proposed, incorporating three key interventions: promoting condom use, screening unaware infected individuals, and providing treatment for those infected. The main goal of this control approach is to reduce the populations of susceptible and infected individuals. Numerical simulations are performed, and the results are provided to validate the theoretical analysis discussed throughout the chapter. The findings presented in this chapter contribute to the ongoing research by Chorfi, Abdelmalek, and Bendoukha, and are currently available as a preprint [14].

2.1 Mathematical HIV/AIDS model

In this section, we examine the fourth-order model introduced in [14], with its corresponding diagram presented in Figure (2.1). This model has been discussed in various studies, includ-

ing those in [7, 14, 41, 50, 55]. Okosun *et al.* improved the model in [50] by incorporating time-dependent control parameters (such as condom use, screening of unaware infectives, and treatment of infectives) under the assumption that AIDS patients could also transmit the disease recklessly. They analyzed this modified model and applied optimal control to evaluate the potential effects of these three control measures on HIV spread [41]. The authors in [55] utilized Lyapunov functions combined with the Volterra-Lyapunov matrix properties to demonstrate the global stability of the fourth-order model by Okosun *et al.* [41]. The model assumes a total population of size $N(t)$ at time t, which is divided into four sub-populations: susceptible individuals $S(t)$, infective individuals unaware of their infection $I_1(t)$, HIV-positive individuals aware of their infection $I_2(t)$, and individuals with AIDS $A(t)$. Thus, the total population is represented as $N(t) = S(t) + I_1(t) + I_2(t) + A(t)$.

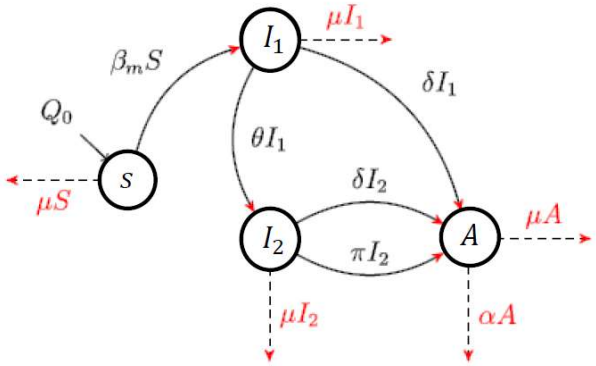


Figure 2.1: Flow diagram for HIV/AIDS disease transmission model.

The model dynamics are described by the ODE system:

$$\begin{cases} \dfrac{dS(t)}{dt} = Q_0 - \beta_m S(t) - \mu S(t), \\ \dfrac{dI_1(t)}{dt} = \beta_m S(t) - (\theta + \mu + \delta)\, I_1(t), \\ \dfrac{dI_2(t)}{dt} = \theta I_1(t) - (\delta + \mu + \pi)\, I_2(t), \\ \dfrac{dA(t)}{dt} = \delta I_1(t) + \delta I_2(t) + \pi I_2(t) - (\alpha + \mu)\, A(t), \end{cases} \tag{2.1}$$

where

$$\beta_m = \frac{(1 - u_1)(\beta_1 c_1 I_1 + \beta_2 c_2 I_2 + \beta_3 c_3 A)}{N}, \tag{2.2}$$

with initial conditions

$$S(0) = S_0, A(0) = A_0,\ I_i(0) = I_{0i},\ \text{for } i = 1, 2. \tag{2.3}$$

The terms c_i (for $i = 1, 2, 3$) represent the number of sexual partners for susceptible individuals interacting with unaware infectives, aware infectives, and individuals with AIDS, respectively, in each time period. Similarly, β_i (for $i = 1, 2, 3$) denote the interaction probabilities between susceptible individuals and unaware infectives, aware infectives, and AIDS individuals, respectively. The parameter Q_0 is the constant rate of immigration of the susceptibles. It is important to note that β_m includes a control parameter $u_1 \in [0, 1]$, which reflects the effectiveness of condom use by susceptible individuals as a preventive measure. The parameter θ represents the detection rate of unaware infectives through screening, which leads them to become aware infectives. The rate π measures how aware infectives, who are undergoing treatment, transition to the AIDS class in each period. Additionally, δ indicates the rate at which untreated infectives progress to AIDS. The parameter μ represents the natural mortality rate that is unrelated to HIV/AIDS, while α stands for the death rate due to AIDS. It is assumed that the contact rate between susceptibles and AIDS individuals is much lower than the rate with aware infectives, which in turn is lower than the rate with unaware infectives ($\beta_3 \ll \beta_2 \ll \beta_1$). This assumption reflects that infected individuals, once aware of their condition, may adopt preventive measures and alter their behavior, reducing their contribution to the spread of the infection. Additionally, it is assumed that individuals in the AIDS class have lower sexual activity.

Now, we describe that all solutions of the system with non-negative initial data will remain non-negative for all time.

2.2 Positivity and well-posedness of solutions

The system (2.1) represents the population of living organisms, and it is essential to prove that all solutions with non-negative initial values will remain non-negative over time.

2.2.1 Positivity of solutions

Theorem 14 *If $S(0) \geq 0$, $I_1(0) \geq 0$, $I_2(0) \geq 0$ and $A(0) \geq 0$, the solutions $S(t)$, $I_1(t)$, $I_2(t)$ and $A(t)$ of system (2.1) are positive for all $t \geq 0$.*

Proof. Based on the first equation of system (2.1), we can deduce that

$$\frac{dS(t)}{dt} + (\beta_m + \mu)\, S(t) \geq 0. \tag{2.4}$$

Multiplying inequality (2.4) by $\exp\left(\mu t + \int_0^t \beta_m(s)ds\right)$ yields

$$\frac{dS(t)}{dt} \exp\left(\mu t + \int_0^t \beta_m(s)ds\right) + \exp\left(\mu t + \int_0^t \beta_m(s)ds\right)(\beta_m + \mu)\, S(t) \geq 0. \tag{2.5}$$

Hence,

$$\frac{d}{dt}\left[S(t) \exp\left(\mu t + \int_0^t \beta_m(s)ds\right)\right] \geq 0. \tag{2.6}$$

Integrating (2.6) leads to

$$S(t) \geq S(0) \exp\left(-\mu t - \int_0^t \beta_m(s)ds\right).$$

Consequently, the solution $S(t)$ remains positive. By applying the same steps to the other equations of system (2.1), we obtain

$$I_1(t) \geq I_1(0) \exp(-(\theta + \delta + \mu)t) \geq 0,$$

$$I_2(t) \geq I_2(0) \exp(-(\pi + \delta + \mu)t) \geq 0,$$

and

$$A(t) \geq A(0) \exp(-(\alpha + \mu)t) \geq 0.$$

It can be observed that all solutions remain positive for all $t \geq 0$. This concludes the proof.

■

2.2.2 Well-Posedness of solutions in a feasible region

We aim to analyze system (2.1) in a suitable feasible region Υ of biological interest.

Theorem 15 *The feasible region* Υ *is defined by*

$$\Upsilon = \left\{ (S, I_1, I_2,\ A) \in \mathbb{R}^4_+ : S + I_1 + I_2 + A \leq \frac{Q_0}{\mu} \right\},$$

with non-negative initial conditions (2.3), it is positively invariant.

Proof. Let $(S(t), I_1(t), I_2(t), A(t))$ be any solution of (2.1) with positive initial conditions. Given that

$$N(t) = S(t) + I_1(t) + I_2(t) + A(t),$$

the time derivative of $N(t)$ along the solution of (2.1) is

$$\frac{dN(t)}{dt} = \frac{dS(t)}{dt} + \frac{dI_1(t)}{dt} + \frac{dI_2(t)}{dt} + \frac{dA(t)}{dt}.$$

This leads to the inequality

$$\frac{dN(t)}{dt} \leq Q_0 - \mu N(t). \tag{2.7}$$

The solution $N(t)$ to the differential equation (2.7) satisfies

$$N(t) \leq N(0)e^{-\mu t} + \frac{Q_0}{\mu}\left(1 - e^{-\mu t}\right),$$

where $N(0)$ represents the sum of the initial values of the variables. As $t \to \infty$, we have

$$\overline{\lim_{t\to\infty}} N(t) = \limsup_{t\to\infty} N(t) \leq \frac{Q_0}{\mu}. \tag{2.8}$$

It has been shown that all solutions of (2.1) which initiate in $\mathbb{R}^4_+$ are restricted to the region

$$\Upsilon = \left\{ (S, I_1, I_2, A) \in \mathbb{R}^4_+ : S + I_1 + I_2 + A \leq \frac{Q_0}{\mu} \right\}. \tag{2.9}$$

Therefore, the solutions are bounded in the interval $[0, \infty)$. ■

2.3 Existence of equilibrium points and calculation of $\mathscr{R}_0$

In this section, we aim to prove the existence of equilibrium solutions for system (2.1) and calculate the basic reproduction number $\mathscr{R}_0$.

Theorem 16 *Consider the system (2.1) and the basic reproduction number $\mathscr{R}_0$:*

(i) If $\mathscr{R}_0 \leq 1$, the system has a single disease-free equilibrium, $\mathscr{E}_0 = \left(\frac{Q_0}{\mu}, 0, 0, 0\right)$.

(ii) If $\mathscr{R}_0 > 1$, the system has two distinct equilibria: the disease-free equilibrium $\mathscr{E}_0$ and the positive endemic equilibrium $\mathscr{E}_1 = (\overline{S}, \overline{I_1}, \overline{I_2}, \overline{A})$.

Proof. By setting $I_1 = I_2 = A = 0$, the disease free equilibrium can be easily determined as $\mathscr{E}_0 = \left(\frac{Q_0}{\mu}, 0, 0, 0\right)$.

Next, we investigate the existence of a positive equilibrium for system (2.1). If such an equilibrium exists, it is called an endemic equilibrium and is denoted by $\mathscr{E}_1 = (\overline{S}, \overline{I_1}, \overline{I_2}, \overline{A})$. Substituting this into (2.1) gives:

$$Q_0 - \overline{\beta_m}\,\overline{S} - \mu\overline{S} = 0, \tag{2.10}$$

$$\overline{\beta_m}\,\overline{S} - (\theta + \mu + \delta)\,\overline{I_1} = 0, \tag{2.11}$$

$$\theta\overline{I_1} - (\delta + \mu + \pi)\,\overline{I_2} = 0, \tag{2.12}$$

$$\delta\overline{I_1} + \delta\overline{I_2} + \pi\overline{I_2} - (\alpha + \mu)\,\overline{A} = 0, \tag{2.13}$$

where

$$\begin{cases} \overline{S} = \dfrac{Q_0}{\overline{\beta_m} + \mu}, \\ \overline{I_1} = \dfrac{Q_0\overline{\beta_m}}{(\theta + \delta + \mu)(\overline{\beta_m} + \mu)}, \\ \overline{I_2} = \dfrac{Q_0\overline{\beta_m}\theta}{(\theta + \delta + \mu)(\delta + \mu + \pi)(\overline{\beta_m} + \mu)}, \\ \overline{A} = \dfrac{Q_0\overline{\beta_m}((\pi + \delta)(\delta + \theta) + \delta\mu)}{(\alpha + \mu)(\theta + \delta + \mu)(\delta + \mu + \pi)(\overline{\beta_m} + \mu)}, \\ \overline{N} = \dfrac{Q_0 - \alpha\overline{A}}{\mu}. \end{cases} \tag{2.14}$$

By solving system (2.1) at the equilibrium, we obtain $\overline{\beta_m} = 0$ (which corresponds to the DFE) or

$$B_1\overline{\beta_m} + B_0 = 0, \tag{2.15}$$

which implies that

$$\overline{\beta_m} = -\frac{B_0}{B_1}, \tag{2.16}$$

where

$$\begin{cases} B_1 = (\delta+\alpha+\mu)(\theta+\mu+\delta) + \pi(\alpha+\delta+\mu+\theta) > 0, \\ B_0 = (\alpha+\mu)(\pi+\delta+\mu)(\delta+\theta+\mu)(1-\mathscr{R}_0). \end{cases} \tag{2.17}$$

The basic reproductive number, $\mathscr{R}_0$, for the system (2.1) represents the expected number of new infections caused by a typical infected individual in a fully susceptible population. If $\mathscr{R}_0 \leq 1$, we obtain $\overline{\beta_m} \leq 0$, and the system has a disease-free equilibrium $\mathscr{E}_0$. On the other hand, if $\mathscr{R}_0 > 1$, then $\overline{\beta_m} > 0$, and the system admits two distinct equilibria: the disease-free equilibrium $\mathscr{E}_0$ and a unique positive endemic equilibrium $\mathscr{E}1 = (\overline{S}, \overline{I_1}, \overline{I_2}, \overline{A})$.

Now, we apply the next-generation method to calculate the reproduction number $\mathscr{R}_0$ for system (2.1). The calculation is carried out as follows:

$$F(\mathscr{E}_0) = \begin{bmatrix} (1-u_1)\beta_1 c_1 & (1-u_1)\beta_2 c_2 & (1-u_1)\beta_3 c_3 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}, \tag{2.18}$$

and

$$V(\mathscr{E}_0) = \begin{bmatrix} (\theta+\delta+\mu) & 0 & 0 \\ -\theta & (\delta+\mu+\pi) & 0 \\ -\delta & -(\delta+\pi) & (\alpha+\mu) \end{bmatrix}. \tag{2.19}$$

Since $\det(V) = (\theta+\delta+\mu)(\delta+\mu+\pi)(\alpha+\mu) \neq 0$, the inverse of V is given by

$$V^{-1} = \frac{1}{\det(V)} \begin{bmatrix} (\delta+\mu+\pi)(\alpha+\mu) & 0 & 0 \\ \theta(\alpha+\mu) & (\theta+\delta+\mu)(\alpha+\mu) & 0 \\ \theta(\delta+\pi)+\delta(\theta+\mu+\pi) & (\delta+\pi)(\delta+\mu+\pi) & (\theta+\delta+\mu)(\delta+\mu+\pi) \end{bmatrix}. \tag{2.20}$$

Hence, the basic reproduction number $\mathscr{R}_0$ is given by:

$$\mathscr{R}_0 = \rho(FV^{-1}) = \zeta_1 + \zeta_2 + \zeta_3 + \zeta_4, \tag{2.21}$$

where

$$\begin{aligned}
\zeta_1 &= \frac{(1-u_1)\beta_1 c_1}{(\theta+\delta+\mu)}, \\
\zeta_2 &= \frac{(1-u_1)\beta_2 c_2 \theta}{(\theta+\delta+\mu)(\delta+\mu+\pi)}, \\
\zeta_3 &= \frac{(1-u_1)\beta_3 c_3 \theta(\delta+\pi)}{(\theta+\delta+\mu)(\delta+\mu+\pi)(\alpha+\mu)}, \\
\zeta_4 &= \frac{(1-u_1)\beta_3 c_3 \delta}{(\theta+\delta+\mu)(\alpha+\mu)}.
\end{aligned}$$

■

2.4 Stability analysis of equilibria

In this section, we investigate the stability of the Disease-free equilibrium $\mathscr{E}_0$ and endemic equilibrium $\mathscr{E}_1$ of system (2.1).

2.4.1 The local and global asymptotic stability when $\mathscr{R}_0 < 1$

Given that $\mathscr{R}_0 \leq 1$, system (2.1) has a unique disease-free equilibrium $\mathscr{E}_0$. Our analysis aims to study the local and global asymptotic stability of this point. First, the local asymptotic stability of the disease-free $\mathscr{E}_0$ described in the following theorem:

Theorem 17 *For system (2.1), if $\mathscr{R}_0 < 1$, the disease-free equilibrium solution $\mathscr{E}_0$ is locally asymptotically stable .*

Proof. The Jacobian matrix associated with system (2.1), evaluated at the disease-free equilibrium $\mathscr{E}_0$, is given by:

$$J(\mathscr{E}_0) = \begin{bmatrix} -\mu & -\Lambda_1 & -\Lambda_2 & -\Lambda_3 \\ 0 & \Lambda_1 - (\theta+\delta+\mu) & \Lambda_2 & \Lambda_3 \\ 0 & \theta & -(\delta+\mu+\pi) & 0 \\ 0 & \delta & \delta+\pi & -(\alpha+\mu) \end{bmatrix}, \tag{2.22}$$

where $\Lambda_1 = (1-u_1)\beta_1 c_1$, $\Lambda_2 = (1-u_1)\beta_2 c_2$, and $\Lambda_3 = (1-u_1)\beta_3 c_3$. It is clear that $-\mu$ is one of the eigenvalues. Therefore, by eliminating the first row and the first column, the Jacobian matrix simplifies to:

$$J'(\mathscr{E}_0) = \begin{bmatrix} \Lambda_1 - (\theta+\delta+\mu) & \Lambda_2 & \Lambda_3 \\ \theta & -(\delta+\mu+\pi) & 0 \\ \delta & \delta+\pi & -(\alpha+\mu) \end{bmatrix}. \tag{2.23}$$

The characteristic polynomial of this matrix is given by:

$$\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0, \tag{2.24}$$

where

$$\begin{aligned} a_1 &= (\alpha+\mu) + (\delta+\mu+\pi) + (\theta+\delta+\mu)(1-\zeta_1), \\ a_2 &= (\alpha+\mu)(\delta+\mu+\pi) \\ &\quad + (\delta+\mu+\pi)(\theta+\delta+\mu)(1-\zeta_1-\zeta_2) \\ &\quad + (\alpha+\mu)(\theta+\delta+\mu)(1-\zeta_1-\zeta_4) \\ a_3 &= (\theta+\delta+\mu)(\delta+\mu+\pi)(\alpha+\mu)(1-\mathscr{R}_0). \end{aligned}$$

The stability conditions given by the Routh-Hurwitz criterion, as presented in Theorem 7, are stated as follows:

$$a_1 > 0,\ a_3 > 0 \text{ and } a_1 a_2 - a_3 > 0. \tag{2.25}$$

The condition $a_3 > 0$ follows directly from the assumption that $\mathscr{R}_0 < 1$. Since $\zeta_1 > 0$, it follows from equation (2.21) that $\zeta_1 < \mathscr{R}_0$. Thus, if $\mathscr{R}_0 < 1$, the first condition $a_1 > 0$

is satisfied. The third stability condition requires further consideration. Through some algebraic manipulations, we obtain:

$$\begin{aligned} a_1a_2 - a_3 = {} & (\alpha+\mu)^2(\pi+\delta+\mu) + (\alpha+\mu)^2(\theta+\delta+\mu)(1-\zeta_1-\zeta_4) \\ & + (\delta+\mu{+}\pi)^2(\alpha+\mu) + (\delta+\mu{+}\pi)^2(\theta+\delta+\mu)(1-\zeta_1-\zeta_2) \\ & + (\delta+\mu{+}\pi)(\alpha+\mu)(\theta+\delta+\mu)[2(1-\zeta_1)+\zeta_3] \\ & + (\theta+\delta+\mu)^2(\delta+\mu{+}\pi)(1-\zeta_1)(1-\zeta_1-\zeta_2) \\ & + (\theta+\delta+\mu)^2(\alpha+\mu)(1-\zeta_1-\zeta_4)(1-\zeta_1). \end{aligned}$$

Since the parameters $\zeta_1, \zeta_2, \zeta_3$, and ζ_4 are all smaller than $\mathscr{R}_0$, it follows that if $\mathscr{R}_0 < 1$, then the inequality $a_1a_2 - a_3 > 0$ holds. Thus, under the assumption that $\mathscr{R}_0 < 1$, the three Routh-Hurwitz stability conditions in (2.25) are satisfied, which implies that the disease-free equilibrium $\mathscr{E}_0$ is locally asymptotically stable. ■

Second, to investigate the global asymptotic stability of the disease-free equilibrium $\mathscr{E}_0$, one standard approach is to construct a suitable Lyapunov function. However, a more straightforward method is to apply the result provided by Castillo-Chavez *et al.*, specifically Lemma 6.

Theorem 18 *The disease-free equilibrium* $\mathscr{E}_0 = \left(\frac{Q_0}{\mu}, 0, 0, 0\right)$ *is a globally asymptotically stable for the system (2.1) if* $\mathscr{R}_0 < 1$.

Proof. By applying Lemma 6 to the system (2.1), we take into consideration

$$v(t) = S(t) \quad \text{and} \quad w(t) = \begin{bmatrix} I_1(t) \\ I_2(t) \\ A(t) \end{bmatrix}.$$

When $I_1 = I_2 = A = 0$, the uninfected subsystem (i.e the equation for S) becomes

$$\frac{dS}{dt} = Q_0 - \mu S,$$

whish has the solution

$$S(t) = \frac{Q_0}{\mu} + e^{-\mu t}\left(S(0) - \frac{Q_0}{\mu}\right).$$

Clearly $S(t) \to \frac{Q_0}{\mu}$ as $t \to \infty$ regardless of the initial value $S(0)$. Therefore, this demonstrates that condition $(\mathbf{C_1})$ in Lemma 6 for the system (2.1).

Next, the right-hand side of the infectious subsysteme (i,e the equations for I_1, I_2, A), can be written as

$$\begin{aligned}
\frac{dw}{dt} = G(v,w) &= \begin{bmatrix} \frac{dI_1}{dt} \\ \frac{dI_2}{dt} \\ \frac{dA}{dt} \end{bmatrix} \\
&= \begin{bmatrix} -(\theta+\delta+\mu)I_1 + \frac{1-u_1}{N}\beta_1 c_1 \frac{Q_0}{\mu} I_1 + \frac{1-u_1}{N}\beta_2 c_2 \frac{Q_0}{\mu} I_2 + \frac{1-u_1}{N}\beta_3 c_3 \frac{Q_0}{\mu} A \\ -\beta_m \frac{Q_0}{\mu} + \beta_m S \\ \theta I_1 - (\theta+\delta+\mu) I_2 \\ \delta I_1 + (\delta+\pi) I_2 - (\alpha+\mu) A \end{bmatrix} \\
&= \begin{bmatrix} -(\theta+\delta+\mu) + \frac{1-u_1}{N}\beta_1 c_1 \frac{Q_0}{\mu} & \frac{1-u_1}{N}\beta_2 c_2 \frac{Q_0}{\mu} & \frac{1-u_1}{N}\beta_3 c_3 \frac{Q_0}{\mu} \\ \theta & -(\theta+\delta+\mu) & 0 \\ \delta & (\delta+\pi) & -(\alpha+\mu) \end{bmatrix} \times \begin{bmatrix} I_1 \\ I_2 \\ A \end{bmatrix} \\
&\quad - \begin{bmatrix} \beta_m \frac{Q_0}{\mu} - \beta_m S \\ 0 \\ 0 \end{bmatrix} \\
&= Aw - \hat{G}(v,w),
\end{aligned}$$

where

$$A = \begin{bmatrix} -(\theta+\delta+\mu) + \frac{1-u_1}{N}\beta_1 c_1 \frac{Q_0}{\mu} & \frac{1-u_1}{N}\beta_2 c_2 \frac{Q_0}{\mu} & \frac{1-u_1}{N}\beta_3 c_3 \frac{Q_0}{\mu} \\ \theta & -(\theta+\delta+\mu) & 0 \\ e\delta & (\delta+\pi) & -(\alpha+\mu) \end{bmatrix},$$

and

$$\hat{G}(v,w) = \begin{bmatrix} \beta_m \frac{Q_0}{\mu} - \beta_m S \\ 0 \\ 0 \end{bmatrix}.$$

It is clear that $S \leq \dfrac{Q_0}{\mu}$, and thus it follows that

$$\hat{G}(v, w) \geq 0, \quad \text{for all} \quad (v, w) \in \mathbb{R}^3_+.$$

Additionally, we observe that the matrix A is an M-matrix since all its off-diagonal elements are non-negative. Therefore, the conditions $(\mathbf{C_1})$ and $(\mathbf{C_2})$ are satisfied. By Lemma 6, the disease-free equilibrium $\mathscr{E}_0$ is globally asymptotically stable provided that $\mathscr{R}_0 < 1$. ■

2.4.2 The local and global asymptotic stability when $\mathscr{R}_0 > 1$

As previously stated, for $\mathscr{R}_0 > 1$, system (2.1) has two equilibrium points: the disease-free equilibrium $\mathscr{E}_0$ and the endemic equilibrium $\mathscr{E}_1(\overline{S}, \overline{I_1}, \overline{I_2}, \overline{A})$. We now proceed to investigate the local asymptotic stability of these equilibria, as established in the following theorem.

Theorem 19 *For system (2.1), if $\mathscr{R}_0 > 1$, $\mathscr{E}_0$ is unstable and $\mathscr{E}_1 = (\overline{S}, \overline{I_1}, \overline{I_2}, \overline{A})$ is locally asymptotically stable.*

Proof. If $\mathscr{R}_0 > 1$, as shown in the proof of Theorem (17), $\mathscr{E}_0$ is clearly unstable. Therefore, the second equilibrium point $\mathscr{E}_1 = (\overline{S}, \overline{I_1}, \overline{I_2}, \overline{A})$ requires further examination. The Jacobian matrix corresponding to system (2.1), evaluated at $\mathscr{E}_1$ is given by:

$$J(\mathscr{E}_1) = \begin{pmatrix} -\overline{G} - \mu & -\overline{F_1} + \overline{J_1} & -\overline{F_2} + \overline{J_1} & -\overline{F_3} + \overline{J_1} \\ \overline{G} & \overline{F_1} - \overline{J_1} - B & \overline{F_2} - \overline{J_1} & \overline{F_3} - \overline{J_1} \\ 0 & \theta & -C & 0 \\ 0 & \delta & D & -E \end{pmatrix},$$

where $B = \theta + \delta + \mu, C = \delta + \mu + \pi, D = \delta + \pi, E = \alpha + \mu$, and

$$\begin{cases} \overline{G} = \dfrac{(\overline{N} - \overline{S})(1-u_1)(\beta_1 c_1 \overline{I_1} + \beta_2 c_2 \overline{I_2} + \beta_3 c_3 \overline{A})}{\overline{N}^2}, \\ \overline{F_1} = \dfrac{(1-u_1)\beta_1 c_1}{\overline{N}} \overline{S}, \\ \overline{J_1} = \dfrac{(1-u_1)(\beta_1 c_1 \overline{I_1} + \beta_2 c_2 \overline{I_2} + \beta_3 c_3 \overline{A})}{\overline{N}^2} \overline{S}, \\ \overline{F_2} = \dfrac{(1-u_1)\beta_2 c_2}{\overline{N}} \overline{S}, \\ \overline{F_3} = \dfrac{(1-u_1)\beta_3 c_3}{\overline{N}} \overline{S}. \end{cases}$$

The characteristic equation associated with $J(\mathscr{E}_1^{\circ})$ is

$$\lambda^4 + p_1\lambda^3 + p_2\lambda^2 + p_3\lambda + p_4 = 0, \tag{2.26}$$

where

$$p_1 = B + C + \overline{G} + \mu + E - \overline{F_1} + \overline{J_1}, \tag{2.27}$$

$$\begin{aligned} p_2 = {} & \mu\left(B - \overline{F_1}\right) + C\mu + CE + \mu E + \left(BC - C\overline{F_1} - \theta\overline{F_2}\right) \\ & + \left(BE - \delta\overline{F_3} - E\overline{F_1}\right) + (C + B + E)\left(\overline{J_1} + \overline{G}\right), \end{aligned} \tag{2.28}$$

$$\begin{aligned} p_3 = {} & \mu\left(BC - C\overline{F_1} - \theta\overline{F_2}\right) + C\mu E \\ & + (CE + \mu(B + C + \alpha) + C\delta + \theta D + \theta E)\,\overline{J_1} \\ & + \left(BCE - CE\overline{F_1} - \theta D\overline{F_3} - \theta E\overline{F_2} - C\delta\overline{F_3}\right) \\ & + \mu\left(BE - \delta\overline{F_3} - E\overline{F_1}\right) + (BC + BE + CE)\,\overline{G}, \end{aligned} \tag{2.29}$$

and

$$\begin{aligned} p_4 = {} & BC\overline{G}E + \left(BC\mu E - C\mu E\overline{F_1} - \theta\mu D\overline{F_3} - \theta\mu E\overline{F_2} - C\mu\delta\overline{F_3}\right) \\ & + (C\mu\delta + C\mu E + \theta\mu D + \theta\mu E)\,\overline{J_1}. \end{aligned} \tag{2.30}$$

Moreover, by multiplying equation (2.11) by $E\theta$ and using (2.12) we obtain

$$\frac{(1-u_1)(\beta_1 c_1 \overline{I_1} E\theta + \beta_2 c_2 \overline{I_2} E\theta + \beta_3 c_3 \overline{A} E\theta)}{\overline{N}} \overline{S} = (\theta + \mu + \delta)\,\overline{I_1} E\theta.$$

This implies that

$$\frac{(1-u_1)(\beta_1 c_1(\delta+\mu+\pi)\overline{I_2}E+\beta_2 c_2\overline{I_2}E\theta+\beta_3 c_3\overline{A}E\theta)}{\overline{N}}\overline{S}$$
$$=(\theta+\mu+\delta)(\delta+\mu+\pi)\overline{I_2}E.$$

Thus, from (2.13), we obtain

$$\overline{A}E\theta=\overline{I_2}\left[\delta(\delta+\mu+\pi)+\theta(\pi+\delta)\right],$$

leading to

$$CE\overline{F_1}+E\theta\overline{F_2}+\delta C\overline{F_3}+\theta D\overline{F_3}=BCE. \tag{2.31}$$

From (2.31), we have

$$\overline{F_1}<B, \tag{2.32}$$

$$C\overline{F_1}+\theta\overline{F_2}<BC, \tag{2.33}$$

and

$$E\overline{F_1}+\delta\overline{F_3}<BE. \tag{2.34}$$

Substituting (2.31) into (2.27)-(2.30) leads to the coefficients

$$\begin{aligned}
p_1&=\left(B-\overline{F_1}\right)+C+\overline{G}+\mu+E+\overline{J_1},\\
p_2&=\mu\left(B-\overline{F_1}\right)+C\mu+CE+\mu E+\left(BC-C\overline{F_1}-\theta\overline{F_2}\right)\\
&\quad+\left(BE-\delta\overline{F_3}-E\overline{F_1}\right)+(C+B+E)\left(\overline{J_1}+\overline{G}\right),\\
p_3&=\mu\left[\left(BC-C\overline{F_1}-\theta\overline{F_2}\right)+\left(BE-\delta\overline{F_3}-E\overline{F_1}\right)\right]\\
&\quad+(CE+\mu(B+C+\alpha)+C\delta+\theta D+\theta E)\,\overline{J_1}\\
&\quad+(BC+BE+CE)\,\overline{G}+\mu CE,\\
p_4&=BCGE+(C\delta+CE+\theta D+\theta E)\,\mu\overline{J_1}.
\end{aligned}$$

From equations (2.32) to (2.34), it is clear that p_1, p_2, p_3, and p_4 are all positive(no changes in signs). Accordingly, by applying Descartes' rule of signs, as stated in Lemma 7, equation (2.26) has four negative real roots. As a result, it follows that $\mathscr{E}_1$ is locally asymptotically stable. ■

Our goal now is to establish that the endemic equilibrium of the HIV model is globally asymptotically stable. It is important to note that the classical approach using Lyapunov functions, in conjunction with the properties of the Volterra-Lyapunov matrix [45, 46], provides a robust framework for proving the global stability of this endemic equilibrium. Additional details are provided below.

We will study the system (2.1) within the biologically feasible domain.

$$\Upsilon = \left\{ (S, I_1, I_2,\ A) \in \mathbb{R}^4_+ : S + I_1 + I_2 + A \leq \frac{Q_0}{\mu} \right\},$$

which is clearly a positively invariant subset of $\mathbb{R}^4$. Moreover, $N = \overline{N} = \dfrac{Q_0}{\mu}$ as $t \to \infty$. Thus, we have the following limiting system:

$$\begin{aligned}
\frac{dS}{dt} &= Q_0 - (1-u_1)\frac{1}{\overline{N}}\left(\beta_1 c_1 I_1 + \beta_2 c_2 I_2 + \beta_3 c_3 A\right) S - \mu S, \\
\frac{dI_1}{dt} &= (1-u_1)\frac{1}{\overline{N}}\left(\beta_1 c_1 I_1 + \beta_2 c_2 I_2 + \beta_3 c_3 A\right) S - (\theta + \delta + \mu) I_1, \\
\frac{dI_2}{dt} &= \theta I_1 - (\delta + \mu + \pi) I_2, \\
\frac{dA}{dt} &= \delta I_1 + \delta I_2 + \pi I_2 - \mu A.
\end{aligned}$$

To establish the global stability result, we propose the following Lyapunov function.

$$\mathcal{V} = m_1 \left(S - \overline{S}\right)^2 + m_2 \left(I_1 - \overline{I_1}\right)^2 + m_3 \left(I_2 - \overline{I_2}\right)^2 + m_4 \left(A - \overline{A}\right)^2, \tag{2.35}$$

where m_1, m_2, m_3 and m_4 are positive constants. Calculating the time derivative of V along the trajectories of systeme (2.1), we obtain

$$\begin{aligned}
\mathcal{V}' &= 2m_1 \left(S - \overline{S}\right) S' + 2m_2 \left(I_1 - \overline{I_1}\right) I_1' + 2m_3 \left(I_2 - \overline{I_2}\right) I_2' + 2m_4 \left(A - \overline{A}\right) A' \\
&= 2m_1 \left(S - \overline{S}\right) \left[\frac{1-u_1}{\overline{N}} \left(-\beta_1 c_1 \left(I_1 S - \overline{I_1}\ \overline{S} \right) - \beta_2 c_2 \left(I_2 S - \overline{I_2}\ \overline{S} \right) \right. \right. \\
&\quad \left. \left. -\beta_3 c_3 \left(AS - \overline{A}\ \overline{S} \right) \right) - \mu \left(S - \overline{S} \right) \right] \\
&\quad + 2m_2 \left(I_1 - \overline{I_1}\right) \left[\frac{1-u_1}{N^*} \left(-\beta_1 c_1 \left(I_1 S - \overline{I_1}\ \overline{S} \right) - \beta_2 c_2 \left(I_2 S - \overline{I_2}\ \overline{S} \right) \right. \right. \\
&\quad \left. \left. -\beta_3 c_3 \left(AS - \overline{A}\ \overline{S} \right) \right) - (\theta + \delta + \mu) \left(I_1 - \overline{I_1} \right) \right] \\
&\quad + 2m_3 \left(I_2 - \overline{I_2}\right) \left[\theta \left(I_1 - \overline{I_1} \right) - (\delta + \mu + \pi) \left(I_2 - \overline{I_2} \right) \right] \\
&\quad + 2m_4 \left(A - \overline{A}\right) \left[\delta \left(I_1 - \overline{I_1} \right) + \delta \left(I_2 - \overline{I_2} \right) + \pi \left(I_2 - \overline{I_2} \right) - (\mu + \alpha) \left(A - \overline{A} \right) \right].
\end{aligned}$$

Then, we add the expression $\beta_1 c_1 I_1 \overline{S}, \beta_2 c_2 I_2 \overline{S}$ and $\beta_3 c_3 A \overline{S}$ into the first and second square brackets. As a result, we obtain

$$
\begin{aligned}
\mathcal{V}' =& 2m_1 \left(S-\overline{S}\right)\left[\frac{1-u_1}{\overline{N}}\left(-\beta_1 c_1\left(I_1 S-\overline{I_1}\ \overline{S}\right)+\beta_1 c_1 I_1 \overline{S}-\beta_1 c_1 I_1 \overline{S}\right)\right. \\
& -\beta_2 c_2\left(I_2 S-\overline{I_2}\ \overline{S}\right)+\beta_2 c_2 I_2 \overline{S}-\beta_2 c_2 I_2 \overline{S}-\beta_3 c_3\left(A S-\overline{A}\ \overline{S}\right) \\
& \left.+\beta_3 c_3 A \overline{S}-\beta_3 c_3 A \overline{S}\right)-\mu\left(S-\overline{S}\right)\Big] \\
& +2m_2\left(I_1-\overline{I_1}\right)\times\left[\frac{1-u_1}{\overline{N}}\left(-\beta_1 c_1\left(I_1 S-\overline{I_1}\ \overline{S}\right)+\beta_1 c_1 I_1 \overline{S}-\beta_1 c_1 I_1 \overline{S}\right.\right. \\
& -\beta_2 c_2\left(I_2 S-\overline{I_2}\ \overline{S}\right)+\beta_2 c_2 I_2 \overline{S}-\beta_2 c_2 I_2 \overline{S}-\beta_3 c_3\left(A S-\overline{A}\ \overline{S}\right). \\
& \left.\left.+\beta_3 c_3 A \overline{S}-\beta_3 c_3 A \overline{S}\right)-(\theta+\delta+\mu)\left(I_1-\overline{I_1}\right)\right] \\
& +2m_3\left(I_2-\overline{I_2}\right)\left[\theta\left(I_1-\overline{I_1}\right)-(\delta+\mu+\pi)\left(I_2-\overline{I_2}\right)\right] \\
& +2m_4\left(A-\overline{A}\right)\left[\delta\left(I_1-\overline{I_1}\right)+\delta\left(I_2-\overline{I_2}\right)+\pi\left(I_2-\overline{I_2}\right)-(\mu+\alpha)\left(A-\overline{A}\right)\right],
\end{aligned}
$$

therefore, we have

$$
\begin{aligned}
\mathcal{V}' =& 2m_1\left(S-\overline{S}\right)\left[\frac{1-u_1}{\overline{N}}\left(-\beta_1 c_1 I_1\left(S-\overline{S}\right)-\beta_1 c_1 \overline{S}\left(I_1-\overline{I_1}\right)-\beta_2 c_2 I_2\left(S-\overline{S}\right)\right.\right. \\
& \left.-\beta_2 c_2 \overline{S}\left(I_2-\overline{I_2}\right)-\beta_3 c_3 A\left(S-\overline{S}\right)-\beta_3 c_3 \overline{S}\left(A-\overline{A}\right)\right)-\mu\left(S-\overline{S}\right)\Big] \\
& +2m_2\left(I_1-\overline{I_1}\right)\left[\frac{1-u_1}{\overline{N}}\left(\beta_1 c_1 I_1\left(S-\overline{S}\right)+\beta_1 c_1 \overline{S}\left(I_1-\overline{I_1}\right)+\beta_2 c_2 I_2\left(S-\overline{S}\right)\right.\right. \\
& \left.\left.+\beta_2 c_2 \overline{S}\left(I_2-\overline{I_2}\right)+\beta_3 c_3 A\left(S-\overline{S}\right)+\beta_3 c_3 \overline{S}\left(A-\overline{A}\right)\right)-(\theta+\delta+\mu)\left(I_1-\overline{I_1}\right)\right] \\
& +2m_3\left(I_2-\overline{I_2}\right)\left[\theta\left(I_1-\overline{I_1}\right)-(\delta+\mu+\pi)\left(I_2-\overline{I_2}\right)\right] \\
& +2m_4\left(A-\overline{A}\right)\left[\delta\left(I_1-\overline{I_1}\right)+\delta\left(I_2-\overline{I_2}\right)+\pi\left(I_2-\overline{I_2}\right)-(\mu+\alpha)\left(A-\overline{A}\right)\right] \\
=& 2m_1\left[\frac{1-u_1}{\overline{N}}\left(-\beta_1 c_1 I_1-\beta_2 c_2 I_2-\beta_3 c_3 A\right)-\mu\right]\left(S-\overline{S}\right)^2 \\
& -2m_1\frac{1-u_1}{\overline{N}}\beta_1 c_1 \overline{S}\left(S-\overline{S}\right)\left(I_1-\overline{I_1}\right)-2m_1\frac{1-u_1}{\overline{N}}\beta_2 c_2 \overline{S}\left(S-\overline{S}\right)\left(I_2-\overline{I_2}\right) \\
& -2m_1\frac{1-u_1}{\overline{N}}\beta_3 c_3 \overline{S}\left(S-\overline{S}\right)\left(A-\overline{A}\right)+2m_2\left[\frac{1-u_1}{\overline{N}}\beta_1 c_1 \overline{S}-(\theta+\delta+\mu)\right]\left(I_1-\overline{I_1}\right)^2 \\
& +2m_2\left[\frac{1-u_1}{\overline{N}}\left(\beta_1 c_1 I_1+\beta_2 c_2 I_2+\beta_3 c_3 A\right)\right]\left(I_1-\overline{I_1}\right)\left(S-\overline{S}\right) \\
& +2m_2\frac{1-u_1}{\overline{N}}\beta_2 c_2 \overline{S}\left(I_1-\overline{I_1}\right)\left(I_2-\overline{I_2}\right)+2m_2\frac{1-u_1}{\overline{N}}\beta_3 c_3 \overline{S}\left(I_1-\overline{I_1}\right)\left(A-\overline{A}\right)
\end{aligned}
$$

$$+ 2m_3\theta\left(I_2-\overline{I_2}\right)\left(I_1-\overline{I_1}\right) - 2m_3\theta(\delta+\mu+\pi)\left(I_2-\overline{I_2}\right)^2 + 2m_4\delta\left(A-\overline{A}\right)\left(I_1-\overline{I_1}\right)$$
$$+ 2m_4(\delta+\pi)\left(A-\overline{A}\right)\left(I_2-\overline{I_2}\right) - 2m_4\left(\alpha+\mu\right)\left(A-\overline{A}\right)^2$$
$$= Y\left(MP+P^TM^T\right)Y^T$$

where $Y = \left[S-\overline{S}, I_1-\overline{I_1}, I_2-\overline{I_2}, A-\overline{A}\right]$, $M = \text{diag}\left(m_1, m_2, m_3, m_4\right)$ and

$$P = \begin{pmatrix} -\beta_m-\mu & -\overline{F_1} & -\overline{F_2} & -\overline{F_3} \\ \beta_m & \overline{F_1}-B & \overline{F_2} & \overline{F_3} \\ 0 & \theta & -C & 0 \\ 0 & \delta & D & -E \end{pmatrix} \tag{2.36}$$

To examine the global asymptotic stability of Y, we proceed by demonstrating that the matrix P defined in Eq.(2.36) is Volterra-Lyapunov stable, or equivalently, that $-P$ is diagonally stable. To achieve this, we prove the following lemmas.

Lemma 9 *For the matrix P defined in Eq.(2.36), let us consider $D = -\widetilde{P}$, then D is diagonal stable.*

Proof. From Eq. (2.36), we obtain

$$D = -\tilde{P} = \begin{pmatrix} \beta_m+\mu & \overline{F_1} & \overline{F_2} \\ -\beta_m & -\overline{F_1}+B & -\overline{F_2} \\ 0 & -\theta & C \end{pmatrix}.$$

To prove the diagonal stability of D and based on Lemma (3), we must demonstrate that the following three conditions are satisfied.

Condition 1. We demonstrate that the matrix $\widetilde{D}$ is diagonally stable. To do so, it is required to show that $-\widetilde{D}$ is Volterra-Lyapunov stable:

$$-\widetilde{D} = \begin{bmatrix} -\dfrac{(1-u_1)}{\overline{N}}\left(\beta_1c_1I_1+\beta_2c_2I_2+\beta_3c_3A\right)-\mu & -\overline{F_1} \\ \dfrac{(1-u_1)}{\overline{N}}\left(\beta_1c_1I_1+\beta_2c_2I_2+\beta_3c_3A\right) & \overline{F_1}-B \end{bmatrix}.$$

Clearly $-\widetilde{D}_{11} = -\dfrac{(1-u_1)}{\overline{N}}\left(\beta_1c_1I_1+\beta_2c_2I_2+\beta_3c_3A\right)-\mu < 0$, note that $u \in [0,1]$. In addition, from (2.32), we have $-\widetilde{D}_{22} = \overline{F_1}-B < 0$. Also, it is clear that $\det(-\widetilde{D}) > 0$, since

$-\widetilde{D}_{21} > 0$ and $-\widetilde{D}_{12} < 0$. Therefore, $-\widetilde{D}$ is Volterra-Lyapunov stable based on Lemma (3).

Condition 2. We show that the matrix $\widetilde{D^{-1}}$ is diagonal stable. Infact, we show that $-\widetilde{D^{-1}}$ is Volterra-Lyapunov stable .

$$-\widetilde{D^{-1}} = \frac{1}{\det(D)} \begin{bmatrix} -\widetilde{D_{11}^{-1}} & -\widetilde{D_{12}^{-1}} \\ -\widetilde{D_{21}^{-1}} & -\widetilde{D_{22}^{-1}} \end{bmatrix}, \tag{2.37}$$

where:

$$\begin{aligned} -\widetilde{D_{11}^{-1}} &= C\overline{F_1} + \overline{F_2}\theta - BC, \\ -\widetilde{D_{12}^{-1}} &= \overline{F_1}C + \overline{F_2}\theta, \\ -\widetilde{D_{21}^{-1}} &= \frac{(1-u_1)}{\overline{N}}\left(-\beta_1 c_1 I_1 - \beta_2 c_2 I_2 - \beta_3 c_3 A\right) C, \\ -\widetilde{D_{22}^{-1}} &= \left(\frac{(1-u_1)}{\overline{N}}\left(-\beta_1 c_1 I_1 - \beta_2 c_2 I_2 - \beta_3 c_3 A\right) - \mu\right) C, \end{aligned}$$

and

$$\det(D) = (\beta_m + \mu)\left(BC - C\overline{F_1} - \overline{F_2}\theta\right) + \beta_m\left(\overline{F_1}C + \overline{F_2}\theta\right). \tag{2.38}$$

According to (2.33), hence, it is clear to see $-\widetilde{D_{11}^{-1}} < 0$, $-\widetilde{D_{22}^{-1}} < 0$ and $\det(D) > 0$. Therefore, $-\widetilde{D^{-1}}$ is volterra-Lyapunov stable based on Lemma (3) .

Condition 3. It is abvious that $D_{33} = C > 0$. Hence, Lemma (5) guarantees that $D = -\widetilde{P}$ is diagonal stable . ■

Lemma 10 *For the matrix P defined (2.36), matrix $H = -\widetilde{P^{-1}}$ is diagonal stable.*

Proof. To prove diagonal stability of H, once again use Lemma (5) as follows:

- $\widetilde{H}$ is diagonal stable.
- $\widetilde{H^{-1}}$ is diagonal stable.
- $H_{33} > 0$.

From (2.36), we obtain

$$H = -\widetilde{P^{-1}} = \frac{1}{\det(-P)} \begin{bmatrix} -\widetilde{P_{11}^{-1}} & -\widetilde{P_{12}^{-1}} & -\widetilde{P_{13}^{-1}} \\ -\widetilde{P_{21}^{-1}} & -\widetilde{P_{22}^{-1}} & -\widetilde{P_{23}^{-1}} \\ -\widetilde{P_{31}^{-1}} & -\widetilde{P_{32}^{-1}} & -\widetilde{P_{33}^{-1}} \end{bmatrix},$$

where

$$
\begin{aligned}
-\widetilde{P_{11}^{-1}} &= CE\overline{F_1} + E\theta\overline{F_2} + \delta C\overline{F_3} + \theta D\overline{F_3} - BCE,\\
-\widetilde{P_{12}^{-1}} &= \overline{F_3}\left[\theta D + \delta C\right] + E\left(\overline{F_1}C + \theta\overline{F_2}\right),\\
-\widetilde{P_{13}^{-1}} &= -B\left[E\overline{F_2} + (\delta+\pi)\overline{F_3}\right],\\
-\widetilde{P_{21}^{-1}} &= \frac{(1-u_1)}{\overline{N}}\left(\beta_1c_1I_1 + \beta_2c_2I_2 + \beta_3c_3A\right)EC,\\
-\widetilde{P_{22}^{-1}} &= \left[\frac{(1-u_1)}{\overline{N}}\left(\beta_1c_1I_1 + \beta_2c_2I_2 + \beta_3c_3A\right) + \mu\right]\mu C,\\
-\widetilde{P_{23}^{-1}} &= \mu^2\overline{F_2} + \mu(\delta+\pi)\overline{F_3},\\
-\widetilde{P_{31}^{-1}} &= \frac{(1-u_1)}{\overline{N}}\left(\beta_1c_1I_1 + \beta_2c_2I_2 + \beta_3c_3A\right)(\mu\theta),\\
-\widetilde{P_{32}^{-1}} &= \left[\frac{(1-u_1)}{\overline{N}}\left(\beta_1c_1I_1 + \beta_2c_2I_2 + \beta_3c_3A\right) + \mu\right](\mu\theta),\\
-\widetilde{P_{33}^{-1}} &= -\mu\left[\overline{F_1}\mu + \overline{F_1}\delta - \mu B\right] + \mu\frac{(1-u_1)}{\overline{N}}\left(\beta_1c_1I_1 + \beta_2c_2I_2 + \beta_3c_3A\right)B.
\end{aligned}
$$

and

$$
-\widetilde{H} = \frac{1}{\det(-P)}\begin{bmatrix} \widetilde{P_{11}^{-1}} & \widetilde{P_{21}^{-1}} \\ \widetilde{P_{12}^{-1}} & \widetilde{P_{22}^{-1}} \end{bmatrix}. \tag{2.39}
$$

Now, we show that the $-\widetilde{H}$ is volterra-Lyapunov stable. As know

$$
\widetilde{P_{11}^{-1}} = BCE - CE\overline{F_1} - E\theta\overline{F_2} - \delta C\overline{F_3} - \theta D\overline{F_3}.
$$

From (2.31), it is clear to see $\widetilde{P_{11}^{-1}} = 0$, It is obvious that $\widetilde{P_{12}^{-1}} < 0$, $\widetilde{P_{22}^{-1}} < 0$ and since $\det(-P) = (\beta_m + \mu)\,\widetilde{P^{-1}}_{11} - \beta_m\widehat{P^{-1}}_{12} > 0$. one can conclude that $-\widetilde{H}$ is volterra-Lyapunov stable.

Our Next Goal here is to show that $-\widetilde{H^{-1}}$ is volterra-Lyapunov stable. Let us consider

$$
-\widetilde{H^{-1}} = \frac{1}{\det(H)}\begin{bmatrix} -h_{11} & -h_{12} \\ -h_{21} & -h_{22} \end{bmatrix}, \tag{2.40}
$$

where

$$
\begin{aligned}
-h_{11} =& E(\mu+\beta_m)\left[\mu\left(C\delta\overline{F_3} + \theta D\overline{F_3} + CE\overline{F_1} + \theta E\overline{F_2} - BCE\right) - BCE\beta_m\right],\\
-h_{12} =& (\delta\overline{F_3} + E\overline{F_1})\left[\mu\left(C\delta\overline{F_3} + \theta D\overline{F_3} + CE\overline{F_1} + \theta E\overline{F_2} - BCE\right) - BCE\beta_m\right],\\
-h_{21} =& -E\beta_m\left[\mu\left(C\delta\overline{F_3} + \theta D\overline{F_3} + CE\overline{F_1} + \theta E\overline{F_2} - BCE\right) - BCE\beta_m\right],\\
-h_{22} =& -(\delta\overline{F_3} - BE + E\overline{F_1})\left[\mu\left(C\delta\overline{F_3} + \theta D\overline{F_3} + CE\overline{F_1} + \theta E\overline{F_2} - BCE\right) - BCE\beta_m\right],
\end{aligned}
$$

According to (2.31) and (2.34), we obtain

$$\begin{aligned}
-h_{11} =& -E^2(\mu+\beta_m)BC\beta_m < 0,\\
-h_{12} =& -(\delta\overline{F_3}+E\overline{F_1})BCE\beta_m < 0,\\
-h_{21} =& E^2\beta_m^2 BC > 0,\\
-h_{22} =& (\delta\overline{F_3}+E\overline{F_1}-BE)BCE\beta_m < 0,
\end{aligned}$$

$$\det(H) = \frac{1}{(\det(-P))^3}\beta_m CEh_{12} + \frac{1}{(\det(-P))^3}\beta_m\theta E\left[\beta_m E\overline{F_2}+\beta_m D\overline{F_3}\right]. \tag{2.41}$$

Hence, it is clear to see $\det(H) > 0$, one can conclude that $-\widetilde{H^{-1}}$ is volterra-Lyapunov stable. ■

Theorem 20 *The matrix P defined in Eq. (2.36) is volterra-Lyapunov stable.*

Proof. Based on lemmas (5), (9) and since $-P_{44} = E > 0$, there existe a positive diagonal matrix M such that $M(-P)+(-P)^T M^T > 0$, thus $MP + P^T M^T < 0$. ■

Theorem 21 *The endemic equilibruim, $\mathscr{E}_1 = (\overline{S}, \overline{I_1}, \overline{I_2}, \overline{A})$ of system (2.1) is globally asymptotically stable when $\mathscr{R}_0 > 1$.*

Proof. Based on, Lemma 5, Lemma 9 and Theorem 20, we obtain $\dfrac{d\mathcal{V}}{dt} < 0$ when $X \neq X_{eq}$ and X is not on the S-axis (a set measure zero). It implies that the endemic equilibrium of the model system (2.1) is globally asymptotically stable. ■

2.5 Optimal control of the HIV/AIDS model

Let us now update system (2.1) to include the three control strategies u_1, u_2, and u_3, which denote condom use, screening of unaware infectives. and treatment of aware infectives, respectively. These strategies are aimed at controlling of the spread of the HIV/AIDS epidemic.

The controlled system is given by

$$\begin{cases} \dfrac{dS}{dt} = Q_0 - \beta_m S - \mu S, \\ \dfrac{dI_1}{dt} = \beta_m S - (u_2\theta + \mu + \delta)\, I_1, \\ \dfrac{dI_2}{dt} = u_2\theta I_1 - (\delta + \mu + u_3\pi)\, I_2, \\ \dfrac{dA}{dt} = \delta I_1 + \delta I_2 + u_3\pi I_2 - (\alpha + \mu)\, A, \end{cases} \tag{2.42}$$

subject to the initial conditions

$$S(0) = S_0, I_1(0) = I_{01}, I_2(0) = I_{02}, A(0) = A_0.$$

Let us also defind the objective functional as

$$\mathscr{J}(u_1, u_2, u_3) = \int_0^T \left(aI_1 + b_1u_1^2 + b_2u_2^2 + b_3u_3^2\right) dt, \tag{2.43}$$

where T denotes the final time and the coefficients a, b_1, b_2 are positive weights. The term aI_1 represents the cost of infection while $b_1u_1^2$, $b_2u_2^2$, and $b_3u_3^2$ are the costs associated with condom use, screening of unaware infectives and treatment of infectives, respectively. Our objective is to minimize the number of unaware infectives I_1 while also minimizing the cost of the three control measures u_1, u_2 and u_3. We seek an optimal control (u_1^*, u_2^*, u_3^*) such that

$$\mathscr{J}(u_1^*, u_2^*, u_3^*) = \min\left\{\mathscr{J}(u_1, u_2, u_3) : u_1, u_2 \text{ and } u_3 \in \mathscr{U}\right\}, \tag{2.44}$$

where $\mathscr{U}$ is the admissible control set defined as

$$\mathscr{U} = \left\{(u_1, u_2, u_3) : u_i \text{ is measurable, } 0 \leq u_i \leq 1,\ t \in [0, T]\,,\ \text{for } i = 1, 2, 3\right\}.$$

2.5.1 Existence of an optimal control

The existence of the optimal control can be proved using a result by Fleming and Rishel (See Theorem 12).

Lemma 11 *There exists an optimal control* $(u_1^*, u_2^*, u_3^*) \in \mathscr{U}$ *such that*

$$\mathscr{J}(u_1^*, u_2^*, u_3^*) = \min_{(u_1,u_2,u_3)\in\mathscr{U}} \mathscr{J}(u_1, u_2, u_3),$$

subject to the control system (2.42).

Proof. We first check that the following conditions in Theorem 12 hold for system (2.42):

(C1) To prove that the set of controls and the corresponding state variables is nonempty, we will use a simplified version of the existence result (see theorem 11). Let $S' = F_S(t, S, I_1, I_2, A)$, $I_1' = F_{I_1}(t, S, I_1, I_2, A)$, $I_2' = F_{I_2}(t, S, I_1, I_2, A)$ and $A' = F_A(t, S, I_1, I_2, A)$, where F_S, F_{I_1}, F_{I_2} and F_A form the right-hand sides of system (2.42). Let $u_i(t) = c_i$ for $i = 1, 2, 3$ for some constants. Since all parameters are constant and S, I_1, I_2 and A are continuous, then F_S, F_{I_1}, F_{I_2} and F_A are also continuous. Additionally, the partial derivatives $\frac{\partial F_S}{\partial S}$, $\frac{\partial F_S}{\partial I_1}$, $\frac{\partial F_S}{\partial I_2}$, $\frac{\partial F_S}{\partial A}$, $\frac{\partial F_{I_1}}{\partial S}$, $\frac{\partial F_{I_1}}{\partial I_1}$, $\frac{\partial F_{I_1}}{\partial I_2}$, $\frac{\partial F_{I_1}}{\partial A}$, $\frac{\partial F_{I_2}}{\partial S}$, $\frac{\partial F_{I_2}}{\partial I_1}$, $\frac{\partial F_{I_2}}{\partial I_2}$, $\frac{\partial F_{I_2}}{\partial A}$ and $\frac{\partial F_A}{\partial S}$, $\frac{\partial F_A}{\partial I_1}$, $\frac{\partial F_A}{\partial I_2}$, $\frac{\partial F_A}{\partial A}$ are all continuous. Therefore, there exists a unique solution (S, I_1, I_2, A) that satisfies the initial conditions, which implies that the set of controls and corresponding state variables is nonempty.

(C2) By definition, $\mathscr{U}$ is closed. Take any controls $u, v \in \mathscr{U}$ and $\vartheta \in [0, 1]$. We have:

$$0 \leq \vartheta u + (1 - \vartheta)v.$$

Additionally, we observe that:

$$\vartheta u \leq \vartheta \quad \text{and} \quad (1 - \vartheta)v \leq (1 - \vartheta),$$

then:

$$\vartheta u + (1 - \vartheta)v \leq \vartheta + (1 - \vartheta) = 1.$$

Hence:

$$0 \leq \vartheta u + (1 - \vartheta)v \leq 1, \quad \text{for all } u, v \in \mathscr{U} \text{ and } \vartheta \in [0, 1].$$

Therefore, $\mathscr{U}$ is convex and **(C2)** is satisfied.

(C3) Each of the right hand side terms F_S, F_{I_1}, F_{I_2} and F_A of system (2.42) is continuous, bounded above by a sum of the bounded control and state, and can be written as a linear function of u with coefficients depending on time and state solutions.

(C4) The integrand in the objective functional $aI_1 + b_1u_1^2 + b_2u_2^2 + b_3u_3^2$ is clearly convex on $\mathscr{U}$. Finally, there exist constants $C_1, C_2 > 0$ and $\gamma > 1$ such that

$$f(t, I_1, u_1, u_2, u_3) = aI_1 + b_1u_1^2 + b_2u_2^2 + b_3u_3^2 \geq C_1 \left(|u_1(t)|^2 + |u_2(t)|^2 + |u_3|^2\right)^{\gamma/2} - C_2.$$

Since $b_1, b_2, b_3 > 0$ and I_1 is bounded, it suffices to choose $C_1 = \inf_{t\in[0,T]} (b_1, b_2, b_3)$, $C_2 > 0$ which depends on upper bounds of I_1 and $\gamma = 2$. The conditions of Theorem 11 are satisfied for system (2.42). Therefore, we conclude that there exists an optimal control $(u_1^*, u_2^*, u_3^*) \in \mathscr{U}$ such that

$$\mathscr{J}(u_1^*, u_2^*, u_3^*) = \min_{(u_1,u_2,u_3)\in\mathscr{U}} \mathscr{J}(u_1, u_2, u_3).$$

■

2.5.2 Characterization of the optimal control

The necessary conditions that an optimal control problem must satisfy come from Pontryagin's maximum principle Theorem 13. This principle converts the controlled system (2.42) into a problem of minimizing point wise a Hamiltonian $\mathscr{H}$ with respect to the control parameters u_1, u_2 and u_3. The Hamiltonian $\mathscr{H}$ is formulated from the cost functional and the objective functional in order to obtain the optimality condition. We define the adjoint or co-state variables λ_S, λ_{I_1}, λ_{I_2} and λ_A for S, I_1, I_2 and A, respectively. The Hamiltonian is defined as

$$\begin{aligned}\mathscr{H} &= aI_1 + b_1u_1^2 + b_2u_2^2 + b_3u_3^2 + \lambda_S(Q_0 - \beta_m S - \mu S)\\ &+ \lambda_{I_1}(\beta_m S - (u_2\theta + \mu + \delta) I_1) + \lambda_{I_2}(u_2\theta I_1 - (\delta + \mu + u_3\pi) I_2)\\ &+ \lambda_A(\delta I_1 + \delta I_2 + u_3\pi I_2 - (\alpha + \mu) A).\end{aligned} \tag{2.45}$$

The form of the adjoint equations and transversality conditions are standard results that follow from Pontryagin's maximum principle Theorem13. The adjoint system along with the transversality and optimality conditions corresponding to the system (2.42) are stated in the following theorem.

Theorem 22 *For the optimal controls u_1^*, u_2^* and u_3^* that minimizes $\mathscr{J}(u_1, u_2, u_3)$ over $\mathscr{U}$, there exist adjoint variables λ_S, λ_{I_1}, λ_{I_2} and λ_A satisfying*

$$\begin{cases} \dfrac{d\lambda_S}{dt} = \left\{\beta_m - \dfrac{\beta_m S}{N}\right\}(\lambda_S - \lambda_{I_1}) + \mu\lambda_S, \\ \dfrac{d\lambda_{I_1}}{dt} = \dfrac{(1-u_1)\beta_1 c_1 S - \beta_m S}{N}(\lambda_S - \lambda_{I_1}) + \lambda_{I_1}(u_2\theta + \mu + \delta) - u_2\theta\lambda_{I_2} - \delta\lambda_A - a, \\ \dfrac{d\lambda_{I_2}}{dt} = \dfrac{(1-u_1)\beta_2 c_2 S - \beta_m S}{N}(\lambda_S - \lambda_{I_1}) + \lambda_{I_2}(\delta + \mu + u_3\pi) - \lambda_A(\delta + u_3\pi), \\ \dfrac{d\lambda_A}{dt} = \dfrac{(1-u_1)\beta_3 c_3 S - \beta_m S}{N}(\lambda_S - \lambda_{I_1}) + \lambda_A(\alpha + \mu), \end{cases} \tag{2.46}$$

subject to the transversality conditions

$$\lambda_S(T) = \lambda_{I_1}(T) = \lambda_{I_2}(T) = \lambda_A(T) = 0. \tag{2.47}$$

The controls u_1^* , u_2^* and u_3^* satisfy the optimality condition:

$$u_1^* = \max\left\{0, \min\left(1, \frac{(\beta_1 c_1 I_1 + \beta_2 c_2 I_2 + \beta_3 c_3 A)S}{2b_1 N}(\lambda_{I_1} - \lambda_S)\right)\right\}, \tag{2.48}$$

$$u_2^* = \max\left\{0, \min\left(1, \frac{\theta I_1(\lambda_{I_1} - \lambda_{I_2})}{2b_2}\right)\right\}, \tag{2.49}$$

$$u_3^* = \max\left\{0, \min\left(1, \frac{\pi I_2(\lambda_{I_2} - \lambda_A)}{2b_3}\right)\right\}. \tag{2.50}$$

Proof. We differentiate the Hamiltonian function with respect to S, I_1, I_2 and A respectively in our attempts to obtain the differential equation governing the adjoint variables. Evaluate at the optimal control to obtain the characterization of the optimal control given by equation (2.45) by solving equations $\dfrac{\partial \mathscr{H}}{\partial u_i} = 0$, for $i = 1, 2, 3$ In addition, the second derivatives of the Hamiltonian function with respect u_1, u_2, u_3 respectively are all positive, that means the optimal problem is minimum at controls u_1^*, u_2^* and u_3^*. Hence the adjoint system can be obtained as follows:

$$\begin{cases} \dfrac{d\lambda_S}{dt} = -\left(\dfrac{\partial \mathscr{H}}{\partial S}\right), \\ \dfrac{d\lambda_{I_1}}{dt} = -\left(\dfrac{\partial \mathscr{H}}{\partial I_1}\right), \\ \dfrac{d\lambda_{I_2}}{dt} = -\left(\dfrac{\partial \mathscr{H}}{\partial I_2}\right), \\ \dfrac{d\lambda_A}{dt} = -\left(\dfrac{\partial \mathscr{H}}{\partial A}\right). \end{cases}$$

$$
\begin{cases}
\dfrac{d\lambda_S}{dt} = (1-u_1)\left\{\dfrac{(\beta_1 c_1 I_1 + \beta_2 c_2 I_2 + \beta_3 c_3 A)\, N - (\beta_1 c_1 I_1 + \beta_2 c_2 I_2 + \beta_3 c_3 A)\, S}{N^2}\right\}(\lambda_S - \lambda_{I_1}) \\
\qquad + \mu\lambda_S, \\
\dfrac{d\lambda_{I_1}}{dt} = -a + (1-u_1)\left\{\dfrac{\beta_1 c_1 N - (\beta_1 c_1 I_1 + \beta_2 c_2 I_2 + \beta_3 c_3 A)}{N^2} S\right\}(\lambda_S - \lambda_{I_1}) + \lambda_{I_1}(u_2\theta + \mu + \delta) \\
\qquad - u_2\theta\lambda_{I_2} - \lambda_A\delta, \\
\dfrac{d\lambda_{I_2}}{dt} = (1-u_1)\left\{\dfrac{\beta_2 c_2 N - (\beta_1 c_1 I_1 + \beta_2 c_2 I_2 + \beta_3 c_3 A)}{N^2} S\right\}(\lambda_S - \lambda_{I_1}) + \lambda_{I_2}(\delta + \mu + u_3\pi) \\
\qquad - \lambda_A(\delta + u_3\pi), \\
\dfrac{d\lambda_A}{dt} = (1-u_1)\left\{\dfrac{\beta_3 c_3 N - (\beta_1 c_1 I_1 + \beta_2 c_2 I_2 + \beta_3 c_3 A)}{N^2} S\right\}(\lambda_S - \lambda_{I_1}) + \lambda_A(\alpha + \mu).
\end{cases}
$$

The transversality conditions (or boundary conditions) are

$$\lambda_S(T) = \lambda_{I_1}(T) = \lambda_{I_2}(T) = \lambda_A(T) = 0.$$

To get the characterization of the optimal control, we solve $\dfrac{\partial \mathscr{H}}{\partial u_i} = 0$ at $u_i = u_i^*$, for $i = 1, 2, 3$. The first control is obtained as

$$
\begin{aligned}
&\frac{\partial \mathscr{H}}{\partial u_1} = 0, \\
&2b_1 u_1^* + \lambda_S \frac{(\beta_1 c_1 I_1 + \beta_2 c_2 I_2 + \beta_3 c_3 A)}{N} S - \lambda_{I_1} \frac{(\beta_1 c_1 I_1 + \beta_2 c_2 I_2 + \beta_3 c_3 A)}{N} S = 0.
\end{aligned}
$$

This implies that

$$u_1^* = \frac{(\beta_1 c_1 I_1 + \beta_2 c_2 I_2 + \beta_3 c_3 A)}{2b_1 N} S(\lambda_{I_1} - \lambda_S).$$

Other controls for u_2 and u_3 obtained similarly. Thus

$$
\begin{aligned}
\frac{\partial \mathscr{H}}{\partial u_2} &= 2b_2 u_2^* - \theta I_1 \lambda_{I_1} + \theta I_1 \lambda_{I_2} = 0, \\
u_2^* &= \frac{\theta I_1 (\lambda_{I_1} - \lambda_{I_2})}{2b_2}.
\end{aligned}
$$

and

$$
\begin{aligned}
\frac{\partial \mathscr{H}}{\partial u_3} &= 2b_3 u_3^* - \pi I_2 \lambda_{I_2} + \pi I_2 \lambda_A = 0, \\
u_3^* &= \frac{\pi I_2 (\lambda_{I_2} - \lambda_A)}{2b_3}.
\end{aligned}
$$

In order to satisfy the given bounds for the control functions, i.e $0 \leq u_i(t) \leq 1$, for $i = 1, 2, 3$, the optimal control is restricted to:

$$u_1^* = \max\left\{0, \min\left(1, \frac{(\beta_1 c_1 I_1 + \beta_2 c_2 I_2 + \beta_3 c_3 A)}{2b_1 N} S\left(\lambda_{I_1} - \lambda_S\right)\right)\right\},$$
$$u_2^* = \max\left\{0, \min\left(1, \frac{\theta I_1\left(\lambda_{I_1} - \lambda_{I_2}\right)}{2b_2}\right)\right\},$$
$$u_3^* = \max\left\{0, \min\left(1, \frac{\pi I_2\left(\lambda_{I_2} - \lambda_A\right)}{2b_3}\right)\right\}.$$

■

2.6 Numerical simulations

In this section, we present the numerical results obtained from the stability analysis of the equilibrium points of the system under study. We also solve the optimality conditions derived from the mathematical model to gain a deeper understanding of the system's dynamics. These results underscore the interplay between theoretical predictions and computational validation, forming a basis for further analysis and implications.

2.6.1 Simulation of stability analysis

We first *consider* the case where $\mathscr{R}_0 < 1$, using the parameter values provided in Table (2.1). The initial values for the state variables are set as $S(0) = 800$, $I_1(0) = 40$, $I_2(0) = 45$, and $A(0) = 0$. The model's dynamics are illustrated in Figure (2.2). The figure demonstrates that the population approaches the disease-free equilibrium $\mathscr{E}_0 = (10000, 0, 0, 0)$. The Disease-Free Equilibrium (DFE) is clearly locally asymptotically stable whenever $\mathscr{R}_0 < 1$. This numerical verification supports the global asymptotic stability result for the disease-free equilibrium as outlined in Theorem 18.

Next, we *consider* the case where $\mathscr{R}_0 > 1$, using the parameter values provided in Table (2.2). The same initial conditions are applied. The dynamics resulting from the model are shown in Figures (2.3) and (2.4) for different values of the control parameter. These figures

demonstrate that the population approaches the endemic equilibrium $\mathscr{E}_1$ when $\mathscr{R}_0 > 1$. The endemic equilibrium $\mathscr{E}_1$ is globally asymptotically stable whenever $\mathscr{R}_0 > 1$, which aligns with the analytical findings previously discussed in Theorem 21.

Table 2.1: **Parameter values for the stability simulation in the case $\mathscr{R}_0 < 1$.**

Parameter	Q_0	β_1	β_2	β_3	c_1	c_2	c_3	θ	π	δ	α	μ
Values	2000	0.20	0.15	0.12	1	1	1	0.015	0.6	0.1	1	0.2
Reference	[50]	[41]	[50]	[41]	[41]	[41]	[48]	[50]	[41]	[50]	[50]	-

Table 2.2: **Parameter values for the stability simulation in the case $\mathscr{R}_0 > 1$.**

Parameter	Q_0	β_1	β_2	β_3	c_1	c_2	c_3	θ	π	δ	α	μ
Values	2000	1.344	0.15	0.12	3	2	1	0.015	0.6	0.1	1	0.02
Reference	[50]	[50]	[50]	[41]	[48]	[48]	[48]	[50]	[41]	[50]	[50]	[50]

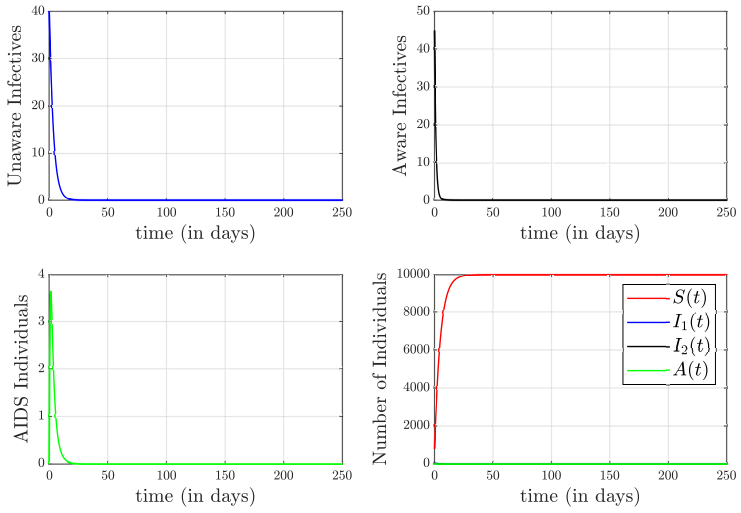


Figure 2.2: The behavior of the system (2.1) for control values in the range $0 \leq u_1 \leq 1$. In each case, the disease-free equilibrium solution is $\mathscr{E}_0 = (10000, 0, 0, 0)$.

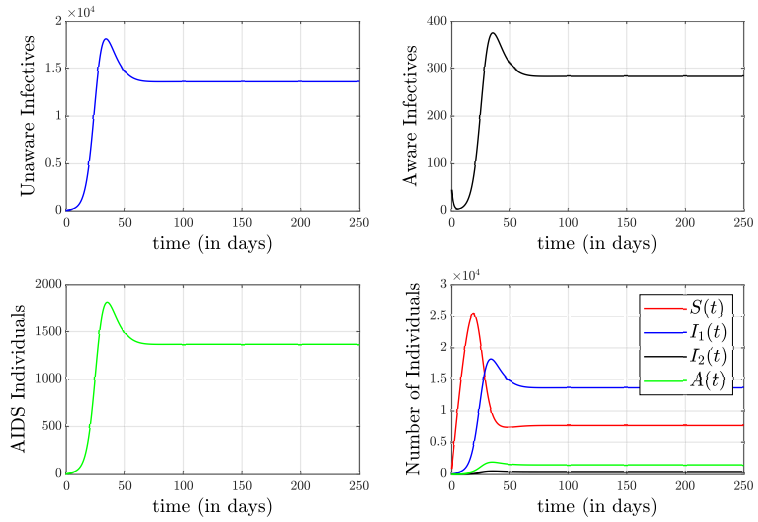


Figure 2.3: The behavior of the system (2.1) for $u_1 = 0.9$. In each case, $\mathscr{R}_0 = 3.0013 > 1$ and the positive endemic equilibrium solution is $\mathscr{E}_1 = (7665.8, 13679, 284.9820, 13690)$.

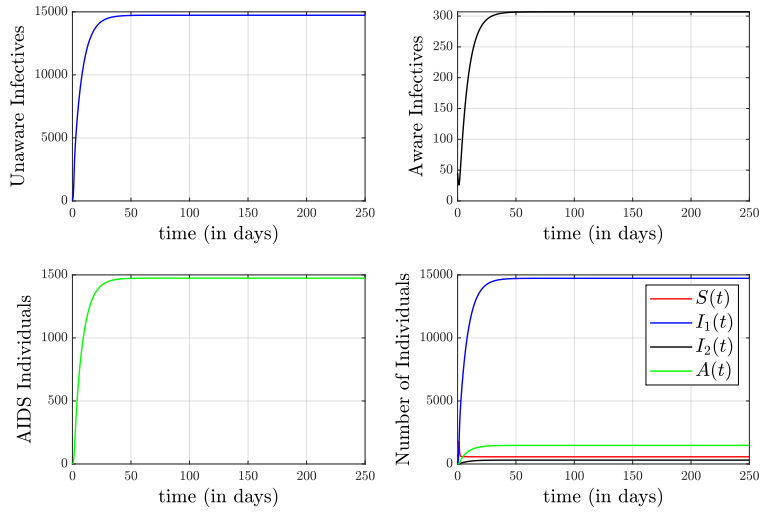


Figure 2.4: The behavior of the system (2.1) for $u_1 = 0$. In each case, $\mathscr{R}_0 = 30.0128 > 1$, and the positive endemic equilibrium solution is $\mathscr{E}_1 = (569.3279, 14730, 306.8848, 1474.3)$.

2.6.2 Optimal control simulation

In this subsection, we conduct numerical simulations of the controlled system (2.42) with and without optimal control. The optimal control solution is obtained by solving the optimality

system, which includes both the state system and the adjoint system. An iterative method is employed to solve this system. We start by solving the state equations with an initial guess for the controls over the simulated time using the forward fourth-order Runge-Kutta method. Due to the transversality conditions (2.49), the adjoint equations are solved using the backward fourth-order Runge-Kutta method, based on the current iteration's solution of the state equations. The controls are then updated using a convex combination of the previous controls and the values from the characterizations (2.48)-(2.50). This process is repeated, and the iterations are terminated when the current states, adjoint states, and control values have sufficiently converged. Next, we numerically investigate the effect of the two optimal control strategies on the spread of the disease in a population. The first strategy applies all three control interventions (u_1, u_2, u_3), while the second strategy uses only the last two controls (u_2, u_3). For the simulation, we chose the weight factors as $a = 800$, $b_1 = 35$, $b_2 = 55$, and $b_3 = 75$, along with the parameter values from Table (2.2). The initial state variables are set as $(S(0), I_1(0), I_2(0), A(0)) = (800, 40, 45, 0)$.

Strategy A: In this strategy, all three control measures (u_1, u_2, u_3) were applied to minimize the objective function $\mathscr{J}$. As illustrated in Figure (2.5), the control strategy results in a significant reduction in the number of infected individuals. Figure (2.6) presents the control profile, where the first control u_1 remains constant from day 1 until the end of the 100-day simulation period, while the controls u_2 and u_3 gradually decrease from their upper bounds after 50 and 72 days, respectively.

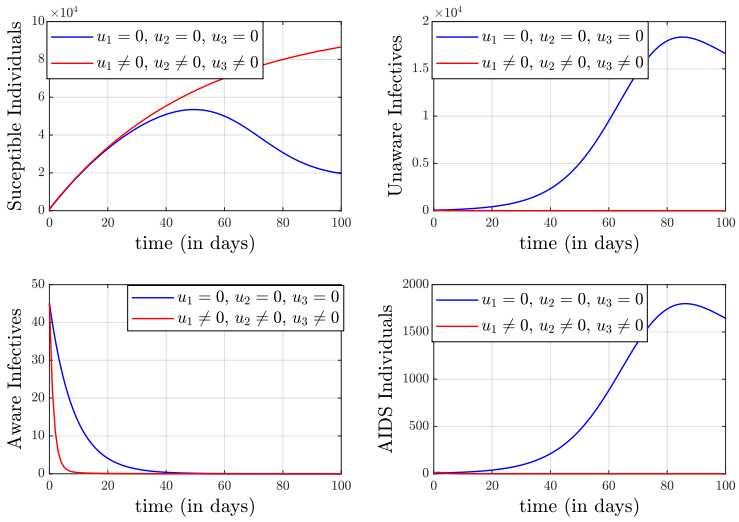


Figure 2.5: Simulations of the HIV/AIDS model illustrating the impact of control **strategy A** on disease transmission.

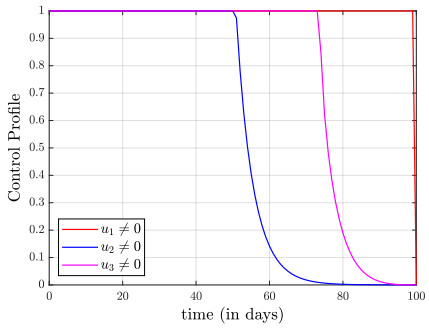


Figure 2.6: The control profile corresponding to **strategy A**.

Strategy B: In this strategy, we optimized the objective function $\mathscr{J}$ by utilizing only the screening control u_2 and the treatment control u_3, while keeping the condom use control u_1 fixed at zero. As depicted in Figure (2.7), we observe a noticeable increase in both unaware and aware infected individuals, as well as in the AIDS population, when compared to the uncontrolled scenario. This increase was anticipated due to the lack of condom use, which is a critical measure in curbing the spread of the infection. Figure (2.8) shows that both u_2 and u_3 remain at their upper bounds throughout the entire simulation period. These findings suggest that this strategy is not effective in containing the spread of the disease.

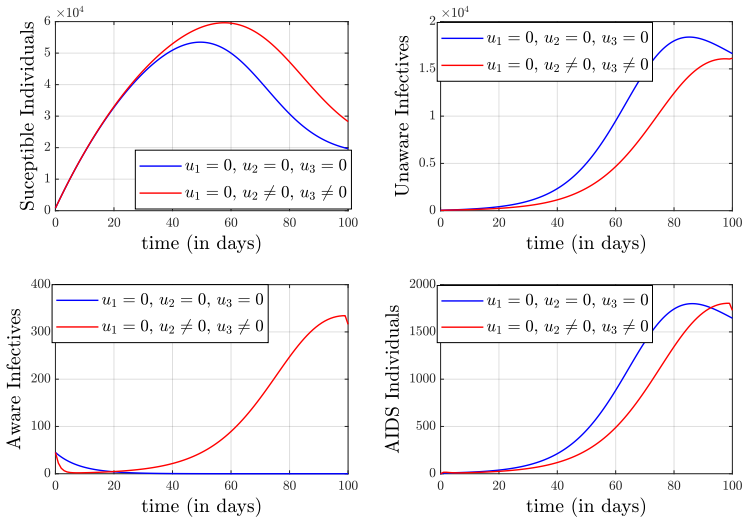


Figure 2.7: Simulations of the HIV/AIDS model illustrating the impact of control **strategy B** on the spread of the disease.

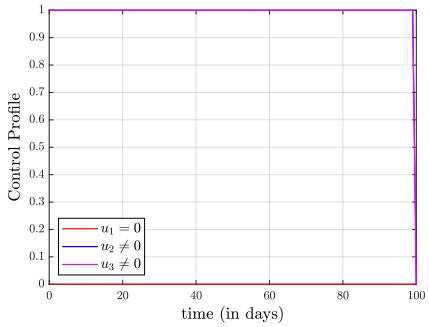


Figure 2.8: The control profile corresponding to **strategy B**.

Chapter 3

The optimal control of an HIV/AIDS reaction-diffusion epidemic model

In this chapter, we consider an HIV/AIDS reaction-diffusion system that was developed by adding a diffusion term to the ordinary differential equation model discussed in the previous chapter and included in the preprint [14]. The model variables become functions of both space and time, allowing for the tracking of population concentrations as well as their spatial spread. We establish the local and global stability of the system and introduce an optimal control strategy. The study begins with an investigation into the existence and uniqueness of solutions. We then establish estimates for the positive strong solution of the controlled system using semigroup theory of operators. Additionally, we employ minimal sequence techniques to demonstrate the existence of an optimal control. In doing so, we establish the necessary optimality conditions for the developed scheme.

The results that will be discussed in this chapter have been published in an international journal [13].

3.1 Reaction-Diffusion HIV/AIDS model

In this section, we consider the following reaction-diffusion HIV/AIDS model:

$$\begin{cases} \dfrac{\partial S(t,x)}{\partial t} - d_1\Delta S(t,x) = Q_0 - \beta_m S(t,x) - \mu S(t,x), \quad (t,x) \in Q, \\ \dfrac{\partial I_1(t,x)}{\partial t} - d_2\Delta I_1(t,x) = \beta_m S(t,x) - (\theta+\mu+\delta) I_1(t,x), \quad (t,x) \in Q, \\ \dfrac{\partial I_2(t,x)}{\partial t} - d_3\Delta I_2(t,x) = \theta I_1(t,x) - (\delta+\mu+\pi) I_2(t,x), \quad (t,x) \in Q, \\ \dfrac{\partial A(t,x)}{\partial t} - d_4\Delta A(t,x) = \delta I_1(t,x) + \delta I_2(t,x) + \pi I_2(t,x) - (\alpha+\mu) A(t,x), \quad (t,x) \in Q, \end{cases} \tag{3.1}$$

where $Q = [0,T] \times \Omega$ and Ω is an open bounded subset from $\mathbb{R}^m$, $m \leq 3$, with the boundary $\partial\Omega$ sufficiently smooth. It is supplemented with the homogeneous Neumann boundary conditions

$$\frac{\partial S(t,x)}{\partial \eta} = \frac{\partial I_1(t,x)}{\partial \eta} = \frac{\partial I_2(t,x)}{\partial \eta} = \frac{\partial A(t,x)}{\partial \eta} = 0, \quad (t,x) \in \Sigma = [0,T] \times \partial\Omega, \tag{3.2}$$

where η is the unit normal vector on $\partial\Omega$. The corresponding initial conditions are

$$S(0,x) = S_0(x), \ I_1(0,x) = I_{01}(x), \ I_2(0,x) = I_{02}(x) \text{ and } A(0,x) = A_0(x). \tag{3.3}$$

In the proposed model, S, I_1, I_2, and A are positive functions of both time and space representing the population distributions of four classes of people: susceptibles, infectives who are not aware of their infection, HIV positive individuals who are aware of their infection, and individuals with AIDS, respectively. This model is constructed by adding the diffusion terms $-d_1\Delta S(t,x)$, $-d_2\Delta I_1(t,x)$, $-d_3\Delta I_2(t,x)$, and $-d_4\Delta A(t,x)$ to the ODE model (2.1). In this context, Δ denotes the Laplacian operator over Ω and the parameters d_i for $i = 1,2,3,4$ represent the diffusivity constants modeling the movement of a certain class as a result of its distribution. It is important to note that the formulation of the proposed model assumes that the movement of the individuals in each class is only affected by the distribution of the same class and not by any of the other class distributions, which in vector form is usually represented by a diagonal diffusivity matrix.

3.2 Local stability of the equilibria

In this section, we aim to demonstrate the local asymptotic stability of the Disease-free equilibrium $\mathscr{E}_0$ and the endemic equilibrium $\mathscr{E}_1$ for system (3.1)-(3.3). Let $0 = \lambda_0 \leq \lambda_1 \leq \lambda_2 \leq .....$ be the eigenvalues Laplacian operator Δ with Neumann boundaries on Ω. Note that the first eigenfunction is a constant which is why the corresponding eigenvalue is equal to zero. The normalized eigenfunctions corresponding to λ_i are denoted by $\Phi_{ij}, 1 \leq j \leq m_i$. These functions are the solutions of

$$\begin{cases} \Delta\Phi_{ij} = \lambda_i \Phi_{ij}, \text{ in } \Omega \\ \dfrac{\partial \Phi_{ij}}{\partial \nu} = 0, \text{in } \partial\Omega. \end{cases} \tag{3.4}$$

The eigenfunctions are normalized according to

$$\int_\Omega \Phi_{ij}^2(x)dx = 1. \tag{3.5}$$

The set of eigenfunctions $\{\Phi_{ij} : 1 \leq j \leq m_i\}$ forms a complete orthonormal basis in $L^2(\Omega)$. In order to establish the local asymptotic stability of the equilibruim point of system (3.1)-(3.3), we must examine all the eigenvalues of the linearizing operator and if they all have negative real parts, then the solution is locally asymptotically stable. The linearizing operator of system (3.1)-(3.3) at any equilibrium point $\mathscr{E} = (\widetilde{S}, \widetilde{I}_1, \widetilde{I}_2, \widetilde{A})$ may be given by

$$\mathcal{L}(\mathscr{E}) = \begin{pmatrix} \begin{pmatrix} -\widetilde{G} - \mu \\ -d_1\Delta \end{pmatrix} & -\widetilde{F}_1 + \widetilde{M}_1 & -\widetilde{F}_2 + \widetilde{M}_1 & -\widetilde{F}_3 + \widetilde{M}_1 \\ G & \begin{pmatrix} \widetilde{F}_1 - \widetilde{M}_1 - d_2\Delta \\ -(\theta + \delta + \mu) \end{pmatrix} & \widetilde{F}_2 - \widetilde{M}_1 & \widetilde{F}_3 - \widetilde{M}_1 \\ 0 & \theta & \begin{pmatrix} -(\delta + \mu + \pi) \\ -d_3\Delta \end{pmatrix} & 0 \\ 0 & \delta & \delta + \pi & \begin{pmatrix} -(\alpha + \mu) \\ -d_4\Delta \end{pmatrix} \end{pmatrix},$$

where

$$\begin{cases} \widetilde{G} = \dfrac{(\widetilde{N}-\widetilde{S})(1-u_1)(\beta_1 c_1 \widetilde{I}_1 + \beta_2 c_2 \widetilde{I}_2 + \beta_3 c_3 \widetilde{A})}{\widetilde{N}^2}, \\ \widetilde{F}_1 = \dfrac{(1-u_1)\beta_1 c_1}{\widetilde{N}}\widetilde{S}, \\ \widetilde{M}_1 = \dfrac{(1-u_1)(\beta_1 c_1 \widetilde{I}_1 + \beta_2 c_2 \widetilde{I}_2 + \beta_3 c_3 \widetilde{A})}{\widetilde{N}^2}\widetilde{S}, \\ \widetilde{F}_2 = \dfrac{(1-u_1)\beta_2 c_2}{\widetilde{N}}\widetilde{S}, \\ \widetilde{F}_3 = \dfrac{(1-u_1)\beta_3 c_3}{\widetilde{N}}\widetilde{S}. \end{cases}$$

Using the eigenfunction expansion method [1, 20], which we described in the first chapter , the Jacobian matrix of system (3.1)-(3.3), which is given by

$$J_i(\mathscr{E}) = \begin{pmatrix} \begin{pmatrix} -\widetilde{G}-\mu \\ -d_1\lambda_i \end{pmatrix} & -\widetilde{F}_1 + \widetilde{M}_1 & -\widetilde{F}_2 + \widetilde{M}_1 & -\widetilde{F}_3 + \widetilde{M}_1 \\ \widetilde{G} & \begin{pmatrix} \widetilde{F}_1 - \widetilde{M}_1 - d_2\lambda_i \\ -(\theta+\delta+\mu) \end{pmatrix} & \widetilde{F}_2 - \widetilde{M}_1 & \widetilde{F}_3 - \widetilde{M}_1 \\ 0 & \theta & \begin{pmatrix} -(\delta+\mu+\pi) \\ -d_3\lambda_i \end{pmatrix} & 0 \\ 0 & \delta & \delta+\pi & \begin{pmatrix} -(\alpha+\mu) \\ -d_4\lambda_i \end{pmatrix} \end{pmatrix}. \quad (3.6)$$

Now, we compute the basic reproduction number of the proposed model (3.1)-(3.3), given its important role in understanding the stability of the system (3.1)-(3.3). This is achieved using the next generation method. Matrix F is given as

$$F = (1-u_1)\begin{bmatrix} \beta_1 c_1 & \beta_2 c_2 & \beta_3 c_3 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}. \quad (3.7)$$

For all $i \geqslant 0$, the matrix V_i given by

$$V_i = \begin{bmatrix} (\theta+\delta+\mu+d_2\lambda_i) & 0 & 0 \\ -\theta & (\delta+\mu+\pi+d_3\lambda_i) & 0 \\ -\delta & -(\delta+\pi) & (\alpha+\mu+d_4\lambda_i) \end{bmatrix}. \quad (3.8)$$

The term $\mathscr{R}_i$ is defined as the spectral radius of matrix FV_i^{-1} for all $i \geqslant 0$. Thus, we get

$$\mathscr{R}_i = \rho(FV_i^{-1}) = A_i + B_i + C_i + D_i, \tag{3.9}$$

where

$$\begin{cases} A_i = \dfrac{(1-u_1)\beta_1 c_1}{(\theta+\delta+\mu+d_2\lambda_i)}, \\ B_i = \dfrac{(1-u_1)\beta_2 c_2 \theta}{(\theta+\delta+\mu+d_2\lambda_i)\,(\delta+\mu+\pi+d_3\lambda_i)}, \\ C_i = \dfrac{(1-u_1)\beta_3 c_3 \theta\,(\delta+\pi)}{(\theta+\delta+\mu+d_2\lambda_i)\,(\delta+\mu+\pi+d_3\lambda_i)\,(\alpha+\mu+d_4\lambda_i)}, \\ D_i = \dfrac{(1-u_1)\beta_3 c_3 \delta}{(\theta+\delta+\mu+d_2\lambda_i)\,(\alpha+\mu+d_4\lambda_i)}. \end{cases} \tag{3.10}$$

For $i = 0$, from (3.9), we have $\mathscr{R}_0 = A_0 + B_0 + C_0 + D_0$, where

$$\begin{cases} A_0 = \dfrac{(1-u_1)\beta_1 c_1}{(\theta+\delta+\mu)}, \\ B_0 = \dfrac{(1-u_1)\beta_2 c_2 \theta}{(\theta+\delta+\mu)\,(\delta+\mu+\pi)}, \\ C_0 = \dfrac{(1-u_1)\beta_3 c_3 \theta\,(\delta+\pi)}{(\theta+\delta+\mu+)\,(\delta+\mu+\pi)\,(\alpha+\mu)}, \\ D_0 = \dfrac{(1-u_1)\beta_3 c_3 \delta}{(\theta+\delta+\mu)\,(\alpha+\mu)}. \end{cases}$$

The following theorem establishes the local stability of the equilibrium points for system (3.1)-(3.3).

Theorem 23 *For system (3.1)-(3.3):*

(i) *If $\mathscr{R}_0 < 1$, the disease-free equilibrium solution $\mathscr{E}_0$ is locally asymptotically stable.*

(ii) If $\mathscr{R}_0 > 1$, $\mathscr{E}_0$ is unstable and the positive endemic equilibrium $\mathscr{E}_1$ is locally asymptotically stable.

Proof. (i) The Jacobian matrix for the system (3.1)-(3.3) evaluated at $\mathscr{E}_0$, for all $i \geqslant 0$ is given by

$$J_i(\mathscr{E}_0) = \begin{pmatrix} -(\mu+d_1\lambda_i) & -\Lambda_1 & -\Lambda_2 & -\Lambda_3 \\ 0 & \Lambda_1-(\theta+\delta+\mu+d_2\lambda_i) & \Lambda_2 & \Lambda_3 \\ 0 & \theta & -(\delta+\mu+\pi+d_3\lambda_i) & 0 \\ 0 & \delta & \delta+\pi & -(\alpha+\mu+d_4\lambda_i) \end{pmatrix},$$

where $\Lambda_1 = (1-u_1)\beta_1 c_1, \Lambda_2 = (1-u_1)\beta_2 c_2, \Lambda_3 = (1-u_1)\beta_3 c_3$. It is clear that $-(\mu + d_1\lambda_i)$ is an eigenvalue. Hence, by removing the first column and the first row, the Jacobian matrix reduces to

$$J_i^{'}(\mathscr{E}_0) = \begin{pmatrix} \Lambda_1 - (\theta + \delta + \mu + d_2\lambda_i) & \Lambda_2 & \Lambda_3 \\ \theta & -(\delta + \mu + \pi + d_3\lambda_i) & 0 \\ \delta & \delta + \pi & -(\alpha + \mu + d_4\lambda_i) \end{pmatrix}.$$

Therefore, we may calculate the eigenvalues of the reduced matrix. Solving the eigenvalues of $J_i^{'}(E_0)$ requires that:

$$\det(J_i^{'}(\mathscr{E}_0) - \xi I) = 0,$$

which leads to the following characteristic polynomial:

$$\xi^3 + m_{i,1}\xi^2 + m_{i,2}\xi + m_{i,3} = 0, \text{ for all } i \geqslant 0, \tag{3.11}$$

where

$$\begin{aligned} m_{i,1} &= (\alpha + \mu + d_4\lambda_i) + (\delta + \mu + \pi + d_3\lambda_i) + (\theta + \delta + \mu + d_2\lambda_i)(1 - A_i), \\ m_{i,2} &= (\alpha + \mu + d_4\lambda_i)(\delta + \mu + \pi + d_3\lambda_i) \\ &+ (\alpha + \mu + d_4\lambda_i)(\theta + \delta + \mu + d_2\lambda_i)(1 - A_i) \\ &+ (\delta + \mu + \pi + d_3\lambda_i)(\theta + \delta + \mu + d_2\lambda_i)(1 - A_i) - \Lambda_2\theta - \delta\Lambda_3, \\ m_{i,3} &= (\theta + \delta + \mu + d_2\lambda_i)(\delta + \mu + \pi + d_3\lambda_i)(\alpha + \mu + d_4\lambda_i)(1 - R_i). \end{aligned}$$

We apply the Routh–Hurwitz stability conditions Theorem 7.

$$m_{i,1} > 0, \quad m_{i,3} > 0, \quad m_{i,1}m_{i,2} - m_{i,3} > 0. \tag{3.12}$$

By examining conditions (3.12) for equation (3.11), $m_{i,3} > 0$ will result if $\mathscr{R}_i < 1$.

We rewrite $m_{i,2}$ as

$$\begin{aligned} m_{i,2} &= (\alpha + \mu + d_4\lambda_i)(\delta + \mu + \pi + d_3\lambda_i) \\ &+ (\delta + \mu + \pi + d_3\lambda_i)(\theta + \delta + \mu + d_2\lambda_i)(1 - A_i - D_i) \\ &+ (\alpha + \mu + d_4\lambda_i)(\theta + \delta + \mu + d_2\lambda_i)(1 - A_i - D_i). \end{aligned}$$

Since $A_i > 0$, for all $i \geqslant 0$, then with respect to (3.9), we can conclude $A_i < \mathscr{R}_i$. Thus, if $\mathscr{R}_i < 1$, then $m_{i,1} > 0$. Finally, we investigate the third stability condition. With some algebraic computations, we have

$$\begin{aligned} m_{i,1}m_{i,2} - m_{i,3} &= (\alpha+\mu+d_4\lambda_i)^2(\pi+\delta+\mu+d_3\lambda_i) \\ &+ (\alpha+\mu+d_4\lambda_i)^2(\theta+\delta+\mu+d_2\lambda_i)(1-A_i-D_i) \\ &+ (\delta+\mu+\pi+d_3\lambda_i)^2(\alpha+\mu+d_4\lambda_i) \\ &+ (\delta+\mu+\pi+d_3\lambda_i)^2(\theta+\delta+\mu+d_2\lambda_i)(1-A_i-B_i) \\ &+ (\delta+\mu+\pi+d_3\lambda_i)(\alpha+\mu+d_4\lambda_i)(\theta+\delta+\mu+d_2\lambda_i)[2(1-A_i)+C_i]. \\ &+ (\theta+\delta+\mu+d_2\lambda_i)^2(\delta+\mu+\pi+d_3\lambda_i)(1-A_i)(1-A_i-B_i) \\ &+ (\theta+\delta+\mu+d_2\lambda_i)^2(\alpha+\mu+d_4\lambda_i)(1-A_i-D_i)(1-A_i). \end{aligned}$$

All the parameters A_i, B_i, C_i and D_i are smaller than $\mathscr{R}_i$. For $i = 0$, conditions (3.12) are satisfied if $\mathscr{R}_0 < 1$, since $\mathscr{R}_i \leq \mathscr{R}_0$ for all $i \geqslant 0$. Hence, if $\mathscr{R}_0 < 1$, from the above relation, we conclude $m_{i,1}m_{i,2} - m_{i,3} > 0$. With these assumptions, all the stability conditions (3.12) are satisfied and the disease-free equilibrium $\mathscr{E}_0$ is locally asymptotically stable.

(ii) The Jacobian matrix for system (3.1)-(3.3) evaluated at $\mathscr{E}_1$ for all $i \geqslant 0$ is given by:

$$J_i(\mathscr{E}_1) = \begin{pmatrix} -\overline{G}-\mu-\lambda_i d_1 & -\overline{F}_1+\overline{M}_1 & -\overline{F}_2+\overline{M}_1 & -\overline{F}_3+\overline{M}_1 \\ \overline{G} & \overline{F}_1-\overline{M}_1-B-\lambda_i d_2 & \overline{F}_2-\overline{M}_1 & \overline{F}_3-\overline{M}_1 \\ 0 & \theta & -C-\lambda_i d_3 & 0 \\ 0 & \delta & D & -E-\lambda_i d_4 \end{pmatrix},$$

where $B = \theta+\delta+\mu, C = \delta+\mu+\pi, D = \delta+\pi, E = \alpha+\mu$, and

$$\begin{cases} \overline{G} = \dfrac{(\overline{N}-\overline{S})(1-u_1)(\beta_1 c_1\overline{I_1}+\beta_2 c_2\overline{I_2}+\beta_3 c_3\overline{A})}{\overline{N}^2}, \\ \overline{F}_1 = \dfrac{(1-u_1)\beta_1 c_1}{\overline{N}}\overline{S}, \\ \overline{M}_1 = \dfrac{(1-u_1)(\beta_1 c_1\overline{I_1}+\beta_2 c_2\overline{I_2}+\beta_3 c_3\overline{A})}{\overline{N}^2}\overline{S}, \\ \overline{F}_2 = \dfrac{(1-u_1)\beta_2 c_2}{\overline{N}}\overline{S}, \\ \overline{F}_3 = \dfrac{(1-u_1)\beta_3 c_3}{\overline{N}}\overline{S}. \end{cases}$$

The characteristic equation of the variational matrix $J_i(\mathscr{E}_1)$ for all $i \geqslant 0$ can be written as

$$\xi^4 + q_{i,1}\xi^3 + q_{i,2}\xi^2 + q_{i,3}\xi + q_{i,4} = 0, \text{ for all } i \geqslant 0, \tag{3.13}$$

where

$$q_{i,1} = \left(B - \overline{F}_1\right) + C + \overline{G} + \mu + E + \overline{M}_1 + \lambda_i \left(d_1 + d_2 + d_3 + d_4\right),$$

$$\begin{aligned} q_{i,2} &= \lambda_i^2 \left(d_1d_2 + d_1d_3 + d_1d_4 + d_2d_3 + d_2d_4 + d_3d_4\right) + \left(BC - C\overline{F}_1 - \theta\overline{F}_2\right) \\ &+ \left(BE - E\overline{F}_1 - \delta\overline{F}_3\right) + \left(B - \overline{F}_1\right)\left[\lambda_i d_3 + \lambda_i d_1 + \lambda_i d_4 + \mu\right] \\ &+ \lambda_i d_2 \left(C + \overline{G} + \mu + E\right) + \left(C + \overline{G} + \mu + \overline{M}_1\right)\lambda_i d_4 + \left(\mu + \overline{G} + E + \overline{M}_1\right)\lambda_i d_3 \\ &+ \left(\overline{M}_1 + E + C\right)\lambda_i d_1 + C\mu + CE + \mu E + (B + C + E)\left(\overline{G} + \overline{M}_1\right), \end{aligned}$$

$$\begin{aligned} q_{i,3} &= \left(B - \overline{F}_1\right)\left[\lambda_i^2 \left(d_1d_3 + d_1d_4 + d_3d_4\right) + \lambda_i\mu\left(d_4 + d_3\right)\right] + \lambda_i^2 d_1d_4\left(C + \overline{M}_1\right) \\ &+ \lambda_i^2 d_2d_4\left(C + \overline{G} + \mu\right) + \lambda_i^2 d_3d_4\left(\overline{G} + \mu + \overline{M}_1\right) + \lambda_i^2 d_2d_3\left(\mu + E + \overline{G}\right) \\ &+ \lambda_i^2 d_1d_2\left(E + C\right) + \lambda_i^2 d_1d_3\left(E + \overline{M}_1\right) + \lambda_i^3\left(d_1d_2d_3 + d_1d_2d_4 + d_1d_3d_4 + d_2d_3d_4\right) \\ &+ \left(BC - C\overline{F}_1 - \theta\overline{F}_2\right)\left[\lambda_i\left(d_1 + d_4\right) + \mu\right] + \left(BE - E\overline{F}_1 - \delta\overline{F}_3\right)\left[\lambda_i\left(d_1 + d_3\right) + \mu\right] \\ &+ \lambda_i d_1\left[E\overline{M}_1 + C\overline{M}_1 + \theta\overline{M}_1 + \delta\overline{M}_1 + CE\right] + \lambda_i d_2\left[\mu E + CE + C\mu + C\overline{G} + \overline{G}E\right] \\ &+ \lambda_i d_3\left[\mu\overline{M}_1 + E\overline{M}_1 + \delta\overline{M}_1 + \mu E + B\overline{G} + \overline{G}E\right] + (BC + BE)\left(\overline{M}_1 + \overline{G}\right) \\ &+ \lambda_i d_4\left[\mu\overline{M}_1 + C\overline{M}_1 + \theta\overline{M}_1 + C\mu + C\overline{G} + B\overline{G}\right] + CE\left(\overline{G} + \mu\right) + \left(CE - \alpha\delta\right)\overline{M}_1, \end{aligned}$$

$$\begin{aligned} q_{i,4} &= \lambda_i^4 d_1d_2d_3d_4 + \lambda_i^3\left(\overline{G}d_2d_3d_4 + Cd_1d_2d_4 + \mu d_2d_3d_4 + Ed_1d_2d_3 + \overline{M}_1d_1d_3d_4\right) \\ &+ \left(\lambda_i^2 d_1d_3 + \mu\lambda_i d_3\right)\left(BE - \delta\overline{F}_3 - E\overline{F}_1\right) + \lambda_i^2 d_1d_2CE + BCE\overline{G} \\ &+ \lambda_i^2 d_1d_4\left(\theta\overline{M}_1 + C\overline{M}_1\right) + \lambda_i^2 d_1d_3\left(\delta\overline{M}_1 + E\overline{M}_1\right) + \lambda_i^2 d_3d_4\left(\mu\overline{M}_1 + B\overline{G}\right) \\ &+ \lambda_i^2 d_2d_4C\left(\mu + \overline{G}\right) + \lambda_i^2 d_2d_3\left(E\overline{G} + \mu E\right) + \lambda_i d_4\left(C\mu\overline{M}_1 + \theta\mu\overline{M}_1 + BC\overline{G}\right). \\ &+ \left(\lambda_i^2 d_3d_4\mu + \lambda_i^3 d_1d_3d_4\right)\left(B - \overline{F}_1\right) + \left(BCE - C\delta\alpha - \theta\alpha D\right)\overline{M}_1 \\ &+ \left(\lambda_i d_4\mu + \lambda_i^2 d_1d_4\right)\left(BC - C\overline{F}_1 - \theta\overline{F}_2\right) + \lambda_i d_1\overline{M}_1\left(\theta D + \theta E + C\delta + CE\right) \\ &+ \lambda_i d_2CE\left(\overline{G} + \mu\right) + \lambda_i d_3\left(\mu\delta\overline{M}_1 + \mu E\overline{M}_1 + B\overline{G}E\right). \end{aligned}$$

It is clear that $q_{i,1}, q_{i,2}, q_{i,3}$ and $q_{i,4}$ are positive for all $i \geqslant 0$ (no changes in signs). By **Descartes rule of signs** (See.Lemma 7), equation (3.13) has four negative real roots. Hence, $\mathscr{E}_1$ is locally asymptotically stable when $\mathscr{R}_0 > 1$. ■

3.3 Global stability of the equilibria

In this section, we analyze the global stability of the disease-free equilibrium $\mathscr{E}_0$ and the endemic equilibrium $\mathscr{E}_1$ of system (3.1)-(3.3).

3.3.1 Global asymptotic stability of the disease-free equilibrium

The aim here is to show that every solution of (3.1)-(3.3) with an arbitrary positive initial condition converges asymptotically towards $\mathscr{E}_0$. The global asymptotic stability of equilibrium solution $\mathscr{E}_0$ can be proved using the Theorem 6 in the presence of a diffusion term.

Theorem 24 *If $\mathscr{R}_0 < 1$, the disease-free equilibrium solution $\mathscr{E}_0$ is a globally asymptotically stable equilibrium for system (3.1)-(3.3).*

Proof. consider

$$v(t,x) = S(t,x), \quad w(t,x) = \begin{bmatrix} I_1(t,x) \\ I_2(t,x) \\ A\ (t,x) \end{bmatrix}. \tag{3.14}$$

When $I_1 = I_2 = A = 0$, we get the following reaction-diffusion equation (the uninfected subsystem)

$$\begin{cases} \dfrac{\partial S}{dt} = d_1 \Delta S + Q_0 - \mu S, \quad (t,x) \in Q, \\ \\ \dfrac{\partial S(t,x)}{\partial \eta} = 0, \quad (t,x) \in \Sigma. \end{cases} \tag{3.15}$$

From Lemma 2 (see [31]), $S(t,x)$ tends to $S_0(x)$ uniformly for $x \in \overline{\Omega}$ as $t \to \infty$. We can obtain that v_{eq} is globally asymptotically stable.

Next, the right-hand side of the infectious subsystem (i.e the equations for I_1, I_2 and A can be written as

$$\frac{\partial w}{\partial t}=G_i(v,w)=\begin{bmatrix} \beta_m-(\theta+\delta+\mu+d_2\lambda_i)\,I_1-\beta_m\dfrac{Q_0}{\mu}+\beta_m S \\ \\ \theta I_1-(\delta+\mu+\pi+d_3\lambda_i)\,I_2 \\ \\ \delta I_1+\delta I_2+\pi I_2-(\alpha+\mu+d_4\lambda_i)\,A \end{bmatrix},\ \text{for } i=0,1,...$$

$$\frac{\partial w}{\partial t}=\begin{bmatrix} \begin{pmatrix} \dfrac{(1-u_1)}{N}\beta_1 c_1\dfrac{Q_0}{\mu} \\ -(\delta+\theta+\mu+d_2\lambda_i) \end{pmatrix} & \dfrac{(1-u_1)}{N}\beta_2 c_2\dfrac{Q_0}{\mu} & \dfrac{(1-u_1)}{N}\beta_3 c_3\dfrac{Q_0}{\mu} \\ \\ \theta & -(\delta+\mu+\pi+d_3\lambda_i) & 0 \\ \\ \delta & \delta+\pi & -(\alpha+\mu+d_4\lambda_i) \end{bmatrix} \tag{3.16}$$

$$\times\begin{bmatrix} I_1 \\ I_2 \\ A \end{bmatrix}-\begin{bmatrix} \beta_m\dfrac{Q_0}{\mu}-\beta_m S \\ 0 \\ 0 \end{bmatrix}.$$

We obtain

$$\frac{\partial w}{\partial t}=G_i(v,w)=M_i\,w-\hat{G}(v,w),\ \text{for } i=0,1,..., \tag{3.17}$$

where

$$M_i=\begin{bmatrix} \begin{pmatrix} \dfrac{(1-u_1)}{N}\beta_1 c_1\dfrac{Q_0}{\mu} \\ -(\theta+\delta+\mu+d_2\lambda_i) \end{pmatrix} & \dfrac{(1-u_1)}{N}\beta_2 c_2\dfrac{Q_0}{\mu} & \dfrac{(1-u_1)}{N}\beta_3 c_3\dfrac{Q_0}{\mu} \\ \\ \theta & -(\delta+\mu+\pi+d_3\lambda_i) & 0 \\ \\ \delta & \delta+\pi & -(\alpha+\mu+d_4\lambda_i) \end{bmatrix}, \tag{3.18}$$

and

$$\hat{G}(v,w) = \begin{bmatrix} \beta_m \dfrac{Q_0}{\mu} - \beta_m S \\ 0 \\ 0 \end{bmatrix}. \tag{3.19}$$

It is obvious that $S(t,x) \leq \dfrac{Q_0}{\mu}$. Hence, $\hat{G}(v,w) \geq 0$ for all $(v,w) \in Q$. We also notice that the matrix M_i in as M-matrix for $i \geq 0$, Since all its off-diagonal elements are non-negative. Then, $\mathscr{E}_0$ is globally asymptotically stable. ■

3.3.2 Global asymptotic stability of the endemic equilibrium model

In this subsection, we investigate the global asymptotic stability of the endemic equilibrium $\mathscr{E}_1$ when $\mathscr{R}_0 > 1$.

Theorem 25 *If $\mathscr{R}_0 > 1$, the endemic equilibrium $\mathscr{E}_1$ of system (3.1)-(3.3) is globally asymptotically stable.*

Proof. First, let

$$\mathcal{W}(t) = \int_\Omega \left[m_1 \left(S - \overline{S}\right)^2 + m_2 \left(I_1 - \overline{I_1}\right)^2 + m_3 \left(I_2 - \overline{I_2}\right)^2 + m_4 \left(A - \overline{A}\right)^2 \right] dx,$$

where m_1, m_2, m_3, and m_4 are positive constants. To prove that $\mathscr{E}_1$ is globally asymptotically stable, we need to establish that $\mathcal{W}(t)$ is a Lyapunov functional. Differentiating $\mathcal{W}(t)$ with respect to time yields

$$\frac{d\mathcal{W}(t)}{dt} = \int_\Omega \left[2m_1 \frac{\partial S}{\partial t}\left(S - \overline{S}\right) + 2m_2 \frac{\partial I_1}{\partial t}\left(I_1 - \overline{I}_1\right) + 2m_3 \frac{\partial I_2}{\partial t}\left(I_2 - \overline{I}_2\right) + 2m_4 \frac{\partial A}{\partial t}\left(A - \overline{A}\right) \right] dx.$$

Substituting the time derivatives with their values from (3.1) leads to

$$\begin{aligned} \frac{d\mathcal{W}(t)}{dt} &= \int_\Omega \left[2m_1 \left(-\beta_m S - \mu S + d_1 \Delta S\right)\left(S - \overline{S}\right) \right] \\ &+ \int_\Omega \left[2m_2 \left(\beta_m S - (\theta + \delta + \mu) I_1 + d_2 \Delta I_1\right)\left(I_1 - \overline{I_1}\right) \right] dx \\ &+ \int_\Omega \left[2m_3 \left(\theta I_1 - (\theta + \delta + \pi) I_2 + d_3 \Delta I_2\right)\left(I_2 - \overline{I_2}\right) \right] \\ &+ \int_\Omega \left[2m_4 \left(\delta I_1 + (\delta + \pi) I_2 - (\mu + \alpha) A + d_4 \Delta A\right)\left(A - \overline{A}\right) \right] dx, \end{aligned}$$

and we have

$$\begin{aligned}\frac{d\mathcal{W}(t)}{dt} &= \int_\Omega \left[2m_1 d_1 \Delta S \left(S - \overline{S}\right)\right] dx + \int_\Omega \left[2m_2 d_2 \Delta I_1 \left(I_1 - \overline{I_1}\right)\right] dx \\ &+ \int_\Omega \left[2m_3 d_3 \Delta I_2 \left(I_2 - \overline{I_2}\right)\right] dx + \int_\Omega \left[2m_4 d_4 \Delta A \left(A - \overline{A}\right)\right] dx \\ &+ \int_\Omega \left[2m_1 \left(-\beta_m S - \mu S\right) \left(S - \overline{S}\right)\right] dx \\ &+ \int_\Omega \left[2m_2 \left(\beta_m S - (\theta + \delta + \mu) I_1\right) \left(I_1 - \overline{I_1}\right)\right] dx \\ &+ \int_\Omega \left[2m_3 \left(\theta I_1 - (\theta + \delta + \pi) I_2\right) \left(I_2 - \overline{I_2}\right)\right] dx \\ &+ \int_\Omega \left[2m_4 \left(\delta I_1 + (\delta + \pi) I_2 - (\mu + \alpha) A\right) \left(A - \overline{A}\right)\right] dx, \\ &= I + J.\end{aligned}$$

The first part is

$$I = I_1 + I_2 + I_3 + I_4, \tag{3.20}$$

where

$$\begin{aligned}I_1 &= 2 \int_\Omega m_1 d_1 \Delta S \left(S - \overline{S}\right) dx, \\ I_2 &= 2 \int_\Omega m_2 d_2 \Delta I_1 \left(I_1 - \overline{I_1}\right) dx, \\ I_3 &= 2 \int_\Omega m_3 d_3 \Delta I_2 \left(I_2 - \overline{I_2}\right) dx,\end{aligned}$$

and

$$I_4 = 2 \int_\Omega m_4 d_4 \Delta A \left(A - \overline{A}\right) dx.$$

The second part is

$$\begin{aligned}J &= \int_\Omega \left[2m_1 \left(-\beta_m S - \mu S\right) \left(S - \overline{S}\right)\right] dx \\ &+ \int_\Omega \left[2m_2 \left(\beta_m S - (\theta + \delta + \mu) I_1\right) \left(I_1 - \overline{I_1}\right)\right] dx \\ &+ \int_\Omega \left[2m_3 \left(\theta I_1 - (\theta + \delta + \pi) I_2\right) \left(I_2 - \overline{I_2}\right)\right] dx \\ &+ \int_\Omega \left[2m_4 \left(\delta I_1 + (\delta + \pi) I_2 - (\mu + \alpha) A\right) \left(A - \overline{A}\right)\right] dx.\end{aligned} \tag{3.21}$$

We start by looking at I. Using Green's formula and assuming the Neumann boundary conditions in (3.3), we obtain

$$\begin{aligned} I &= -2m_1d_1\int_\Omega |\nabla S|^2\,dx - 2m_2d_2\int_\Omega |\nabla I_1|^2\,dx - 2m_3d_3\int_\Omega |\nabla I_2|^2\,dx - 2m_4d_4\int_\Omega |\nabla A|^2\,dx, \\ &= -\int_\Omega \left[2m_1d_1\,|\nabla S|^2 + 2m_2d_2\,|\nabla I_1|^2 + 2m_3d_3\,|\nabla I_2|^2 + 2m_4d_4\,|\nabla A|^2\right] dx < 0. \end{aligned} \tag{3.22}$$

Here, it is observed that the second part, $J \leq 0$, was proven in the previous chapter. This leads to $\dfrac{d\mathcal{W}}{dt} \leq 0$. Also, $\dfrac{d\mathcal{W}}{dt} = 0$ if and only if $S = \overline{S}$, $I_1 = \overline{I_1}$, $I_2 = \overline{I_2}$, and $A = \overline{A}$. Then, the largest compact invariant set in $\Gamma = \left\{(S, I_1, I_2, A) \mid \dfrac{d\mathcal{W}}{dt} = 0\right\}$ is the singleton $\mathscr{E}_1$. Hence, it follows from LaSalle's invariance principle Theorem 6, we conclude $\mathscr{E}_1$ is globally asymptotically stable when $\mathscr{R}_0 > 1$. ■

3.4 Mathematical model and optimal control

Consider model (3.1)-(3.3) with three control strategies: condom use u_1, screening of unaware infectives u_2, and treatment of aware infectives u_3. These control strategies aim to control the spread of the HIV/AIDS epidemic. The resulting system is given by

$$\begin{cases} \dfrac{\partial S}{\partial t} - d_1\Delta S = Q_0 - \beta_m S(t,x) - \mu S, \quad (t,x) \in Q, \\ \dfrac{\partial I_1}{\partial t} - d_2\Delta I_1 = \beta_m S - (u_2\theta + \mu + \delta)I_1, \quad (t,x) \in Q, \\ \dfrac{\partial I_2}{\partial t} - d_3\Delta I_2 = u_2\theta I_1 - (\delta + \mu + u_3\pi)I_2, \quad (t,x) \in Q, \\ \dfrac{\partial A}{\partial t} - d_4\Delta A = \delta I_1 + \delta I_2 + u_3\pi I_2 - (\alpha + \mu)A, \quad (t,x) \in Q, \end{cases} \tag{3.23}$$

with homogeneous Neumann boundary conditions

$$\frac{\partial S(t,x)}{\partial \eta} = \frac{\partial I_1(t,x)}{\partial \eta} = \frac{\partial I_2(t,x)}{\partial \eta} = \frac{\partial A(t,x)}{\partial \eta} = 0, \quad (t,x) \in \Sigma = [0,T] \times \partial\Omega, \tag{3.24}$$

and initial conditions

$$S(0,x) = S_0(x),\ I_1(0,x) = I_{01}(x),\ I_2(0,x) = I_{02}(x) \text{ and } A(0,x) = A_0(x),\ x \in \Omega. \tag{3.25}$$

Our class of admissible controls is

$$\mathscr{U} = \left\{(u_1, u_1, u_3) \in L^2(Q) : 0 \leq u_i \leq 1, \text{ for } i = 1,2,3\right\}. \tag{3.26}$$

The objective functional is defined as

$$\begin{aligned}\mathscr{J}\left(S, I_1, I_2, A, (u_1, u_2, u_3)\right) = &\int_Q \left[K_1 S + K_2 I_1 + K_3 I_2 + K_4 A\right] dtdx \\ &+ M_1 \left\|u_1\right\|^2_{L^2(Q)} + M_2 \left\|u_2\right\|^2_{L^2(Q)} + M_3 \left\|u_3\right\|^2_{L^2(Q)},\end{aligned} \tag{3.27}$$

where K_1, K_2, K_3, and K_4 are constant weights, and $M_1 \left\|u_1\right\|^2_{L^2(Q)}$ $M_2 \left\|u_2\right\|^2_{L^2(Q)}$ and $M_3 \left\|u_3\right\|^2_{L^2(Q)}$ denote the costs associated with these controls. We seek to find the optimal control $u_i^*, i = 1, 2, 3$ in an appropriate control set such that

$$\mathscr{J}\left(S^*, I_1^*, I_2^*, A^*, (u_1^*, u_2^*, u_3^*)\right) = \inf_{(u_1, u_2, u_3) \in \mathscr{U}} \mathscr{J}\left(S, I_1, I_2, A, (u_1, u_2, u_3)\right), \tag{3.28}$$

subject to system (3.23)-(3.25).

3.4.1 Existence and uniqueness of a strong nonnegative solution.

The existence of a strong solution and well as the positivity and boundedness of solutions, which is necessary since model (3.23)-(3.25) describes populations that must remain nonnegative and bounded at all times. Let $B : D(B) \subset \left(L^2(\Omega)\right)^4 \longmapsto \left(L^2(\Omega)\right)^4$ denote the linear operator defined by

$$B = \begin{pmatrix} d_1\Delta & 0 & 0 & 0 \\ 0 & d_2\Delta & 0 & 0 \\ 0 & 0 & d_3\Delta & 0 \\ 0 & 0 & 0 & d_4\Delta \end{pmatrix}, \tag{3.29}$$

with

$$D(B) = \left\{(S, I_1, I_2, A) \in \left(H^2(\Omega)\right)^4, \frac{\partial S}{\partial \eta} = \frac{\partial I_1}{\partial \eta} = \frac{\partial I_2}{\partial \eta} = \frac{\partial A}{\partial \eta} = 0, \text{ a.e } x \in \partial\Omega\right\}. \tag{3.30}$$

Also, let $z = (S, I_1, I_2, A)$, $z^0 = (S_0, I_{01}, I_{02}, A_0)$ and $f(t, z) = (f_1(t, z), f_2(t, z), f_3(t, z), f_4(t, z))$ with

$$\begin{cases} f_1(t, z) = Q_0 - \beta_m S - \mu S, \\ f_2(t, z) = \beta_m S - (u_2\theta + \mu + \delta) I_1, \\ f_3(t, z) = u_2\theta I_1 - (\delta + \mu + u_3\pi) I_2, \\ f_4(t, z) = \delta I_1 + \delta I_2 + u_3\pi I_2 - (\alpha + \mu) A, \end{cases} \tag{3.31}$$

where $z \in D(f) = \left\{ z \in (L^2(\Omega))^4 : f(t,z) \in (L^2(\Omega))^4 \right\}$. Then, problem (3.23)-(3.25) can be rewritten in the space $(L^2(\Omega))^4$ in the form

$$\begin{cases} \dfrac{\partial z}{\partial t} = Bz + f(t,z), \quad t \in [0,T] \\ z(0) = z^0 \in D(B). \end{cases} \tag{3.32}$$

Theorem 26 *Let Ω be a bounded domain from $\mathbb{R}^m$, $m \leq 3$, with a boundary of class $C^{2+\xi}, \xi \succ 0$. As initial data of system are nonnegative, then for given control $u = (u_1, u_2, u_3) \in \mathscr{U}$, problem (3.23)-(3.25) admits a unique globally positive strong solution z satisfying $z \in W^{1,2}\left([0,T]; (L^2(\Omega))^4\right)$, such that*

$$S(t,x) \in L^\infty(Q) \cap L^2\left(0,T; H^2(\Omega)\right) \cap L^\infty\left(0,T; H^1(\Omega)\right), \tag{3.33}$$

$$I_1(t,x) \in L^\infty(Q) \cap L^2\left(0,T; H^2(\Omega)\right) \cap L^\infty\left(0,T; H^1(\Omega)\right), \tag{3.34}$$

$$I_2(t,x) \in L^\infty(Q) \cap L^2\left(0,T; H^2(\Omega)\right) \cap L^\infty\left(0,T; H^1(\Omega)\right), \tag{3.35}$$

$$A(t,x) \in L^\infty(Q) \cap L^2\left(0,T; H^2(\Omega)\right) \cap L^\infty\left(0,T; H^1(\Omega)\right). \tag{3.36}$$

Moreover, there exists a positive constant C corresponding to state variable z, such that

$$\left\| \frac{\partial S}{\partial t} \right\|_{L^2(Q)} + \|S\|_{L^2(0,T;H^2(\Omega))} + \|S\|_{H^1(\Omega)} + \|S\|_{L^\infty(Q)} \leq C, \tag{3.37}$$

$$\left\| \frac{\partial I_1}{\partial t} \right\|_{L^2(Q)} + \|I_1\|_{L^2(0,T;H^2(\Omega))} + \|I_1\|_{H^1(\Omega)} + \|I_1\|_{L^\infty(Q)} \leq C, \tag{3.38}$$

$$\left\| \frac{\partial I_2}{\partial t} \right\|_{L^2(Q)} + \|I_2\|_{L^2(0,T;H^2(\Omega))} + \|I_2\|_{H^1(\Omega)} + \|I_2\|_{L^\infty(Q)} \leq C, \tag{3.39}$$

$$\left\| \frac{\partial A}{\partial t} \right\|_{L^2(Q)} + \|A\|_{L^2(0,T;H^2(\Omega))} + \|A\|_{H^1(\Omega)} + \|A\|_{L^\infty(Q)} \leq C. \tag{3.40}$$

Proof. As the operator B defined in (3.29)-(3.30) is dissipating, self-adjoint from [51] and generates a C_0- semigroup of contractions on $(L^2(\Omega))^4$, in addition $|S|, |I_1|, |I_2|, |A| \leq N$, thus the function $f = (f_1, f_2, f_3, f_4)$ becomes Lipschitz continuous in $z = (S, I_1, I_2, A)$ uniformly with respect to $t \in [0,T]$. Therefore, problem (3.23)-(3.25) admits a unique strong solution (see Theorem 9)

$$z = (S, I_1, I_2, A) \in W^{1,2}\left([0,T]; \left(L^2(\Omega)\right)^4\right) \cap L^2\left(0,T; (H^2(\Omega))^4\right). \tag{3.41}$$

(i) Let us now prove that S, I_1, I_2, and A are bounded uniformly in $L^{\infty}(Q)$. Let

$$M = \max\left\{\|f_1\|_{L^{\infty}(Q)}, \|S_0(x)\|_{L^{\infty}(\Omega)}\right\}, \tag{3.42}$$

and $\left\{\tilde{S}(t), t \geq 0\right\}$ is the semigroup generated by the operator B_1: $D(B_1) \subset L^2(\Omega) \longmapsto L^2(\Omega)$, where $B_1 S = d_1 \Delta S$ and

$$D(B_1) = \left\{S \in H^2(\Omega), \frac{\partial S}{\partial \eta} = 0, \text{on } \partial\Omega\right\}.$$

It is obvious that the function $V_1(t,x) = S(t,x) - Mt - \|S_0(x)\|_{L^{\infty}(\Omega)}$ satisfies the Cauchy problem

$$\begin{cases} \dfrac{\partial V_1(t,x)}{\partial t} = d_1 \Delta V_1(t,x) + f_1(t, z(t,x)) - M, \ (t,x) \in Q, \\ V_1(0,x) = S_0(x) - \|S_0(x)\|_{L^{\infty}(\Omega)}. \end{cases} \tag{3.43}$$

This system admits a unique strong solution defined by

$$V_1(t,x) = \tilde{S}(t)(S_0(x) - \|S_0(x)\|_{L^{\infty}(\Omega)}) + \int_0^t \tilde{S}(t-s)(f_1(s, z(s,x)) - M)ds.$$

Since $S_0(x) - \|S_0(x)\|_{L^{\infty}(\Omega)} \leq 0$ and $f_1(s, z(s,x)) - M \leq 0$, we have $V_1(t,x) \leq 0, \forall (t,x) \in Q$. Similarly, we can prove that the function $V_2(t,x) = S(t,x) + Mt + \|S_0(x)\|_{L^{\infty}(\Omega)}$ is nonnegative. Then,

$$|S(t,x)| \leq Mt + \|S_0(x)\|_{L^{\infty}(\Omega)}, \ \forall (t,x) \in Q,$$

which implies that

$$S(t,x) \in L^{\infty}(Q). \tag{3.44}$$

We can employ similar methods to prove that $I_1(t,x) \in L^{\infty}(Q)$, $I_2(t,x) \in L^{\infty}(Q)$, and $A(t,x) \in L^{\infty}(Q)$.

(ii) We further show that $S(t,x) \in L^{\infty}(0,T; H^1(\Omega))$, $I_1(t,x) \in L^{\infty}(0,T; H^1(\Omega))$, $I_2(t,x) \in L^{\infty}(0,T; H^1(\Omega))$, and $A(t,x) \in L^{\infty}(0,T; H^1(\Omega))$. From the first equation of (3.1), we obtain

$$\int_0^t \int_{\Omega} \left|\frac{\partial S}{\partial t} - d_1 \Delta S\right|^2 dsdx = \int_0^t \int_{\Omega} |Q_0 - \beta_m S - \mu S|^2 dsdx,$$

and then

$$\begin{aligned}&\int_0^t\int_\Omega\left|\frac{\partial S}{\partial t}\right|^2 dsdx - 2d_1\int_0^t\int_\Omega\frac{\partial S}{\partial t}\Delta S dsdx + d_1^2\int_0^t\int_\Omega|\Delta S|^2\,dsdx\\&=\int_0^t\int_\Omega|Q_0-\beta_m S-\mu S|^2\,dsdx.\end{aligned}\tag{3.45}$$

On the other hand, Green's formula enables us to obtain

$$-2d_1\int_0^t\int_\Omega\frac{\partial S}{dt}\Delta S dsdx = d_1\int_\Omega|\nabla S|^2\,dx - d_1\int_\Omega|\nabla S_0(x)|^2\,dx.\tag{3.46}$$

Substituting (3.46) into (3.45), we obtain

$$\begin{aligned}&\int_0^t\int_\Omega\left|\frac{\partial S}{\partial t}\right|^2 dsdx + d_1\int_\Omega|\nabla S|^2 + d_1^2\int_0^t\int_\Omega|\Delta S|^2\,dsdx\\&=d_1\int_\Omega|\nabla S_0(x)|^2\,dx+\int_0^t\int_\Omega|Q_0-\beta_m S-\mu S|^2\,dsdx.\end{aligned}$$

Since $S, I_1, I_2, A \in L^\infty(Q)$ are bounded and $S_0(x) \in H^2(\Omega)$, we deduce that

$$S \in L^\infty\left(0,T;H^1(\Omega)\right).\tag{3.47}$$

We use (3.41), (3.44), and (3.47) to obtain $S \in L^2(0,T;H^2(\Omega)) \cap L^\infty(Q) \cap L^\infty(0,T;H^1(\Omega))$. We conclude that inequality (3.37) holds. We may obtain the same results for I_1, I_2, and A.

(iii) Now, we show the nonnegativeness of I_1. We set $I_1 = I_1^+ - I_1^-$ with

$$I_1^+(t,x) = \sup\{0, I_1(t,x)\},$$

$$I_1^-(t,x) = -\inf\{0, I_1(t,x)\}.$$

We multiply $\dfrac{\partial I_1}{\partial t} = d_2\Delta I_1 + \beta_m S - (u_2\theta+\mu+\delta)I_1$ by I_1^- and integrate over Ω to obtain

$$\begin{aligned}&-\frac{1}{2}\frac{d}{\mathrm{d}t}\left(\int_\Omega\left(I_1^-\right)^2(t,x)\mathrm{d}x\right)\\&=\int_\Omega\left|d_2\nabla I_1^-(t,x)\right|^2\,\mathrm{d}x+\int_\Omega\left[(u_2\theta+\mu+\delta)\left(I_1^-\right)^2\right](t,x)\mathrm{d}x\\&\quad-\int_\Omega\left[\beta_m S\left(I_1^-\right)^2\right](t,x)\mathrm{d}x.\end{aligned}$$

Then, we have

$$-\frac{1}{2}\frac{d}{\mathrm{d}t}\left(\int_{\Omega}\left(I_1^-\right)^2(t,x)\mathrm{d}x\right)\geq-\int_{\Omega}\left[\beta_m S\left(I_1^-\right)^2\right](t,x)\mathrm{d}x.$$

Hence,

$$\frac{1}{2}\frac{d}{\mathrm{d}t}\left(\int_{\Omega}\left(I_1^-\right)^2(t,x)\mathrm{d}x\right)\leq\|\beta_m S\|_{L^\infty(Q)}\int_{\Omega}\left[\left(I_1^-\right)^2\right](t,x)\mathrm{d}x.$$

By integrating again on $[0,t]$ with $t<T$ and using the Gronwall inequality, we obtain

$$\int_{\Omega}\left(I_1^-\right)^2(t,x)\mathrm{d}x\leq e^{2t\|\beta_m S\|_{L^\infty(Q)}}\int_{\Omega}\left(I_1^-\right)^2(0,x)\mathrm{d}x.$$

Then, $I_1^-=0$, and we deduce that $I_1(t,x)\geq 0,\forall(t,x)\in Q$. In addition, the system

$$\begin{cases}\dfrac{\partial S}{\partial t}=d_1\Delta S+Q_0-\beta_m S-\mu S, & (t,x)\in Q,\\ \dfrac{\partial I_2}{\partial t}=d_3\Delta I_2+u_2\theta I_1-(\delta+\mu+u_3\pi)\,I_2, & (t,x)\in Q,\\ \dfrac{\partial A}{\partial t}=d_4\Delta A+\delta I_1+\delta I_2+u_3\pi I_2-(\alpha+\mu)\,A, & (t,x)\in Q,\end{cases}\tag{3.48}$$

can be written in the form

$$\begin{cases}\dfrac{\partial S}{\partial t}=d_1\Delta S+\phi_1(S,I_2,A), & (t,x)\in Q,\\ \dfrac{\partial I_2}{\partial t}=d_3\Delta I_2+\phi_2(S,I_2,A), & (t,x)\in Q,\\ \dfrac{\partial A}{\partial t}=d_4\Delta A+\phi_3(S,I_2,A), & (t,x)\in Q.\end{cases}\tag{3.49}$$

It is easy to see that the functions $\phi_1(S,I_2,A)$,$\phi_2(S,I_2,A)$, and $\phi_3(S,I_2,A)$ are continuously differentiable, satisfying $\phi_1(0,I_2,A)=Q_0\geq 0$,and $\phi_2(S,0,A)=u_2\theta I_1\geq 0$, $\phi_3(S,I_2,0)=\delta I_1+\delta I_2+u_3\pi I_2\geq 0$, for all S,I_2, and $A\geq 0$. Since the initial data of system (3.48) are nonnegative, we deduce the positivity of S,I_2, and A (see Lemma 8) and thus we conclude that $S(t,x)\geq 0,I_1(t,x)\geq 0,I_2(t,x)\geq 0$ and $A(t,x)\geq 0,\forall(t,x)\in Q$. This completes the proof. ■

3.4.2 Existence of the optimal solution

The existence of an optimal solution is established in the following theorem.

Theorem 27 *Under the hypotheses of Theorem 26, the optimal control problem (3.23)-(3.28) admits an optimal solution* $(S^*,I_1^*,I_2^*,A^*,(u_1^*,u_2^*,u_3^*))$.

Proof. Since u_1, u_2, u_3, S, I_1, I_2, and A are bounded uniformly in $L^\infty(Q)$ and $\mathscr{J}(S, I_1, I_2, A, u_1, u_2, u_3)$ is bounded from below, there exists a minimizing sequence $\{u_1^n, u_2^n, u_3^n\}_{n\geq 1} \subset \mathscr{U}$ such that

$$\lim_{n\longrightarrow\infty} \mathscr{J}(S^n, I_1^n, I_2^n, A^n, (u_1^n, u_2^n, u_3^n)) = \inf_{(u_1,u_2,u_3)\in\mathscr{U}} \mathscr{J}(S, I_1, I_2, A, (u_1, u_2, u_3)). \tag{3.50}$$

Here, (S^n, I_1^n, I_2^n, A^n) is the solution of the following system:

$$\begin{cases} \dfrac{\partial S^n}{\partial t} - d_1\Delta S^n = Q_0 - \beta_m^n S^n - \mu S^n, & (t,x)\in Q, \\ \dfrac{\partial I_1^n}{\partial t} - d_2\Delta I_1^n = \beta_m^n S^n - (u_2^n\theta + \mu + \delta) I_1^n, & (t,x)\in Q, \\ \dfrac{\partial I_2^n}{\partial t} - d_3\Delta I_2^n = u_2^n\theta I_1^n - (\delta + \mu + u_3^n\pi) I_2^n, & (t,x)\in Q, \\ \dfrac{\partial A^n}{\partial t} - d_4\Delta A^n = \delta I_1^n + \delta I_2^n + u_3^n\pi I_2^n - (\alpha+\mu) A^n, & (t,x)\in Q, \end{cases} \tag{3.51}$$

with homogeneous Neumann boundary conditions

$$\frac{\partial S^n(t,x)}{\partial \eta} = \frac{\partial I_1^n(t,x)}{\partial \eta} = \frac{\partial I_2^n(t,x)}{\partial \eta} = \frac{\partial A^n(t,x)}{\partial \eta} = 0, (t,x)\in[0,T]\times\partial\Omega, \tag{3.52}$$

and initial conditions

$$S^n(0,x) = S_0, I_1^n(0,x) = I_{01}, I_2^n(0,x) = I_{02}, A^n(0,x) = A_0, x\in\Omega. \tag{3.53}$$

It follows from Theorem 26 that $S^n, I_1^n, I_2^n, A^n \in W^{1,2}\left([0,T]; \left(L^2(\Omega)\right)^4\right)$, which implies that $S^n, I_1^n, I_2^n, A^n \in C([0,T]; L^2(\Omega))$. Furthermore, from (3.37)-(3.40), we deduce that S^n, I_1^n, I_2^n, and A^n are all uniformly bounded, that is, there exists a positive constant C independent of n such that

$$\left\|\frac{\partial S^n}{\partial t}\right\|_{L^2(Q)} + \|S^n\|_{L^2(0,T,H^2(\Omega))} + \|S^n\|_{L^\infty(Q)} + \|S^n\|_{H^1(\Omega)} \leq C, \tag{3.54}$$

$$\left\|\frac{\partial I_1^n}{\partial t}\right\|_{L^2(Q)} + \|I_1^n\|_{L^2(0,T,H^2(\Omega))} + \|I_1^n\|_{L^\infty(Q)} + \|I_1^n\|_{H^1(\Omega)} \leq C, \tag{3.55}$$

$$\left\|\frac{\partial I_2^n}{\partial t}\right\|_{L^2(Q)} + \|I_2^n\|_{L^2(0,T,H^2(\Omega))} + \|I_2^n\|_{L^\infty(Q)} + \|I_2^n\|_{H^1(\Omega)} \leq C, \tag{3.56}$$

$$\left\|\frac{\partial A^n}{\partial t}\right\|_{L^2(Q)} + \|A^n\|_{L^2(0,T,H^2(\Omega))} + \|A^n\|_{L^\infty(Q)} + \|A^n\|_{H^1(\Omega)} \leq C. \tag{3.57}$$

By virtue of (3.54)-(3.57), we can further obtain the equicontinuity of the family $\{(S^n(t), I_1^n(t), I_2^n(t), A^n(t))\}$. The fact that $H^1(\Omega)$ is compactly embedded into $L^2(\Omega)$ implies that $\{(S^n(t), I_1^n(t), I_2^n(t), A^n(t))\}_{n\geq 1}$ is relatively compact in $(L^2(\Omega))^4$ and $\|S^n\|_{L^2(\Omega)} \leq C, \|I_1^n\|_{L^2(\Omega)} \leq C, \|I_2^n\|_{L^2(\Omega)} \leq C$ and $\|A^n\|_{L^2(\Omega)} \leq C$, $\forall t \in [0;T]$. Then, by the Ascoli-Arzela theorem (see [11]), there exist $(S^*, I_1^*, I_2^*, A^*) \in (C([0,T]; L^2(\Omega))^4$ and a subsequence of $\{(S^n(t), I_1^n(t), I_2^n(t), A^n(t))\}_{n\geq 1}$, still denoted by itself, such that

$$\begin{cases} \lim\limits_{n\longmapsto\infty} \sup_{t\in[0,T]} \|S^n(t) - S^*(t)\|_{L^2(\Omega)} = 0, \\ \lim\limits_{n\longmapsto\infty} \sup_{t\in[0,T]} \|I_1^n(t) - I_1^*(t)\|_{L^2(\Omega)} = 0, \\ \lim\limits_{n\longmapsto\infty} \sup_{t\in[0,T]} \|I_2^n(t) - I_2^*(t)\|_{L^2(\Omega)} = 0, \\ \lim\limits_{n\longmapsto\infty} \sup_{t\in[0,T]} \|A^n(t) - A^*(t)\|_{L^2(\Omega)} = 0. \end{cases} \tag{3.58}$$

The boundedness of $\Delta S^n, \Delta I_1^n, \Delta I_2^n$, and ΔA^n in $L^2(Q)$ implies it is weakly convergent in $L^2(Q)$ on a subsequence. Then, for all distributions φ,

$$\begin{cases} \int\limits_Q \varphi \Delta S^n = \int\limits_Q S^n \Delta\varphi \longmapsto \int\limits_Q S^* \Delta\varphi = \int\limits_Q \varphi \Delta S^*, \\ \int\limits_Q \varphi \Delta I_1^n = \int\limits_Q I_1^n \Delta\varphi \longmapsto \int\limits_Q I_1^* \Delta\varphi = \int\limits_Q \varphi \Delta I_1^*, \\ \int\limits_Q \varphi \Delta I_2^n = \int\limits_Q I_2^n \Delta\varphi \longmapsto \int\limits_Q I_2^* \Delta\varphi = \int\limits_Q \varphi \Delta I_2^*, \\ \int\limits_Q \varphi \Delta A^n = \int\limits_Q A^n \Delta\varphi \longmapsto \int\limits_Q A^* \Delta\varphi = \int\limits_Q \varphi \Delta A^*. \end{cases} \tag{3.59}$$

This implies that

$$\begin{cases} \Delta S^n \longmapsto \Delta S^* \text{ weakly in } L^2(Q), \\ \Delta I_1^n \longmapsto \Delta I_1^* \text{ weakly in } L^2(Q), \\ \Delta I_2^n \longmapsto \Delta I_2^* \text{ weakly in } L^2(Q), \\ \Delta A^n \longmapsto \Delta A^* \text{ weakly in } L^2(Q). \end{cases} \tag{3.60}$$

From (3.54)-(3.57), we obtain

$$\begin{cases} \dfrac{\partial S^n}{\partial t} \longmapsto \dfrac{\partial S^*}{\partial t} \text{weakly in } L^2(Q), \\ \dfrac{\partial I_1^n}{\partial t} \longmapsto \dfrac{\partial I_1^*}{\partial t} \text{weakly in } L^2(Q), \\ \dfrac{\partial I_2^n}{\partial t} \longmapsto \dfrac{\partial I_2^*}{\partial t} \text{weakly in } L^2(Q), \\ \dfrac{\partial A^n}{\partial t} \longmapsto \dfrac{\partial A^*}{\partial t} \text{weakly in } L^2(Q). \end{cases} \tag{3.61}$$

$$\begin{cases} S^n \longmapsto S^* \text{ weakly in } L^2\left(0,T,H^2(\Omega)\right), \\ I_1^n \longmapsto I_1^* \text{ weakly in } L^2\left(0,T,H^2(\Omega)\right), \\ I_2^n \longmapsto I_2^* \text{ weakly in } L^2\left(0,T,H^2(\Omega)\right), \\ A^n \longmapsto A^* \text{ weakly in } L^2\left(0,T,H^2(\Omega)\right). \end{cases} \tag{3.62}$$

$$\begin{cases} S^n \longmapsto S^* \text{ weakly star in } L^\infty\left(0,T,H^1(\Omega)\right), \\ I_1^n \longmapsto I_1^* \text{ weakly star in } L^\infty\left(0,T,H^1(\Omega)\right), \\ I_2^n \longmapsto I_2^* \text{ weakly star in } L^\infty\left(0,T,H^1(\Omega)\right), \\ A^n \longmapsto A^* \text{ weakly star in } L^\infty\left(0,T,H^1(\Omega)\right). \end{cases} \tag{3.63}$$

We now show that

$$\begin{cases} I_1^n S^n \longmapsto I_1^* S^* \text{ strongly in } L^2(Q), \\ I_2^n S^n \longmapsto I_2^* S^* \text{ strongly in } L^2(Q), \\ A^n S^n \longmapsto A^* S^* \text{ strongly in } L^2(Q). \end{cases} \tag{3.64}$$

Noting that

$I_1^n S^n - I_1^* S^* = S^n\left(I_1^n - I_1^*\right) + I_1^*\left(S^n - S^*\right), I_2^n S^n - I_2^* S^* = S^n\left(I_2^n - I_2^*\right) + I_2^*\left(S^n - S^*\right),$ *and* $A^n S^n - A^* S^* = S^n\left(A^n - A^*\right) + A^*\left(S^n - S^*\right)$, we make use of the convergences $S^n \longmapsto S^*$strongly in $L^2(Q)$, $I_1^n \longmapsto I_1^*$ strongly in $L^2(Q)$,$I_2^n \longmapsto I_2^*$ strongly in $L^2(Q)$, and $A^n \longmapsto A^*$ strongly in $L^2(Q)$.

Furthermore, S^n, I_1^n, I_2^n, and A^n are all uniformly bounded in $L^\infty(Q)$. We obtain (3.64). Moreover, since u_1^n, u_2^n, and u_3^n are all bounded in $L^2(Q)$, there exist functions u_1^*, u_2^*,u_3^* and a subsequence of $\{u_1^n, n \geq 1\}$, $\{u_2^n, n \geq 1\}$, and $\{u_3^n, n \geq 1\}$, still denoted by themselves, such that

$$\begin{cases} u_1^n \longmapsto u_1^* \text{ weakly in } L^2(Q), \\ u_2^n \longmapsto u_2^* \text{ weakly in } L^2(Q), \\ u_3^n \longmapsto u_3^* \text{ weakly in } L^2(Q). \end{cases} \tag{3.65}$$

Meanwhile, since $\mathscr{U}$ is a convex closed set in $L^2(Q)$, it is weakly closed. Hence, (3.65) implies that $u^* = (u_1^*, u_2^*, u_3^*) \in \mathscr{U}$. We can further show that

$$\begin{cases} u_2^n I_1^n \longmapsto u_2^* I_1^* \text{ weakly in } L^2(Q), \\ u_3^n I_2^n \longmapsto u_3^* I_2^* \text{ weakly in } L^2(Q). \end{cases} \tag{3.66}$$

We write

$$u_2^n I_1^n - u_2^* I_1^* = u_2^n \left(I_1^n - I_1^*\right) + I_1^* \left(u_2^n - u_2^*\right),$$

$$u_3^n I_2^n - u_3^* I_2^* = u_3^n \left(I_2^n - I_2^*\right) + I_2^* \left(u_3^n - u_3^*\right).$$

The term I_1^n strongly converges to I_1^* in $L^2(Q)$, I_2^n strongly converges to I_2^* in $L^2(Q)$, u_2^n weakly converges to u_2^* in $L^2(Q)$, and u_3^n weakly converges to u_3^* in $L^2(Q)$. We obtain (3.66). Similarly, we can show that $\beta_m^n S^n \longmapsto \beta_m^* S^*$weakly in $L^2(Q)$.

Now, sending $n \longmapsto +\infty$ in (3.51)-(3.53), we find that (S^*, I_1^*, I_2^*, A^*) are a solution of (3.23)-(3.25) corresponding to $(u_1^*, u_2^*, u_3^*) \in \mathscr{U}$. Therefore,

$$\begin{aligned}
\mathscr{J}\left(S^*, I_1^*, I_2^*, A^*, (u_1^*, u_2^*, u_3^*)\right) &= \int_Q \left[K_1 S^* + K_2 I_1^* + K_3 I_2^* + K_4 A^*\right] dtdx \\
&+ M_1 \left\|u_1^*\right\|_{L^2(Q)}^2 + M_2 \left\|u_2^*\right\|_{L^2(Q)}^2 + M_3 \left\|u_3^*\right\|_{L^2(Q)}^2 \\
&\leq \liminf_{n \longrightarrow \infty} \int_Q \left[K_1 S^n + K_2 I_1^n + K_3 I_2^n + K_4 A^n\right] dtdx \\
&+ M_1 \left\|u_1^n\right\|_{L^2(Q)}^2 + M_2 \left\|u_2^n\right\|_{L^2(Q)}^2 + M_3 \left\|u_3^n\right\|_{L^2(Q)}^2 \\
&= \lim_{n \longrightarrow \infty} \int_Q \left[K_1 S^n + K_2 I_1^n + K_3 I_2^n + K_4 A^n\right] dxdt \\
&+ M_1 \left\|u_1^n\right\|_{L^2(Q)}^2 + M_2 \left\|u_2^n\right\|_{L^2(Q)}^2 + M_3 \left\|u_3^n\right\|_{L^2(Q)}^2 \\
&= \inf_{(u_1,u_2,u_3) \in \mathscr{U}} \mathscr{J}\left(S, I_1, I_2, A, (u_1, u_2, u_3)\right).
\end{aligned}$$

This shows that $\mathscr{J}$ attains its minimum at $(S^*, I_1^*, I_2^*, A^*, (u_1^*, u_2^*, u_3^*))$. We deduce that $(S^*, I_1^*, I_2^*, A^*, (u_1^*, u_2^*, u_3^*))$ verifies problem (3.23)-(3.25) and minimizes the objective functional (3.27). The proof is complete. ■

3.4.3 Derivation of optimal control

We aim to identify an optimal control $u^* = (u_1^*, u_2^*, u_3^*) \in \mathscr{U}$ that satisfies condition (3.28)where $\mathscr{U}$ is the set of admissible controls defined in (3.26). This optimization problem is subject to the state system (3.23)-(3.25), with state functions in $L^2\left((0,T), H^1(\Omega)\right)$ and corresponding

time derivatives in $L^2((0,T), H^1(\Omega)^*)$. To determine u^* we must solve an optimality system that includes the state PDEs, adjoint PDEs, and the optimal control characterization. Additionally, we require the sensitivity system, which involves differentiating the control-to-state map $u \to (S, I_1, I_2, A)(u)$. By utilizing this system and the objective functional, we derive the adjoint system. Subsequently, we employ the sensitivity and adjoint systems to simplify the derivative of the map $u \to \mathscr{J}(u)$, ultimately achieving the desired optimal control characterization. These derivatives are calculated as directional derivatives. Below, we provide a an overview of the derivation of the sensitivity and adjoint equations, and the control characterization.

Sensitivity system

Given a control $u = (u_1, u_2, u_3) \in \mathscr{U}$, consider another control $u + \varepsilon k$ in $\mathscr{U}$ for $\varepsilon > 0$ with $k = (k_1, k_2, k_3) \in L^2(Q)$, represents a perturbation. Using the control-to-state map, we define $(S^\varepsilon, I_1^\varepsilon, I_2^\varepsilon, A^\varepsilon) = (S, I_1, I_2, A)(u + \varepsilon k)$. We then define the sensitivity functions, which are Gateaux derivatives of the control-to-state map:

$$\frac{S^\varepsilon - S}{\varepsilon} \to \psi_1, \frac{I_1^\varepsilon - I_1}{\varepsilon} \longrightarrow \psi_2, \frac{I_2^\varepsilon - I_2}{\varepsilon} \to \psi_3, \frac{A^\varepsilon - A}{\varepsilon} \longrightarrow \psi_4, \text{as } \epsilon \to 0.$$

We also have:

$$S^\varepsilon \to S, I_1^\varepsilon \to I_1, I_2^\varepsilon \to I_2 \text{ and } A^\varepsilon \to A.$$

The sensitivity functions $\psi = (\psi_1, \psi_2, \psi_3, \psi_4)$ satisfy a that corresponds to the linearized form of the state equations. See works by Li and Yong[33], Lions [34] and De Silva et al.[47] provide validation for the convergence of these quotients and the existence of the sensitivity functions and their corresponding PDEs. These equations are utilized to derive PDEs for the adjoint $\lambda = (\lambda_1, \lambda_2, \lambda_3, \lambda_4)$ where each adjoint variable is associated with a state variable.

We now derive equations for the sensitivity functions by forming their coefficients and then passing the limit. In order to do so we utilize system (3.23)-(3.25) to write equations for $(S^\epsilon, I_1^\epsilon, I_2^\epsilon, A^\epsilon)$and then form equations for the sensitivity coefficients. The sensitivity system

is :

$$\begin{cases} (\psi_1)_t - d_1\Delta\psi_1 = -(\beta_m+\mu)\,\psi_1 - \dfrac{S\beta_1 c_1\,(1-u_1)}{N}\psi_2 - \dfrac{S\beta_2 c_2\,(1-u_1)}{N}\psi_3 \\ \\ -\dfrac{S\beta_3 c_3\,(1-u_1)}{N}\psi_4 + \dfrac{Sk_1}{N}\left(\beta_1 c_1 I_1 + \beta_2 c_2 I_2 + \beta_3 c_3 A\right), \\ \\ (\psi_2)_t - d_2\Delta\psi_2 = \beta_m\psi_1 + \left(\dfrac{S\beta_1 c_1\,(1-u_1)}{N} - (\delta+\mu+\theta u_{_2})\right)\psi_2 + \dfrac{S\beta_2 c_2\,(1-u_1)}{N}\psi_3 \\ \\ +\dfrac{S\beta_3 c_3\,(1-u_1)}{N}\psi_4 - \dfrac{Sk_1}{N}\left(\beta_1 c_1 I_1 + \beta_2 c_2 I_2 + \beta_3 c_3 A\right) - \theta I_1 k_2, \\ \\ (\psi_3)_t - d_3\Delta\psi_3 = \theta u_2\psi_2 - (\delta+\mu+\pi u_3)\psi_3 - \pi I_2 k_3 + \theta I_1 k_2, \\ \\ (\psi_4)_t - d_4\Delta\psi_4 = \delta\psi_2 + (\delta+\pi u_3)\,\psi_3 - \pi I_2 k_3 - (\alpha+\mu)\psi_4, \end{cases} \tag{3.67}$$

with initial and homogeneous Neumann boundary conditions

$$\begin{aligned} &\psi_1(0,x) = \psi_2(0,x) = \psi_3(0,x) = \psi_4(0,x) = 0, \text{ for } x \in \Omega \\ &\frac{\partial\psi_1}{\partial\eta} = \frac{\partial\psi_2}{\partial\eta} = \frac{\partial\psi_3}{\partial\eta} = \frac{\partial\psi_4}{\partial\eta} = 0, \text{on } [0,T]\times\partial\Omega. \end{aligned} \tag{3.68}$$

We can now write the sensitivity system in vector form as follows:

$$\mathcal{L}\begin{pmatrix}\psi_1\\ \psi_2\\ \psi_3\\ \psi_4\end{pmatrix} = \begin{pmatrix} \dfrac{Sk_1}{N}\left(\beta_1 c_1 I_1 + \beta_2 c_2 I + \beta_3 c_3 A\right) \\ -\dfrac{Sk_1}{N}\left(\beta_1 c_1 I_1 + \beta_2 c_2 I_2 + \beta_3 c_3 A\right) - \theta I_1 k_2 \\ -\pi I_2 k_3 + \theta I_1 k_2 \\ -\pi I_2 k_3 \end{pmatrix}, \tag{3.69}$$

where

$$\mathcal{L}\begin{pmatrix}\psi_1\\ \psi_2\\ \psi_3\\ \psi_4\end{pmatrix} = \begin{pmatrix}(\psi_1)_t - d_1\Delta\psi_1\\ (\psi_2)_t - d_2\Delta\psi_2\\ (\psi_3)_t - d_3\Delta\psi_3\\ (\psi_4)_t - d_4\Delta\psi_4\end{pmatrix} + M\begin{pmatrix}\psi_1\\ \psi_2\\ \psi_3\\ \psi_4\end{pmatrix}.$$

The term M denotes the matrix given by

$$M = \begin{pmatrix} (\beta_m+\mu) & \frac{S\beta_1 c_1 (1-u_1)}{N} & \frac{S\beta_2 c_2 (1-u_1)}{N} & \frac{S\beta_3 c_3 (1-u_1)}{N} \\ -\beta_m & -\frac{S\beta_1 c_1 (1-u_1)}{N} + (\delta+\mu+\theta u_2) & -\frac{S\beta_2 c_2 (1-u_1)}{N} & -\frac{S\beta_3 c_3 (1-u_1)}{N} \\ 0 & -\theta u_2 & (\delta+\mu+\pi u_3) & 0 \\ 0 & -\delta & -(\delta+\pi u_3) & \alpha+\mu \end{pmatrix}.$$

Adjoint system

The adjoint variables $\lambda = (\lambda_1, \lambda_2, \lambda_3, \lambda_4)$ where each adjoint variable is associated with a state variable (S, I_1, I_2, A). The adjoint operator $\mathcal{L}^*$ is obtained from the relation:

$$\langle \lambda, \mathcal{L}\psi \rangle = \langle \mathcal{L}^*\lambda, \psi \rangle \tag{3.70}$$

in the appropriate weak $L^2(Q)$ sense and $\langle ., . \rangle$ is the $L^2(Q)$ inner product. The right-hand side of the adjoint system is determined by taking derivatives of the objective functional's integrand with respect to the states.

$$\begin{aligned} \frac{\partial}{\partial S}(K_1 S + K_2 I_1 + K_3 I_2 + K_4 A + M_1 u_1^2 + M_2 u_2^2 + M_3 u_3^2) &= K_1, \\ \frac{\partial}{\partial I_1}(K_1 S + K_2 I_1 + K_3 I_2 + K_4 A + M_1 u_1^2 + M_2 u_2^2 + M_3 u_3^2) &= K_2, \\ \frac{\partial}{\partial I_2}(K_1 S + K_2 I_1 + K_3 I_2 + K_4 A + M_1 u_1^2 + M_2 u_2^2 + M_3 u_3^2) &= K_3, \\ \frac{\partial}{\partial A}(K_1 S + K_2 I_1 + K_3 I_2 + K_4 A + M_1 u_1^2 + M_2 u_2^2 + M_3 u_3^2) &= K_4. \end{aligned}$$

Expression (3.70) is employed to derive the operators in the adjoint system. This involves applying integration by parts to $\langle \lambda, \mathcal{L}\psi \rangle$and the boundary conditions of the sensitivity equations. The adjoint system obtained this way is:

$$\mathcal{L}^* \begin{pmatrix} \lambda_1 \\ \lambda_2 \\ \lambda_3 \\ \lambda_4 \end{pmatrix} = \begin{pmatrix} K_1 \\ K_2 \\ K_3 \\ K_4 \end{pmatrix}. \tag{3.71}$$

where

$$\mathcal{L}^* \begin{pmatrix} \lambda_1 \\ \lambda_2 \\ \lambda_3 \\ \lambda_4 \end{pmatrix} = \begin{pmatrix} -(\lambda_1)_t - d_1 \Delta(\lambda_1) \\ -(\lambda_2)_t - d_2 \Delta(\lambda_2) \\ -(\lambda_3)_t - d_3 \Delta(\lambda_3) \\ -(\lambda_4)_t - d_4 \Delta(\lambda_4) \end{pmatrix} + M^T \begin{pmatrix} \lambda_1 \\ \lambda_2 \\ \lambda_3 \\ \lambda_4 \end{pmatrix}. \tag{3.72}$$

In the integration by parts, the adjoints must be defined as zero at the final time $t = T$. Thus, the transversality (final time) conditions are given by:

$$\lambda_1(T,x) = \lambda_2(T,x) = \lambda_3(T,x) = \lambda_4(T,x) = 0, \text{in } \Omega, \tag{3.73}$$

and the boundary conditions by:

$$\frac{\partial \lambda_1}{\partial \eta} = \frac{\partial \lambda_2}{\partial \eta} = \frac{\partial \lambda_3}{\partial \eta} = \frac{\partial \lambda_4}{\partial \eta} = 0, \text{on } [0,T] \times \partial\Omega. \tag{3.74}$$

Optimal control characterization

We now derive an expression for the optimal control $u^* = (u_1^*, u_2^*, u_3^*)$ as a function of the state and adjoint variables.

Theorem 28 *Let u^* be an optimal control of (3.23)-(3.27) and let (S^*, I_1^*, I_2^*, A^*) be the optimal state, that is (S^*, I_1^*, I_2^*, A^*) is the solution to (3.23)-(3.27) with the control u^*. Then,*

$$\begin{aligned} u_1^* &= \min\left[1, \max\left(\frac{1}{2M_1}\left(\frac{S^*}{N^*}(\lambda_2 - \lambda_1)(\beta_1 c_1 I_1^* + \beta_2 c_2 I_2^* + \beta_3 c_3 A^*)\right), 0\right)\right], \\ u_2^* &= \min\left[1, \max\left(\frac{1}{2M_2}(\lambda_2 - \lambda_3)\theta I_1^*, 0\right)\right], \\ u_3^* &= \min\left[1, \max\left(\frac{1}{2M_3}(\lambda_4 + \lambda_3)\pi I_2^*, 0\right)\right]. \end{aligned} \tag{3.75}$$

Proof. The derivative of the map $u \to \mathscr{J}(u)$ at u^* in the direction k is :

$$\lim_{\varepsilon \to 0^+} \frac{\mathscr{J}(u^* + \varepsilon k) - \mathscr{J}(u^*)}{\varepsilon},$$

with

$$\begin{aligned} J(u^* + \varepsilon k) = \int_Q \big[& K_1 S^\varepsilon + K_2 I_1^\varepsilon + K_3 I_2^\varepsilon + K_4 A^\varepsilon + M_1 (u_1^* + \varepsilon k_1)^2 \\ & + M_2 (u_2^* + \varepsilon k_2)^2 + M_3 (u_3^* + \varepsilon k_3)^2 \big] \, dtdx, \end{aligned}$$

$$\mathscr{J}\left(u^*\right)=\int_Q\left[K_1S^*+K_2I_1^*+K_3I_2^*+K_4A^*+M_1\left(u_1^*\right)^2+M_2\left(u_2^*\right)^2+M_3\left(u_3^*\right)^2\right]dtdx.$$

The superscript * on the state variables indicates optimality, meaning the state solution at the optimal characterization. To determine the optimal control, we aim to find u^* such that :

$$\lim_{\varepsilon\to0^+}\frac{\mathscr{J}\left(u^*+\varepsilon k\right)-\mathscr{J}\left(u^*\right)}{\varepsilon}\geq0.$$

The positivity of the derivative is due to the fact that $\mathscr{J}(u^*)$ is minimum among all $\mathscr{J}(u)$, $u\in\mathscr{U}$. By utilizing the sensitivity and adjoint systems, we derive a characterization for u^* in the following way:

$$0\leq\lim_{\varepsilon\to0^+}\frac{\mathscr{J}\left(u^*+\varepsilon k\right)-\mathscr{J}\left(u^*\right)}{\varepsilon}.$$

Substituting‘ $\mathscr{J}\left(u^*+\epsilon k\right)$ and $\mathscr{J}\left(u^*\right)$, we obtain

$$0\leq\lim_{\varepsilon\to0^+}\int_Q\left[K_1\frac{S^\varepsilon-S^*}{\varepsilon}+K_2\frac{I_1^\varepsilon-I_1^*}{\varepsilon}+K_3\frac{I_2^\varepsilon-I_2^*}{\varepsilon}+K_4\frac{A^\varepsilon-A^*}{\varepsilon}\right.$$
$$\left.+2M_1k_1u_1^*+2M_2k_2u_2^*+2M_3k_3u_3^*+M_1\varepsilon k_1^2+M_2\varepsilon k_2^2+M_3\varepsilon k_3^2\right]dtdx.$$

Passing to the limit:

$$0\leq\int_Q\left[K_1\psi_1+K_2\psi_2+K_3\psi_3+K_4\psi_4+2M_1k_1u_1^*+2M_2k_2u_2^*+2M_3k_3u_3^*\right]dtdx.$$

Rearranging in matrix form:

$$0\leq\int_Q\left[\left(\psi_1,\psi_2,\psi_3,\psi_4\right)\left(K_1,K_2,K_3,K_4\right)^T+2M_1k_1u_1^*+2M_2k_2u_2^*+2M_3k_3u_3^*\right]dtdx.$$

Using the fact that $\left(K_1,K_2,K_3,K_4\right)^T$ is the right hand side of the adjoint operator:

$$0\leq\int_Q\left[\left(\psi_1,\psi_2,\psi_3,\psi_4\right)\mathcal{L}^*\left(\lambda_1,\lambda_2,\lambda_3,\lambda_4\right)^T+2M_1k_1u_1^*+2M_2k_2u_2^*+2M_3k_3u_3^*\right]dtdx.$$

Using the adjoint relation (3.70) in the appropriate weak sense:

$$0\leq\int_Q\left[\left(\lambda_1,\lambda_2,\lambda_3,\lambda_4\right)\mathcal{L}\left(\psi_1,\psi_2,\psi_3,\psi_4\right)^T+2M_1k_1u_1^*+2M_2k_2u_2^*+2M_3k_3u_3^*\right]dtdx.$$

Substituting the sensitivity operator by its right hand side:

$$0\leq\int_Q\left(\lambda_1,\lambda_2,\lambda_3,\lambda_4\right)\begin{pmatrix}\frac{S^*k_1}{N^*}\left(\beta_1c_1I_1^*+\beta_2c_2I_2^*+\beta_3c_3A^*\right)\\-\frac{S^*k_1}{N^*}\left(\beta_1c_1I_1^*+\beta_2c_2I_2^*+\beta_3c_3A^*\right)-\theta I_1^*k_2\\-\pi I_2^*k_3+\theta I_1^*k_2\\-\pi I_2^*k_3\end{pmatrix}dtdx$$
$$+\int_Q\left[2M_1k_1u_1^*+2M_2k_2u_2^*+2M_3k_1u_3^*\right]dtdx.$$

Rearranging:

$$0 \leq \int_Q \left[k_1 \left(\frac{S^*}{N^*} (\lambda_1 - \lambda_2) (\beta_1 c_1 I_1^* + \beta_2 c_2 I_2^* + \beta_3 c_3 A^*) + 2M_1 u_1^* \right) \right] dtdx$$
$$+ \int_Q \left[k_2 \left((-\lambda_2 \theta + \lambda_3 \theta) I_1^* + 2u_2^* M_2 \right) + k_3 \left(-(\lambda_4 + \lambda_3) \pi I_2^* + 2u_3^* M_3 \right) \right] dtdx.$$

This has to be true for all $k \in L^2(Q)$ on the interior of the control set. In particular, if $k \geqslant 0$, then the term in the brackets must also be nonnegative

$$\frac{S^*}{N^*} (\lambda_1 - \lambda_2) (\beta_1 c_1 I_1^* + \beta_2 c_2 I_2^* + \beta_3 c_3 A^*) + 2M_1 u_1^* \geqslant 0,$$
$$(-\lambda_2 \theta + \lambda_3 \theta) I_1^* + 2u_2^* M_2 \geqslant 0,$$
$$-(\lambda_4 + \lambda_3) \pi I_2^* + 2u_3^* M_3 \geqslant 0.$$

And if $k \leqslant 0$, then:

$$\frac{S^*}{N^*} (\lambda_1 - \lambda_2) (\beta_1 c_1 I_1^* + \beta_2 c_2 I_2^* + \beta_3 c_3 A^*) + 2M_1 u_1^* \leqslant 0,$$
$$(-\lambda_2 \theta + \lambda_3 \theta) I_1^* + 2u_2^* M_2 \leqslant 0,$$
$$-(\lambda_4 + \lambda_3) \pi I_2^* + 2u_3^* M_3 \leqslant 0.$$

So we must necessarily have:

$$\frac{S^*}{N^*} (\lambda_1 - \lambda_2) (\beta_1 c_1 I_1^* + \beta_2 c_2 I_2^* + \beta_3 c_3 A^*) + 2M_1 u_1^* = 0,$$
$$(-\lambda_2 \theta + \lambda_3 \theta) I_1^* + 2u_2^* M_2 = 0,$$
$$-(\lambda_4 + \lambda_3) \pi I_2^* + 2u_3^* M_3 = 0.$$

Which leads to:

$$\begin{aligned} u_1^* &= \frac{1}{2M_1} \left(\frac{S^*}{N^*} (\lambda_2 - \lambda_1) (\beta_1 c_1 I_1^* + \beta_2 c_2 I_2^* + \beta_3 c_3 A^*) \right), \\ u_2^* &= \frac{1}{2M_2} (\lambda_2 - \lambda_3) \theta I_1^*, \\ u_3^* &= \frac{1}{2M_3} (\lambda_4 + \lambda_3) \pi I_2^*. \end{aligned}$$

Due to the boundedness of the control we obtain the following optimal control characterization:

$$\begin{aligned} u_1^* &= \min \left[1, \max \left(\frac{1}{2M_1} \left(\frac{S^*}{N^*} (\lambda_2 - \lambda_1) (\beta_1 c_1 I_1^* + \beta_2 c_2 I_2^* + \beta_3 c_3 A^*) \right), 0 \right) \right], \\ u_2^* &= \min \left[1, \max \left(\frac{1}{2M_2} (\lambda_2 - \lambda_3) \theta I_1^*, 0 \right) \right], \\ u_3^* &= \min \left[1, \max \left(\frac{1}{2M_3} (\lambda_4 + \lambda_3) \pi I_2^*, 0 \right) \right]. \end{aligned} \tag{3.76}$$

■

3.5 Numerical simulations

In the numerical simulations, we discuss the global asymptotic stability of the system equilibria (3.1)-(3.3) using two sets of parameter values chosen from Table (3.1). We consider the following initial conditions

$$\begin{aligned} S(0,x) &= 200 + 8sin(x), \\ I_1(0,x) &= 40 + cos(x), \\ I_2(0,x) &= 45 + cos(x), \\ A(0,x) &= 10 + cos(x). \end{aligned} \tag{3.77}$$

Table 3.1: **Parameter values**

Parameter	Q_0	β_1	β_2	β_3	c_1	c_2	c_3	θ	π	δ	α	μ
First set of values	50	0.20	0.15	0.12	1	1	1	0.015	0.6	0.1	1	0.2
Reference	-	[41]	[50]	[41]	[41]	[41]	[48]	[50]	[41]	[50]	[50]	-
Second set of values	50	1.344	0.15	0.12	3	2	1	0.015	0.6	0.1	1	0.02
Reference	-	[50]	[50]	[41]	[48]	[48]	[48]	[50]	[41]	[50]	[50]	[50]

We take $d_1 = d_2 = d_3 = d_4 = 0.001, u_1 = 0.9, x \in [0, 50]$ and $t \in [0, 300]$. Firstly, for the first set of parameter values (i.e., the second row in Table (3.1)), we obtain $\mathscr{R}_0 = 0.0678 < 1$. In this case, system (3.1)-(3.3) has a unique disease-free equilibrium point $\mathscr{E}_0 = (250, 0, 0, 0)$. From figure (3.1), we can see that the solution of system (3.1)-(3.3) approaches the disease-free equilibrium as $t \to \infty$. This result is consistent with theorem (24).i.e. $\mathscr{E}_0$ is globally asymptotically stable.

Secondly, for the second set of parameter values (i.e., the fourth row in Table (3.1)), we find $\mathscr{R}_0 = 3.0013 > 1$. In this case, system (3.1)-(3.3) has a unique endemic equilibrium point $\mathscr{E}_1(193.4817, 341.7064, 7.1189, 38.3861)$. as illustrated in figure (3.2), we can see that the solution of system (3.1)-(3.3) converges to this endemic equilibrium as $t \to \infty$. This

observation aligns with our theoretical findings in theorem (25), indicating that $\mathscr{E}_1$ is globally asymptotically stable.

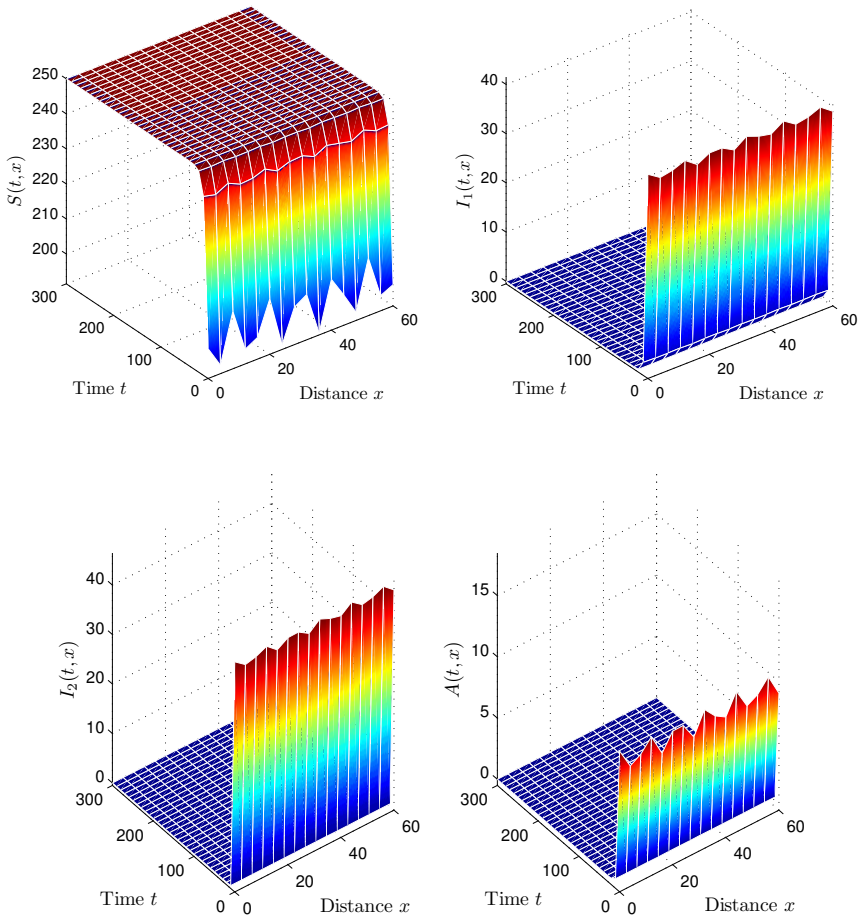


Figure 3.1: The equilibrium $\mathscr{E}_0$ is globally asymptotically stable

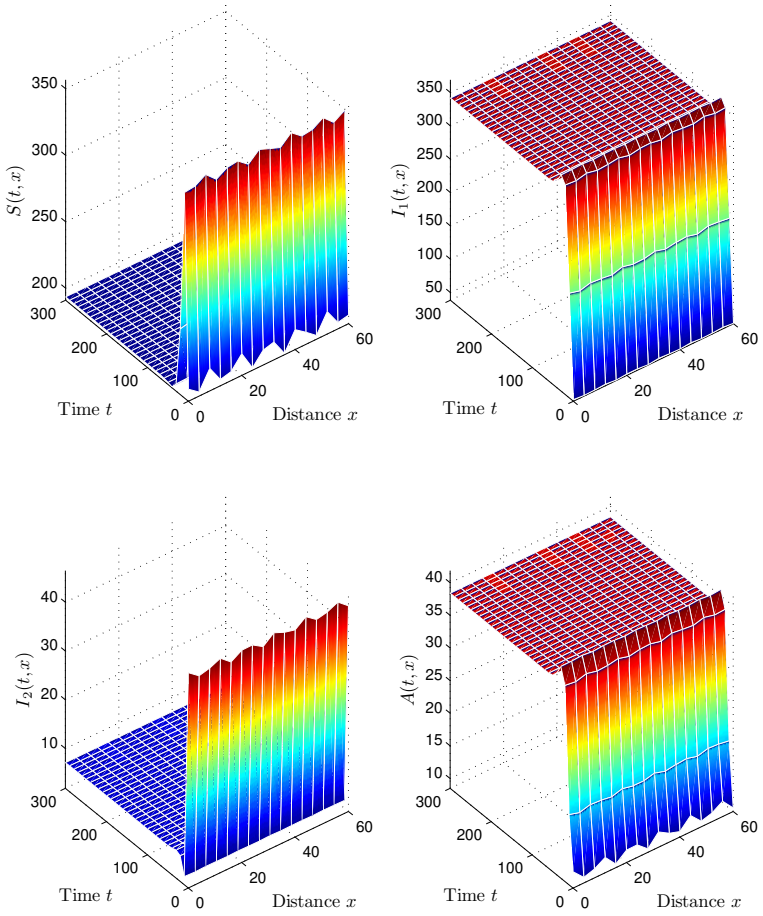


Figure 3.2: The equilibrium $\mathscr{E}_1$ is globally asymptotically stable

Conclusion

This thesis is devoted to studying the stability and optimal control problems for an HIV/AIDS epidemic model, both in the absence and presence of a diffusion terms. Rigorous mathematical results have been established for the model.

Our first contribution is to derive sufficient conditions for asymptotic stability of epidemic by means of the stability theory in ODE and PDE cases. It has been proven that the model always has one disease-free equilibrium point, denoted as $\mathscr{E}_0$, which is locally asymptotically stable when $\mathscr{R}_0 < 1$ and unstable when $\mathscr{R}_0 > 1$. Additionally, it has been shown that the model possesses an endemic equilibrium point $\mathscr{E}_1$, when $\mathscr{R}_0 > 1$, and this equilibrium is locally asymptotically stable. Through the application of Lyapunov functions and the theory of Volterra-Lyapunov stable matrices, the global asymptotic stability of the proposed model in both ODE and PDE cases has been discussed. It has been demonstrated that if $\mathscr{R}_0 < 1$, $\mathscr{E}_0$ is globally asymptotically stable, and if $\mathscr{R}_0 > 1$, $\mathscr{E}_1$ is globally asymptotically stable.

Our second contribution in this work, of this thesis applying optimal control theory to the proposed model in ODE and PDE cases, We proposed an optimal controller that incorporates three distinct measures to combat the spread of HIV/AIDS: the use of condoms, screening individuals who are unaware of their infection status, and providing treatment to those who are infected. The goal of the optimal controller is to minimize the size of both the susceptible and infected populations. In the ODE controlled model case, we demonstrated the existence of an optimal control, where Pontryagin's Maximum Principle is used to identify the optimal controls. As a result, the optimal strategies for the control inputs were determined. In the case of the PDE controlled model, using the theory of semigroups of operators, the existence

of a global positive strong solution is established. Furthermore, the existence of the optimal control problem was established using functional analysis methods. Thus, the necessary optimality conditions for the proposed scheme were derived.

Perspectives

In the future, we will tackle the interresting questions:

- Applying different control strategies, calculating the cost for each strategy, and selecting the optimal strategy for disease control at the lowest cost. Additionally, we will perform numerical simulations in the case of PDE.
- It would be interesting to apply optimal control strategies to a reaction-diffusion epidemic model with time fractional.

Bibliographie

[1] S. Abdelmalek and S. Bendoukha, Global asymptotic stability of a diffusive SVIR epidemic model with immigration of individuals, *Electronic Journal of Differential Equations*, (2016), 1-14.

[2] S. Abdelmalek, *Existence Globale des Solutions des Systemes de Reaction - Diffusion via des Methodes Fonctionnelle*, Thesis. January (2008).

[3] R. M. Anderson, G. F. Medley and R. M. May, preliminary study of the transmission dynamics of the human immunodeficiency virus (HIV), the causative agent of AIDS, *IMA J. Math. Appl. Med. Biol.*, **3** (1986), 229-263.

[4] S. Aniţa, V. Arnăutu and V. Capasso, *An introduction to optimal control problems in life sciences and economics: From mathematical models to numerical simulation with MATLAB.*, Springer Science, Business Media, 2011.

[5] Z. Bai, R. Peng and X. Zhao, A reaction-diffusion malaria model with seasonality and incubation period, *J. Math. Biol*, **77** (2018), 201–228.

[6] A. Berman and R. J. Plemmons, Nonnegative matrices in the mathematical sciences, *Society of Industrial and applied Mathematics*, Philadelphia, (1994).

[7] A. Babaei, H. Jafari and M. Ahmadi, A fractional order HIV/AIDS model based on the effect of screening of unaware infectives, Mathematical Methods in the Applied Sciences **42** (2019), 2334-2343.

[8] W. E. Boyce and R. C. Diprima, *Elementary Differential Equations and Boundary Value Problems*, John Wiley and Sons, New York, 2009.

[9] J. C. Butcher, On the convergence of numerical solutions to ordinary differential equations, *Mathematics of Computation*, **20** (1966), 1-10.

[10] J. C. Butcher. A multistep generalization of Runge-Kutta methods with four or five stages. *Journal of the ACM*, **14** (1967), 84-99.

[11] H. Brezis, P. G. Ciarlet and J. L. Lions, *Analyse Fonctionnelle: Théorie et Applications*, vol 91, Dunod, Paris, 1999.

[12] V. Barbu, *Mathematical methods in optimization of differential systems*, Mathematics and Its Applications , Springer, New York, 2012.

[13] N. Chorfi, S. Bendoukha and S. Abdelmalek, The optimal control of an HIV/AIDS reaction-diffusion epidemic model, *Discrete and Continuous Dynamical Systems-S*, (2024).

[14] N. Chorfi, S. Abdelmalek and S. Bendoukha, Stability analysis and optimal control of an HIV/AIDS epidemic model, preprint, 2023, 2304.08251.

[15] N. Chorfi, S. Bendoukha and S. Abdelmalek, An optimal control problem for a reaction-diffusion HIV/AIDS system, *IEEE International Conference on Recent Advances in Mathematics and Informatics(ICRAMI' 2021)*, September 21-22, 2021 at Tebessa, Algeria. https://ieeexplore.ieee.org/document/9585972

[16] N. Chorfi, S. Abdelmalek and S. Bendoukha, Stability analysis and an optimal control applied to the spread of HIV/AIDS model, *African Conference on Dynamical Systems and Ordinary Differential Equations (ACDSODE'21), March 20-23, 2021, Bejaia university, Algeria.* https://asdcod21.sciencesconf.org/

[17] N. Chorfi, S. Abdelmalek and S. Bendoukha, Stability analysis and an optimal control of fractional-Order modified HIV/AIDS model, *International on Pure and Applied*

Mathematical (IC-PAM'21), May 26-27, 2021, Ourgla, Algeria.
https://ic-pam.sciencesconf.org/

[18] N. Chorfi, S. Abdelmalek and S. Bendoukha, Stability analysis for reaction-diffusion HIV/AIDS system, *National Conference on Pure and Applied Mathematics (CNMPA'2021)*, April 15, 2021 at Tebessa university, Algeria. http://cnmpa2021.x10.bz

[19] C. Castillo-Chavez, Z. Feng and W. Huang, On the computation of R_0 and its role on global stability, in Mathematical Approaches for Emerging and Re-emerging Infectious Diseases: An Introduction, *IMA Volumes in Mathematics and Its Applications*, **125** (2002), 229–250.

[20] R. G. Casten and C. J. Holland, Stability properties of solutions to systems of reaction-diffusion equations, *SIAM J. Appl. Math*, **33** (1977), 353-364.

[21] J. Canada, J. L. Gamez, and J. A. Montero, A study of an optimal control problem for diffusive nonlinear elliptic equations of logistic type, *SIAM journal on control and optimization*, **36** (1998), 1171-1189.

[22] L. Djebara, Asymptotic stability of an epidemic reaction-diffusion model. 2021. PhD Thesis.

[23] P. Van den Driessche and J. Watmough, Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission, *Mathematical Biosciences*, **180** (2002), 29-48.

[24] P. Van den Driessche and Z. Shua, Global stability of infectious disease models using lyapunov functions, *SIAM Journal on Applied Mathematics*, **73** (2013), 1513–1532.

[25] F. Dai and B. Liu, Global solvability and optimal control to a haptotaxis cancer invasion model with two cancer cell species, *Applied Mathematics and Optimization*, **84** (2021), 2379-2443.

[26] W. H. Fleming and R. W. Rishel, *Deterministic and Stochastic Optimal Control*, Springer, New York, 1975.

[27] D. Henry, Geometric theory of semilinear parabolic equations, Lecture Notes in Mathematics 840, Springer-Verlag, Berlin-New York, (1981).

[28] W. M. Haddad, V. Chellaboina and Q. Hui, *Nonnegative and Compartmental Dynamical Systems*, Princeton University Press, Princeton, New Jersey, (2010).

[29] A. M. Kramer, M. Andrew and al., Spatial spread of the West Africa Ebola epidemic, *Royal Society Open Science*, **3** (2016), 160294.

[30] H. K. Khalil, *Nonlinear Systems*, Third Edition, Prentice Hall, (2002).

[31] Y. Lou and X.-Q. Zhao, A reaction–diffusion malaria model with incubation period in the vector population, *J. Math. Biol*, **62** (2011), 543-568.

[32] S. Lenhart and J. T. Workman, *Optimal Control Applied to Biological Models*, Chapman and Hall/CRC, 2007.

[33] X. Li and J. Yong, *Optimal control theory for infinite dimensional systems*, Springer Science, Business Media, 2012.

[34] J. L. Lions, *Optimal control of systems governed by partial differential equations*, Springer-Verlag, 1971.

[35] S. Lenhart, S. Stojanovic and V. Protopopescu, A minimax problem for semi linear non local competitive systems, *Applied Math and Optimization*, **28** (1993), 113-132.

[36] R. S. Laugesen, *Spectral Theory of Partial Differential Equations Lecture Notes*, University of Illinois at Urbana-Champaign, (2012).

[37] A. Leung and S. Stojanovic, Optimal control for elliptic volterra-lotka type equations, *Journal of mathematical analysis and applications*, **173** (1993), 603-619.

[38] A. M. Ljapunov, *Stability of motion, with a contribution by V. A. Pliss and an introduction by V. P. Basov. Translated from the Russian by Flavian Abramovici and Michael Shimshoni*, Mathematics in Science and Engineering, Vol. 30, Academic Press, New York, 1966.

[39] M. Martcheva, Introduction to mathematical epidemiology, Vol. 61, Springer, New York, (2015).

[40] M. McAsey, L. Mou and W. Han, Convergence of the forward-backward sweep method in optimal control, *Computational Optimization and Applications*, **53** (2012), 207-226.

[41] K. O. Okosun, O. D. Makinde and I. Takaidza, Impact of optimal control on the treatment of HIV/AIDS and screening of unaware infectives, *Applied Mathematical Modelling*, **37** (2013), 3802-3820.

[42] M. Pierre, Global existence in reaction-diffusion systems with control of mass: a survey, *Milan Journal of Mathematics*, **78** (2010), 417-455.

[43] A. Pazy, *Semi groups of Linear Operators and Applications to Partial Differential Equations*, Applied Mathematical Sciences, 44, Springer-Verlag, New York, 1983.

[44] A. S. S. Rao, Mathematical modelling of AIDS epidemic in India, *Current Science*, **84** (2003), 1192-1197.

[45] R. Redheffer, Volterra multipliers I, *SIAM Journal on Algebraic Discrete Methods*, **6** (1985), 592–611.

[46] R. Redheffer, Volterra multipliers II, *SIAM Journal on Algebraic Discrete Methods*, **6** (1985), 612–623.

[47] D. Silva, K. R. Phan, T. V. Phan and S. Lenhart, Advection control in parabolic PDE systems for competitive populations, *Discrete , Continuous Dynamical Systems-Series B* **22** (2017), 1049-1072.

[48] R. Safiel, E. S. Massawe and O. Makinde, Modelling the effect of screening and treatment on transmission of HIV/AIDS infection in a population, *American Journal of Mathematics and Statistics*, **2** (2012), 75-88.

[49] A. Shair, A. Ambrosetti, *A textbook on ordinary Differential Equations*, Springer Cham Heidelberg, University of texas atsan, (2014).

[50] A. Tripathi, R. Naresh and D. Sharma, Modeling the effect of screening of unaware infectives on the spread of HIV infection. Applied mathematics and computation, 2007, 184(2), 1053-1068.

[51] I. I. Vrabie, *Co-Semi groups and Applications*, Elsevier, 2003.

[52] X. Wang, Solving optimal control problems with MATLAB: Indirect methods. Technical report, ISE Dept, NCSU, 2009.

[53] S. Wiggins and M. Golubitsky, *Introduction to Applied Nonlinear Dynamical Systems and Chaos*, 2^{nd} edition, Springer, New York, 2003.

[54] H. Xiang and B. Liu, Solving the inverse problem of an SIS epidemic reaction–diffusion model by optimal control methods, *Computers and Mathematics with Applications*, **70** (2015), 805-819.

[55] M. S. Zahedi and N. S. Kargar, The Volterra–Lyapunov matrix theory for global stability analysis of a model of the HIV/AIDS, *International Journal of Biomathematics*, **10** (2017), 1750002.

[56] X. B. Zhang, G. Wang and H. Zhu, Optimal control of a diffusive eco-epidemiological predator prey model, *Int. J. Biomath* **13**(2020), 2050065: 1-22.

[57] M. Zhou, H. Xiang and Z. Li, Optimal control strategies for a reaction–diffusion epidemic system, *Nonlinear Analysis: Real World Applications*, **46** (2019), 446-464.