Age structured population dynamics with applications in epidemiology

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Preface

The work described in this thesis was carried out in the School of Mathematical and Statistical Sciences, North-West University, Mafikeng Campus, from February 2021 to June 2022 under the supervision of Doctor Rodrigue Yves M'pika Massoukou and the co-supervision of Professor Suares Clovis Oukouomi Noutchie.

This study represents the original work by the author and has not otherwise been submitted in any form for any degree or diploma to any tertiary institution. Where use has been made of the work of others, it is duly acknowledged in the text.

Abstract

Models describing the dynamics of biological phenomena that evolve in stages have been studied extensively using time-delay mathematical models. Recently, these models have evolved into age structured models with age dependent variables. Various mathematical tools have been employed to study these models and investigate the effects of age structure. This work explores two age structured models to address the issues of latent infection of cells by Human Immuno-deficiency Virus (HIV) and the effects of latent Tuberculosis (TB) infection on the dynamics of HIV. We consider models discussed on the transmission dynamics of HIV by multiple cell types through two transmission routes within-host and on the co-epidemic of HIV and TB. Latency of infected cells provides a major challenge to the elimination of HIV within-host since the virus persists at low levels within the latent population. Furthermore, the spread of viral particles through each transmission route may facilitate the progression of the disease due to continued infection of cells by infected cells or free viral particles. Investigating the dynamics of a HIV and TB co-epidemic provides insights into the effects of latency and the long term behavior of the synergistic relationship between HIV and TB. In this work, we extend the integer order systems of differential equations studied in [Xia, 2017] and [Xiaoyan, 2013] to fractional order. The within-host dynamics are described by a system of Caputo fractional derivatives while the co-epidemic by a system of Caputo-Fabrizio fractional derivatives. The equilibrium points of each system are obtained and the reproduction numbers of the diseases are computed. It is shown that the reproduction number of HIV through each transmission route contribute to the reproduction number of HIV through each cell type. Furthermore, the local asymptotic stability of the disease-free equilibrium is established.

Keywords: Age structure, Fractional differential equations, Laplace transform, Lipschitz continuity, Second mean value theorem, Reproduction number, Local asymptotic stability.

Declaration 1 - Plagiarism

I, Madito Gladstone Thabo declare that

1. The research reported in this dissertation, except where otherwise indicated, is my original research.
2. This dissertation has not been submitted for any degree or examination at any other university.
3. This dissertation does not contain other persons' data, images, graphs or other information, unless specifically acknowledged as being sourced from other persons.
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Declaration 2 - Publications

Papers in preparation:

1. A Caputo fractional model for an age structured dynamics of HIV infection within host through two transmission routes and target cell types
2. A Caputo-Fabrizio fractional model for an age structured population dynamics of an HIV-TB co-epidemic

Dedication

This work is dedicated to the Madito family.

Acknowledgements

I would like to thank my family for their support throughout the course of writing this dissertation. Thanks to my supervisor Dr. Rodrigue Yves M'pika Massoukou and co-supervisor Prof. Suares Clovis Oukouomi Noutchie for their inputs, discussions and guidance through the valley of dynamical systems. A special thanks to Dr. Richard Guiem for his efforts, suggestions and guidance from integers to fractions. I am grateful to the National Research Foundation for the generous scholarship to support my studies. I also want to thank the North-West University for the opportunity to study at the institution and financial support to complete my studies.

Contents

Chapter 1

Introduction

This chapter provides a brief review of the literature on the reproduction number, age structure, fractional derivatives and the evolution of models describing the dynamics of HIV. Furthermore, it outlines the necessary information about what will be covered in each chapter of the work.

Mathematical modeling of population dynamics involves systems of ordinary differential equations (ODEs), partial differential equations (PDEs) or a hybrid system which consists of ODEs and PDEs. These models often describe the population dynamics by grouping of individuals within the population into compartments based on their shared characteristics. When investigating biological phenomena like infectious disease epidemics, the movement of individuals from compartment to compartment occurs at different rates and depends on parameters such as the birth rates, death rates, transition rate and transmission rates between individuals susceptible to the disease and infectives capable of transmitting the disease. The evolution of a disease is described by systems of differential equations and analysis of these systems yields useful results such as the basic reproduction number. The basic reproduction number is the number of secondary infections as a result of a single infective during its entire period of infection. This can be utilized to study the progression of the diseases and discuss the stability of the equilibria of the system. Various factors such as the parameters of the model affect the reproduction number, thus impacting the progression of the disease. The next generation matrix technique is used to compute the basic reproduction number. This is possible only for system of ODEs. However, systems of PDEs and hybrid systems pose a different challenge in the computation of the basic reproduction number and alternative approaches are considered (see [Chunyang, 2020], [Massoukou, 2018], [Junyuan, 2018], [Xiaoyan, 2012]).

Other factors that can affect the reproduction number include the age or spatial structure of the population. When infectious diseases are transmitted but remain dormant or require some incubation period within an individual for some time before the individual becomes infectious, this individual falls in the age latency infection class. Models describing population dynamics with age latency are deemed to have age structure. This dissertation studies the effects of age structure on the dynamics of some infectious diseases within a population using fractional differential equations. Fractional differential equations yield better results than classical systems when modeling biological phenomena [Atangana, 2013], [Baleanu, 2020], [Sin, 2018], [Behzad, 2020]. There are various definitions and formulations of fractional derivatives which have been developed and studied, see [Kai, 2010], [Mahto, 2012] for a summary of fractional derivatives. Mathematical tools such as fractional derivatives have formed a critical part in the mathematical modeling of HIV, TB and other biological phenomena involving super-diffusion or sub-diffusion processes.

HIV infection within-host occurs in stages where the key stages are viral entry into the cell, replication and release of viral particles. Entry into susceptible cells occurs either through interaction with free viral particles or contact with infected cells which are ready for release of viral particles. Cells in the replication stage of the life cycle of HIV cannot transmit viral particles to other cells and hence do not actively contribute to the transmission of the disease within-host. These cells are grouped according to the stage of replication which determines the age latency of the cell. Furthermore, some of the cells do not become latent and are capable of transmitting the disease once infected. Since different cell types are capable of spreading HIV [Xia, 2017], [Yijun, 2017], the age latency plays a crucial role in the progression of the disease, hence the time since infection for each cell-type is different. A model describing the dynamics of HIV infection within-host through two transmission routes and a general model investigating the transmission of HIV within-host by multiple cell types and two transmission routes were proposed in [Junyuan, 2018], [Xia, 2017] and [Yijun, 2017], respectively. In [Baleanu, 2020], a fractional model of the within-host dynamics of HIV infection by a single cell type through two transmission routes is considered. In this work, we consider a Caputo fractional model for the within-host dynamics of age structured HIV infection by two cell types and transmission routes.

Epidemics of diseases often occur in completely susceptible populations. However, when diseases occur concurrently, we have a co-epidemic as the dynamics of one disease affect those of the other disease. HIV and TB are two such diseases where TB infection of HIV infectives affects the dynamics of HIV infection and HIV infection of TB infectives impacts on the dynamics of TB infection within a population. Since the TB spreads either through transmission of bacteria from active TB infectives to susceptible individuals or activation of latent TB bacteria in the fraction of individuals who have been infected with TB but cannot transmit it to others [Xiaoyan, 2012], [Zhang, 2015]. The complex dynamics of the HIV/TB co-epidemic have been simplified in the model proposed in [Xiaoyan, 2013], the defects of the simplified model are discussed and some results about the effects of each disease of the dynamics of the other are investigated. The critical assumptions of the model involves the treatment of HIV to recovery of HIV infectives but not for co-infectives. Furthermore, death due to disease occurs only in co-infectives since infected individuals undergo treatment and co-infected individuals do not. We extend the classical system considered in this model to a Caputo-Fabrizio fractional system.

This dissertation is composed of five (5) chapters. The first chapter presents the introduction related to mathematical modeling of population dynamics and the literature on HIV-TB. Chapter 2 provides a summary of useful results, definitions and theorems used throughout the text. Chapter 3 investigates the spread of HIV infection within host through two transmission routes and cell types with the incorporation of age structure, whereas Chapter 4 studies the co-epidemic of HIV and TB with age structure. The well-posedness of the models, including the boundedness of the solutions, positivity of solutions, existence and uniqueness of solutions, and stability analysis of the disease-free equilibrium are investigated in Chapter 3 and Chapter 4. Chapter 5 discusses some theoretical results derived in Chapter 3 and Chapter 4, and provides a thorough conclusion to the dissertation.

Chapter 2

Preliminaries

This chapter provides useful mathematical tools which are used throughout this work, including definitions (extracted from [Kai, 2010], unless otherwise stated) and some theorems.

Definition 2.1. *The function* $\Gamma : (0, \infty) \to \mathbb{R}$ *defined by*

$$\Gamma(\nu) := \int_0^\infty t^{\nu-1} e^{-t} dt,$$

is called Euler's Gamma function.

Definition 2.2. *The function* $B : (0, \infty) \times (0, \infty) \to \mathbb{R}$ *defined by*

$$B(x, y) := \int_0^1 t^{x-1}(1-t)^{y-1} dt = \frac{\Gamma(x)\Gamma(y)}{\Gamma(x+y)},$$

is called Euler's Beta function.

Definition 2.3 (Convolution)**.** *The convolution of functions* f *and* g *denoted by* $f * g$ *is given by*

$$(f * g)(t) = \int_0^t f(t-s)g(s)ds.$$

Theorem 2.4 (Second mean value theorem, [Hetmaniok, 2012]). *Consider continuous functions f and g, such that f is monotonic on $[a,b]$. Then there exists a point $c \in [a,b]$ such that*

$$\int\limits_a^b f(t)g(t)dt = \inf_{t\in[a,c]}\{f(t)\}\int\limits_a^c g(t)dt + \sup_{t\in[c,b]}\{f(t)\}\int\limits_c^b g(t)dt.$$

Definition 2.5 (Lipschitz continuity, [Baleanu, 2020]). *Let $(\mathbb{X}, ||\cdot||_{\mathbb{X}})$ be a normed space. A mapping $A : \mathbb{X} \to \mathbb{X}$ is Lipschitz continuous if and only if there exists a positive constant $M > 0$ such that A satisfies the Lipschitz condition,*

$$||Ax - Ay||_{\mathbb{X}} \leq M||x - y||_{\mathbb{X}},$$

for every $x, y \in \mathbb{X}$.

Definition 2.6. [*Kai, 2010*] *For $p \geq 1$, $\mathbb{L}_p[a,b]$ denotes the Lebesgue space defined as:*

$$\mathbb{L}_p[a,b] := \left\{ f : [a,b] \to \mathbb{R} \middle| f \quad \textit{is measurable on} \quad [a,b] \quad \textit{and} \quad \int\limits_a^b |f(t)|^p dt < \infty \right\}.$$

In particular, for $p = \infty$,

$$\mathbb{L}_\infty[a,b] := \left\{ f : [a,b] \to \mathbb{R} \middle| f \quad \textit{is measurable on} \quad [a,b] \quad \textit{and essentially bounded on} \quad [a,b] \right\}.$$

Furthermore, $\mathbb{L}_p^+$ denotes the positive cone of $\mathbb{L}_p[a,b]$ and is defined as:

$$\mathbb{L}_p^+[a,b] := \left\{ f : [a,b] \to \mathbb{R}_+ \middle| f \quad \textit{is measurable on} \quad [a,b] \quad \textit{and} \quad \int\limits_a^b |f(t)|^p dt < \infty \right\}.$$

Definition 2.7. [*Kai, 2010*] *For $p \geq 1$, the $\mathbb{L}_p$-norm denoted by $||\cdot||_p$, on $\mathbb{L}_p[a,b]$ is given by:*

$$||f||_p := \left(\int\limits_a^b |f(t)|^p dt \right)^{\frac{1}{p}}.$$

Definition 2.8. [*Kai, 2010*] *Let $\mathbb{X}$ be a normed space. Consider the space of functions $H^\nu[a,b]$ defined as*

$$H^\nu[a,b] = \{ f \in \mathbb{X} : ||f(x) - f(y)||_{\mathbb{X}} \leq ||x - y||_{\mathbb{X}}^\nu \quad \textit{for all} \quad x, y \in \mathbb{X} \}.$$

$H^\nu[a,b]$ is the called the Hölder space of order ν.

Definition 2.9. [Kai, 2010] *The operator* $I^{\nu} : \mathbb{L}_1[a,b] \to \mathbb{R}$ *defined by:*

$$I^{\nu} f(t) := \frac{1}{\Gamma(\nu)} \int\limits_a^b (t-x)^{\nu-1} f(x)dx, \quad \textit{where} \quad t \in [a,b], \nu \in \mathbb{R}_+,$$

is called the Riemann-Liouville fractional integral operator of order ν*.*

Definition 2.10. [Kai, 2010] *The operator* ${}^{C}D_t^{\nu}$ *defined by:*

$${}^{C}D_t^{\nu} f(t) := I^{m-\nu} \frac{d^m f(t)}{dt^m},$$

where $\nu > 0$*,* $m = \lceil \nu \rceil$ *and* $\frac{d^m f(t)}{dt^m} \in \mathbb{L}_1[a,b]$*, is called the Caputo differential operator of order* ν*.*

Definition 2.11. [Caputo, 2015], [Losada, 2015] *Let* $f \in H^1[0,h]$ *and* $\nu \in (0,1)$*, then the Caputo-Fabrizio fractional derivative of* f *is given as:*

$${}^{CF}D_t^{\nu} f(t) = \frac{2M(\nu)}{(2-\nu)(1-\nu)} \int\limits_0^t f'(s) \exp\left\{ -\frac{\nu}{1-\nu}(t-s) \right\} ds \quad \textit{for} \quad t \in [0,h],$$

where $M(\nu)$ *is the order dependent normalization function.*

Definition 2.12. [Schiff, 1999] *Consider a function* $f : [0,\infty) \to \mathbb{R}$ *and* $s > 0$*. The Laplace transform of* f *is defined by:*

$$F(s) := \mathcal{L}\{f(t)\} = \int\limits_0^{\infty} e^{-st} f(t)dt,$$

and the inverse Laplace transform $\mathcal{L}^{-1}$ *satisfies* $\mathcal{L}^{-1}\{F(s)\} = \mathcal{L}^{-1}\{\mathcal{L}\{f(t)\}\} = f(t)$*.*

Definition 2.13. *The Laplace transform of the Caputo fractional derivative is given by*

$$\mathcal{L}\{{}^{C}D_t^{\nu} f(t)\} = s^{\nu}\mathcal{L}\{f(t)\} - \sum_{k=1}^{m} s^{\nu-k} f^{(k-1)}(0),$$

where $m = \lceil \nu \rceil$*.*

Definition 2.14. [Losada, 2015] *The Laplace transform of the Caputo-Fabrizio fractional derivative is given by*

$$\mathcal{L}\{{}^{CF}D_t^{\nu} f(t)\} = \frac{B(\nu)}{\nu + (1-\nu)s} \Big(s\mathcal{L}\{f(t)\} - f(0) \Big),$$

where $B(\nu) = \frac{2-\nu}{2M(\nu)}$*.*

Definition 2.15. *The Laplace transform of the Mittag-Leffler function of order* ν*, defined by*

$$E_\nu(-\lambda t^\nu) = \sum_{j=0}^{\infty} \frac{(-\lambda t^\nu)^j}{\Gamma(j\nu + 1)},$$

is given by,

$$\mathcal{L}\{E_\nu(-\lambda t^\nu)\} = \frac{s^{\nu-1}}{s^\nu + \lambda}.$$

Theorem 2.16 (Stability of fractional linear systems)**.** *Consider an* N*-dimensional system of fractional differential equations* $D_t^\nu f(t) = Af(t)$*, where* A *is an arbitrary constant* $N \times N$ *matrix. The real solution* $f(t) = 0$ *of the system is asymptotically stable if and only if all distinct eigenvalues* λ_j *for* $j = 1, 2, \ldots, N$ *of the matrix* A *satisfy the condition* $|arg(\lambda_j)| > \frac{\nu\pi}{2}$.

Theorem 2.17. [*Kai, 2010*] *Let* $\nu \in (0, 1)$*. Moreover let* $\psi_0 \in \mathbb{X}$*,* $K > 0$ *and* $h^* > 0$*. Define*

$$G := \{\psi(t) \in \mathbb{X} : t \in [0, h^*], ||\psi(t) - \psi_0||_{\mathbb{X}} \leq K\},$$

and let the function $f : G \to \mathbb{X}$ *be continuous and fulfill a Lipschitz condition*

$$||f(\psi_1(t)) - f(\psi_2(t))||_{\mathbb{X}} \leq M||\psi_1(t) - \psi_2(t)||_{\mathbb{X}},$$

with some constant $M > 0$*. Furthermore, define*

$$L = \sup_{\psi \in \mathbb{X}} ||f(\psi(t))||_{\mathbb{X}} \quad \textit{and} \quad h := \begin{cases} h^* \quad \textit{if} \quad L = 0, \\ \min\left\{h^*, \left(\frac{K\Gamma(\nu+1)}{L}\right)^{\frac{1}{\nu}}\right\} \quad \textit{else}. \end{cases}$$

Then, there exists a uniquely defined function $\psi \in C[0, h]$ *solving the fractional initial value problem* $D_t^\nu \psi(t) = f(\psi(t))$ *with initial condition* $\psi(0) = \psi_0$*.*

Note 1. *See* [*Mahto, 2012*], [*Sin, 2018*] *for further discussions on the existence and uniqueness of solutions*

Chapter 3

Caputo fractional model for age structured dynamics of HIV latent infection through two transmission routes and cell types

This chapter focuses on a Caputo fractional model of HIV infection transmission by two cell types and transmission routes. We consider various aspects of the model which are investigated in four (4) sections. The first section discusses the formulation of the model and assumptions; whereas the second section explores the well-posedness of the model by investigating the positivity, boundedness, existence and uniqueness of solutions to the system of fractional differential equations. In the third section the existence of equilibria is proven and the basic reproduction number is derived. The last section explores the stability of the disease-free equilibrium using a linearization technique.

3.1 Introduction

It is widely known that HIV transmission within-host occurs by infection of CD4$^+$ T-cells, which are the largest white blood cells [Baleanu, 2020], [Yijun, 2017]. However, HIV can infect various types of cells within-host such as Macrophages and dendritic cells [Yijun, 2017]. Though HIV also infects these cells, transmission mainly occurs through CD4$^+$ cells and has the most destructive effect on these cells, causing the immune system to weaken and the body becomes susceptible to other infections (we consider the co-infection of HIV and TB in Chapter 4 of the work). Macrophages have been identified as responsible for HIV transmission in the later stages of viral infection [Yijun, 2017], hence we consider the transmission of HIV by CD4$^+$ T-cells and Macrophages in this chapter. Time delay models have been developed to study the impact of HIV infection by Macrophages and recently the incorporation of age structure in mathematical models has enabled better description of produced viral particles and of the infected or latently infected cell mortality [Hetmaniok, 2012], [Xiaoyan, 2012], [Zhang, 2015]. Not only can HIV be transmitted by multiple cell types in the body, transmission also occurs in various means, cell-to-cell transmission and cell-to-virus transmission. Cell-to-cell transmission occurs when infected cells interact with susceptible cells and viral particles are transferred from the infected cells, enabling the reproduction of HIV through multiple cells. Alternatively, infected cells can release viral particles into the blood stream, which then infect susceptible cells. The transmission of HIV either through cell-to-cell or cell-to-virus transmission routes is crucial in the development of medication for control of HIV infection. In [Yijun, 2017] a general model is developed for HIV transmission by multiple cells and two transmission routes to n cell types. We extend this model of first order system of hybrid differential equations to a fractional order system of differential equations. Fractional order systems have been shown to produce better results when modelling natural phenomena than classical or integer order systems [?], [Baleanu, 2020], [Changpin, 2007], [Kai, 2010], [Sin, 2018], [Behzad, 2020].

3.1.1 Model formulation

We investigate a model describing the dynamics of HIV infection through two transmission routes, namely cell-to-cell transmission and cell-to-free virus transmission [Elaiw, 2016], [Chunyang, 2020], [Elaiw, 2017], [Junyuan, 2018], [Xia, 2017], by different cell types [Rahmat, 2019], [Xia, 2017], [Yijun, 2017]. The population of free virions at time t is denoted by $V(t)$, whereas the total population of host cells is divided into 6 compartments. The population of target Type 1 cells which are susceptible to HIV infection is denoted by $T_1(t)$ and the susceptible population of Type 2 cells is denoted as $T_2(t)$. We denote the population of latently infected Type 1 cells of latency age a by $L_1(a,t)$ and the population of latently infected Type 2 cells of latency age b is denoted by $L_2(b,t)$ [Xia, 2017], [Xiaoyan, 2013], the last 2 compartments consist of the productively infected Type 1 and Type 2 cells, which are denoted by $I_1(t)$ and $I_2(t)$, respectively. The system written in terms of the Caputo fractional derivatives (see [Baleanu, 2020], [Changpin, 2007], [Rahmat, 2019], [Behzad, 2020] for other fractional models of HIV transmission) as the fractional initial value problem below:

$$ {}^{C}D_t^{\nu}T_1(t) = \Lambda_1 - \mu_1 T_1(t) - \beta_1 T_1(t)V(t) - \kappa_1 T_1(t)I_1(t), \tag{3.1}$$

$$ {}^{C}D_t^{\nu}T_2(t) = \Lambda_2 - \mu_2 T_2(t) - \beta_2 T_2(t)V(t) - \kappa_2 T_2(t)I_2(t), \tag{3.2}$$

$$ {}^{C}\partial_t^{\nu}L_1(a,t) + {}^{C}\partial_a^{\nu}L_1(a,t) = \rho_1(a)L_1(a,t) - (\alpha_1(a) + d_1(a))L_1(a,t), \tag{3.3}$$

$$ {}^{C}\partial_t^{\nu}L_2(b,t) + {}^{C}\partial_b^{\nu}L_2(b,t) = \rho_2(b)L_2(b,t) - (\alpha_2(b) + d_2(b))L_2(b,t), \tag{3.4}$$

$$ {}^{C}D_t^{\nu}I_1(t) = (1-f_1)(\beta_1 T_1(t)V(t) + \kappa_1 T_1(t)I_1(t)) + \int_0^{\infty} \alpha_1(a)L_1(a,t)da - \delta_1 I_1(t), \tag{3.5}$$

$$ {}^{C}D_t^{\nu}I_2(t) = (1-f_2)(\beta_2 T_2(t)V(t) + \kappa_2 T_2(t)I_2(t)) + \int_0^{\infty} \alpha_2(b)L_2(b,t)db - \delta_2 I_2(t), \tag{3.6}$$

$$ {}^{C}D_t^{\nu}V(t) = N_1\delta_1 I_1(t) + N_2\delta_2 I_2(t) - \mu_V V(t). \tag{3.7}$$

with the recruitment of cells into the populations of latently infected cells for all time given by

$$ L_i(0,t) = f_i(\beta_i T_i(t)V(t) + \kappa_i T_i(t)I_i(t)), \quad \text{with} \quad i = 1,2 $$

and initial conditions

$$T_1(0) \in \mathbb{R}_+, T_2(0) \in \mathbb{R}_+, L_1(a,0) \in \mathbb{L}_1^+(0,\infty), L_2(b,0) \in \mathbb{L}_1^+(0,\infty), I_1(0) \in \mathbb{R}_+,$$

$$I_2(0) \in \mathbb{R}_+ \quad \text{and} \quad V(0) \in \mathbb{R}_+.$$

For $l \in \{a, t\}$, the Caputo fractional derivative is given by

$${}^C D_l^{\nu} f(l) := I^{1-\nu} \frac{df(l)}{dl} = \frac{1}{\Gamma(\nu)} \int\limits_0^l (l-x)^{\nu-1} \frac{df(l)}{dl} dx,$$

and the partial Caputo fractional derivative is given by

$${}^C \partial_l^{\nu} f(l) = I^{1-\nu} \frac{\partial f(l)}{\partial l} = \frac{1}{\Gamma(\nu)} \int\limits_0^l (l-x)^{\nu-1} \frac{\partial f(l)}{\partial l} dx,$$

for all $\nu \in (0,1)$. The rates of change of the viral and host cell populations depend on the recruitment rates Λ_1 and Λ_2, death rates μ_1 and μ_2, transmission rates per contact with free virion β_1 and β_2, and the transmission rates per contact with productively infected cell κ_1 and κ_2 of target Type 1 and Type 2 cells, respectively. The age of latency dependent parameters $\rho_1(a)$ and $\rho_2(b)$, denote the proliferation rate of latently infected target Type 1 and Type 2 cells of age a and b, respectively [Junyuan, 2018]. Transition of latently infected cells to productive infection occurs at rates $\alpha_1(a)$ and $\alpha_2(b)$, and death of latently infected cells of different age occurs at the rates $d_1(a)$ and $d_2(b)$ for Type 1 and Type 2 cells, respectively. When infection occurs a fraction $f_1 \in (0,1)$ and $f_2 \in (0,1)$ of target Type 1 and Type 2 cells, respectively, become latently infected and a fraction of cell that become infected can produce virions without undergoing latency delay. Death of productively infected cells occurs at δ_1 and δ_2 for infected Type 1 and Type 2 cells, respectively. When some of the infected cells die, they burst and release virions into the plasma, so the total number of virions a cell produces during its entire life cycle is given by N_1 and N_2 productively infected Type 1 and Type 2 cells, respectively. Production of virions by productively infected cells contributes to the migration of viral particles into the free virion population, however clearence of free viral particles from the compartment occurs at the rate μ_V [Xia, 2017], [Yijun, 2017].

We provide below a list of assumptions for the model regarding the dynamics of the disease [Chunyang, 2020]:

(A1) The initial population of recruited latently infected Type 1 cells is given by

$$L_1(0,0) = f_1(\beta_1 T_1(0)V(0) + \kappa_1 T_1(0)I_1(0)).$$

(A2) The initial population of recruited latently infected Type 2 cells is given by

$$L_2(0,0) = f_2(\beta_2 T_2(0)V(0) + \kappa_2 T_2(0)I_2(0)).$$

(A3) The age of latency dependent parameters ρ_1, ρ_2, α_1, α_2, d_1, $d_2 \in \mathbb{L}_\infty^+(0,\infty)$.

(A4) The latently infected Type 1 and Type 2 cells populations remain relatively stable during treatment provided

$$\sup_{a\in(0,\infty)} \{\rho_1(a)\} \leq \inf_{a\in(0,\infty)} \{d_1(a)\},$$

and

$$\sup_{b\in(0,\infty)} \{\rho_2(b)\} \leq \inf_{b\in(0,\infty)} \{d_2(b)\},$$

which is due to the suppression of replication within infected cells by medication inhibiting viral replication during latency.

3.2 Well-posedness of the model

3.2.1 Boundedness of solutions

Let $\mathbb{X} = \mathbb{R}^2 \times (\mathbb{L}_1(0,\infty))^2 \times \mathbb{R}^3$ be a Banach space and let $\mathbb{X}_+ = \mathbb{R}_+^2 \times (\mathbb{L}_1^+(0,\infty))^2 \times \mathbb{R}_+^3$ be the positive cone of $\mathbb{X}$. Consider a continuous function $\phi : \mathbb{R}_+ \times \mathbb{X}_+ \to \mathbb{X}_+$, with initial condition

$$\psi(0) = (T_1(0), T_2(0), L_1(a,0), L_2(b,0), I_1(0), I_2(0), V(0))^T \in \mathbb{X}_+,$$

given as:

$$\phi(t, \psi(0)) = (T_1(t), T_2(t), L_1(a,t), L_2(b,t), I_1(t), I_2(t), V(t))^T = \psi(t).$$

The system, (3.1) - (3.7) can be re-written as

$$ {}^{C}D_t^{\nu}\psi(t) = f(\psi(t)), \tag{3.8}$$

with

$$ {}^{C}D_t^{\nu}\psi(t) = \begin{pmatrix} {}^{C}D_t^{\nu}T_1(t) \\ {}^{C}D_t^{\nu}T_2(t) \\ {}^{C}\partial_t^{\nu}L_1(a,t) \\ {}^{C}\partial_t^{\nu}L_2(b,t) \\ {}^{C}D_t^{\nu}I_1(t) \\ {}^{C}D_t^{\nu}I_2(t) \\ {}^{C}D_t^{\nu}V(t) \end{pmatrix},$$

and

$$ f(\psi(t)) := \begin{pmatrix} f_1(\psi(t)) \\ f_2(\psi(t)) \\ f_3(\psi(t)) \\ f_4(\psi(t)) \\ f_5(\psi(t)) \\ f_6(\psi(t)) \\ f_7(\psi(t)) \end{pmatrix}$$

$$ = \begin{pmatrix} \Lambda_1 - \mu_1 T_1(t) - (\beta_1 V(t) + \kappa_1 I_1(t))T_1(t) \\ \Lambda_2 - \mu_2 T_2(t) - (\beta_2 V(t) + \kappa_2 I_2(t))T_2(t) \\ (\rho_1(a) - \alpha_1(a) - d_1(a))L_1(a,t) - {}^{C}\partial_a^{\nu}L_1(a,t) \\ (\rho_2(b) - \alpha_2(b) - d_2(b))L_2(b,t) - {}^{C}\partial_b^{\nu}L_2(b,t) \\ (1-f_1)(\beta_1 V(t) + \kappa_1 I_1(t))T_1(t) + \int_0^{\infty}\alpha_1(a)L_1(a,t)da - \delta_1 I_1(t) \\ (1-f_2)(\beta_2 V(t) + \kappa_2 I_2(t))T_2(t) + \int_0^{\infty}\alpha_2(b)L_2(b,t)db - \delta_2 I_2(t) \\ N_1\delta_1 I_1(t) + N_2\delta_2 I_2(t) - \mu_V V(t) \end{pmatrix}.$$

Using the norm on $\mathbb{X}$, we have

$$||\phi(t,\psi(0))||_{\mathbb{X}} = ||\psi(t)||_{\mathbb{X}} = |T_1(t)| + |T_2(t)| + ||L_1(t)||_1 + ||L_2(t)||_1 + |I_1(t)| + |I_2(t)| + |V(t)|.$$

Consequently, we have

$$||\psi(t)||_{\mathbb{X}} = T_1(t) + T_2(t) + \int_0^\infty L_1(a,t)da + \int_0^\infty L_2(b,t)db + I_1(t) + I_2(t) + V(t).$$

Applying the Caputo fractional derivative of order $\nu \in (0,1)$, leads to

$$\begin{aligned} {}^C D_t^\nu ||\psi(t)||_{\mathbb{X}} = & {}^C D_t^\nu T_1(t) + {}^C D_t^\nu T_2(t) + \int_0^\infty {}^C\partial_t^\nu L_1(a,t)da + \int_0^\infty {}^C\partial_t^\nu L_2(b,t)db + {}^C D_t^\nu I_1(t) \\ & + {}^C D_t^\nu I_2(t) + {}^C D_t^\nu V(t). \end{aligned}$$

Making use of (3.1) - (3.7), we obtain

$$\begin{aligned} {}^C D_t^\nu ||\psi(t)||_{\mathbb{X}} = \quad & \Lambda_1 - \mu_1 T_1(t) - (\beta_1 V(t) + \kappa_1 I_1(t))T_1(t) + \Lambda_2 - \mu_2 T_2(t) \\ & - (\beta_2 V(t) + \kappa_2 I_2(t))T_2(t) - \int_0^\infty {}^C\partial_a^\nu L_1(a,t)da \\ & + \int_0^\infty (\rho_1(a) - \alpha_1(a) - d_1(a))L_1(a,t)da - \int_0^\infty {}^C\partial_b^\nu L_2(b,t)db \\ & + \int_0^\infty (\rho_2(b) - \alpha_2(b) - d_2(b))L_2(b,t)db + (1-f_1)(\beta_1 V(t) + \kappa_1 I_1(t))T_1(t) \\ & + \int_0^\infty \alpha_1(a)L_1(a,t)da - \delta_1 I_1(t) + (1-f_2)(\beta_2 V(t) + \kappa_2 I_2(t))T_2(t) \\ & + \int_0^\infty \alpha_2(b)L_2(b,t)db - \delta_2 I_2(t) + N_1\delta_1 I_1(t) + N_2\delta_2 I_2(t) - \mu_V V(t), \end{aligned}$$

and hence

$$\begin{aligned} {}^C D_t^\nu ||\psi(t)||_{\mathbb{X}} = & \Lambda_1 - \mu_1 T_1(t) + \Lambda_2 - \mu_2 T_2(t) - \int_0^\infty {}^C\partial_a^\nu L_1(a,t)da - \int_0^\infty {}^C\partial_b^\nu L_2(b,t)db \\ & + \int_0^\infty (\rho_1(a) - d_1(a))L_1(a,t)da + \int_0^\infty (\rho_2(b) - d_2(b))L_2(b,t)db \\ & - f_1(\beta_1 T_1(t)V(t) + \kappa_1 T_1(t)I_1(t)) - f_2(\beta_2 T_2(t)V(t) + \kappa_2 T_2(t)I_2(t)) \\ & - \delta_1 I_1(t) - \delta_2 I_2(t) + N_1\delta_1 I_1(t) + N_2\delta_2 I_2(t) - \mu_V V(t). \end{aligned}$$

Clearly,

$$\begin{aligned}{}^{C}D_t^{\nu}||\psi(t)||_{\mathbb{X}} \leq &\Lambda_1 - \mu_1 T_1(t) + \Lambda_2 - \mu_2 T_2(t) - \int\limits_0^{\infty} (d_1(a) - \rho_1(a)) L_1(a,t) da - \mu_V V(t) \\ &- \int\limits_0^{\infty} (d_2(b) - \rho_2(b)) L_2(b,t) db - (1-N_1)\delta_1 I_1(t) - (1-N_2)\delta_2 I_2(t),\end{aligned}$$

and thus

$$\begin{aligned}{}^{C}D_t^{\nu}||\psi(t)||_{\mathbb{X}} \leq &\Lambda_1 - \mu_1 T_1(t) + \Lambda_2 - \mu_2 T_2(t) - c_1 \int\limits_0^{\infty} L_1(a,t) da - c_2 \int\limits_0^{\infty} L_2(b,t) db \\ &- (1-N_1)\delta_1 I_1(t) - (1-N_2)\delta_2 I_2(t) - \mu_V V(t),\end{aligned}$$

where

$$c_1 = \inf_{a \in \mathbb{R}_+} \{d_1(a)\} - \sup_{a \in \mathbb{R}_+} \{\rho_1(a)\} \quad \text{and} \quad c_2 = \inf_{b \in \mathbb{R}_+} \{d_2(b)\} - \sup_{b \in \mathbb{R}_+} \{\rho_2(b)\}.$$

Therefore

$${}^{C}D_t^{\nu}||\psi(t)||_{X} \leq \Lambda_1 + \Lambda_2 - c_3 \Bigg(T_1(t) - T_2(t) - \int\limits_0^{\infty} L_1(a,t) da - \int\limits_0^{\infty} L_2(b,t) db - I_1(t) - I_2(t) - V(t) \Bigg),$$

with $c_3 = \min\{\mu_1, \mu_2, c_1, c_2, (1-N_1)\delta_1, (1-N_2)\delta_2, \mu_V\}$. Hence,

$${}^{C}D_t^{\nu}||\psi(t)||_{\mathbb{X}} \leq \Lambda_1 + \Lambda_2 - c_3 ||\psi(t)||_{\mathbb{X}}.$$

Applying the Laplace transform, we obtain

$$\mathcal{L}\{{}^{C}D_t^{\nu}||\psi(t)||_{\mathbb{X}}\} \leq \mathcal{L}\{\Lambda_1 + \Lambda_2\} - c_3 \mathcal{L}\{||\psi(t)||_{\mathbb{X}}\}.$$

It follows from the Laplace transform of the Caputo fractional derivative that

$$s^{\nu} \mathcal{L}\{||\psi(t)||_{\mathbb{X}}\} - s^{\nu-1} ||\psi(0)||_{\mathbb{X}} \leq \frac{\Lambda_1 + \Lambda_2}{s} - c_3 \mathcal{L}\{||\psi(t)||_{\mathbb{X}}\},$$

that is,

$$\mathcal{L}\{||\psi(t)||_{\mathbb{X}}\}(s^{\nu} + c_3) \leq s^{\nu-1} ||\psi(0)||_{\mathbb{X}} + \frac{\Lambda_1 + \Lambda_2}{s},$$

and then

$$\mathcal{L}\{||\psi(t)||_{\mathbb{X}}\} \leq \frac{s^{\nu-1}||\psi(0)||_{\mathbb{X}}}{s^{\nu}+c_3} + \frac{(\Lambda_1+\Lambda_2)s^{\nu-1}}{s^{\nu}(s^{\nu}+c_3)}.$$

Making use of the Laplace transform of the Mittag-Leffler function, it follows that

$$\begin{aligned}\mathcal{L}\{||\psi(t)||_{\mathbb{X}}\} &\leq ||\psi(0)||_{\mathbb{X}}\mathcal{L}\{E_{\nu}(-c_3t^{\nu})\} + (\Lambda_1+\Lambda_2)\mathcal{L}\left\{\frac{t^{\nu-1}}{\Gamma(\nu)}\right\}\mathcal{L}\{E_{\nu}(-c_3t^{\nu})\},\\ &= ||\psi(0)||_{\mathbb{X}}\mathcal{L}\{E_{\nu}(-c_3t^{\nu})\} + \frac{\Lambda_1+\Lambda_2}{\Gamma(\nu)}\mathcal{L}\{t^{\nu-1} * E_{\nu}(-c_3t^{\nu})\},\end{aligned}$$

where $t^{\nu-1} * E_{\nu}(-c_3t^{\nu})$ is the convolution of $t^{\nu-1}$ and $E_{\nu}(-c_3t^{\nu})$. Applying the inverse Laplace transform yields

$$||\psi(t)||_{\mathbb{X}} \leq ||\psi(0)||_{\mathbb{X}}E_{\nu}(-c_3t^{\nu}) + \frac{\Lambda_1+\Lambda_2}{\Gamma(\nu)}t^{\nu-1} * E_{\nu}(-c_3t^{\nu}),$$

where

$$\begin{aligned}t^{\nu-1} * E_{\nu}(-c_3t^{\nu}) &= \int_0^t (t-s)^{\nu-1}E_{\nu}(-c_3s^{\nu})ds,\\ &= \int_0^t (t-s)^{\nu-1}\sum_{j=0}^{\infty}\frac{(-c_3s^{\nu})^j}{\Gamma(j\nu+1)}ds,\\ &= \sum_{j=0}^{\infty}\frac{(-c_3)^j}{\Gamma(j\nu+1)}\int_0^t (t-s)^{\nu-1}s^{j\nu}ds.\end{aligned}$$

Let $s = tx$, then we have

$$\begin{aligned}t^{\nu-1} * E_{\nu}(-c_3t^{\nu}) &= \sum_{j=0}^{\infty}\frac{(-c_3)^j}{\Gamma(j\nu+1)}\int_0^1 t^{\nu-1}(1-x)^{\nu-1}(xt)^{j\nu}(tdx),\\ &= \sum_{j=0}^{\infty}\frac{(-c_3)^j}{\Gamma(j\nu+1)}\int_0^1 t^{j\nu+\nu}(1-x)^{\nu-1}x^{j\nu}dx,\\ &= \sum_{j=0}^{\infty}\frac{(-c_3)^j t^{j\nu+\nu}}{\Gamma(j\nu+1)}\int_0^1 (1-x)^{\nu-1}x^{j\nu}dx,\\ &= \sum_{j=0}^{\infty}\frac{(-c_3)^j t^{j\nu+\nu}}{\Gamma(j\nu+1)}\int_0^1 (1-x)^{\nu-1}x^{(j\nu+1)-1}dx.\end{aligned}$$

Using the definition of the Beta function,

$$B(p,q) := \int_0^1 (1-x)^{p-1}x^{q-1}dx = \frac{\Gamma(p)\Gamma(q)}{\Gamma(p+q)},$$

it follows that

$$\begin{aligned} t^{\nu-1} * E_\nu(-c_3t^\nu) &= \sum_{j=0}^{\infty} \frac{(-c_3)^j t^{j\nu+\nu}}{\Gamma(j\nu+1)} \frac{\Gamma(\nu)\Gamma(j\nu+1)}{\Gamma(j\nu+\nu+1)}, \\ &= \sum_{j=0}^{\infty} \frac{\Gamma(\nu)(-c_3)^j t^{j\nu+\nu}}{\Gamma(j\nu+\nu+1)}, \\ &= \sum_{k=1}^{\infty} \frac{\Gamma(\nu)(-c_3)^{k-1} t^{\nu k}}{\Gamma(k\nu+1)}, \\ &= \frac{\Gamma(\nu)}{-c_3} \sum_{k=1}^{\infty} \frac{(-c_3t^\nu)^k}{\Gamma(k\nu+1)}. \end{aligned}$$

Observe that

$$\begin{aligned} E_\nu(-c_3t^\nu) &= \sum_{j=0}^{\infty} \frac{(-c_3t^\nu)^j}{\Gamma(j\nu+1)}, \\ &= 1 + \sum_{j=1}^{\infty} \frac{(-c_3t^\nu)^j}{\Gamma(j\nu+1)}, \end{aligned}$$

and substituting this into the convolution yields

$$t^{\nu-1} * E_\nu(-c_3t^\nu) = \frac{\Gamma(\nu)}{c_3}(1 - E_\nu(-c_3t^\nu)).$$

Therefore,

$$\begin{aligned} ||\psi(t)||_{\mathbb{X}} &\leq ||\psi(0)||_{\mathbb{X}} E_\nu(-c_3t^\nu) + \frac{\Lambda_1+\Lambda_2}{c_3}(1 - E_\nu(-c_3t^\nu)), \\ &= \frac{\Lambda_1+\Lambda_2}{c_3} + \left(||\psi(0)||_{\mathbb{X}} - \frac{\Lambda_1+\Lambda_2}{c_3}\right) E_\nu(-c_3t^\nu), \end{aligned}$$

and taking the limit as $t \to \infty$ leads to

$$\lim_{t\to\infty} ||\psi(t)||_{\mathbb{X}} \leq \frac{\Lambda_1+\Lambda_2}{c_3},$$

since $\lim_{t\to\infty} E_\nu(-c_3t^\nu) = 0$ [Kai, 2010]. This concludes that the solution $\psi(t)$ is bounded.

Therefore, if we denote by G the state space of (3.8) then we have

$$G = \left\{ \psi(t) \in \mathbb{X}_+ : ||\psi(t)||_{\mathbb{X}} \leq \frac{\Lambda_1+\Lambda_2}{c_3} \right\}.$$

3.2.2 Positivity of solutions

Here the purpose is to establish the positivity of the solution of (3.8). Observe that the right-hand side of (3.8) can be decomposed as

$$f(\psi(t)) = \mathfrak{L}\psi(t) + \mathfrak{M}(\psi(t)),$$

where

$$\mathfrak{L} = \begin{pmatrix} -\mu_1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & -\mu_2 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -{}^{C}\partial_a^{\nu} + m_1(a) & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -{}^{C}\partial_b^{\nu} + m_2(b) & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\delta_1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -\delta_2 & 0 \\ 0 & 0 & 0 & 0 & N_1\delta_1 & N_2\delta_2 & -\mu_V \end{pmatrix},$$

and

$$\mathfrak{M}(\psi(t)) = \begin{pmatrix} \Lambda_1 - \beta_1 T_1(t)V(t) - \kappa_1 T_1(t)I_1(t), \\ \Lambda_2 - \beta_2 T_2(t)V(t) - \kappa_2 T_2(t)I_2(t), \\ 0 \\ 0 \\ (1-f_1)(\beta_1 T_1(t)V(t) + \kappa_1 T_1(t)I_1(t)) + \int_0^{\infty} \alpha_1(a)L_1(a,t)da \\ (1-f_2)(\beta_2 T_2(t)V(t) + \kappa_2 T_2(t)I_2(t)) + \int_0^{\infty} \alpha_2(b)L_2(b,t)db \\ 0 \end{pmatrix},$$

where $m_1(a) = \alpha_1(a) + d_1(a) - \rho_1(a)$ and $m_2(b) = \alpha_2(b) + d_2(b) - \rho_2(b)$. Clearly, it is sufficient to have $\mathfrak{L}\mathbb{X}_+ \subset \mathbb{X}_+$ and $\mathfrak{M}(\mathbb{X}_+) \subset \mathbb{X}_+$ to construct a positive solution. Since $\mathcal{L}$ is a Metzler matrix, it follows that $\mathcal{L}$ is a positive operator and hence $\mathfrak{L}\mathbb{X}_+ \subset \mathbb{X}_+$. To show that $\mathfrak{M}(\mathbb{X}_+) \subset \mathbb{X}_+$, we require $\Lambda_i - \beta_i T_i(t)V(t) - \kappa_i T_i(t)I_i(t) > 0$ for all $i = 1,2$. We have

$$\begin{aligned} \Lambda_i - (\beta_i V(t) + \kappa_i I_i(t))T_i(t) &> \Lambda_i - (\beta_i |V(t)| + \kappa_i |I_i(t)|)|T_i(t)| \\ &> \Lambda_i - (\beta_i ||\psi(t)||_{\mathbb{X}} + \kappa_i ||\psi(t)||_{\mathbb{X}})||\psi(t)||_{\mathbb{X}} \end{aligned}$$

$$
\begin{aligned}
&= \Lambda_i - (\beta_i + \kappa_i)||\psi(t)||^2_{\mathbb{X}} \\
&> \Lambda_i - (\beta_i + \kappa_i)\left(\frac{\Lambda_1 + \Lambda_2}{c_3}\right)^2,
\end{aligned}
$$

and hence $\Lambda_i - \beta_i T_i(t)V(t) - \kappa_i T_i(t)I_i(t) > 0$ for all $i = 1, 2$, provided that

$$\frac{\Lambda_i}{(\Lambda_1 + \Lambda_2)^2} > \frac{\beta_i + \kappa_i}{c_3^2}.$$

Therefore $\mathfrak{M}(\mathbb{X}_+) \subset \mathbb{X}_+$. It follows that the state space G is positively invariant provided

$$\frac{\Lambda_i}{(\Lambda_1 + \Lambda_2)^2} > \frac{\beta_i + \kappa_i}{c_3^2},$$

for all $i = 1, 2$, are satisfied.

3.2.3 Existence and uniqueness of solutions

Theorem 3.1. *The function f is Lipschitz continuous in $\mathbb{X}_+$.*

Proof. Let $\psi(t), \psi^*(t) \in \mathbb{X}_+$. Since $f_1(\mathbb{X}_+) \subseteq \mathbb{R}_+$, it follows from (3.8) that

$$
\begin{aligned}
|f_1(\psi(t)) - f_1(\psi^*(t))| =& |\Lambda_1 - \mu_1 T_1(t) - \beta_1 T_1(t)V(t) - \kappa_1 T_1(t)I_1(t) - (\Lambda_1 - \mu_1 T_1^*(t) - \\
& \beta_1 T_1^*(t)V^*(t) - \kappa_1 T_1^*(t)I_1^*(t))| \\
=& | - \mu_1(T_1(t) - T_1^*(t)) - \beta_1(T_1(t)V(t) - T_1^*(t)V^*(t)) \\
& - \kappa_1(T_1^*(t)I_1^*(t) - T_1^*(t)I_1^*(t))| \\
=& | - \mu_1(T_1(t) - T_1^*(t)) - \beta_1(T_1(t)V(t) - T_1(t)V^*(t) + T_1(t)V^*(t) - \\
& T_1^*(t)V^*(t)) - \kappa_1(T_1(t)I_1(t) - T_1(t)I_1^*(t) + T_1(t)I_1^*(t) \\
& - T_1^*(t)I_1^*(t))|,
\end{aligned}
$$

therefore it follows that

$$
\begin{aligned}
|f_1(\psi(t)) - f_1(\psi^*(t))| \leq& \mu_1|T_1(t) - T_1^*(t)| + \beta_1|T_1(t)||V(t) - V^*(t)| + \beta_1|T_1(t) \\
& - T_1^*(t)||V^*(t)| + \kappa_1|T_1(t)||I_1(t) - I_1^*(t)| \\
& + \kappa_1|T_1(t) - T_1^*(t)||I_1^*(t)|.
\end{aligned}
$$

Since $\psi(t)$ is bounded, there exist positive constants $C_{T_1}, C_{T_2}, C_{L_1}, C_{L_2}, C_{I_1}, C_{I_2}$ and C_V such that, $|T_1(t)| \leq C_{T_1}, |T_2(t)| \leq C_{T_2}, ||L_1(t)||_1 \leq C_{L_1}, ||L_2(t)||_1 \leq C_{L_2}, |I_1(t)| \leq C_{I_1}, |I_2(t)| \leq C_{I_2}$ and $|V(t)| \leq C_V$. It follows that,

$$\begin{aligned}|f_1(\psi(t)) - f_1(\psi^*(t))| \leq & \mu_1|T_1(t) - T_1^*(t)| + \beta_1 C_{T_1}|V_1(t) - V_1^*(t)| + \beta_1 C_V|T_1(t) - T_1^*(t)| \\ & + \kappa_1 C_{T_1}|I_1(t) - I_1^*(t)| + \kappa_1 C_{I_1}|T_1(t) - T_1^*(t)| \\ \leq & (\mu_1 + \beta_1 C_V + \kappa_1 C_{I_1})|T_1(t) - T_1^*(t)| + \beta_1 C_{T_1}|V_1(t) - V_1^*(t)| \\ & + \kappa_1 C_{T_1}|I_1(t) - I_1^*(t)| \\ \leq & M_{T_1}|T_1(t) - T_1^*(t)| + M_{T_1}|V_1(t) - V_1^*(t)| + M_{T_1}|I_1(t) - I_1^*(t)| \\ = & M_{T_1}(|T_1(t) - T_1^*(t)| + |V_1(t) - V_1^*(t)| + |I_1(t) - I_1^*(t)|) \\ \leq & M_{T_1}||\psi(t) - \psi^*(t)||_{\mathbb{X}},\end{aligned}$$

where

$$M_{T_1} = \max\{\mu_1 + \beta_1 C_V + \kappa_1 C_{I_1}, \beta_1 C_{T_1}, \kappa_1 C_{T_1}\};$$

therefore f_1 is Lipschitz continuous in $\mathbb{R}_+$. Similarly,

$$|f_2(\psi(t)) - f_2(\psi^*(t))| \leq M_{T_2}||\psi(t) - \psi^*(t)||_{\mathbb{X}},$$

where

$$M_{T_2} = \max\{\mu_2 + \beta_2 C_V + \kappa_1 C_{I_2}, \beta_2 C_{T_2}, \kappa_2 C_{T_2}\},$$

that is, f_2 is Lipschitz continuous in $\mathbb{R}_+$. Since $f_3(\mathbb{X}_+) \in \mathbb{L}_1(0, \infty)$, it follows that

$$\begin{aligned}||f_3(\psi(t)) - f_3(\psi^*(t))||_1 = & ||\rho_1 L_1(t) - (\alpha_1 + d_1)L_1(t) - {}^C\partial_a^\nu L_1(t) - (\rho_1 L_1^*(t) \\ & - (\alpha_1 + d_1)L_1^*(t) - {}^C\partial_a^\nu L_1^*(t))||_1 \\ = & ||(\rho_1 - \alpha_1 - d_1)(L_1(t) - L_1^*(t)) - {}^C\partial_a^\nu(L_1(t) - L_1^*(t))||_1 \\ = & || - (\alpha_1 + d_1 - \rho_1)(L_1(t) - L_1^*(t)) - {}^C\partial_a^\nu(L_1(t) - L_1^*(t))||_1 \\ = & ||(\alpha_1 + d_1 - \rho_1)(L_1(t) - L_1^*(t)) + {}^C\partial_a^\nu(L_1(t) - L_1^*(t))||_1 \\ \leq & ||(\alpha_1 + d_1 - \rho_1)(L_1(t) - L_1^*(t))||_1 + ||I^{1-\nu}\partial_a(L_1(t) - L_1^*(t))||_1 \\ = & ||m_1(L_1(t) - L_1^*(t))||_1 + ||I^{1-\nu}\partial_a(L_1(t) - L_1^*(t))||_1,\end{aligned}$$

since $m_1(a) = \alpha_1(a) + d_1(a) - \rho_1(a)$. It follows from $0 < m_1(a) \leq \sup\limits_{a\in[0,\infty)}\{m_1(a)\}$, that

$$\int\limits_0^\infty (m_1(a))|L_1(a,t) - L_1^*(a,t)|da \leq \sup_{a\in[0,\infty)}\{m_1(a)\}\int\limits_0^\infty |L_1(a,t) - L_1^*(a,t)|da,$$

and hence

$$||m_1(L_1(t) - L_1^*(t))||_1 \leq \sup_{a\in[0,\infty)}\{m_1(a)\}||L_1(t) - L_1^*(t)||_1.$$

This leads to

$$\begin{aligned}||f_3(t,\psi(t)) - f_3(t,\psi^*(t))||_1 \leq& \sup_{a\in[0,\infty)}\{m_1(a)\}||L_1(t) - L_1^*(t)||_1\\ &+\int_0^\infty |I^{1-\nu}\partial_s(L_1(s,t) - L_1^*(s,t))|da\\ \leq& \sup_{a\in[0,\infty)}\{m_1(a)\}||L_1(t) - L_1^*(t)||_1\\ &+\int_0^\infty \left|\frac{1}{\Gamma(1-\nu)}\int_0^a (a-s)^{-\nu}\partial_a(L_1(s,t) - L_1^*(s,t))ds\right|da.\end{aligned}$$

Observing that

$$\begin{aligned}\int_0^a (a-s)^{-\nu}\partial_s(L_1(s,t) - L_1^*(s,t))ds =&\left[-\frac{(a-s)^{-\nu+1}}{-\nu+1}\partial_s(L_1(s,t) - L_1^*(s,t))\right]_0^a\\ &+\int_0^a \frac{(a-s)^{-\nu+1}}{-\nu+1}\partial_s^2(L_1(s,t) - L_1^*(s,t))ds\end{aligned}$$

and applying the Theorem (2.4) to the integral term yields

$$\begin{aligned}\int_0^a \frac{(a-s)^{-\nu+1}}{-\nu+1}\partial_s^2(L_1(s,t) - L_1^*(s,t))ds =& \frac{(a-0)^{-\nu+1}}{-\nu+1}\int_0^c \partial_s^2(L_1(s,t) - L_1^*(s,t))ds\\ =& \frac{a^{-\nu+1}}{-\nu+1}\left[\partial_s(L_1(s,t) - L_1^*(s,t))\right]_0^c,\end{aligned}$$

where $c \in (0,a)$. Hence

$$\begin{aligned}\int_0^a (a-s)^{-\nu}\partial_s(L_1(s,t) - L_1^*(s,t))ds =&\left[-\frac{(a-s)^{-\nu+1}}{-\nu+1}\partial_s(L_1(s,t) - L_1^*(s,t))\right]_0^a\\ &+\left[\frac{a^{-\nu+1}}{-\nu+1}\partial_s(L_1(s,t) - L_1^*(s,t))\right]_0^c\\ =&\frac{a^{-\nu+1}}{-\nu+1}\partial_a(L_1(c,t) - L_1^*(c,t))\\ =&\frac{a^{-\nu+1}}{-\nu+1}\frac{L_1(a,t) - L_1^*(a,t) - (L_1(0,t) - L_1^*(0,t))}{a-0}\end{aligned}$$

$$= \frac{a^{-\nu}}{-\nu+1}[L_1(a,t) - L_1^*(a,t) - (L_1(0,t) - L_1^*(0,t))].$$

Therefore

$$||f_3(\psi(t)) - f_3(\psi^*(t))||_1 \leq \sup_{a\in[0,\infty)} \{m_1(a)\}||L_1(t) - L_1^*(t)||_1 + \int\limits_0^\infty \Bigg| \frac{a^{-\nu}}{(1-\nu)\Gamma(1-\nu)} \times [L_1(a,t) - L_1^*(a,t) - (L_1(0,t) - L_1^*(0,t))] \Bigg| da;$$

that is,

$$||f_3(\psi(t)) - f_3(\psi^*(t))||_1 \leq \sup_{a\in[0,\infty)} \{m_1(a)\}||L_1(t) - L_1^*(t)||_1 + \int\limits_0^\infty \frac{a^{-\nu}}{\Gamma(2-\nu)}|L_1(a,t) - L_1^*(a,t) - (L_1(0,t) - L_1^*(0,t))| da.$$

It follows from (3.3) that $L_1(a,t)$ is differentiable with respect to a. Therefore, $L_1(a,t)$ is continuous with respect to a. By continuity of $L_1(a,t) - L_1^*(a,t)$ at $a = 0$, for any arbitrary $\epsilon > 0$, there exists a $\delta > 0$ such that $|L_1(a,t) - L_1^*(a,t) - (L_1(0,t) - L_1^*(0,t))| < \epsilon$ whenever $a < \delta$, hence

$$\begin{aligned}
||f_3(\psi(t)) - f_3(\psi^*(t))||_1 &< \sup_{a\in[0,\infty)} \{m_1(a)\}||L_1(t) - L_1^*(t)||_1 + \lim_{w\to\infty} \int\limits_0^w \frac{a^{-\nu}}{\Gamma(2-\nu)} \epsilon da \\
&= \sup_{a\in[0,\infty)} \{m_1(a)\}||L_1(t) - L_1^*(t)||_1 + \lim_{w\to\infty} \frac{\epsilon}{\Gamma(2-\nu)} \int\limits_0^w a^{-\nu} da \\
&= \sup_{a\in[0,\infty)} \{m_1(a)\}||L_1(t) - L_1^*(t)||_1 + \lim_{w\to\infty} \frac{\epsilon}{\Gamma(2-\nu)} \left[\frac{a^{1-\nu}}{1-\nu}\right]\Bigg|_0^w \\
&= \sup_{a\in[0,\infty)} \{m_1(a)\}||L_1(t) - L_1^*(t)||_1 + \lim_{w\to\infty} \frac{\epsilon}{\Gamma(2-\nu)} \frac{w^{1-\nu}}{1-\nu}.
\end{aligned}$$

Choosing

$$\epsilon = \frac{C_{L_1}||L_1(t) - L_1^*(t)||_1}{w^{1-\nu}},$$

leads to,

$$\begin{aligned}
||f_3(\psi(t)) - f_3(\psi^*(t))||_1 &< \sup_{a\in[0,\infty)} \{m_1(a)\}||L_1(t) - L_1^*(t)||_1 + \lim_{w\to\infty} \frac{C_{L_1}||L_1(t) - L_1^*(t)||_1}{(1-\nu)\Gamma(2-\nu)} \\
&= \left[\sup_{a\in[0,\infty)} \{m_1(a)\} + \frac{C_{L_1}}{(1-\nu)\Gamma(2-\nu)}\right]||L_1(t) - L_1^*(t)||_1
\end{aligned}$$

$$< \left[\sup_{a\in[0,\infty)} \{m_1(a)\} + \frac{C_{L_1}}{(1-\nu)\Gamma(2-\nu)} \right] ||\psi(t) - \psi^*(t)||_{\mathbb{X}}$$
$$= M_{L_1}||\psi(t) - \psi^*(t)||_{\mathbb{X}},$$

where

$$M_{L_1} = \sup_{a\in[0,\infty)} \{m_1(a)\} + \frac{C_{L_1}}{\Gamma(\nu)},$$

and hence f_3 is Lipschitz continuous in $\mathbb{L}_1(0,\infty)$. In a similar way,

$$||f_4(\psi(t)) - f_4(\psi^*(t))||_1 < M_{L_2}||\psi(t) - \psi^*(t)||_{\mathbb{X}},$$

where $m_2(b) = \alpha_2(b) + d_2(b) - \rho_2(b)$ and

$$M_{L_2} = \sup_{b\in[0,\infty)} \{m_2(b)\} + \frac{C_{L_2}}{(1-\nu)\Gamma(2-\nu)},$$

hence f_4 is Lipschitz continuous in $\mathbb{L}_1(0,\infty)$. Since $f_5(\mathbb{X}_+) \subseteq \mathbb{R}_+$, it follows that

$$\begin{aligned}
|f_5(\psi(t)) - f_5(\psi^*(t))| =& \Bigg|(1-f_1)(\beta_1 T_1(t)V(t) + \kappa_1 T_1(t)I_1(t)) + \int_0^\infty \alpha_1(a)L_1(a,t)da - \\
& \delta_1 I_1(t) - ((1-f_1)(\beta_1 T_1(t)V(t) + \kappa_1 T_1(t)I_1(t)) \\
& + \int_0^\infty \alpha_1(a)L_1(a,t)da - \delta_1 I_1(t))\Bigg| \\
=& \Bigg|(1-f_1)[\beta_1(T_1(t)V(t) - T_1^*(t)V^*(t)) + \kappa_1(T_1(t)I_1(t) - T_1^*(t)I_1^*(t))] \\
& + \int_0^\infty \alpha_1(a)(L_1(a,t) - L_1^*(a,t))da - \delta_1(I_1(t) - I_1^*(t))\Bigg| \\
=& \Bigg|(1-f_1)[\beta_1(T_1(t)V(t) - T_1(t)V^*(t) + T_1(t)V^*(t) - T_1^*(t)V^*(t)) \\
& + \kappa_1(T_1(t)I_1(t) - T_1(t)I_1^*(t) + T_1(t)I_1^*(t) - T_1^*(t)I_1^*(t))] \\
& + \int_0^\infty \alpha_1(a)(L_1(a,t) - L_1^*(a,t))da - \delta_1(I_1(t) - I_1^*(t))\Bigg|. \\
=& \Bigg|(1-f_1)[\beta_1(T_1(t)(V(t) - V^*(t)) + (T_1(t) - T_1^*(t))V^*(t)) \\
& + \kappa_1(T_1(t)(I_1(t) - I_1^*(t)) + (T_1(t) - T_1^*(t))I_1^*(t))]
\end{aligned}$$

$$\begin{aligned}
&+\int_0^\infty \alpha_1(a)(L_1(a,t)-L_1^*(a,t))da-\delta_1(I_1(t)-I_1^*(t))\Big| \\
=&(1-f_1)[\beta_1|T_1(t)||V(t)-V^*(t)|+|T_1(t)-T_1^*(t)||V^*(t)|+\kappa_1|T_1(t)| \\
&\times|I_1(t)-I_1^*(t)|+|T_1(t)-T_1^*(t)||I_1^*(t)|] \\
&+\int_0^\infty \alpha_1(a)|L_1(a,t)-L_1^*(a,t)|da-\delta_1|I_1(t)-I_1^*(t)|
\end{aligned}$$

This leads to

$$|f_5(\psi(t))-f_5(\psi^*(t))|\leq(1-f_1)[\beta_1C_{T_1}|V(t)-V^*(t)|+C_V|T_1(t)-T_1^*(t)|+\kappa_1C_{T_1}|I_1(t)- I_1^*(t)|+C_{I_1}|T_1(t)-T_1^*(t)|]+\sup_{a\in[0,\infty)}\{\alpha_1(a)\}\int_0^\infty|L_1(a,t)-L_1^*(a,t)|da-\delta_1|I_1(t)-I_1^*(t)|;$$

that is,

$$\begin{aligned}
|f_5(\psi(t))-f_5(\psi^*(t))|\leq&(1-f_1)(\beta_1C_V+\kappa_1C_{I_1})|T_1(t)-T_1^*(t)|+(1-f_1)\beta_1C_{T_1}|V(t)- \\
&V^*(t)|+[(1-f_1)\kappa_1C_{T_1}-\delta_1]|I_1(t)-I_1^*(t)| \\
&+\sup_{a\in[0,\infty)}\{\alpha_1(a)\}||L_1(t)-L_1^*(t)||_1 \\
\leq&M_{I_1}(|T_1(t)-T_1^*(t)|+|V(t)-V^*(t)|+|I_1(t)-I_1^*(t)| \\
&+||L_1(t)-L_1^*(t)||_1) \\
\leq&M_{I_1}||\psi(t)-\psi^*(t)||_{\mathbb{X}},
\end{aligned}$$

where

$$M_{I_1}=\max\left\{(1-f_1)(\beta_1C_V+\kappa_1C_{I_1}),(1-f_1)\beta_1C_{T_1},(1-f_1)\kappa_1C_{T_1}-\delta_1,\sup_{a\in[0,\infty)}\{\alpha_1(a)\}\right\}.$$

Therefore f_5 is Lipschitz continuous in $\mathbb{R}_+$. Similarly,

$$|f_6(\psi(t))-f_6(\psi^*(t))|\leq M_{I_2}||\psi(t)-\psi^*(t)||_{\mathbb{X}},$$

where

$$M_{I_2}=\max\left\{(1-f_2)(\beta_2C_V+\kappa_2C_{I_2}),(1-f_2)\beta_2C_{T_2},(1-f_2)\kappa_2C_{T_2}-\delta_2,\sup_{b\in[0,\infty)}\{\alpha_2(b)\}\right\},$$

that is, f_6 is Lipschitz continuous in $\mathbb{R}_+$. Since $f_7(\mathbb{X}_+) \subseteq \mathbb{R}_+$, it follows that

$$\begin{aligned}|f_7(\psi(t)) - f_7(\psi^*(t))| =& |N_1\delta_1 I_1(t) + N_2\delta_2 I_2(t) - \mu_V V(t) - (N_1\delta_1 I_1(t) + N_2\delta_2 I_2(t) \\ & - \mu_V V(t))| \\ =& |N_1\delta_1(I_1(t) - I_1^*(t)) + N_2\delta_2(I_2(t) - I_2^*(t)) - \mu_V(V(t) - V^*(t))| \\ \leq& N_1\delta_1|I_1(t) - I_1^*(t)| + N_2\delta_2|I_2(t) - I_2^*(t)| + \mu_V|V(t) - V^*(t)|,\end{aligned}$$

with

$$M_V = \max\{N_1\delta_1, N_2\delta_2, \mu_V\},$$

then it follows that,

$$\begin{aligned}|f_7(\psi(t)) - f_7(\psi^*(t))| &\leq M_V(|I_1(t) - I_1^*(t)| + |I_2(t) - I_2^*(t)| + |V(t) - V^*(t)|) \\ &\leq M_V||\psi(t) - \psi^*(t)||_{\mathbb{X}},\end{aligned}$$

that is, f_7 is Lipschitz continuous in $\mathbb{R}_+$.
Therefore,

$$\begin{aligned}||f(\psi(t)) - f(\psi^*(t))||_{\mathbb{X}} =& |f_1(\psi(t)) - f_1(\psi^*(t))| + |f_2(\psi(t)) - f_2(\psi^*(t))| + ||f_3(\psi(t)) - \\ & f_3(\psi^*(t))||_1 + ||f_4(\psi(t)) - f_4(\psi^*(t))||_1 + |f_5(\psi(t)) - f_5(\psi^*(t))| + \\ & |f_6(\psi(t)) - f_6(\psi^*(t))| + |f_7(\psi(t)) - f_7(\psi^*(t))| \\ \leq& (M_{T_1} + M_{T_2} + M_{L_1} + M_{L_2} + M_{I_1} + M_{I_2} + M_V)||\psi(t) - \psi^*(t)||_{\mathbb{X}} \\ =& M||\psi(t) - \psi^*(t)||_{\mathbb{X}},\end{aligned}$$

with

$$M = M_{T_1} + M_{T_2} + M_{L_1} + M_{L_2} + M_{I_1} + M_{I_2} + M_V.$$

This completes the proof. □

Theorem 3.2. *Let*

$$L = \sup_{\psi \in \mathbb{X}} ||f(\psi(t))||_{\mathbb{X}}, h = \left(\frac{(\Lambda_1 + \Lambda_2)\Gamma(\nu + 1)}{c_3 L}\right)^{\frac{1}{\nu}},$$

and the set G defined by

$$G = \left\{\psi(t) \in \mathbb{X}_+ : t \in [0, h], ||\psi(t) - \psi(0)||_{\mathbb{X}} \leq \frac{\Lambda_1 + \Lambda_2}{c_3}\right\}.$$

There exists a unique solution $\psi(t) \in G$ of (3.8) with initial condition $\psi(0) = \psi_0$.

Proof. Let $t \in [0, h]$. Consider the function ψ of the form

$$\psi(t) := \psi(0) + \frac{1}{\Gamma(\nu)} \int\limits_0^t (t-s)^{\nu-1} f(\psi(s)) ds.$$

We proceed to show that the solution $\psi(t) \in G$. We have,

$$\begin{aligned} ||\psi(t) - \psi(0)||_{\mathbb{X}} &= \left|\left| \frac{1}{\Gamma(\nu)} \int\limits_0^t (t-s)^{\nu-1} f(\psi(s)) ds \right|\right|_{\mathbb{X}} \\ &\leq \frac{1}{\Gamma(\nu)} \int\limits_0^t (t-s)^{\nu-1} ||f(\psi(s))||_{\mathbb{X}} ds, \end{aligned}$$

Furthermore, It follows that

$$\begin{aligned} ||\psi(t) - \psi(0)||_{\mathbb{X}} &\leq \frac{1}{\Gamma(\nu)} \left(\left[-\frac{(t-s)^{\nu}}{\nu} ||f(\psi(s))||_{\mathbb{X}} \right]_0^t + \int\limits_0^t \frac{(t-s)^{\nu}}{\nu} \frac{d}{ds} ||f(\psi(s))||_{\mathbb{X}} ds \right) \\ &= \frac{1}{\Gamma(\nu)} \left(\frac{t^{\nu}}{\nu} ||f(\psi(0))||_{\mathbb{X}} + \int\limits_0^t \frac{(t-s)^{\nu}}{\nu} \frac{d}{ds} ||f(\psi(s))||_{\mathbb{X}} ds \right). \end{aligned}$$

Applying the Theorem 2.4 on the integral leads to,

$$\int\limits_0^t \frac{(t-s)^{\nu}}{\nu} \frac{d}{ds} ||f(\psi(s))||_{\mathbb{X}} ds = \frac{(t-0)^{\nu}}{\nu} \int\limits_0^t \frac{d}{ds} ||f(\psi(s))||_{\mathbb{X}} ds,$$

that is,

$$\begin{aligned} ||\psi(t) - \psi(0)||_{\mathbb{X}} &= \frac{1}{\Gamma(\nu)} \left(\frac{t^{\nu}}{\nu} ||f(\psi(0))||_{\mathbb{X}} + \frac{t^{\nu}}{\nu} \int\limits_0^t \frac{d}{ds} ||f(\psi(s))||_{\mathbb{X}} ds \right) \\ &= \frac{t^{\nu}}{\nu\Gamma(\nu)} \left(||f(\psi(0))||_{\mathbb{X}} + \Big[||f(\psi(s))||_{\mathbb{X}} \Big]_0^t \right) \\ &= \left(\frac{t^{\nu}}{\Gamma(\nu+1)} \right) ||f(\psi(t))||_{\mathbb{X}}. \end{aligned}$$

Since $0 \leq t \leq h$, it follows that $t^{\nu} \leq h^{\nu}$. Therefore,

$$||\psi(t) - \psi(0)||_{\mathbb{X}} \leq \left(\frac{h^{\nu}}{\Gamma(\nu+1)} \right) ||f(\psi(t))||_{\mathbb{X}}$$

$$\leq \left(\frac{h^{\nu} L}{\Gamma(\nu+1)}\right).$$

Substituting $h = \left(\frac{(\Lambda_1+\Lambda_2)\Gamma(\nu+1)}{c_3 L}\right)^{\frac{1}{\nu}}$, yeilds

$$||\psi(t) - \psi(0)||_{\mathbb{X}} \leq \frac{\Lambda_1 + \Lambda_2}{c_3},$$

and hence $\psi(t) \in G$. Define the function f by $f : G \to \mathbb{X}_+$. For $\psi(t), \psi^*(t) \in G$, it follows from the Lipschitz continuity of f that:

$$\begin{aligned}
||f(\psi(t)) - f(\psi^*(t))||_{\mathbb{X}} &\leq M||\psi(t) - \psi^*(t)||_{\mathbb{X}} \\
&= M||\psi(t) - \psi(0) + \psi(0) - \psi^*(t)||_{\mathbb{X}} \\
&\leq M(||\psi(t) - \psi(0)||_{\mathbb{X}} + ||\psi(0) - \psi^*(t)||_{\mathbb{X}}) \\
&= M(||\psi(t) - \psi(0)||_{\mathbb{X}} + ||\psi^*(t) - \psi(0)||_{\mathbb{X}}) \\
&\leq M\left(\frac{\Lambda_1 + \Lambda_2}{c_3} + \frac{\Lambda_1 + \Lambda_2}{c_3}\right) \\
&= \frac{2M(\Lambda_1 + \Lambda_2)}{c_3} \\
&= M\delta,
\end{aligned}$$

where $\delta = \frac{2(\Lambda_1+\Lambda_2)}{c_3}$. For $\epsilon = M\delta$, there exists $\delta = \frac{\epsilon}{M}$ so that

$$||\psi(t) - \psi^*(t)||_{\mathbb{X}} \leq \delta \quad \text{yields} \quad ||f(\psi(t)) - f(\psi^*(t))||_{\mathbb{X}} \leq \epsilon,$$

and hence f is continuous in $\mathbb{X}_+$. Therefore, it follows from Theorem 2.17 that there exists a unique solution of (3.8). □

3.3 Equilibria and basic reproduction numbers

In this section we derive the equilibrium points of the system (3.1) - (3.7) and the basic reproduction numbers of the disease through each transmission route.

3.3.1 Equilibria

The equilibrium states of the system (3.1) - (3.7) satisfy

$$^{C}D_t^{\nu}T_1(t) = {}^{C}D_t^{\nu}T_2(t) = {}^{C}\partial_t^{\nu}L_1(a,t) = {}^{C}\partial_t^{\nu}L_2(a,t) = {}^{C}D_t^{\nu}I_1(t) = {}^{C}D_t^{\nu}I_2(t) = {}^{C}D_t^{\nu}V(t) = 0;$$

that is,

$$0 = \Lambda_1 - \mu_1 T_1^* - \beta_1 T_1^* V^* - \kappa_1 T_1^* I_1^*, \tag{3.9}$$

$$0 = \Lambda_2 - \mu_2 T_2^* - \beta_2 T_2^* V^* - \kappa_2 T_2^* I_2^*, \tag{3.10}$$

$$^{C}D_a^{\nu}L_1^*(a) = -m_1(a)L_1^*(a), \tag{3.11}$$

$$^{C}D_b^{\nu}L_2^*(b) = -m_2(b)L_2^*(b), \tag{3.12}$$

$$0 = (1-f_1)(\beta_1 T_1^* V^* + \kappa_1 T_1^* I_1^*) + \int\limits_0^\infty \alpha_1(a)L_1^*(a)da - \delta_1 I_1^*, \tag{3.13}$$

$$0 = (1-f_2)(\beta_2 T_2^* V^* + \kappa_2 T_2^* I_2^*) + \int\limits_0^\infty \alpha_2(b)L_2^*(b)db - \delta_2 I_2^*, \tag{3.14}$$

$$0 = N_1\delta_1 I_1^* + N_2\delta_2 I_2^* - \mu_V V^*. \tag{3.15}$$

Taking the Laplace transform of (3.11) leads to

$$\mathcal{L}\{^{C}D_a^{\nu}L_1^*(a)\} = -\mathcal{L}\{m_1(a)L_1^*(a)\}.$$

It follows from the Laplace transform of the Caputo fractional derivative that

$$s^{\nu}\mathcal{L}\{L_1^*(a)\} - s^{\nu-1}L_1^*(0) = -\mathcal{L}\{m_1(a)L_1^*(a)\},$$

where

$$L_1^*(0) = f_1(\beta_1 T_1^* V^* + \kappa_1 T_1^* I_1^*).$$

It follows that

$$\mathcal{L}\{L_1^*(a)\} = \frac{1}{s}L_1^*(0) - \frac{1}{s^{\nu}}\mathcal{L}\{m_1(a)L_1^*(a)\},$$

and hence

$$\mathcal{L}\{L_1^*(a)\} = \mathcal{L}\{L_1^*(0)\} - \mathcal{L}\left\{\frac{a^{\nu-1}}{\Gamma(\nu)}\right\}\mathcal{L}\{m_1(a)L_1^*(a)\},$$

that is,

$$\mathcal{L}\{L_1^*(a)\} = \mathcal{L}\{L_1^*(0)\} - \frac{1}{\Gamma(\nu)}\mathcal{L}\{a^{\nu-1} * m_1(a)L_1^*(a)\}.$$

Thus taking the inverse Laplace transform yields

$$\begin{aligned}
L_1^*(a) &= L_1^*(0) - \frac{1}{\Gamma(\nu)}a^{\nu-1} * m_1(a)L_1^*(a),\\
&= L_1^*(0) - \frac{1}{\Gamma(\nu)}\int_0^a (a-s)^{\nu-1}m_1(s)L_1^*(s)ds,\\
&= L_1^*(0) - \frac{1}{\Gamma(\nu)}\left(\left[-\frac{(a-s)^\nu}{\nu}m_1(s)L_1^*(s)\right]_0^a + \int_0^a \frac{(a-s)^\nu}{\nu}\frac{d}{ds}\{m_1(s)L_1^*(s)\}ds\right)\\
&= L_1^*(0) - \frac{1}{\Gamma(\nu)}\left(\frac{a^\nu}{\nu}m_1(0)L_1^*(0) + \int_0^a \frac{(a-s)^\nu}{\nu}\frac{d}{ds}\{m_1(s)L_1^*(s)\}ds\right).
\end{aligned}$$

It follows from Theorem 2.4 that

$$\int_0^a \frac{(a-s)^\nu}{\nu}\frac{d}{ds}\{m_1(s)L_1^*(s)\}ds = \frac{(a-0)^\nu}{\nu}\int_0^a \frac{d}{ds}\{m_1(s)L_1^*(s)\}ds,$$

and therefore we get

$$\begin{aligned}
L_1^*(a) &= L_1^*(0) - \frac{1}{\Gamma(\nu)}\left(\frac{a^\nu}{\nu}m_1(0)L_1^*(0) + \frac{a^\nu}{\nu}\int_0^a \frac{d}{ds}\{m_1(s)L_1^*(s)\}ds\right)\\
&= L_1^*(0) - \frac{a^\nu}{\nu\Gamma(\nu)}\left(m_1(0)L_1^*(0) + \Big[m_1(s)L_1^*(s)\Big]_0^a\right)\\
&= L_1^*(0) - \frac{a^\nu}{\Gamma(\nu+1)}m_1(a)L_1^*(a).
\end{aligned}$$

Solving for $L_1^*(a)$ yields

$$L_1^*(a) = L_1^*(0)\left(1 + \frac{a^\nu m_1(a)}{\Gamma(\nu+1)}\right)^{-1}.$$

Since

$$\left(1 + \frac{a^\nu m_1(a)}{\Gamma(\nu+1)}\right)^{-1} = \sum_{j=0}^{\infty}\left(-\frac{a^\nu m_1(a)}{\Gamma(\nu+1)}\right)^j = \sum_{j=0}^{\infty}(-1)^j\left(\frac{a^\nu m_1(a)}{\Gamma(\nu+1)}\right)^j,$$

provided

$$\left|\frac{a^\nu m_1(a)}{\Gamma(\nu+1)}\right| < 1,$$

then

$$L_1^*(a) = L_1^*(0)\sum_{j=0}^{\infty}\left(-\frac{a^{\nu}m_1(a)}{\Gamma(\nu+1)}\right)^j = L_1^*(0)\sigma_1(a), \quad \text{provided} \quad \left|\frac{a^{\nu}m_1(a)}{\Gamma(\nu+1)}\right| < 1, \quad (3.16)$$

where the probability of a Type 1 cell being latently infected some time units after infection [Xiaoyan, 2013] is given as

$$\sigma_1(a) = \sum_{j=0}^{\infty}\left(-\frac{a^{\nu}m_1(a)}{\Gamma(\nu+1)}\right)^j.$$

We then deduce that

$$\begin{aligned}\int_0^{\infty}\alpha_1(a)L_1^*(a)da &= \int_0^{\infty}\alpha_1(a)L_1^*(0)\sigma_1(a)da\\ &= \int_0^{\infty}\alpha_1(a)f_1(\beta_1T_1^*V^* + \kappa_1T_1^*I_1^*)\sigma_1(a)da\\ &= f_1(\beta_1T_1^*V^* + \kappa_1T_1^*I_1^*)\int_0^{\infty}\alpha_1(a)\sigma_1(a)da\\ &= \xi_1f_1(\beta_1T_1^*V^* + \kappa_1T_1^*I_1^*),\end{aligned}$$

where the probability of latently infected Type 1 cells transitioning to productively infected cells is denoted by,

$$\xi_1 = \int_0^{\infty}\alpha_1(a)\sigma_1(a)da.$$

Substituting ξ_1 into (3.13) leads to

$$0 = (1-f_1)(\beta_1T_1^*V^* + \kappa_1T_1^*I_1^*) + \xi_1f_1(\beta_1T_1^*V^* + \kappa_1T_1^*I_1^*) - \delta_1I_1^*,$$

and hence we obtain

$$(1+\xi_1f_1-f_1)(\beta_1T_1^*V^* + \kappa_1T_1^*I_1^*) = \delta_1I_1^*,$$

that is,

$$\beta_1T_1^*V^* + \kappa_1T_1^*I_1^* = \frac{\delta_1I_1^*}{1+\xi_1f_1-f_1}.$$

Substituting into (3.9) yields a relation between the populations of infected and uninfected Type 1 cells,

$$(\Lambda_1 - \mu_1 T_1^*)(1 + \xi_1 f_1 - f_1) = \delta_1 I_1^*,$$

and hence

$$T_1^* = \frac{\Lambda_1}{\mu_1} - \frac{\delta_1}{\mu_1(1 + \xi_1 f_1 - f_1)} I_1^* = \left(1 - \frac{\kappa_1 I_1^*}{\mu_1 \mathcal{R}_1^{CC}}\right) T_1^0, \tag{3.17}$$

where

$$T_1^0 = \frac{\Lambda_1}{\mu_1} \quad \text{and} \quad \mathcal{R}_1^{CC} = \frac{\Lambda_1}{\mu_1}(1 + \xi_1 f_1 - f_1)\frac{\kappa_1}{\delta_1}.$$

We provide similar results by solving (3.10) to obtain the equilibrium population of latently infected Type 2 cells as,

$$L_2^*(b) := L_2^*(0) \sum_{j=0}^{\infty} \left(- \frac{b^\nu m_2(b)}{\Gamma(\nu+1)} \right)^j = L_2^*(0)\sigma_2(b), \tag{3.18}$$

where the probability of a Type 2 cell being latently infected some time units after infection is given by,

$$\sigma_2(b) = \sum_{j=0}^{\infty} \left(- \frac{b^\nu m_2(b)}{\Gamma(\nu+1)} \right)^j = \sum_{j=0}^{\infty} (-1)^j \left(\frac{b^\nu m_2(b)}{\Gamma(\nu+1)} \right)^j,$$

and the probability of latently infected Type 2 cells transitioning to productively infected cells is denoted by,

$$\xi_2 = \int_0^\infty \alpha_2(b)\sigma_2(b)db.$$

Substituting ξ_2 into (3.14) leads to

$$0 = (1 - f_2)(\beta_2 T_2^* V^* + \kappa_2 T_2^* I_2^*) + \xi_2 f_2(\beta_2 T_2^* V^* + \kappa_2 T_2^* I_2^*) - \delta_2 I_2^*,$$

and hence we obtain

$$(1 + \xi_2 f_2 - f_2)(\beta_2 T_2^* V^* + \kappa_2 T_2^* I_2^*) = \delta_2 I_2^*,$$

that is,

$$\beta_2 T_2^* V^* + \kappa_2 T_2^* I_2^* = \frac{\delta_2 I_2^*}{1 + \xi_2 f_2 - f_2}.$$

Substituting into (3.10) yields a relation between the populations of infected and uninfected Type 2 cells,

$$(\Lambda_2 - \mu_2 T_2^*)(1 + \xi_2 f_2 - f_2) = \delta_2 I_2^*,$$

the equilibrium population of uninfected Type 2 cells is also related to the population of infected Type 2 cells by,

$$T_2^* = \frac{\Lambda_2}{\mu_2} - \frac{\delta_2}{\mu_2(1+\xi_2 f_2 - f_2)} I_2^* = \left(1 - \frac{\kappa_2 I_2^*}{\mu_2 \mathcal{R}_2^{CC}}\right) T_2^0, \tag{3.19}$$

where

$$T_2^0 = \frac{\Lambda_2}{\mu_2} \quad \text{and} \quad \mathcal{R}_2^{CC} = \frac{\Lambda_2}{\mu_2}(1+\xi_2 f_2 - f_2)\frac{\kappa_2}{\delta_2}.$$

From equation (3.15), we get

$$V^* = \frac{N_1 \delta_1}{\mu_V} I_1^* + \frac{N_2 \delta_2}{\mu_V} I_2^*. \tag{3.20}$$

It follows that the equilibrium states of the system (3.1) - (3.7) are generated by

$$\begin{pmatrix} T_1^* \\ T_2^* \\ L_1^*(a) \\ L_2^*(b) \\ I_1^* \\ I_2^* \\ V^* \end{pmatrix} = \begin{pmatrix} \left(1 - \frac{\kappa_1 I_1^*}{\mu_1 \mathcal{R}_1^{CC}}\right) T_1^0 \\ \left(1 - \frac{\kappa_2 I_2^*}{\mu_2 \mathcal{R}_2^{CC}}\right) T_2^0 \\ L_1^*(0)\sigma_1(a) \\ L_2^*(0)\sigma_2(b) \\ I_1^* \\ I_2^* \\ \frac{N_1\delta_1}{\mu_V} I_1^* + \frac{N_2\delta_2}{\mu_V} I_2^* \end{pmatrix}, \tag{3.21}$$

where

$$L_1^*(0) = f_1(\beta_1 T_1^* V^* + \kappa_1 T_1^* I_1^*), \quad L_2^*(0) = f_2(\beta_2 T_2^* V^* + \kappa_2 T_2^* I_2^*).$$

I_1^* and I_2^* are determined as follows:

Case 1 ($I_1^* = 0$ and $I_2^* = 0$): The disease-free equilibrium E^0 is given as

$$E^0 = \left(\frac{\Lambda_1}{\mu_1}, \frac{\Lambda_2}{\mu_2}, 0, 0, 0, 0, 0\right)^T = \left(T_1^0, T_2^0, 0, 0, 0, 0, 0\right)^T. \tag{3.22}$$

Case 2 ($I_1^* \neq 0$ and $I_2^* = 0$): The Type 1 cell dominated endemic equilibrium E_1^* is given by

$$E_1^* = \left(\left(1 - \frac{\kappa_1 I_1^*}{\mu_1 \mathcal{R}_1^{CC}}\right) T_1^0, \frac{\Lambda_2}{\mu_2}, L_1^*(0)\sigma_1(a), 0, I_1^*, 0, \frac{N_1\delta_1}{\mu_V} I_1^*\right)^T. \tag{3.23}$$

Case 3 ($I_1^* = 0$ and $I_2^* \neq 0$): The Type 2 cell dominated endemic equilibrium E_2^* is given by

$$E_2^* = \left(\frac{\Lambda_1}{\mu_1}, \left(1 - \frac{\kappa_2 I_2^*}{\mu_2 \mathcal{R}_2^{CC}}\right)T_2^0, 0, L_2^*(0)\sigma_2(b), 0, I_2^*, \frac{N_2\delta_2}{\mu_V}I_2^*\right)^T. \tag{3.24}$$

Case 4 ($I_1^* \neq 0$ and $I_2^* \neq 0$): The coexistence-cell endemic equilibrium E_3^* is given by

$$E_3^* = \begin{pmatrix} \left(1 - \frac{\kappa_1 I_1^*}{\mu_1 \mathcal{R}_1^{CC}}\right)T_1^0 \\ \left(1 - \frac{\kappa_2 I_2^*}{\mu_2 \mathcal{R}_2^{CC}}\right)T_2^0 \\ L_1^*(0)\sigma_1(a) \\ L_2^*(0)\sigma_2(b) \\ I_1^* \\ I_2^* \\ \frac{N_1\delta_1}{\mu_V}I_1^* + \frac{N_2\delta_2}{\mu_V}I_2^* \end{pmatrix}. \tag{3.25}$$

3.3.2 Basic reproduction numbers and existence of equilibria

Here, the aim is to explore the relationship between the basic reproduction numbers of the disease through each transmission route and to prove the existence of equilibria of the system (3.1) - (3.7). To do this, we first substitute (3.20) into (3.17) to obtain

$$\mu_V\Lambda_1 - \mu_V\mu_1 T_1^* - \beta_1 T_1^*(N_1\delta_1 I_1^* + N_2\delta_2 I_2^*) - \mu_V\kappa_1 T_1^* I_1^* = 0,$$

which reduces to

$$\mu_V\Lambda_1 - T_1^*[\mu_V\mu_1 + (\beta_1 N_1\delta_1 + \mu_V\kappa_1)I_1^* + \beta_1 N_2\delta_2 I_2^*] = 0,$$

and hence

$$T_1^* = \frac{\mu_V\Lambda_1}{\mu_V\mu_1 + (\beta_1 N_1\delta_1 + \mu_V\kappa_1)I_1^* + \beta_1 N_2\delta_2 I_2^*}. \tag{3.26}$$

Next, we substitute (3.20) into (3.13) to obtain

$$(1 + \xi_1 f_1 - f_1)[\beta_1 T_1^*(N_1\delta_1 I_1^* + N_2\delta_2 I_2^*) + \mu_V\kappa_1 T_1^* I_1^*] - \mu_V\delta_1 I_1^* = 0,$$

which reduces to

$$(1 + \xi_1 f_1 - f_1)[(\beta_1 N_1\delta_1 + \mu_V\kappa_1)I_1^* + \beta_1 N_2\delta_2 I_2^*]T_1^* - \mu_V\delta_1 I_1^* = 0,$$

and hence

$$T_1^* = \frac{\mu_V \delta_1 I_1^*}{(1+\xi_1 f_1 - f_1)[(\beta_1 N_1 \delta_1 + \mu_V \kappa_1) I_1^* + \beta_1 N_2 \delta_2 I_2^*]}. \tag{3.27}$$

Equating (3.26) and (3.27) yields

$$\frac{\mu_V \Lambda_1}{\mu_V \mu_1 + (\beta_1 N_1 \delta_1 + \mu_V \kappa_1) I_1^* + \beta_1 N_2 \delta_2 I_2^*} = \frac{\mu_V \delta_1 I_1^*}{1+\xi_1 f_1 - f_1} \times \frac{1}{(\beta_1 N_1 \delta_1 + \mu_V \kappa_1) I_1^* + \beta_1 N_2 \delta_2 I_2^*},$$

and hence,

$$\begin{aligned} \mu_V \Lambda_1 (1+&\xi_1 f_1 - f_1)[(\beta_1 N_1 \delta_1 + \mu_V \kappa_1) I_1^* + \beta_1 N_2 \delta_2 I_2^*] \\ &= \mu_V \delta_1 I_1^* [\mu_V \mu_1 + (\beta_1 N_1 \delta_1 + \mu_V \kappa_1) I_1^* + \beta_1 N_2 \delta_2 I_2^*]. \end{aligned}$$

This is equivalent to

$$\begin{aligned} &(\beta_1 N_1 \delta_1 + \mu_V \kappa_1) \delta_1 I_1^{*2} + [\mu_1 \mu_V \delta_1 - \Lambda_1 (1+\xi_1 f_1 - f_1)(\beta_1 N_1 \delta_1 + \mu_V \kappa_1)] I_1^* \\ &- \Lambda_1 (1+\xi_1 f_1 - f_1) \beta_1 N_2 \delta_2 I_2^* + \delta_1 \beta_1 N_2 \delta_2 I_1^* I_2^* = 0; \end{aligned}$$

that is,

$$A_1 I_1^{*2} + B_1 I_1^* - C_1 I_2^* + D_1 I_1^* I_2^* = 0,$$

where

$$\begin{aligned} &A_1 = (\beta_1 N_1 \delta_1 + \mu_V \kappa_1) \delta_1, \quad B_1 = \mu_1 \mu_V \delta_1 - \Lambda_1 (1+\xi_1 f_1 - f_1)(\beta_1 N_1 \delta_1 + \mu_V \kappa_1), \\ &C_1 = \Lambda_1 (1+\xi_1 f_1 - f_1) \beta_1 N_2 \delta_2 \quad \text{and} \quad D_1 = \delta_1 \beta_1 N_2 \delta_2. \end{aligned}$$

It follows that

$$B_1 I_1^* - C_1 I_2^* + D_1 I_1^* I_2^* = -A_1 I_1^{*2} < 0,$$

and hence,

$$I_2^* (C_1 - D_1 I_1^*) > B_1 I_1^*. \tag{3.28}$$

The following possibilities are discussed:

(i) Assuming $B_1 > 0$ and dividing (3.28) by B_1 results in

$$I_2^* \frac{C_1 - D_1 I_1^*}{B_1} > I_1^* > 0,$$

and hence $C_1 - D_1 I_1^* > 0$. It follows from $B_1 > 0$ that

$$\mu_1 \mu_V \delta_1 - \Lambda_1(1 + \xi_1 f_1 - f_1)(\beta_1 N_1 \delta_1 + \mu_V \kappa_1) > 0,$$

which yields,

$$1 - \frac{\Lambda_1}{\mu_1}(1 + \xi_1 f_1 - f_1)\left(\frac{\beta_1 N_1}{\mu_V} + \frac{\kappa_1}{\delta_1}\right) > 0;$$

that is, $\mathcal{R}_1 < 1$, where

$$\mathcal{R}_1 = \frac{\Lambda_1}{\mu_1}(1 + \xi_1 f_1 - f_1)\left(\frac{\beta_1 N_1}{\mu_V} + \frac{\kappa_1}{\delta_1}\right) = \mathcal{R}_1^{CV} + \mathcal{R}_1^{CC},$$

with

$$\mathcal{R}_1^{CV} = \frac{\Lambda_1}{\mu_1}(1 + \xi_1 f_1 - f_1)\frac{\beta_1 N_1}{\mu_V}.$$

It follows from $C_1 - D_1 I_1^* > 0$ that

$$I_1^* < \frac{C_1}{D_1} = \frac{\Lambda_1(1 + \xi_1 f_1 - f_1)}{\delta_1};$$

that is,

$$I_1^* < \frac{\mu_1}{\kappa_1}\mathcal{R}_1^{CC}.$$

(ii) Assuming $B_1 < 0$ and dividing (3.28) by B_1 leads to,

$$I_2^* \frac{C_1 - D_1 I_1^*}{B_1} < I_1^*.$$

It follows that

$$0 < I_2^* \frac{C_1 - D_1 I_1^*}{B_1} < I_1^* \quad \text{or} \quad I_2^* \frac{C_1 - D_1 I_1^*}{B_1} < 0 < I_1^*;$$

which yields

$$C_1 - D_1 I_1^* < 0 \quad \text{or} \quad C_1 - D_1 I_1^* > 0,$$

respectively. Equivalently, we have $C_1 - D_1 I_1^* \neq 0$, which leads to $I_1^* \neq \frac{D_1}{C_1} = \frac{\mu_1}{\kappa_1}\mathcal{R}_1^{CC}$. It follows from $B_1 < 0$ that $\mathcal{R}_1 > 1$. Therefore, $\mathcal{R}_1 > 1$ and $I_1^* \neq \frac{\mu_1}{\kappa_1}\mathcal{R}_1^{CC}$.

Similar calculations following the substitution of (3.20) into (3.10) and (3.14), lead to the following:

(iii)

$$\mathcal{R}_2 < 1 \quad \text{and} \quad I_2^* < \frac{\mu_2}{\kappa_2}\mathcal{R}_2^{CC},$$

where

$$\mathcal{R}_2 = \frac{\Lambda_2}{\mu_2}(1+\xi_2 f_2 - f_2)\frac{\beta_2 N_2}{\mu_V} + \frac{\kappa_2}{\delta_2} = \mathcal{R}_2^{CV} + \mathcal{R}_2^{CC},$$

with

$$\mathcal{R}_2^{CV} = \frac{\Lambda_2}{\mu_2}(1+\xi_2 f_2 - f_2)\frac{\beta_2 N_2}{\mu_V}.$$

(iv) $\mathcal{R}_2 > 1$ and $I_2^* \neq \frac{\mu_2}{\kappa_2}\mathcal{R}_2^{CC}$.
Combining results from (i), (ii), (iii) and (iv) allows us to state the following proposition.

Proposition 3.3. *The equilibria of the system exists provided the following:*

(a) The disease-free equilibrium E^0, always exists regardless of (i)-(iv).

(b) The Type 1 cell dominated endemic Equilibrium E_1^* exists whenever (i) or (ii) is satisfied.

(c) The Type 2 cell dominated endemic Equilibrium E_2^* exists whenever (ii) or (iii) is satisfied.

(d) The dual cell endemic Equilibrium E_3^* exists whenever (i) or (ii), and (iii) or (iv), are satisfied.

3.4 Stability of the disease-free equilibrium

This section focuses of the local asymptotic stability of the disease-free equilibrium point. To achieve this, we employ the linearization technique around the equilibrium.

Let

$$\tilde{T}_1(t), \tilde{T}_2(t), \tilde{L}_1(a,t), \tilde{L}_2(b,t), \tilde{I}_1(t), \tilde{I}_2(t) \quad \text{and} \quad \tilde{V}(t),$$

be perturbations of

$$T_1(t), T_2(t), L_1(a,t), L_2(b,t), I_1(t), I_2(t) \quad \text{and} \quad V(t),$$

respectively, so that

$$\tilde{T}_1(t) = T_1(t) - T_1, \tilde{T}_2(t) = T_2(t) - T_2, \tilde{L}_1(a,t) = L_1(a,t) - L_1(a), \tilde{L}_2(b,t) = L_2(b,t) - L_2(b),$$

$$\tilde{I}_1(t) = I_1(t) - I_1, \tilde{I}_2(t) = I_2(t) - I_2 \quad \text{and} \quad \tilde{V}(t) = V(t) - V,$$

where $E = (T_1, T_2, L_1(a), L_2(b), I_1, I_2, V)^T$ is the equilibrium point. The perturbations satisfy the fractional system,

$$\begin{aligned}
{}^{C}D_t^{\nu}\tilde{T}_1(t) =& -[\tilde{T}_1(t)(\mu_1 + \beta_1 V + \kappa_1 I_1) + T_1(\beta_1\tilde{V} + \kappa_1\tilde{I}_1(t))], && (3.29)\\
{}^{C}D_t^{\nu}\tilde{T}_2(t) =& -[\tilde{T}_2(t)(\mu_2 + \beta_2 V + \kappa_2 I_2) + T_2(\beta_2\tilde{V} + \kappa_2\tilde{I}_2(t))], && (3.30)\\
{}^{C}\partial_t^{\nu}\tilde{L}_1(a,t) =& -m_1(a)\tilde{L}_1(a,t) - {}^{C}\partial_a^{\nu}\tilde{L}_1(a,t), && (3.31)\\
{}^{C}\partial_t^{\nu}\tilde{L}_2(b,t) =& -m_2(b)\tilde{L}_2(b,t) - {}^{C}\partial_b^{\nu}\tilde{L}_2(b,t), && (3.32)\\
{}^{C}D_t^{\nu}\tilde{I}_1(t) =& (1-f_1)[\tilde{T}_1(t)(\beta_1 V + \kappa_1 I_1) + T_1(\beta_1\tilde{V} + \kappa_1\tilde{I}_1(t))]\\
&+ \int_0^{\infty}\alpha_1(a)\tilde{L}_1(a,t)da - \delta_1\tilde{I}_1(t), && (3.33)\\
{}^{C}D_t^{\nu}\tilde{I}_2(t) =& (1-f_2)[\tilde{T}_2(t)(\beta_2 V + \kappa_2 I_2) + T_2(\beta_2\tilde{V} + \kappa_2\tilde{I}_2(t))]\\
&+ \int_0^{\infty}\alpha_2(b)\tilde{L}_2(b,t)db - \delta_2\tilde{I}_2(t), && (3.34)\\
{}^{C}D_t^{\nu}\tilde{V}(t) =& N_1\delta_1\tilde{I}_1(t) + N_2\delta_2\tilde{I}_2(t) - \mu_V\tilde{V}(t), && (3.35)
\end{aligned}$$

after neglecting perturbation terms of order greater than or equal to 2, with boundary conditions

$$\tilde{L}_1(0,t) = f_1[\tilde{T}_1(t)(\beta_1 V + \kappa_1 I_1) + T_1(\beta_1\tilde{V} + \kappa_1\tilde{I}_1)],$$

and

$$\tilde{L}_2(0,t) = f_2[\tilde{T}_2(t)(\beta_2 V + \kappa_2 I_2) + T_2(\beta_2\tilde{V} + \kappa_2\tilde{I}_2)].$$

Suppose the solutions of the fractional system (3.29) - (3.35) are of the form,

$$\tilde{T}_1(t) = \bar{T}_1 E_{\nu}(\lambda t^{\nu}), \tilde{T}_2(t) = \bar{T}_2 E_{\nu}(\lambda t^{\nu}), \tilde{L}_1(a,t) = \bar{L}_1(a) E_{\nu}(\lambda t^{\nu}),$$

$\tilde{L}_2(b,t) = \bar{L}_2(b)E_\nu(\lambda t^\nu), \tilde{I}_1(t) = \bar{I}_1 E_\nu(\lambda t^\nu), \tilde{I}_2(t) = \bar{I}_2 E_\nu(\lambda t^\nu)$ and $\tilde{V}(t) = \bar{V}E_\nu(\lambda t^\nu)$, with initial conditions $\bar{T}_1, \bar{T}_2, \bar{L}_1(a), \bar{L}_2(b), \bar{I}_1, \bar{I}_2$, and $\bar{V}$. Since any function $f(t) = \bar{f}E_\nu(\lambda t^\nu)$ with initial condition $\bar{f} = f(0)$ satisfies the fractional equation ${}^C D_t^\nu f(t) = \lambda f(t)$, then it follows that,

$$\lambda\bar{T}_1 = -[\bar{T}_1(\mu_1 + \beta_1 V + \kappa_1 I_1) + T_1(\beta_1\bar{V} + \kappa_1\bar{I}_1)], \tag{3.36}$$

$$\lambda\bar{T}_2 = -[\bar{T}_2(\mu_2 + \beta_2 V + \kappa_2 I_2) + T_2(\beta_2\bar{V} + \kappa_2\bar{I}_2)], \tag{3.37}$$

$$\lambda\bar{L}_1(a) = -m_1(a)\bar{L}_1(a) - {}^C D_a^\nu \bar{L}_1(a), \tag{3.38}$$

$$\lambda\bar{L}_2(b) = -m_2(b)\bar{L}_2(b) - {}^C D_b^\nu \bar{L}_2(b), \tag{3.39}$$

$$\lambda\bar{I}_1 = (1-f_1)[\bar{T}_1(\beta_1 V + \kappa_1 I_1) + T_1(\beta_1\bar{V} + \kappa_1\bar{I}_1)] + \int_0^\infty \alpha_1(a)\bar{L}_1(a)da - \delta_1\bar{I}_1, \tag{3.40}$$

$$\lambda\bar{I}_2 = (1-f_2)[\bar{T}_2(\beta_2 V + \kappa_2 I_2) + T_2(\beta_2\bar{V} + \kappa_2\bar{I}_2)] + \int_0^\infty \alpha_2(b)\bar{L}_2(b)db - \delta_2\bar{I}_2, \tag{3.41}$$

$$\lambda\bar{V} = N_1\delta_1\bar{I}_1 + N_2\delta_2\bar{I}_2 - \mu_V\bar{V}, \tag{3.42}$$

with boundary conditions

$$\bar{L}_1(0) = f_1[\bar{T}_1(\beta_1 V + \kappa_1 I_1) + T_1(\beta_1\bar{V} + \kappa_1\bar{I}_1)],$$

and

$$\bar{L}_2(0) = f_2[\bar{T}_2(\beta_2 V + \kappa_2 I_2) + T_2(\beta_2\bar{V} + \kappa_2\bar{I}_2)].$$

Theorem 3.4. *The disease-free equilibrium, E^0, is locally asymptotically stable.*

Proof. The disease-free equilibrium is given by

$$E^0 = (T_1^0, T_2^0, 0, 0, 0, 0, 0)^T = \left(\frac{\Lambda_1}{\mu_1}, \frac{\Lambda_2}{\mu_2}, 0, 0, 0, 0, 0\right)^T.$$

It follows from (3.36) - (3.42) that

$$\lambda\bar{T}_1 = -\bar{T}_1\mu_1 - T_1^0(\beta_1\bar{V} + \kappa_1\bar{I}_1), \tag{3.43}$$

$$\lambda\bar{T}_2 = -\bar{T}_2\mu_2 - T_2^0(\beta_2\bar{V} + \kappa_2\bar{I}_2), \tag{3.44}$$

$$\lambda\bar{L}_1(a) = -m_1(a)\bar{L}_1(a) - {}^C D_a^\nu \bar{L}_1(a), \tag{3.45}$$

$$\lambda \bar{L}_2(b) = -m_2(b)\bar{L}_2(b) - {}^C D_b^\nu \bar{L}_2(b), \tag{3.46}$$

$$\lambda \bar{I}_1 = (1-f_1)T_1^0(\beta_1 \bar{V} + \kappa_1 \bar{I}_1) + \int\limits_0^\infty \alpha_1(a)\bar{L}_1(a)da - \delta_1 \bar{I}_1, \tag{3.47}$$

$$\lambda \bar{I}_2 = (1-f_2)T_2^0(\beta_2 \bar{V} + \kappa_2 \bar{I}_2) + \int\limits_0^\infty \alpha_2(b)\bar{L}_2(b)db - \delta_2 \bar{I}_2, \tag{3.48}$$

$$\lambda \bar{V} = N_1\delta_1 \bar{I}_1 + N_2 \delta_2 \bar{I}_2 - \mu_V \bar{V}, \tag{3.49}$$

with boundary conditions

$$\bar{L}_1(0) = f_1 T_1^0(\beta_1 \bar{V} + \kappa_1 \bar{I}_1),$$

and

$$\bar{L}_2(0) = f_2 T_2^0(\beta_2 \bar{V} + \kappa_2 \bar{I}_2).$$

From (3.43) and (3.44) we get, respectively,

$$(\lambda + \mu_1)\bar{T}_1 = -(\beta_1 \bar{V} + \kappa_1 \bar{I}_1)T_1^0 < 0 \quad \text{and} \quad (\lambda + \mu_2)\bar{T}_2 = -(\beta_2 \bar{V} + \kappa_2 \bar{I}_2)T_2^0 < 0.$$

Therefore

$$\lambda < -\mu_1 < 0 \quad \text{and} \quad \lambda < -\mu_2 < 0;$$

that is, $\arg(\lambda) = \pi > \frac{\pi\nu}{2}$ for every $\nu \in (0,1)$.

From (3.45) we obtain,

$$\bar{L}_1(a) = \bar{L}_1(0)\sigma_{1,\lambda}(a), \quad \text{where} \quad \sigma_{1,\lambda}(a) = \sum_{k=0}^\infty \left(-\frac{a^\nu(m_1(a)+\lambda)}{\Gamma(\nu+1)}\right)^k,$$

with

$$\left| -\frac{a^\nu(m_1(a)+\lambda)}{\Gamma(\nu+1)} \right| < 1, \quad \text{or equivalently,} \quad \frac{\Gamma(\nu+1)}{a^\nu} - m_1(a) > \lambda > -\frac{\Gamma(\nu+1)}{a^\nu} - m_1(a).$$

Consider the integral

$$\begin{aligned}\int\limits_0^\infty \alpha_1(a)\bar{L}_1(a)da &= \int\limits_0^\infty \alpha_1(a)\bar{L}_1(0)\sigma_{1,\lambda}(a)da \\ &= \bar{L}_1(0)\int\limits_0^\infty \alpha_1(a)\sigma_{1,\lambda}(a)da\end{aligned}$$

$$= \bar{L}_1(0)\xi_{1,\lambda},$$

where $\xi_{1,\lambda} = \int_0^\infty \alpha_1(a)\sigma_{1,\lambda}(a)da$. This allows equation (3.47) to be rewritten as,

$$\lambda\bar{I}_1 = (1 + \xi_{1,\lambda}f_1 - f_1)T_1^0(\beta_1\bar{V} + \kappa_1\bar{I}_1) - \delta_1\bar{I}_1. \tag{3.50}$$

Similarly, from (3.46) we obtain

$$\bar{L}_2(b) = \bar{L}_2(0)\sigma_{2,\lambda}(b), \quad \text{where} \quad \sigma_{2,\lambda}(b) = \sum_{k=0}^{\infty}\left(- \frac{b^\nu(m_2(b) + \lambda)}{\Gamma(\nu+1)}\right)^k,$$

with

$$\left| - \frac{b^\nu(m_2(b) + \lambda)}{\Gamma(\nu+1)}\right| < 1, \quad \text{or equivalently,} \quad \frac{\Gamma(\nu+1)}{b^\nu} - m_2(b) > \lambda > -\frac{\Gamma(\nu+1)}{b^\nu} - m_2(b),$$

and $\xi_{2,\lambda} = \int_0^\infty \alpha_2(b)\sigma_{2,\lambda}(b)db$. Thus equation (3.48) can be rewritten as

$$\lambda\bar{I}_2 = (1 + \xi_{2,\lambda}f_2 - f_2)T_2^0(\beta_2\bar{V} + \kappa_2\bar{I}_2) - \delta_2\bar{I}_2. \tag{3.51}$$

Let $\bar{\xi}_{1,\lambda} = 1 + \xi_{1,\lambda}f_1 - f_1$ and $\bar{\xi}_{2,\lambda} = 1 + \xi_{2,\lambda}f_2 - f_2$. Eliminating $\bar{V}$ from equation (3.49) and (3.50) yields

$$(\lambda + \mu_V)(\lambda + \delta_1)\bar{I}_1 = \bar{\xi}_{1,\lambda}T_1^0\beta_1(N_1\delta_1\bar{I}_1 + N_2\delta_2\bar{I}_2) + \bar{\xi}_{1,\lambda}T_1^0\kappa_1(\lambda + \mu_V)\bar{I}_1,$$

which simplifies to,

$$[(\lambda + \mu_V)(\lambda + \delta_1) - \beta_1\bar{\xi}_{1,\lambda}T_1^0N_1\delta_1 - \bar{\xi}_{1,\lambda}T_1^0\kappa_1(\lambda + \mu_V)]\bar{I}_1 = \bar{\xi}_{1,\lambda}T_1^0\beta_1N_2\delta_2\bar{I}_2. \tag{3.52}$$

Similarly, eliminating $\bar{V}$ from equation (3.49) and (3.51) leads to,

$$[(\lambda + \mu_V)(\lambda + \delta_2) - \beta_2\bar{\xi}_{2,\lambda}T_2^0N_2\delta_2 - \bar{\xi}_{2,\lambda}T_2^0\kappa_2(\lambda + \mu_V)]\bar{I}_2 = \bar{\xi}_{2,\lambda}T_2^0\beta_2N_1\delta_1\bar{I}_1. \tag{3.53}$$

It follows from (3.52) and (3.53) that

$$[(\lambda + \mu_V)(\lambda + \delta_1) - \beta_1\bar{\xi}_{1,\lambda}T_1^0N_1\delta_1 - \bar{\xi}_{1,\lambda}T_1^0\kappa_1(\lambda + \mu_V)][(\lambda + \mu_V)(\lambda + \delta_2) - \beta_2\bar{\xi}_{2,\lambda}T_2^0N_2\delta_2$$
$$- \bar{\xi}_{2,\lambda}T_2^0\kappa_2(\lambda + \mu_V)] = [\bar{\xi}_{1,\lambda}T_1^0\beta_1N_2\delta_2][\bar{\xi}_{2,\lambda}T_2^0\beta_2N_1\delta_1],$$

that is,

$$\frac{[\bar{\xi}_{1,\lambda}T_1^0\beta_1N_2\delta_2][\bar{\xi}_{2,\lambda}T_2^0\beta_2N_1\delta_1]}{(\lambda + \mu_V)(\lambda + \delta_2) - \beta_2\bar{\xi}_{2,\lambda}T_2^0N_2\delta_2 - \bar{\xi}_{2,\lambda}T_2^0\kappa_2(\lambda + \mu_V)} = (\lambda + \mu_V)(\lambda + \delta_1) - \beta_1\bar{\xi}_{1,\lambda}T_1^0N_1\delta_1$$

$$- \bar{\xi}_{1,\lambda} T_1^0 \kappa_1 (\lambda + \mu_V).$$

This leads to the characteristic equation

$$\frac{\bar{\xi}_{1,\lambda} T_1^0 \beta_1 N_2 \delta_2}{(\lambda+\mu_V)^2(\lambda+\delta_1)(\lambda+\delta_2)} \times \frac{\bar{\xi}_{2,\lambda} T_2^0 \beta_2 N_1 \delta_1}{\left[1 - \frac{\beta_2 \bar{\xi}_{2,\lambda} T_2^0 N_2 \delta_2}{(\lambda+\mu_V)(\lambda+\delta_2)} - \frac{\bar{\xi}_{2,\lambda} T_2^0 \kappa_2}{\lambda+\delta_2}\right]} + \left[\frac{\beta_1 \bar{\xi}_{1,\lambda} T_1^0 N_1 \delta_1}{(\lambda+\mu_V)(\lambda+\delta_1)} + \frac{\bar{\xi}_{1,\lambda} T_1^0 \kappa_1}{\lambda+\delta_1}\right] = 1; \tag{3.54}$$

that is,

$$C^0(\lambda) = 1, \tag{3.55}$$

where

$$C^0(\lambda) = \frac{[\bar{\xi}_{1,\lambda} T_1^0 \beta_1 N_2 \delta_2][\bar{\xi}_{2,\lambda} T_2^0 \beta_2 N_1 \delta_1]}{(\lambda+\mu_V)^2(\lambda+\delta_1)(\lambda+\delta_2)\left[1 - \frac{\beta_2 \bar{\xi}_{2,\lambda} T_2^0 N_2 \delta_2}{(\lambda+\mu_V)(\lambda+\delta_2)} - \frac{\bar{\xi}_{2,\lambda} T_2^0 \kappa_2}{\lambda+\delta_2}\right]} + \left[\frac{\beta_1 \bar{\xi}_{1,\lambda} T_1^0 N_1 \delta_1}{(\lambda+\mu_V)(\lambda+\delta_1)} + \frac{\bar{\xi}_{1,\lambda} T_1^0 \kappa_1}{\lambda+\delta_1}\right].$$

Let

$$A_0(\lambda) = \frac{[T_1^0 \beta_1 N_2 \delta_2][T_2^0 \beta_2 N_1 \delta_1]\bar{\xi}_{1,\lambda}\bar{\xi}_{2,\lambda}}{(\lambda+\mu_V)^2(\lambda+\delta_1)(\lambda+\delta_2)}, \quad A_1(\lambda) = \bar{\xi}_{1,\lambda}\left(\frac{\beta_1 N_1 \delta_1}{(\lambda+\mu_V)(\lambda+\delta_1)} + \frac{\kappa_1}{\lambda+\delta_1}\right)T_1^0 \quad \text{and}$$

$$A_2(\lambda) = \bar{\xi}_{2,\lambda}\left(\frac{\beta_2 N_2 \delta_2}{(\lambda+\mu_V)(\lambda+\delta_2)} + \frac{\kappa_2}{\lambda+\delta_2}\right)T_2^0,$$

so that

$$C^0(\lambda) = \frac{A_0(\lambda)}{1 - A_2(\lambda)} + A_1(\lambda). \tag{3.56}$$

To find the solutions λ that satisfy the characteristic equation (3.55), we consider the following cases.

3.4.1 Case 1 ($\lambda \in \mathbb{R}$):

Consider the Caputo derivative of $C^0(\lambda)$ with respect to λ,

$${}^C D_\lambda^\nu C^0(\lambda) = I^{1-\nu} D_\lambda C^0(\lambda) = I^{1-\nu} D_\lambda \left[\frac{A_0(\lambda)}{1 - A_2(\lambda)} + A_1(\lambda)\right].$$

We compute $D_\lambda[C^0(\lambda)]$ as follows,

$$\begin{aligned}D_\lambda\bigg[\frac{A_0(\lambda)}{1-A_2(\lambda)}+A_1(\lambda)\bigg] =&\frac{D_\lambda[A_0(\lambda)](1-A_2(\lambda))-A_1(\lambda)D_\lambda[1-A_2(\lambda)]}{(1-A_2(\lambda))^2}\\ &+D_\lambda[A_1(\lambda)]\\ =&\frac{D_\lambda[A_0(\lambda)](1-A_2(\lambda))+A_0(\lambda)D_\lambda[A_2(\lambda)]}{(1-A_2(\lambda))^2}\\ &+D_\lambda[A_1(\lambda)],\end{aligned}$$

which reduces to

$$D_\lambda\bigg[\frac{A_0(\lambda)}{1-A_2(\lambda)}+A_1(\lambda)\bigg]=\frac{D_\lambda[A_0(\lambda)]}{1-A_2(\lambda)}+\frac{A_0(\lambda)}{(1-A_2(\lambda))^2}D_\lambda[A_2(\lambda)]+D_\lambda[A_1(\lambda)]. \quad (3.57)$$

We observe that,

$$\begin{aligned}D_\lambda[A_1(\lambda)] =&D_\lambda\bigg[\frac{\bar{\xi}_{1,\lambda}}{\lambda+\delta_1}\bigg(\frac{\beta_1N_1\delta_1}{\lambda+\mu_V}+\kappa_1\bigg)T_1^0\bigg]\\ =&D_\lambda\bigg[\frac{\bar{\xi}_{1,\lambda}}{\lambda+\delta_1}\bigg]\bigg(\frac{\beta_1N_1\delta_1}{\lambda+\mu_V}+\kappa_1\bigg)T_1^0+\bigg(\frac{\bar{\xi}_{1,\lambda}}{\lambda+\delta_1}\bigg)D_\lambda\bigg[\frac{\beta_1N_1\delta_1}{\lambda+\mu_V}+\kappa_1\bigg]T_1^0\\ =&\bigg(\frac{D_\lambda[\bar{\xi}_{1,\lambda}](\lambda+\delta_1)-\bar{\xi}_{1,\lambda}D_\lambda[\lambda+\delta_1]}{(\lambda+\delta_1)^2}\bigg)\bigg(\frac{\beta_1N_1\delta_1}{\lambda+\mu_V}+\kappa_1\bigg)T_1^0\\ &-\bigg(\frac{\bar{\xi}_{1,\lambda}}{\lambda+\delta_1}\bigg)\frac{\beta_1N_1\delta_1}{(\lambda+\mu_V)^2}T_1^0\\ =&\bigg(\frac{D_\lambda[\bar{\xi}_{1,\lambda}](\lambda+\delta_1)-\bar{\xi}_{1,\lambda}}{(\lambda+\delta_1)^2}\bigg)\bigg(\frac{\beta_1N_1\delta_1}{\lambda+\mu_V}+\kappa_1\bigg)T_1^0-\bigg(\frac{\bar{\xi}_{1,\lambda}}{\lambda+\delta_1}\bigg)\frac{\beta_1N_1\delta_1}{(\lambda+\mu_V)^2}T_1^0.\end{aligned}$$

Computing the derivative of $\bar{\xi}_{1,\lambda}$ yields,

$$\begin{aligned}D_\lambda[\bar{\xi}_{1,\lambda}] &= D_\lambda[1+\xi_{1,\lambda}f_1-f_1]\\ &= f_1D_\lambda\bigg[\int_0^\infty \alpha_1(a)\sigma_{1,\lambda}(a)da\bigg]\\ &= f_1D_\lambda\bigg[\int_0^\infty \frac{\alpha_1(a)}{1+\frac{a^\nu(m_1(a)+\lambda)}{\Gamma(\nu+1)}}da\bigg]\\ &= -f_1\int_0^\infty \frac{\alpha_1(a)a^\nu}{\Gamma(\nu+1)\Big(1+\frac{a^\nu(m_1(a)+\lambda)}{\Gamma(\nu+1)}\Big)^2}da,\end{aligned}$$

which leads to

$$D_\lambda[\bar{\xi}_{1,\lambda}] = -f_1\int_0^\infty \frac{\alpha_1(a)a^\nu}{\Gamma(\nu+1)}\sigma_{1,\lambda}^2(a)da = -f_1||\gamma_{1,\lambda}||_1,$$

where

$$\gamma_{1,\lambda}(a) = \frac{\alpha_1(a)a^{\nu}}{\Gamma(\nu+1)}\sigma^2_{1,\lambda}(a).$$

Therefore it follows that,

$$D_\lambda[A_1(\lambda)] = \Big(-f_1||\gamma_{1,\lambda}||_1 - \frac{\bar{\xi}_{1,\lambda}}{\lambda+\delta_1}\Big)\Big(\frac{\beta_1 N_1\delta_1}{\lambda+\mu_V}+\kappa_1\Big)T_1^0 - \Big(\frac{\bar{\xi}_{1,\lambda}}{\lambda+\delta_1}\Big)\frac{\beta_1 N_1 \delta_1}{(\lambda+\mu_V)^2}T_1^0,$$

that is,

$$\begin{aligned} D_\lambda[A_1(\lambda)] = -&\Bigg[\Big(f_1||\gamma_{1,\lambda}||_1 + \frac{\bar{\xi}_{1,\lambda}}{\lambda+\delta_1}\Big)\Big(\frac{\beta_1 N_1\delta_1}{\lambda+\mu_V}+\kappa_1\Big)T_1^0 \\ &+\Big(\frac{\bar{\xi}_{1,\lambda}}{\lambda+\delta_1}\Big)\frac{\beta_1 N_1\delta_1}{(\lambda+\mu_V)^2}T_1^0\Bigg] < 0, \end{aligned} \tag{3.58}$$

provided $\lambda+\delta_1 > 0$ and $\lambda+\mu_V>0$. Similarly, we have

$$\begin{aligned} D_\lambda[A_2(\lambda)] = -&\Bigg[\Big(f_2||\gamma_{2,\lambda}||_1 + \frac{\bar{\xi}_{2,\lambda}}{\lambda+\delta_2}\Big)\Big(\frac{\beta_2 N_2\delta_2}{\lambda+\mu_V}+\kappa_2\Big)T_2^0 \\ &+\Big(\frac{\bar{\xi}_{2,\lambda}}{\lambda+\delta_2}\Big)\frac{\beta_2 N_2\delta_2}{(\lambda+\mu_V)^2}T_2^0\Bigg] < 0, \end{aligned} \tag{3.59}$$

where

$$\gamma_{2,\lambda}(b) = \frac{\alpha_2(b)b^{\nu}}{\Gamma(\nu+1)}\sigma^2_{2,\lambda}(b),$$

provided $\lambda+\delta_2>0$ and $\lambda+\mu_V>0$.

The derivative of $A_0(\lambda)$ is given as,

$$\begin{aligned} D_\lambda[A_0(\lambda)] = &D_\lambda\Bigg[\frac{[T_1^0\beta_1 N_2\delta_2][T_2^0\beta_2 N_1\delta_1]\bar{\xi}_{1,\lambda}\bar{\xi}_{2,\lambda}}{(\lambda+\mu_V)^2(\lambda+\delta_1)(\lambda+\delta_2)}\Bigg] \\ =&\frac{[T_1^0\beta_1 N_2\delta_2][T_2^0\beta_2 N_1\delta_1]}{(\lambda+\mu_V)^4(\lambda+\delta_1)^2(\lambda+\delta_2)^2}(D_\lambda[\bar{\xi}_{1,\lambda}\bar{\xi}_{2,\lambda}](\lambda+\mu_V)^2(\lambda+\delta_1)(\lambda+\delta_2) \\ &-\bar{\xi}_{1,\lambda}\bar{\xi}_{2,\lambda}D_\lambda[(\lambda+\mu_V)^2(\lambda+\delta_1)(\lambda+\delta_2)]). \end{aligned}$$

Therefore from

$$\begin{aligned} D_\lambda[\bar{\xi}_{1,\lambda}\bar{\xi}_{2,\lambda}] &= D_\lambda[\bar{\xi}_{1,\lambda}]\bar{\xi}_{2,\lambda} + \bar{\xi}_{1,\lambda}D_\lambda[\bar{\xi}_{2,\lambda}] \\ &= -(f_1||\gamma_{1,\lambda}||_1\bar{\xi}_{2,\lambda} + \bar{\xi}_{1,\lambda}f_2||\gamma_{2,\lambda}||_1) < 0, \end{aligned}$$

and

$$D_\lambda[(\lambda+\mu_V)^2(\lambda+\delta_1)(\lambda+\delta_2)] = D_\lambda[(\lambda)^2](\lambda+\delta_1)(\lambda+\delta_2)$$

$$\begin{aligned}&+(\lambda+\mu_V)^2 D_\lambda[(\lambda+\delta_1)(\lambda+\delta_2)]\\ =&2(\lambda+\mu_V)(\lambda+\delta_1)(\lambda+\delta_2)\\ &+(\lambda+\mu_V)^2[(\lambda+\delta_2)+(\lambda+\delta_1)]\\ >&0,\end{aligned}$$

it follows that,

$$\begin{aligned}-(f_1||\gamma_{1,\lambda}||_1\bar{\xi}_{2,\lambda}+\bar{\xi}_{1,\lambda}f_2||\gamma_{2,\lambda}||_1)(\lambda+\mu_V)^2(\lambda+\delta_1)(\lambda+\delta_2)&\\ -\bar{\xi}_{1,\lambda}\bar{\xi}_{2,\lambda}D_\lambda[(\lambda+\mu_V)^2(\lambda+\delta_1)(\lambda+\delta_2)]&<0,\end{aligned}$$

and hence, $D_\lambda[A_0(\lambda)]<0$. We have

$$\frac{A_0(\lambda)}{(1-A_2(\lambda))^2}D_\lambda[A_2(\lambda)]+D_\lambda[A_1(\lambda)]<0,$$

and hence we observe that

$$D_\lambda[C^0(\lambda)]=\frac{D_\lambda[A_0(\lambda)]}{1-A_2(\lambda)}+\frac{A_0(\lambda)}{(1-A_2(\lambda))^2}D_\lambda[A_2(\lambda)]+D_\lambda[A_1(\lambda)].$$

Therefore

$$D_\lambda[C^0(\lambda)]<0 \quad \text{if and only if} \quad 1-A_2(\lambda)>0. \tag{3.60}$$

It follows that $C^0(\lambda)$ is a decreasing function of λ whenever $A_2(\lambda)<1$. Let λ^* be a solution to the characteristic equation such that

$$1>C^0(0) \quad \text{whenever} \quad \lambda^*<0 \quad \text{and} \quad C^0(0)>1 \quad \text{whenever} \quad \lambda^*>0.$$

For $\lambda^*<0$, we have

$$\frac{A_0(0)}{1-A_2(0)}+A_1(0)<1;$$

which implies

$$0<A_0(0)<(1-A_1(0))(1-A_2(0)). \tag{3.61}$$

It follows that, either $A_1(0)<1 \quad \text{and} \quad A_2(0)<1$ or $A_1(0)>1 \quad \text{and} \quad A_2(0)>1$.
Equivalently, either $\mathcal{R}_1<1 \quad \text{and} \quad \mathcal{R}_2<1$ or $\mathcal{R}_1>1 \quad \text{and} \quad \mathcal{R}_2>1$.
It follows from

$$\arg(\lambda^*)=\pi>\frac{\pi\nu}{2} \quad \text{for all} \quad \nu\in(0,1),$$

that E^0 is locally asymptotically stable whenever either $\mathcal{R}_1 < 1 \quad \text{and} \quad \mathcal{R}_2 < 1$ or $\mathcal{R}_1 > 1 \quad \text{and} \quad \mathcal{R}_2 > 1$. However, only the condition $\mathcal{R}_1 < 1 \quad \text{and} \quad \mathcal{R}_2 < 1$ is biologically feasible and the condition $\mathcal{R}_1 > 1 \quad \text{and} \quad \mathcal{R}_2 > 1$ is neglected.

Likewise, for $\lambda^* > 0$, we have

$$\frac{A_0(0)}{1 - A_2(0)} + A_1(0) > 1;$$

which implies

$$A_0(0) > (1 - A_1(0))(1 - A_2(0)).$$

It follows that, either

$$A_1(0) > 1 \quad \text{and} \quad A_2(0) < 1$$

or

$$A_1(0) < 1 \quad \text{and} \quad A_2(0) > 1.$$

Equivalently, either

$$\mathcal{R}_1 > 1 \quad \text{and} \quad \mathcal{R}_2 < 1$$

or

$$\mathcal{R}_1 < 1 \quad \text{and} \quad \mathcal{R}_2 > 1.$$

It follows from

$$\arg(\lambda^*) = 0 < \frac{\pi\nu}{2} \quad \text{for all} \quad \nu \in (0, 1),$$

that E^0 is unstable whenever either $\mathcal{R}_1 < 1 \quad \text{and} \quad \mathcal{R}_2 < 1$ or $\mathcal{R}_1 > 1 \quad \text{and} \quad \mathcal{R}_2 > 1$.

3.4.2 Case 2 ($\lambda \in \mathbb{C}$):

Let $\lambda = x + \iota y$ with $y \neq 0$. Consider the following,

$$\bar{\xi}_{1,xy} = 1 + \xi_{1,xy} f_1 - f_1,$$

which yields

$$\bar{\xi}_{1,xy} = 1 - f_1 + f_1 \int_0^\infty \frac{\alpha_1(a)}{1 + \frac{a^\nu (m_1(a) + x + \iota y)}{\Gamma(\nu+1)}} da,$$

$$= 1 - f_1 + f_1 \int\limits_0^\infty \frac{\alpha_1(a)}{1 + \frac{a^\nu (m_1(a)+x)}{\Gamma(\nu+1)} + \iota \frac{a^\nu y}{\Gamma(\nu+1)}} da,$$

$$= 1 - f_1 + f_1 \int\limits_0^\infty \frac{\alpha_1(a)\left[1 + \frac{a^\nu (m_1(a)+x)}{\Gamma(\nu+1)} - \iota \frac{a^\nu y}{\Gamma(\nu+1)}\right]}{\left(1 + \frac{a^\nu (m_1(a)+x)}{\Gamma(\nu+1)}\right)^2 + \left(\frac{a^\nu y}{\Gamma(\nu+1)}\right)^2} da$$

this leads to

$$\begin{aligned}\bar{\xi}_{1,xy} =& 1 - f_1 + f_1 \int\limits_0^\infty \frac{\alpha_1(a)\left[1 + \frac{a^\nu (m_1(a)+x)}{\Gamma(\nu+1)}\right]}{\left(1 + \frac{a^\nu (m_1(a)+x)}{\Gamma(\nu+1)}\right)^2 + \left(\frac{a^\nu y}{\Gamma(\nu+1)}\right)^2} da \\ & - \iota f_1 \int\limits_0^\infty \alpha_1(a) \frac{\left[\frac{a^\nu y}{\Gamma(\nu+1)}\right]}{\left(1 + \frac{a^\nu (m_1(a)+x)}{\Gamma(\nu+1)}\right)^2 + \left(\frac{a^\nu y}{\Gamma(\nu+1)}\right)^2} da \\ =& D_{1,xy} - \iota E_{1,xy},\end{aligned}$$

where

$$D_{1,xy} = 1 - f_1 + f_1 \int\limits_0^\infty \frac{\alpha_1(a)\left[1 + \frac{a^\nu (m_1(a)+x)}{\Gamma(\nu+1)}\right]}{\left(1 + \frac{a^\nu (m_1(a)+x)}{\Gamma(\nu+1)}\right)^2 + \left(\frac{a^\nu y}{\Gamma(\nu+1)}\right)^2} da,$$

and

$$E_{1,xy} = f_1 \int\limits_0^\infty \frac{\alpha_1(a)\left[\frac{a^\nu y}{\Gamma(\nu+1)}\right]}{\left(1 + \frac{a^\nu (m_1(a)+x)}{\Gamma(\nu+1)}\right)^2 + \left(\frac{a^\nu y}{\Gamma(\nu+1)}\right)^2} da.$$

Similarly, $\bar{\xi}_{2,xy} = D_{2,xy} - \iota E_{2,xy}$, where

$$D_{2,xy} = 1 - f_2 + f_2 \int_0^\infty \frac{\alpha_2(b)\left[1 + \frac{b^\nu (m_2(b)+x)}{\Gamma(\nu+1)}\right]}{\left(1 + \frac{b^\nu (m_2(b)+x)}{\Gamma(\nu+1)}\right)^2 + \left(\frac{b^\nu y}{\Gamma(\nu+1)}\right)^2} db,$$

and

$$E_{2,xy} = f_2 \int_0^\infty \frac{\alpha_2(b)\left[\frac{b^\nu y}{\Gamma(\nu+1)}\right]}{\left(1 + \frac{b^\nu (m_2(b)+x)}{\Gamma(\nu+1)}\right)^2 + \left(\frac{b^\nu y}{\Gamma(\nu+1)}\right)^2} db.$$

It follows that,

$$\begin{aligned}
A_1(x+\iota y) =& \frac{D_{1,xy} - \iota E_{1,xy}}{(x+\delta_1)+\iota y}\left(\frac{\beta_1 N_1 \delta_1}{(x+\mu_V)+\iota y} + \kappa_1\right)T_1^0 \\
=& \frac{(D_{1,xy} - \iota E_{1,xy})((x+\delta_1)-\iota y)}{(x+\delta_1)^2+y^2}\left(\frac{\beta_1 N_1 \delta_1((x+\mu_V)-\iota y)}{(x+\mu_V)^2+y^2} + \kappa_1\right)T_1^0 \\
=& \frac{(D_{1,xy}(x+\delta_1) + E_{1,xy}y) - \iota(E_{1,xy}(x+\delta_1) + D_{1,xy}y)}{(x+\delta_1)^2+y^2}\left(\frac{\beta_1 N_1 \delta_1 (x+\mu_V)}{(x+\mu_V)^2+y^2}\right. \\
&\left. + \kappa_1 - \iota \frac{\beta_1 N_1 \delta_1 y}{(x+\mu_V)^2+y^2}\right)T_1^0 \\
=& \frac{D_{1,xy}(x+\delta_1) + E_{1,xy}y}{(x+\delta_1)^2+y^2}\left(\frac{\beta_1 N_1 \delta_1 (x+\mu_V)}{(x+\mu_V)^2+y^2} + \kappa_1 - \iota \frac{\beta_1 N_1 \delta_1 y}{(x+\mu_V)^2+y^2}\right)T_1^0 - \\
& \iota \frac{E_{1,xy}(x+\delta_1) + D_{1,xy}y}{(x+\delta_1)^2+y^2}\left(\frac{\beta_1 N_1 \delta_1 (x+\mu_V)}{(x+\mu_V)^2+y^2} + \kappa_1 - \iota \frac{\beta_1 N_1 \delta_1 y}{(x+\mu_V)^2+y^2}\right)T_1^0
\end{aligned}$$

which yields

$$\begin{aligned}
A_1(x+\iota y) =& \left[\frac{D_{1,xy}(x+\delta_1) + E_{1,xy}y}{(x+\delta_1)^2+y^2}\left(\frac{\beta_1 N_1 \delta_1 (x+\mu_V)}{(x+\mu_V)^2+y^2} + \kappa_1\right)T_1^0\right. \\
& \left. - \frac{E_{1,xy}(x+\delta_1) + D_{1,xy}y}{(x+\delta_1)^2+y^2}\left(\frac{\beta_1 N_1 \delta_1 y}{(x+\mu_V)^2+y^2}\right)T_1^0\right] \\
& - \iota\left[\frac{D_{1,xy}(x+\delta_1) + E_{1,xy}y}{(x+\delta_1)^2+y^2}\left(\frac{\beta_1 N_1 \delta_1 y}{(x+\mu_V)^2+y^2}\right)T_1^0\right. \\
& \left. + \frac{E_{1,xy}(x+\delta_1) + D_{1,xy}y}{(x+\delta_1)^2+y^2}\left(\frac{\beta_1 N_1 \delta_1 (x+\mu_V)}{(x+\mu_V)^2+y^2} + \kappa_1\right)T_1^0\right]
\end{aligned}$$

$$=F_{1,xy} - \iota G_{1,xy},$$

where

$$\begin{aligned} F_{1,xy} =& \frac{D_{1,xy}(x+\delta_1) + E_{1,xy}y}{(x+\delta_1)^2+y^2}\left(\frac{\beta_1 N_1 \delta_1 (x+\mu_V)}{(x+\mu_V)^2+y^2} + \kappa_1\right)T_1^0 - \frac{E_{1,xy}(x+\delta_1) + D_{1,xy}y}{(x+\delta_1)^2+y^2} \\ & \left(\frac{\beta_1 N_1 \delta_1 y}{(x+\mu_V)^2+y^2}\right)T_1^0, \end{aligned}$$

and

$$\begin{aligned} G_{1,xy} =& \frac{D_{1,xy}(x+\delta_1) + E_{1,xy}y}{(x+\delta_1)^2+y^2}\left(\frac{\beta_1 N_1 \delta_1 y}{(x+\mu_V)^2+y^2}\right)T_1^0 + \frac{E_{1,xy}(x+\delta_1) + D_{1,xy}y}{(x+\delta_1)^2+y^2} \\ & \left(\frac{\beta_1 N_1 \delta_1 (x+\mu_V)}{(x+\mu_V)^2+y^2} + \kappa_1\right)T_1^0. \end{aligned}$$

Similarly we obtain,

$$A_2(x+\iota y) = F_{2,xy} - \iota G_{2,xy},$$

where

$$\begin{aligned} F_{2,xy} =& \frac{D_{2,xy}(x+\delta_2) + E_{2,xy}y}{(x+\delta_2)^2+y^2}\left(\frac{\beta_2 N_2 \delta_2 (x+\mu_V)}{(x+\mu_V)^2+y^2} + \kappa_2\right)T_2^0 - \frac{E_{2,xy}(x+\delta_2) + D_{2,xy}y}{(x+\delta_2)^2+y^2} \\ & \left(\frac{\beta_2 N_2 \delta_2 y}{(x+\mu_V)^2+y^2}\right)T_2^0, \end{aligned}$$

and

$$\begin{aligned} G_{2,xy} =& \frac{D_{2,xy}(x+\delta_2) + E_{2,xy}y}{(x+\delta_2)^2+y^2}\left(\frac{\beta_2 N_2 \delta_2 y}{(x+\mu_V)^2+y^2}\right)T_2^0 + \frac{E_{2,xy}(x+\delta_2) + D_{2,xy}y}{(x+\delta_2)^2+y^2} \\ & \left(\frac{\beta_2 N_2 \delta_2 (x+\mu_V)}{(x+\mu_V)^2+y^2} + \kappa_2\right)T_2^0. \end{aligned}$$

Suppose $A_0(x+\iota y) = H_{xy} + \iota I_{xy}$, then it follows from (3.56) that,

$$\begin{aligned} C^0(x+\iota y) =& \frac{H_{xy} + \iota I_{xy}}{1 - F_{2,xy} + \iota G_{2,xy}} + F_{1,xy} + \iota G_{1,xy} \\ =& \frac{(H_{xy} + \iota I_{xy})(1 - F_{2,xy} - \iota G_{2,xy})}{(1-F_{2,xy})^2 + G_{2,xy}^2} + F_{1,xy} + \iota G_{1,xy} \\ =& \frac{[H_{xy}(1-F_{2,xy}) + I_{xy}G_{2,xy}] + \iota[I_{xy}(1-F_{2,xy}) - H_{xy}G_{2,xy}]}{(1-F_{2,xy})^2 + G_{2,xy}^2} \\ & + F_{1,xy} + \iota G_{1,xy} \end{aligned}$$

$$=\left[\frac{H_{xy}(1-F_{2,xy})+I_{xy}G_{2,xy}}{(1-F_{2,xy})^2+G_{2,xy}^2}+F_{1,xy}\right]$$
$$+\iota\left[G_{1,xy}+\frac{I_{xy}(1-F_{2,xy})-H_{xy}G_{2,xy}}{(1-F_{2,xy})^2+G_{2,xy}^2}\right],$$

That is,

$$C^0(x+\iota y)=\Re C^0(x+\iota y)+\iota\Im C^0(x+\iota y),$$

where

$$\Re C^0(x+\iota y)=\frac{H_{xy}(1-F_{2,xy})+I_{xy}G_{2,xy}}{(1-F_{2,xy})^2+G_{2,xy}^2}+F_{1,xy}, \tag{3.62}$$

and

$$\Im C^0(x+\iota y)=G_{1,xy}+\frac{I_{xy}(1-F_{2,xy})-H_{xy}G_{2,xy}}{(1-F_{2,xy})^2+G_{2,xy}^2}. \tag{3.63}$$

Thus it follows from (3.55) that, $\Re C^0(x+\iota y)=1$ and $\Im C^0(x+\iota y)=0$. Therefore, we obtain

$$H_{xy}=G_{1,xy}G_{2,xy}+(1-F_{1,xy})(1-F_{2,xy}),$$

and

$$I_{xy}=G_{2,xy}(1-F_{1,xy})-G_{1,xy}(1-F_{2,xy}).$$

Consider the argument of $C^0(x+\iota y)$ given by,

$$\arg(C^0(x+\iota y))=\arg\left(\frac{A_0(x+\iota y)}{1-A_2(x+\iota y)}+A_1(x+\iota y)\right)$$
$$=\arg\left(\frac{A_0(x+\iota y)+A_1(x+\iota y)(1-A_2(x+\iota y))}{1-A_2(x+\iota y)}\right).$$

Since

$$\arg(C^0(x+\iota y))=\arctan\left(\frac{\Im C^0(x+\iota y)}{\Re C^0(x+\iota y)}\right)=0+k\pi,\quad \text{where}\quad k\in\mathbb{Z},$$

it follows that

$$\arg\{A_0(x+\iota y)+A_1(x+\iota y)(1-A_2(x+\iota y))\}=\arg\{1-A_2(x+\iota y)\}+k\pi.$$

Equivalently,

$$\arg\{H_{xy}+F_{1,xy}(1-F_{2,xy})+G_{1,xy}G_{2,xy}+\iota(I_{xy}+F_{1,xy}G_{2,xy}-G_{1,xy}(1-F_{2,xy}))\}$$
$$=\arg\{1-F_{2,xy}+\iota G_{2,xy}\}+k\pi,$$

that is,

$$\arctan\left(\frac{H_{xy}+F_{1,xy}(1-F_{2,xy})+G_{1,xy}G_{2,xy}}{I_{xy}+F_{1,xy}G_{2,xy}-G_{1,xy}(1-F_{2,xy})}\right)=\arctan\left(\frac{G_{2,xy}}{1-F_{2,xy}}\right)+k\pi.$$

Hence

$$\tan\left[\arctan\left(\frac{H_{xy}+F_{1,xy}(1-F_{2,xy})+G_{1,xy}G_{2,xy}}{I_{xy}+F_{1,xy}G_{2,xy}-G_{1,xy}(1-F_{2,xy})}\right)\right]=\tan\left[\arctan\left(\frac{G_{2,xy}}{1-F_{2,xy}}\right)+k\pi\right],$$

yields

$$\frac{H_{xy}+F_{1,xy}(1-F_{2,xy})+G_{1,xy}G_{2,xy}}{I_{xy}+F_{1,xy}G_{2,xy}-G_{1,xy}(1-F_{2,xy})}=\frac{G_{2,xy}}{1-F_{2,xy}}.$$

Substituting H_{xy} and I_{xy} yields,

$$(1-F_{2,xy})(G_{2,xy}-2G_{1,xy}(1-F_{2,xy}))=G_{2,xy}(1-F_{2,xy}+2G_{1,xy}G_{2,xy}),$$

this leads to

$$2G_{1,xy}((1-F_{2,xy})^2+G_{2,xy}^2)=0,$$

therefore $G_{1,xy}=0$. Consequently we have,

$$A_1(x+\iota y)=F_{1,xy},\quad H_{xy}=(1-F_{1,xy})(1-F_{2,xy})\quad\text{and}\quad I_{xy}=G_{2,xy}(1-F_{1,xy}).$$

Furthermore,

$$\begin{aligned}G_{1,xy}=&\frac{D_{1,xy}(x+\delta_1)+E_{1,xy}y}{(x+\delta_1)^2+y^2}\left(\frac{\beta_1N_1\delta_1y}{(x+\mu_V)^2+y^2}\right)T_1^0\\&+\frac{E_{1,xy}(x+\delta_1)+D_{1,xy}y}{(x+\delta_1)^2+y^2}\left(\kappa_1+\frac{\beta_1N_1\delta_1(x+\mu_V)}{(x+\mu_V)^2+y^2}\right)T_1^0=0.\end{aligned}$$

That is,

$$\begin{aligned}(D_{1,xy}(x+\delta_1)+E_{1,xy}y)(\beta_1N_1\delta_1y)+&[E_{1,xy}(x+\delta_1)+D_{1,xy}y]\\&\times[\beta_1N_1\delta_1(x+\mu_V)+\kappa_1((x+\mu_V)^2+y^2)]=0,\end{aligned}$$

which leads to

$$\begin{aligned}&D_{1,xy}y\{\beta_1N_1\delta_1(2x+\mu_V+\delta_1)+\kappa_1[(x+\mu_V)^2+y^2]\}+E_{1,xy}\{\beta_1N_1\delta_1[y^2+(x+\delta_1)(x+\mu_V)]\\&+\kappa_1(x+\delta_1)[(x+\mu_V)^2+y^2]\}=0.\end{aligned}$$

It follows that,

$$\begin{aligned} D_{1,xy}y\{\beta_1 N_1\delta_1(2x+\mu_V+\delta_1)+\kappa_1[(x+\mu_V)^2+y^2]\} =& -E_{1,xy}\{\beta_1 N_1\delta_1[y^2 \\ &+(x+\delta_1)(x+\mu_V)] \\ &+\kappa_1(x+\delta_1)[(x+\mu_V)^2+y^2]\}. \end{aligned}$$

Observe that,

$$E_{1,xy}y = f_1\int\limits_0^\infty \frac{\alpha_1(a)\left[\frac{a^\nu y^2}{\Gamma(\nu+1)}\right]}{\left(1+\frac{a^\nu(m_1(a)+x)}{\Gamma(\nu+1)}\right)^2+\left(\frac{a^\nu y}{\Gamma(\nu+1)}\right)^2}da > 0,$$

therefore from

$$\begin{aligned} D_{1,xy}y^2\{\beta_1 N_1\delta_1(2x+\mu_V+\delta_1)+\kappa_1[(x+\mu_V)^2+y^2]\} =& -E_{1,xy}y\{\beta_1 N_1\delta_1[y^2 \\ &+(x+\delta_1)(x+\mu_V)] \\ &+\kappa_1(x+\delta_1)[(x+\mu_V)^2+y^2]\} < 0, \end{aligned}$$

we obtain $D_{1,xy} < 0$. Consequently we have,

$$D_{1,xy} = 1-f_1+f_1\int\limits_0^\infty \frac{\alpha_1(a)\left[1+\frac{a^\nu(m_1(a)+x)}{\Gamma(\nu+1)}\right]}{\left(1+\frac{a^\nu(m_1(a)+x)}{\Gamma(\nu+1)}\right)^2+\left(\frac{a^\nu y}{\Gamma(\nu+1)}\right)^2}da < 0,$$

that is,

$$1-f_1+f_1\int\limits_0^\infty \frac{\alpha_1(a)\left[1+\frac{a^\nu(m_1(a)+x)}{\Gamma(\nu+1)}\right]}{\left(1+\frac{a^\nu(m_1(a)+x)}{\Gamma(\nu+1)}\right)^2+\left(\frac{a^\nu y}{\Gamma(\nu+1)}\right)^2}da = 1-f_1+f_1\int\limits_0^\infty \alpha_1(a)\times$$

$$\frac{\left[1+\frac{a^\nu m_1(a)}{\Gamma(\nu+1)}\right]}{\left(1+\frac{a^\nu(m_1(a)+x)}{\Gamma(\nu+1)}\right)^2+\left(\frac{a^\nu y}{\Gamma(\nu+1)}\right)^2}da + xf_1\int\limits_0^\infty \frac{\alpha_1(a)\frac{a^\nu}{\Gamma(\nu+1)}}{\left(1+\frac{a^\nu(m_1(a)+x)}{\Gamma(\nu+1)}\right)^2+\left(\frac{a^\nu y}{\Gamma(\nu+1)}\right)^2}da,$$

therefore

$$1 - f_1 + f_1 \int\limits_0^\infty \frac{\alpha_1(a)\left[1 + \frac{a^\nu (m_1(a)+x)}{\Gamma(\nu+1)}\right]}{\left(1 + \frac{a^\nu (m_1(a)+x)}{\Gamma(\nu+1)}\right)^2 + \left(\frac{a^\nu y}{\Gamma(\nu+1)}\right)^2} da = 1 - f_1 + ||J_{1,xy}||_1 + x||K_{1,xy}||_1 < 0,$$

where

$$J_{1,xy}(a) = f_1 \frac{\alpha_1(a)\left[1 + \frac{a^\nu m_1(a)}{\Gamma(\nu+1)}\right]}{\left(1 + \frac{a^\nu (m_1(a)+x)}{\Gamma(\nu+1)}\right)^2 + \left(\frac{a^\nu y}{\Gamma(\nu+1)}\right)^2},$$

and

$$K_{1,xy}(a) = f_1 \frac{\alpha_1(a)\frac{a^\nu}{\Gamma(\nu+1)}}{\left(1 + \frac{a^\nu (m_1(a)+x)}{\Gamma(\nu+1)}\right)^2 + \left(\frac{a^\nu y}{\Gamma(\nu+1)}\right)^2}.$$

Hence we obtain,

$$x < -\frac{1 - f_1 + ||J_{1,xy}||_1}{||K_{1,xy}||_1} < 0. \tag{3.64}$$

It follows that $|\arg(x + \iota y)| \in (\frac{\pi}{2}, \pi)$, that is,

$$|\arg(x + \iota y)| > \frac{\pi\nu}{2}, \quad \text{for all} \quad \nu \in (0, 1).$$

Therefore E^0 is locally asymptotically stable. $\square$

The local asymptotic stability of the disease-free equilibrium, E^0, is determined by the reproduction number through each cell type in Case 1 while it is determined by a characteristic equation in Case 2.

Chapter 4

Caputo-Fabrizio fractional model for an age structured population dynamics of an HIV and TB co-epidemic

This chapter focuses on a model of an HIV and TB co-epidemic in a population with age structure. We consider various aspects of the model which are investigated in four (4) sections as follows. The first discusses the formulation of the model, model parameters, and assumptions; whereas the second section explores the well-posedness of the model by investigating the positivity, boundedness, existence and uniqueness of solutions to the system of fractional differential equations. The third section studies the existence of equilibria and computation of the basic reproduction number. The fourth section explores the stability of the disease free equilibrium using the linearization technique.

4.1 Introduction

Co-epidemics occur when two or more diseases spreading in a community affect the dynamics of the other disease. Individuals in a population can become dually infected with these diseases in a state of co-infection, thus we consider the co-dynamics of the spread of HIV and TB since these diseases often co-exist within a population [Long, 2008], [Williams, 2017]. Community spread of HIV occurs primarily through sexual contact and through other activities that involve exchange of blood between individuals. HIV infection occurs in multiple stages within-host and the disease eventually progresses to AIDS when untreated. Treatment assists in controlling HIV infection, however no cure currently exists for the disease [Rhines, 2018]. TB is a bacterial infection which spreads primarily through the air. When susceptible individuals become infected with TB, they can either be latently infected, which means they are not infectious and TB lies dormant in their bodies, or actively infected and so they can spread the disease to others. Effective treatment options are available for TB and individuals infected TB usually recover from the disease as a result of treatment [Zhang, 2015]. Age structured models describing latently infected TB populations have been developed and studied [Xiaoyan, 2013]. The progression of HIV infection to AIDS weakens the immune system of an individual, thus making the body susceptible to opportunistic diseases such as TB. This can occur either through endogenous activation of latent TB within a HIV infective or infection of HIV infectives by TB as a result of a weakened immune system [Okhuese, 2020]. The co-epidemic of HIV and TB has recently become an area of interest for mathematical epidemiologist as these diseases are particularly dominant in society and TB is the leading cause of death in HIV infectives. In [Xiaoyan, 2013], a simplistic model was proposed which consists of first order hybrid system of differential equations investigating the dynamics of an HIV-TB co-epidemic. Their main concern is the effects of HIV and HIV-TB co-infection in the transmission dynamics of TB. Furthermore, they discuss various defects and limitations in the model. We do not address the issues discussed, however, we extend the model to fractional order system of differential equations and investigate the effects of TB on the dynamics of HIV.

4.1.1 Model formulations

We begin this section with the formulation of a model describing the coepidemic of Human Immuno-Deficiency Virus (HIV) and Tuberculosis (TB) in a population compartmentalized into Susceptibles (S), which are individuals susceptible to both diseases. Exposed (E) individuals structured by latency age of TB, TB infectious (I_1) and HIV infectious (I_2) individuals who are capable of transmitting TB to susceptibles and, HIV to susceptibles and TB infected individuals, respectively. It is assumed that exposed individuals do not infect others with the disease, which simplifies the dynamics of the co-epidemic. The compartment of jointly infected individuals is denoted by (J), which are individuals infected by both HIV and TB. The natural birth rate of the population is denoted by Λ while the death rate is denoted by μ. Susceptible individuals who have sufficient contact with individuals infected with active TB become latently infected at a rate of β_1. Susceptibles become infected with HIV at a rate of β_2 and HIV infectives who receive treatment return into the susceptible class at a rate of α_2. Individuals who are latently infected and actively infected TB receive treatment and return into the susceptible class at the rates $\alpha_0(a)$ and α_1, respectively. Latently infected individuals develop active TB at $\gamma(a)$, which varies with latency age. Progression of actively infected TB patients into the co-infected class occurs at a rate of δ_1 and progression of HIV infectives into co-infection due with active TB occurs at δ_2. It is assumed that infectives do not die from HIV only or active TB only, however co-infectives die at a rate η. Furthermore, it is assumed that co-infectives are incapable of recovery from, or transmission of either disease. The HIV-TB co-epidemic is modelled by the following system of Caputo-Fabrizio fractional differential equations of order ν:

$$ {}^{CF}D_t^{\nu}S(t) = \Lambda - \mu S(t) - \beta_1 S(t)I_1(t) - \beta_2 S(t)I_2(t) + \int\limits_0^{\infty} \alpha_0(a)e(a,t)da + \alpha_1 I_1(t) + \alpha_2 I_2(t), \tag{4.1} $$

$$ {}^{CF}\partial_t^{\nu}e(a,t) + {}^{CF}\partial_a^{\nu}e(a,t) = -(\mu + \gamma(a) + \alpha_0(a))e(a,t), \tag{4.2} $$

$$ {}^{CF}D_t^{\nu}I_1(t) = \int\limits_0^{\infty} \gamma(a)e(a,t)da - \mu I_1(t) - \alpha_1 I_1(t) - \delta_1 I_1(t)I_2(t), \tag{4.3} $$

$$ {}^{CF}D_t^{\nu} I_2(t) = \beta_2 S(t) I_2(t) - \mu I_2(t) - \alpha_2 I_2(t) - \delta_2 I_1(t) I_2(t), \tag{4.4} $$

$$ {}^{CF}D_t^{\nu} J(t) = \delta_1 I_1(t) I_2(t) + \delta_2 I_1(t) I_2(t) - \mu J(t) - \eta J(t), \tag{4.5} $$

with initial conditions $S(0) \in \mathbb{R}_+$, $e(a,0) = e_0(a) \in \mathbb{L}_+^1(0,\infty)$, $I_1(0) \in \mathbb{R}_+$, $I_2(0) \in \mathbb{R}_+$, $J(0) \in \mathbb{R}_+$ and boundary condition $e(0,t) = \beta_1 S(t) I_1(t)$. For $l \in \{a,t\}$, the Caputo-Fabrizio fractional derivative is given by

$$ {}^{CF}D_l^{\nu} f(l) = \frac{2M(\nu)}{(2-\nu)(1-\nu)} \int_0^l \frac{df(s)}{ds} \exp\left\{ -\frac{\nu}{1-\nu}(l-s) \right\} ds, $$

and the partial Caputo-Fabrizio fractional derivative is given by

$$ {}^{C}\partial_l^{\nu} f(l) = \frac{2M(\nu)}{(2-\nu)(1-\nu)} \int_0^l \frac{\partial f(s)}{\partial s} \exp\left\{ -\frac{\nu}{1-\nu}(l-s) \right\} ds, $$

where $M(\nu)$ is the order dependent normalization function and $\nu \in (0,1)$.

Model assumptions:

(B1) Λ, μ, β_1, β_2, α_1, α_2, δ_1, δ_2, $\eta \in (0,\infty)$.

(B2) $\alpha_0(a)$, $\gamma(a) \in \mathbb{L}_+^{\infty}(0,\infty)$.

4.2 Well-posedness of the model

4.2.1 Boundedness of solutions

Let $\mathbb{X} = \mathbb{R} \times \mathbb{L}^1(0,\infty) \times \mathbb{R}^3$ be a Banach space and consider the positive cone $\mathbb{X}_+ = \mathbb{R}_+ \times \mathbb{L}_+^1(0,\infty) \times \mathbb{R}_+^3$. Define a continuous function $\phi : \mathbb{R}_+ \times \mathbb{X}_+ \to \mathbb{X}_+$ given by:

$$ \phi(t, \psi(0)) = (S(t), e(a,t), I_1(t), I_2(t), J(t))^T = \psi(t), $$

with initial condition $\psi(0) = (S(0), e_0(a), I_1(0), I_2(0), J(0))^T$. Let $||\cdot||_{\mathbb{X}}$ be the norm defined on $\mathbb{X}$, we have

$$\begin{aligned}||\psi(t)||_{\mathbb{X}} &= |S(t)| + ||e(a,t)||_1 + |I_1(t)| + |I_2(t)| + |J(t)|,\\ &= S(t) + \int\limits_0^\infty e(a,t)da + I_1(t) + I_2(t) + J(t).\end{aligned}$$

The system of equations (4.1) - (4.5) can be re-written in the abstract form

$$^{CF}D_t^\nu \psi(t) = f(\psi(t)), \tag{4.6}$$

where

$$f(\psi(t)) := \begin{pmatrix} f_1(\psi(t)) \\ f_2(\psi(t)) \\ f_3(\psi(t)) \\ f_4(\psi(t)) \\ f_5(\psi(t)) \end{pmatrix} = \begin{pmatrix} f_1(\psi(t)) \\ -{}^{CF}\partial_a^\nu e(a,t) - (\mu + \gamma(a) + \alpha_0(a))e(a,t) \\ \int_0^\infty \gamma(a)e(a,t)da - \mu I_1(t) - \alpha_1 I_1(t) - \delta_1 I_1(t)I_2(t) \\ \beta_2 S(t)I_2(t) - \mu I_2(t) - \alpha_2 I_2(t) - \delta_2 I_1(t)I_2(t) \\ \delta_1 I_1(t)I_2(t) + \delta_2 I_1(t)I_2(t) - \mu J(t) - \eta J(t) \end{pmatrix},$$

where

$$f_1(\psi(t)) = \Lambda - \mu S(t) - \beta_1 S(t)I_1(t) - \beta_2 S(t)I_2(t) + \int\limits_0^\infty \alpha_0(a)e(a,t)da + \alpha_1 I_1(t) + \alpha_2 I_2(t).$$

Applying the Caputo-Fabrizio fractional derivative on (4.6) yields,

$$\begin{aligned}{}^{CF}D_t^\nu ||\psi(t)||_{\mathbb{X}} =& {}^{CF}D_t^\nu S(t) + \int\limits_0^\infty {}^{CF}\partial_t^\nu e(a,t)da + {}^{CF}D_t^\nu I_1(t) + {}^{CF}D_t^\nu I_2(t) + {}^{CF}D_t^\nu J(t),\\ =& \Lambda - \mu S(t) - \beta_1 S(t)I_1(t) - \beta_2 S(t)I_2(t) + \int\limits_0^\infty \alpha_0(a)e(a,t)da + \alpha_1 I_1(t) +\\ & \alpha_2 I_2(t) - \int\limits_0^\infty {}^{CF}\partial_a^\nu e(a,t)da - \int\limits_0^\infty (\mu + \gamma(a) + \alpha_0(a))e(a,t)da + \int\limits_0^\infty \gamma(a)\\ & \times e(a,t)da - \mu I_1(t) - \alpha_1 I_1(t) - \delta_1 I_1(t)I_2(t) + \beta_2 S(t)I_2(t) - \mu I_2(t) -\\ & \alpha_2 I_2(t) - \delta_2 I_1(t)I_2(t) + \delta_1 I_1(t)I_2(t) + \delta_2 I_1(t)I_2(t) - \mu J(t) - \eta J(t),\\ =& \Lambda - \mu S(t) - \beta_1 S(t)I_1(t) - \int\limits_0^\infty {}^{CF}\partial_a^\nu e(a,t)da - \int\limits_0^\infty \mu e(a,t)da - \mu I_1(t) -\end{aligned}$$

$$\begin{aligned}&\mu I_2(t) - \mu J(t) - \eta J(t),\\ \leq&\Lambda - \mu S(t) - \int_0^\infty \mu e(a,t)da - \mu I_1(t) - \mu I_2(t) - \mu J(t).\end{aligned}$$

That is,

$$\begin{aligned}{}^{CF}D_t^{\nu}||\psi(t)||_{\mathbb{X}} &\leq \Lambda - \mu\left(S(t) + \int_0^\infty e(a,t)da + I_1(t) + I_2(t) + J(t)\right),\\ &\leq \Lambda - \mu||\psi(t)||_{\mathbb{X}}.\end{aligned}$$

Making use of the Laplace transform leads to

$$\mathcal{L}\{{}^{CF}D_t^{\nu}||\psi(t)||_{\mathbb{X}}\} \leq \mathcal{L}\{\Lambda\} - \mu\mathcal{L}\{||\psi(t)||_{\mathbb{X}}\},$$

which implies that

$$\frac{B(\nu)}{\nu + (1-\nu)s}\left(s\mathcal{L}\{||\psi(t)||_{\mathbb{X}}\} - ||\psi(0)||_{\mathbb{X}}\right) \leq \frac{\Lambda}{s} - \mu\mathcal{L}\{||\psi(t)||_{\mathbb{X}}\},$$

and hence

$$\mathcal{L}\{||\psi(t)||_{\mathbb{X}}\}\left(\mu + \frac{sB(\nu)}{\nu + (1-\nu)s}\right) \leq \frac{\Lambda}{s} + \frac{B(\nu)}{\nu + (1-\nu)s}||\psi(0)||_{\mathbb{X}}.$$

It follows that

$$\begin{aligned}\mathcal{L}\{||\psi(t)||_{\mathbb{X}}\} &\leq \frac{\Lambda}{s\left(\mu + \frac{sB(\nu)}{\nu+(1-\nu)s}\right)} + \frac{B(\nu)||\psi(0)||_{\mathbb{X}}}{(\nu + (1-\nu)s)\left(\mu + \frac{sB(\nu)}{\nu+(1-\nu)s}\right)}\\ &= \frac{\Lambda(\nu + (1-\nu)s)}{s(\mu\nu + [\mu(1-\nu) + B(\nu)]s)} + \frac{B(\nu)||\psi(0)||_{\mathbb{X}}}{\mu\nu + [\mu(1-\nu) + B(\nu)]s}.\end{aligned}$$

Consequently, we obtain

$$\begin{aligned}\mathcal{L}\{||\psi(t)||_{\mathbb{X}}\} \leq& \frac{\nu\Lambda}{s(\mu\nu + [\mu(1-\nu) + B(\nu)]s)} + \frac{\Lambda(1-\nu)}{\mu\nu + [\mu(1-\nu) + B(\nu)]s}\\ &+ \frac{B(\nu)||\psi(0)||_{\mathbb{X}}}{\mu\nu + [\mu(1-\nu) + B(\nu)]s}\end{aligned}$$

$$
\begin{aligned}
=&\frac{\nu\Lambda}{s[\mu(1-\nu)+B(\nu)]\left(\frac{\mu\nu}{\mu(1-\nu)+B(\nu)}+s\right)}\\
&+\frac{\Lambda(1-\nu)}{[\mu(1-\nu)+B(\nu)]\left(\frac{\mu\nu}{\mu(1-\nu)+B(\nu)}+s\right)}\\
&+\frac{B(\nu)||\psi(0)||_{\mathbb{X}}}{[\mu(1-\nu)+B(\nu)]\left(\frac{\mu\nu}{\mu(1-\nu)+B(\nu)}+s\right)}\\
=&\frac{\nu\Lambda}{\mu(1-\nu)+B(\nu)}\frac{1}{s\left(\frac{\mu\nu}{\mu(1-\nu)+B(\nu)}+s\right)}\\
&+\frac{\Lambda(1-\nu)}{\mu(1-\nu)+B(\nu)}\frac{1}{\left(\frac{\mu\nu}{\mu(1-\nu)+B(\nu)}+s\right)}\\
&+\frac{B(\nu)||\psi(0)||_{\mathbb{X}}}{\mu(1-\nu)+B(\nu)}\frac{1}{\left(\frac{\mu\nu}{\mu(1-\nu)+B(\nu)}+s\right)}\\
=&\frac{\Lambda}{\mu}\left(\frac{1}{s}-\frac{1}{\frac{\mu\nu}{\mu(1-\nu)+B(\nu)}+s}\right)+\frac{\Lambda(1-\nu)}{\mu(1-\nu)+B(\nu)}\left(\frac{1}{\frac{\mu\nu}{\mu(1-\nu)+B(\nu)}+s}\right)\\
&+\frac{B(\nu)||\psi(0)||_{\mathbb{X}}}{\mu(1-\nu)+B(\nu)}\left(\frac{1}{\frac{\mu\nu}{\mu(1-\nu)+B(\nu)}+s}\right).
\end{aligned}
$$

Application of the inverse Laplace transform yields,

$$
\begin{aligned}
||\psi(t)||_{\mathbb{X}}\leq&\frac{\Lambda}{\mu}\left(1-\exp\left\{\frac{-\mu\nu t}{\mu(1-\nu)+B(\nu)}\right\}\right)\\
&+\frac{\Lambda(1-\nu)}{\mu(1-\nu)+B(\nu)}\exp\left\{\frac{-\mu\nu t}{\mu(1-\nu)+B(\nu)}\right\}\\
&+\frac{B(\nu)||\psi(0)||_{\mathbb{X}}}{\mu(1-\nu)+B(\nu)}\exp\left\{\frac{-\mu\nu t}{\mu(1-\nu)+B(\nu)}\right\}\\
=&\frac{\Lambda}{\mu}+\left(\frac{\Lambda(1-\nu)+B(\nu)||\psi(0)||_{\mathbb{X}}}{\mu(1-\nu)+B(\nu)}-\frac{\Lambda}{\mu}\right)\exp\left\{\frac{-\mu\nu t}{\mu(1-\nu)+B(\nu)}\right\}\\
.
\end{aligned}
$$

We observe that

$$||\psi(t)||_{\mathbb{X}}\leq\frac{\Lambda}{\mu}\quad\text{as}\quad t\to\infty,$$

and hence $\psi(t)$ is bounded for all $t > 0$. Therefore, the state space G of (4.6) is defined by

$$G = \left\{ \psi(t) \in \mathbb{X}_+ : ||\psi(t)||_{\mathbb{X}} \leq \frac{\Lambda}{\mu} \right\}.$$

4.2.2 Positivity of solutions

The aim here is to construct a positive solution of (4.6).

The function f in (4.6) can be decomposed as $f(\psi(t)) = \mathfrak{L}\psi(t) + \mathfrak{M}(\psi(t))$, where

$$\mathfrak{L} = \begin{pmatrix} -\mu & 0 & \alpha_1 & \alpha_2 & 0 \\ 0 & -{}^{CF}\partial_a^{\nu} - (\mu + \gamma(a) + \alpha_0(a)) & 0 & 0 & 0 \\ 0 & 0 & -\mu - \alpha_1 & 0 & 0 \\ 0 & 0 & 0 & -\mu - \alpha_2 & 0 \\ 0 & 0 & 0 & 0 & -\mu - \eta \end{pmatrix}$$

and

$$\mathfrak{M}(\psi(t)) = \begin{pmatrix} \Lambda - \beta_1 S(t) I_1(t) - \beta_2 S(t) I_2(t) + \int_0^\infty \alpha_0(a) e(a,t) da \\ 0 \\ \int_0^\infty \gamma(a) e(a,t) da - \delta_1 I_1(t) I_2(t) \\ \beta_2 S(t) I_2(t) - \delta_2 I_1(t) I_2(t) \\ \delta_1 I_1(t) I_2(t) + \delta_2 I_1(t) I_2(t) \end{pmatrix}.$$

It is enough to show that $\mathfrak{L}\mathbb{X}_+ \subset \mathbb{X}_+$ and $\mathfrak{M}(\mathbb{X}_+) \subset \mathbb{X}_+$ so that the solution of (4.6) is positive. Since $\mathfrak{L}$ satisfies the properties of a Metzler Matrix, thus it follows that $\mathfrak{L}$ is a positive operator and hence $\mathfrak{L}\mathbb{X}_+ \subset \mathbb{X}_+$. To prove that $\mathfrak{M}(\mathbb{X}_+) \subset \mathbb{X}_+$, we consider an arbitrary $\psi(t) \in \mathbb{X}_+$ and show that $\mathfrak{M}(\psi(t)) \in \mathbb{X}_+$. To do this, we require the following:

(i) $\Lambda - \beta_1 S(t) I_1(t) - \beta_2 S(t) I_2(t) + \int_0^\infty \alpha_0(a) e(a,t) da > 0$,

(ii) $\int_0^\infty \gamma(a) e(a,t) da - \delta_1 I_1(t) I_2(t) > 0$,

(iii) $\beta_2 S(t) I_2(t) - \delta_2 I_1(t) I_2(t) > 0$.

Let $\underline{\gamma} = \inf_{a\in[0,\infty)}\{\gamma(a)\}$ and $\underline{\alpha_0} = \inf_{a\in[0,\infty)}\{\alpha_0(a)\}$. From (ii), we have

$$\int_0^\infty \gamma(a)e(a,t)da - \delta_1 I_1(t)I_2(t) > \underline{\gamma}||e(t)||_1 - \frac{\delta_1\Lambda^2}{\mu^2},$$

and hence $\int_0^\infty \gamma(a)e(a,t)da - \delta_1 I_1(t)I_2(t) > 0$, provided that

$$||e(t)||_1 > \frac{\delta_1\Lambda^2}{\underline{\gamma}\mu^2}. \tag{4.7}$$

From (i), we have

$$\begin{aligned}\Lambda - \beta_1 S(t)I_1(t) - \beta_2 S(t)I_2(t) + \int_0^\infty \alpha_0(a)e(a,t)da &> \Lambda - \beta_1\frac{\Lambda^2}{\mu^2} - \beta_2\frac{\Lambda^2}{\mu^2} + \underline{\alpha_0}||e(t)||_1 \\ &> \Lambda - (\beta_1+\beta_2)\frac{\Lambda^2}{\mu^2} + \underline{\alpha_0}\frac{\delta_1\Lambda^2}{\underline{\gamma}\mu^2},\end{aligned}$$

and hence

$$\Lambda - \beta_1 S(t)I_1(t) - \beta_2 S(t)I_2(t) + \int_0^\infty \alpha_0(a)e(a,t)da > 0,$$

provided that

$$\beta_1 + \beta_2 < \frac{\mu^2}{\Lambda} + \frac{\delta_1\underline{\alpha_0}}{\underline{\gamma}}. \tag{4.8}$$

From (iii), we have

$$\beta_2 S(t)I_2(t) - \delta_2 I_1(t)I_2(t) = (\beta_2 S(t) - \delta_2 I_1(t))I_2(t),$$

and hence

$$\beta_2 S(t)I_2(t) - \delta_2 I_1(t)I_2(t) > 0,$$

provided that

$$\beta_2 S(t) - \delta_2 I_1(t) > 0.$$

Since

$$\beta_2 S(t) - \delta_2 I_1(t) > \beta_2 S(t) - \delta_2\frac{\Lambda}{\mu},$$

then

$$\beta_2 S(t) - \delta_2 I_1(t) > 0,$$

provided that

$$S(t) > \frac{\delta_2 \Lambda}{\mu \beta_2}. \tag{4.9}$$

Therefore $\mathfrak{M}(\mathbb{X}_+) \subset \mathbb{X}_+$. It follows that the state space G is positively invariant provided that (4.7), (4.8) and (4.9) are satisfied.

4.2.3 Existence and uniqueness of solutions

We examine the Lipschitz continuity of the function f on $\mathbb{X}_+$. For $\psi(t), \psi^*(t) \in \mathbb{X}_+$, since $f(\psi(t)) \in \mathbb{R}_+$, we have

$$\begin{aligned} |f_1(\psi(t)) - f_1(\psi^*(t))| = \Bigg| & \Lambda - \mu S(t) - \beta_1 S(t) I_1(t) - \beta_2 S(t) I_2(t) + \int_0^\infty \alpha_0(a) e(a,t) da + \\ & \alpha_1 I_1(t) + \alpha_2 I_2(t) - \Big(\Lambda - \mu S^*(t) - \beta_1 S^*(t) I_1^*(t) - \beta_2 S^*(t) I_2^*(t) \\ & + \int_0^\infty \alpha_0(a) e^*(a,t) da + \alpha_1 I_1^*(t) + \alpha_2 I_2^*(t) \Big) \Bigg| \end{aligned}$$

which leads to

$$\begin{aligned} |f_1(\psi(t)) - f_1(\psi^*(t))| = \Bigg| & - \mu (S(t) - S^*(t)) - \beta_1 (S(t) I_1(t) - S^*(t) I_1^*(t)) - \beta_2 (S^*(t) I_2^*(t) \\ & - S^*(t) I_2^*(t)) + \int_0^\infty \alpha_0(a)(e(a,t) - e^*(a,t)) da + \alpha_1 (I_1(t) - I_1^*(t)) \\ & + \alpha_2 (I_2(t) - I_2^*(t)) \Bigg|. \end{aligned}$$

Hence, it follows that

$$\begin{aligned} |f_1(\psi(t)) - f_1(\psi^*(t))| = \Bigg| & - \mu (S(t) - S^*(t)) - \beta_1 (S(t) - S^*(t)) I_1(t) - \beta_1 S(t) (I_1(t) - \\ & I_1^*(t)) - \beta_2 (S^*(t) - S^*(t)) I_2(t) - \beta_2 S^*(t) (I_2(t) - I_2^*(t)) \\ & + \int_0^\infty \alpha_0(a)(e(a,t) - e^*(a,t)) da + \alpha_1 (I_1(t) - I_1^*(t)) \end{aligned}$$

$$+\alpha_2(I_2(t)-I_2^*(t))\Bigg|,$$

thus

$$\begin{aligned}|f_1(\psi(t))-f_1(\psi^*(t))| =&\mu|S(t)-S^*(t)|+\beta_1|S(t)-S^*(t)||I_1(t)|+\beta_1|S(t)||I_1(t)-I_1^*(t)|\\&+\beta_2|S^*(t)-S^*(t)||I_2(t)|+\beta_2|S^*(t)||I_2(t)-I_2^*(t)|\\&+\left|\int_0^\infty \alpha_0(a)(e(a,t)-e^*(a,t))da\right|+\alpha_1|I_1(t)-I_1^*(t)|\\&+\alpha_2|I_2(t)-I_2^*(t)|.\end{aligned}$$

Since the solution $\psi(t)$ is bounded, there exist positive constants C_S, C_{I_1}, C_{I_2} and C_J such that,

$$|S(t)|\leq C_S, ||e(t)||_1\leq C_e, |I_1(t)|\leq C_{I_1}, |I_2(t)|\leq C_{I_2} \quad \text{and} \quad |J(t)|\leq C_J.$$

It follows that,

$$\begin{aligned}|f_1(\psi(t))-f_1(\psi^*(t))| \leq&\mu|S(t)-S^*(t)|+\beta_1C_{I_1}|S(t)-S^*(t)|+\beta_1C_S|I_1(t)-I_1^*(t)|+\\&\beta_2C_{I_2}|S^*(t)-S^*(t)|+\beta_2C_S|I_2(t)-I_2^*(t)|+\sup_{a\in[0,\infty)}\{\alpha_0(a)\}\times\\&\int_0^\infty |e(a,t)-e^*(a,t)|da+\alpha_1|I_1(t)-I_1^*(t)|+\alpha_2|I_2(t)-I_2^*(t)|\\ \leq&(\mu+\beta_1C_{I_1}+\beta_2C_{I_2})|S^*(t)-S^*(t)|+(\beta_1C_S+\alpha_1)|I_1(t)-I_1^*(t)|\\&+(\beta_2C_S+\alpha_2)|I_2(t)-I_2^*(t)|+\sup_{a\in[0,\infty)}\{\alpha_0(a)\}||e(a,t)-e^*(a,t)||_1\\ =&M_S(|S(t)-S^*(t)|+|I_1(t)-I_1^*(t)|+|I_2(t)-I_2^*(t)|+||e(a,t)-\\&e^*(a,t)||_1)\\ \leq&M_S||\psi(t)-\psi^*(t)||_{\mathbb{X}},\end{aligned}$$

where

$$M_S=\max\left\{\mu+\beta_1C_{I_1}+\beta_2C_{I_2}, \beta_1C_S+\alpha_1, \beta_2C_S+\alpha_2, \sup_{a\in[0,\infty)}\{\alpha_0(a)\}\right\}.$$

Therefore f_1 is Lipschitz continuous in $\mathbb{R}_+$. For $\psi(t),\psi^*(t)\in\mathbb{X}_+$, since $f_2(\psi(t))\in\mathbb{R}_+$, we have

$$||f_2(\psi(t))-f_2(\psi^*(t))||_1 =||-(\mu+\gamma+\alpha_0)e(t)-{}^{CF}\partial_a^\nu e(t)-(-(\mu+\gamma+\alpha_0)e^*(t)$$

$$
\begin{aligned}
&- {}^{CF}\partial_a^\nu e^*(t))||_1 \\
=&|| -(\mu+\gamma+\alpha_0)(e(t)-e^*(t)) - {}^{CF}\partial_a^\nu(e(t)-e^*(t))||_1 \\
\leq&||(\mu+\gamma+\alpha_0)(e(t)-e^*(t))||_1 + ||{}^{CF}\partial_a^\nu(e(t)-e^*(t))||_1.
\end{aligned}
$$

Since

$$
\begin{aligned}
{}^{CF}\partial_a^\nu(e(a,t)-e^*(a,t)) &= \frac{M(\nu)}{1-\nu}\int\limits_0^a \partial_s(e(s,t)-e^*(s,t))\exp\left(-\frac{\nu}{1-\nu}(a-s)\right)ds \\
&= \frac{M(\nu)}{1-\nu}\exp\left(-\frac{\nu}{1-\nu}a\right)\int\limits_0^a \partial_s(e(s,t)-e^*(s,t))\exp\left(\frac{\nu}{1-\nu}s\right)ds
\end{aligned}
$$

and

$$
\begin{aligned}
\int\limits_0^a \partial_s(e(s,t)-e^*(s,t))\exp\left(\frac{\nu}{1-\nu}s\right)ds &= \inf_{s\in[0,a]}\left\{\exp\left(\frac{\nu}{1-\nu}s\right)\right\}\int\limits_0^a \partial_a(e(a,t)-e^*(a,t))ds \\
&= e(a,t)-e^*(a,t)-e(0,t)+e^*(0,t),
\end{aligned}
$$

thus

$$
{}^{CF}\partial_a^\nu(e(a,t)-e^*(a,t)) = \frac{M(\nu)}{1-\nu}\exp\left(-\frac{\nu}{1-\nu}a\right)(e(a,t)-e^*(a,t)-e(0,t)+e^*(0,t)).
$$

It follows that

$$
\begin{aligned}
||f_2(\psi(t))-f_2(\psi^*(t))||_1 = &\sup_{a\in[0,\infty)}\{\mu+\gamma(a)+\alpha_0(a)\}\int\limits_0^\infty |e(a,t)-e^*(a,t)|da + \frac{M(\nu)}{1-\nu}\times \\
&\int\limits_0^\infty \left|\exp\left(-\frac{\nu}{1-\nu}a\right)(e(a,t)-e^*(a,t)-e(0,t)+e^*(0,t))\right|da,
\end{aligned}
$$

and hence

$$
\begin{aligned}
||f_2(\psi(t))-f_2(\psi^*(t))||_1 = &\sup_{a\in[0,\infty)}\{\mu+\gamma(a)+\alpha_0(a)\}||e(t)-e^*(t)||_1 + \frac{M(\nu)}{1-\nu}\times \\
&\int\limits_0^\infty \exp\left(-\frac{\nu}{1-\nu}a\right)|e(a,t)-e^*(a,t)-e(0,t)+e^*(0,t)|da
\end{aligned}
$$

It follows from (4.2) that $e(a,t)$ is differentiable with respect to a, and hence $e(a,t)$ is continuous with repect to a. Therefore, by continuity of $e(a,t)-e^*(a,t)$ at $a=0$, for any arbitrary $\epsilon>0$, there exists a $\delta>0$ such that

$$|e(a,t)-e^*(a,t)-(e(0,t)-e^*(0,t))|<\epsilon,$$

whenever $a<\delta$. Hence,

$$\begin{aligned}||f_2(\psi(t))-f_2(\psi^*(t))||_1 <& \sup_{a\in[0,\infty)}\{\mu+\gamma(a)+\alpha_0(a)\}||e(t)-e^*(t)||_1+\frac{M(\nu)}{1-\nu}\times\\ &\int\limits_0^\infty \exp\Big(-\frac{\nu}{1-\nu}a\Big)\epsilon da\\ =& \sup_{a\in[0,\infty)}\{\mu+\gamma(a)+\alpha_0(a)\}||e(t)-e^*(t)||_1-\frac{M(\nu)\epsilon}{1-\nu}\frac{1-\nu}{\nu}\times\\ &\Big\{\exp\Big(-\frac{\nu}{1-\nu}a\Big)\Big\}\Big|_0^\infty\\ =& \sup_{a\in[0,\infty)}\{\mu+\gamma(a)+\alpha_0(a)\}||e(t)-e^*(t)||_1-\frac{M(\nu)\epsilon}{\nu}.\end{aligned}$$

Choosing $\epsilon=C_e||e(t)-e^*(t)||_1$ leads to

$$\begin{aligned}||f_2(\psi(t))-f_2(\psi^*(t))||_1 =& \sup_{a\in[0,\infty)}\{\mu+\gamma(a)+\alpha_0(a)\}||e(t)-e^*(t)||_1-\frac{M(\nu)}{\nu}C_e||e(t)\\ &-e^*(t)||_1\\ =&\Big(\sup_{a\in[0,\infty)}\{\mu+\gamma(a)+\alpha_0(a)\}-\frac{M(\nu)}{\nu}C_e\Big)||e(t)-e^*(t)||_1\\ <&M_e||\psi(t)-\psi^*(t)||_{\mathbb{X}},\end{aligned}$$

where

$$M_e=\sup_{a\in[0,\infty)}\{\mu+\gamma(a)+\alpha_0(a)\}-\frac{M(\nu)}{\nu}C_e.$$

Therefore, f_2 is Lipschitz continuous in $\mathbb{L}_1(0,\infty)$. For $\psi(t),\psi^*(t)\in\mathbb{X}_+$, since $f_3(\psi(t))\in\mathbb{R}_+$, we compute

$$\begin{aligned}|f_3(\psi(t))-f_3(\psi^*(t))| =&\Big|\int\limits_0^\infty \gamma(a)e(a,t)da-\mu I_1(t)-\delta_1 I_1(t)I_2(t)-\alpha_1 I_1(t)\\ &-\Big(\int\limits_0^\infty \gamma(a)e^*(a,t)da-\mu I_1^*(t)-\delta_1 I_1^*(t)I_2^*(t)-\alpha_1 I_1^*(t)\Big)\Big|\end{aligned}$$

$$
\begin{aligned}
&= \Bigg| \int_0^\infty \gamma(a)(e(a,t) - e^*(a,t))da - \mu(I_1(t) - I_1^*(t)) - \delta_1(I_1(t)I_2(t) \\
&\quad - I_1^*(t)I_2^*(t)) - \alpha_1(I_1(t) - I_1^*(t)) \Bigg| \\
&\leq \Bigg| \int_0^\infty \gamma(a)(e(a,t) - e^*(a,t))da \Bigg| + \mu|I_1(t) - I_1^*(t)| + \delta_1|I_1(t)I_2(t) \\
&\quad - I_1^*(t)I_2^*(t)| + \alpha_1|I_1(t) - I_1^*(t)|,
\end{aligned}
$$

which leads to

$$
\begin{aligned}
|f_3(\psi(t)) - f_3(\psi^*(t))| \leq & \sup_{a\in[0,\infty)} \{\gamma(a)\} \int_0^\infty |e(a,t) - e^*(a,t)|da + \mu|I_1(t) - I_1^*(t)| + \delta_1|I_1(t) \\
& \times I_2(t) - I_1^*(t)I_2(t) - I_1^*(t)I_2^*(t) + I_1^*(t)I_2(t)| \\
\leq & \sup_{a\in[0,\infty)} \{\gamma(a)\}||e(t) - e^*(t)||_1 + (\mu + \alpha_1)|I_1(t) - I_1^*(t)| + \delta_1|I_1(t) \\
& - I_1^*(t)||I_2(t)| + |I_1^*(t)||I_2(t) - I_2^*(t)| \\
\leq & \sup_{a\in[0,\infty)} \{\gamma(a)\}||e(t) - e^*(t)||_1 + (\mu + \alpha_1)|I_1(t) - I_1^*(t)| + \delta_1 C_{I_2} \\
& \times |I_1(t) - I_1^*(t)| + \delta_1 C_{I_1}|I_2(t) - I_2^*(t)| \\
\leq & M_{I_1}(||e(t) - e^*(t)||_1 + |I_1(t) - I_1^*(t)| + |I_1(t) - I_1^*(t)| + |I_2(t) \\
& - I_2^*(t)|) \\
\leq & M_{I_1}||\psi(t) - \psi^*(t)||_{\mathbb{X}},
\end{aligned}
$$

where

$$
M_{I_1} = \max\left\{ \sup_{a\in[0,\infty)} \{\gamma(a)\}, \mu + \alpha_1, \delta_1 C_{I_1}, \delta_1 C_{I_2} \right\}.
$$

Therefore f_3 is Lipschitz continuous in $\mathbb{R}_+$. For $\psi(t), \psi^*(t) \in \mathbb{X}_+$, since $f_4(\psi(t)) \in \mathbb{R}_+$, we compute the following

$$
\begin{aligned}
|f_4(\psi(t)) - f_4(\psi^*(t))| = & |\beta_2 S(t)I_2(t) - \mu I_2(t) - \alpha_2 I_2(t) - \delta_2 I_1(t)I_2(t) - (\beta_2 S(t)^* I_2^*(t) \\
& - \mu I_2^*(t) - \alpha_2 I_2^*(t) - \delta_2 I_1^*(t)I_2^*(t))| \\
= & |\beta_2(S(t)I_2(t) - S^*(t)I_2^*(t)) - (\mu + \alpha_2)(I_2(t) - I_2^*(t)) - \delta_2(I_1(t) \\
& \times I_2(t) - I_1^*(t)I_2^*(t))|
\end{aligned}
$$

$$
\begin{aligned}
&=|\beta_2(S(t)I_2(t) - S(t)^*I_2(t) + S^*(t)I_2(t) - S^*(t)I_2^*(t)) - (\mu+\alpha_2) \\
&\quad \times (I_2(t) - I_2^*(t)) - \delta_2(I_1(t)I_2(t) - I_1^*(t)I_2(t) + I_1^*(t)I_2(t) - \\
&\quad I_1^*(t)I_2^*(t))| \\
&\le \beta_2|S(t) - S(t)^*||I_2(t)| + \beta_2|S^*(t)||I_2(t) - I_2^*(t)| + (\mu+\alpha_2)|I_2(t) - \\
&\quad I_2^*(t)| + \delta_2|I_1(t) - I_1^*(t)||I_2(t)| + \delta_2|I_1^*(t)||I_2(t) - I_2^*(t)| \\
&\le \beta_2 C_{I_2}|S(t) - S(t)^*| + \beta_2 C_S|I_2(t) - I_2^*(t)| + (\mu+\alpha_2)|I_2(t) - I_2^*(t)| \\
&\quad + \delta_2 C_{I_2}|I_1(t) - I_1^*(t)| + \delta_2 C_{I_1}|I_2(t) - I_2^*(t)| \\
&\le M_{I_2}(|S(t) - S(t)^*| + |I_2(t) - I_2^*(t)| + |I_2(t) - I_2^*(t)| \\
&\quad + |I_1(t) - I_1^*(t)| + |I_2(t) - I_2^*(t)|) \\
&\le M_{I_2}||\psi(t) - \psi^*(t)||_{\mathbb{X}},
\end{aligned}
$$

where

$$
M_{I_2} = \max\{\beta_2 C_{I_2}, \beta_2 C_S, \mu+\alpha_2, \delta_2 C_{I_2}, \delta_2 C_{I_1}\}.
$$

Therefore f_4 is Lipschitz continuous in $\mathbb{R}_+$. For $\psi(t), \psi^*(t) \in \mathbb{X}_+$, since $f_5(\psi(t)) \in \mathbb{R}_+$, we have

$$
\begin{aligned}
|f_5(\psi(t)) - f_5(\psi^*(t))| &= |\delta_1 I_1(t)I_2(t) + \delta_2 I_1(t)I_2(t) - (\mu+\eta)J(t) - [\delta_1 I_1^*(t)I_2^*(t) + \delta_2 I_1^*(t) \\
&\quad \times I_2^*(t) - (\mu+\eta)J^*(t)]| \\
&= |(\delta_1+\delta_2)[I_1(t)I_2(t) - I_1^*(t)I_2^*(t)] - (\mu+\eta)[J(t) - J^*(t)]| \\
&= |(\delta_1+\delta_2)[I_1(t)I_2(t) - I_1^*(t)I_2(t) + I_1^*(t)I_2(t) - I_1^*(t)I_2^*(t)] - (\mu+\eta) \\
&\quad \times [J(t) - J^*(t)]| \\
&= (\delta_1+\delta_2)|I_1(t) - I_1^*(t)||I_2(t)| + (\delta_1+\delta_2)|I_1^*(t)||I_2(t) - I_2^*(t)| + \\
&\quad (\mu+\eta)|J(t) - J^*(t)| \\
&\le (\delta_1+\delta_2)C_{I_2}|I_1(t) - I_1^*(t)| + (\delta_1+\delta_2)C_{I_1}|I_2(t) - I_2^*(t)| \\
&\quad + (\mu+\eta)|J(t) - J^*(t)| \\
&\le M_J(|I_1(t) - I_1^*(t)| + |I_2(t) - I_2^*(t)| + |J(t) - J^*(t)|) \\
&\le M_J||\psi(t) - \psi^*(t)||_{\mathbb{X}},
\end{aligned}
$$

where

$$
M_J = \max\{(\delta_1+\delta_2)C_{I_2}, (\delta_1+\delta_2)C_{I_1}, \mu+\eta\}.
$$

Therefore f_5 is Lipschitz continuous in $\mathbb{R}_+$. Hence,

$$\begin{aligned}||f(\psi(t))-f(\psi^*(t))||_{\mathbb{X}} =&|f_1(t,\psi(t))-f_1(t,\psi^*(t))|+||f_2(t,\psi(t))-f_2(t,\psi^*(t))||_1+\\ &|f_3(t,\psi(t))-f_3(t,\psi^*(t))|+|f_4(t,\psi(t))-f_4(t,\psi^*(t))|\\ \leq&(M_S+M_e+M_{I_1}+M_{I_2}+M_J)||\psi(t)-\psi^*(t)||_{\mathbb{X}}\\ =&M||\psi(t)-\psi^*(t)||_{\mathbb{X}},\end{aligned}$$

with

$$M=M_S+M_e+M_{I_1}+M_{I_2}+M_J.$$

Theorem 4.1. *Let*

$$L=\sup_{\psi\in\mathbb{X}_+}||f(\psi(t))||_{\mathbb{X}}, h=\frac{\Lambda B(\nu)}{\nu\mu L}+\frac{\nu-1}{\nu}, \frac{\Lambda}{\mu L}\leq 1,$$

and the set G be defined by

$$G=\left\{\psi(t)\in\mathbb{X}_+ : t\in[0,h], ||\psi(t)-\psi(0)||_{\mathbb{X}}\leq\frac{\Lambda}{\mu L}\right\}.$$

There exists a unique solution $\psi(t)\in G$ of (4.6) with initial condition $\psi(0)=\psi_0$.

Proof. Let $t\in[0,h]$. Consider the function ψ of the form

$$\psi(t):=\psi(0)+\frac{1-\nu}{B(\nu)}f(\psi(t))+\frac{\nu}{B(\nu)}\int\limits_a^t f(\psi(s))ds,$$

where $B(\nu)=\frac{2-\nu}{2}M(\nu)$. We want to show that $\psi(t)\in G$. To do this, we compute the following

$$\begin{aligned}||\psi(t)-\psi(0)||_{\mathbb{X}}&=\left|\left|\frac{1-\nu}{B(\nu)}f(\psi(t))+\frac{\nu}{B(\nu)}\int\limits_0^t f(\psi(s))ds\right|\right|_{\mathbb{X}}\\ &\leq\frac{1-\nu}{B(\nu)}||f(\psi(t))||_{\mathbb{X}}+\frac{\nu}{B(\nu)}\int\limits_0^t ||f(\psi(s))||_{\mathbb{X}}ds\\ &=\frac{1-\nu}{B(\nu)}||f(\psi(t))||_{\mathbb{X}}+\frac{\nu}{B(\nu)}\left[(s)||f(\psi(s))||_{\mathbb{X}}|_0^t-\int\limits_0^t s\frac{d}{ds}(||f(\psi(s))||_{\mathbb{X}})ds\right]\end{aligned}$$

$$= \frac{1-\nu}{B(\nu)}||f(\psi(t))||_{\mathbb{X}} + \frac{\nu}{B(\nu)}\left[t||f(\psi(t))||_{\mathbb{X}} - \int\limits_0^t s\frac{d}{ds}(||f(\psi(s))||_{\mathbb{X}})ds\right].$$

The function $g(s) = s$ is monotonic increasing on $[0,t]$, application of Theorem 2.4 yields

$$\int\limits_0^t s\frac{d}{ds}(||f(\psi(s))||_{\mathbb{X}})ds = \inf_{s\in[0,c]}\{s\}\int\limits_0^c \frac{d}{ds}(||f(\psi(s))||_{\mathbb{X}})ds + \sup_{s\in[c,t]}\{s\}\int\limits_c^t \frac{d}{ds}(||f(\psi(s))||_{\mathbb{X}})ds,$$

thus

$$\begin{aligned}\int\limits_0^t s\frac{d}{ds}(||f(\psi(s))||_{\mathbb{X}})ds &= (0)\int\limits_0^c \frac{d}{ds}(||f(\psi(s))||_{\mathbb{X}})ds + (t)\int\limits_c^t \frac{d}{ds}(||f(\psi(s))||_{\mathbb{X}})ds\\ &= t\int\limits_c^t \frac{d}{ds}(||f(\psi(s))||_{\mathbb{X}})ds\\ &= t[||f(\psi(s))||_{\mathbb{X}}]_c^t\\ &= t[||f(\psi(t))||_{\mathbb{X}} - ||f(\psi(c))||_{\mathbb{X}}],\end{aligned}$$

where $c \in [0,t]$. Choosing $c = t$ leads to

$$\int\limits_0^t s\frac{d}{ds}(||f(\psi(s))||_{\mathbb{X}})ds = 0.$$

Therefore

$$||\psi(t) - \psi(0)||_{\mathbb{X}} = \frac{1-\nu}{B(\nu)}||f(\psi(t))||_{\mathbb{X}} + \frac{\nu}{B(\nu)}t||f(\psi(t))||_{\mathbb{X}}.$$

Since $t \le h$, it follows that

$$\begin{aligned}||\psi(t) - \psi(0)||_{\mathbb{X}} &\le \left(\frac{1-\nu}{B(\nu)} + \frac{\nu}{B(\nu)}h\right)||f(\psi(t))||_{\mathbb{X}}\\ &\le \left(\frac{1-\nu}{B(\nu)} + \frac{\nu}{B(\nu)}h\right)L.\end{aligned}$$

With $h = \frac{\Lambda B(\nu)}{\nu\mu L} + \frac{\nu-1}{\nu}$, we have

$$||\psi(t) - \psi(0)||_{\mathbb{X}} \le \frac{\Lambda}{\mu L}.$$

Define the function f by $f : G \to X_+$. For $\psi(t), \psi^*(t) \in G$, it follows from the Lipschitz continuity of f that:

$$||f(\psi(t)) - f(\psi^*(t))||_{\mathbb{X}} \le M||\psi(t) - \psi^*(t)||_{\mathbb{X}}$$

$$
\begin{aligned}
&= M||\psi(t) - \psi(0) + \psi(0) - \psi^*(t)||_{\mathbb{X}} \\
&\leq M(||\psi(t) - \psi(0)||_{\mathbb{X}} + ||\psi(0) - \psi^*(t)||_{\mathbb{X}}) \\
&= M(||\psi(t) - \psi(0)||_{\mathbb{X}} + ||\psi^*(t) - \psi(0)||_{\mathbb{X}}) \\
&\leq M\left(\frac{\Lambda}{\mu L} + \frac{\Lambda}{\mu L}\right) \\
&= \frac{2M\Lambda}{\mu L} \\
&= M\delta,
\end{aligned}
$$

where $\delta = \frac{2\Lambda}{\mu L}$. For $\epsilon = M\delta$, there exists $\delta = \frac{\epsilon}{M}$ so that

$$||\psi(t) - \psi^*(t)||_{\mathbb{X}} \leq \delta \quad \text{yields} \quad ||f(\psi(t)) - f(\psi^*(t))||_{\mathbb{X}} \leq \epsilon.$$

Hence f is continuous, therefore it follows from Theorem 2.17 that there exists a unique solution of (4.6). ☐

4.3 Equilibria and basic reproduction numbers

At equilibrium, we have the following system of equations:

$$\Lambda - \mu S - \beta_1 S I_1 - \beta_2 S I_2 + \int_0^\infty \alpha_0(a)e(a)da + \alpha_1 I_1 + \alpha_2 I_2 = 0, \tag{4.10}$$

$${}^{CF}D_a^\nu e(a) = -(\mu + \gamma(a) + \alpha_0(a))e(a) = -\xi(a)e(a), \tag{4.11}$$

$$\int_0^\infty \gamma(a)e(a)da - \mu I_1 - \alpha_1 I_1 - \delta_1 I_1 I_2 = 0, \tag{4.12}$$

$$\beta_2 S I_2 - \mu I_2 - \alpha_2 I_2 - \delta_2 I_1 I_2 = 0, \tag{4.13}$$

$$\delta_1 I_1 I_2 + \delta_2 I_1 I_2 - \mu J - \eta J = 0. \tag{4.14}$$

Applying the Laplace transform on (4.11) yields

$$\mathcal{L}\{{}^{CF}D_a^\nu e(a)\} := \frac{B(\nu)}{1 - \nu + \nu s}[s\mathcal{L}\{e(a)\} - e(0)] = -\mathcal{L}\{\xi(a)e(a)\},$$

which implies

$$\mathcal{L}\{e(a)\} = \frac{e(0)}{s} - \left(\frac{1-\nu}{B(\nu)s} - \frac{\nu}{B(\nu)}\right)\mathcal{L}\{\xi(a)e(a)\}$$

$$
\begin{aligned}
&= \mathcal{L}\{e(0)\} - \frac{1-\nu}{B(\nu)}\mathcal{L}\{1\}\mathcal{L}\{\xi(a)e(a)\} - \frac{\nu}{B(\nu)}\mathcal{L}\{\xi(a)e(a)\} \\
&= \mathcal{L}\{e(0)\} - \frac{1-\nu}{B(\nu)}\mathcal{L}\{1 * \xi(a)e(a)\} - \frac{\nu}{B(\nu)}\mathcal{L}\{\xi(a)e(a)\}.
\end{aligned}
$$

Taking the inverse Laplace transform leads to

$$e(a) = e(0) - \frac{1-\nu}{B(\nu)}[1 * \xi(a)e(a)] - \frac{\nu}{B(\nu)}[\xi(a)e(a)].$$

However the convolution is given by

$$
\begin{aligned}
1 * \xi(a)e(a) &= \int_0^a \xi(s)e(s)ds \\
&= [s\xi(s)e(s)]_0^a - \int_0^a s\frac{d}{ds}[\xi(s)e(s)]ds \\
&= a\xi(a)e(a) - \int_0^a s\frac{d}{ds}[\xi(s)e(s)]ds.
\end{aligned}
$$

Since the function $g(s) = s$ is monotonic increasing on $[0, a]$, application of Theorem 2.4 yields

$$
\begin{aligned}
\int_0^a s\frac{d}{ds}[\xi(s)e(s)]ds &= \inf_{s\in[0,c]}\{s\}\int_0^c \frac{d}{ds}[\xi(s)e(s)]ds + \sup_{s\in[c,a]}\{s\}\int_c^a \frac{d}{ds}[\xi(s)e(s)]ds \\
&= (0)\int_0^c \frac{d}{ds}[\xi(s)e(s)]ds + (a)\int_c^a \frac{d}{ds}[\xi(s)e(s)]ds \\
&= a\int_c^a \frac{d}{ds}[\xi(s)e(s)]ds \\
&= a[\xi(s)e(s)]_c^a \\
&= a[\xi(a)e(a) - \xi(c)e(c)],
\end{aligned}
$$

where $c \in [0, a]$. Choosing $c = a$ leads to

$$\int_0^a s\frac{d}{ds}[\xi(s)e(s)]ds = 0,$$

and hence the convolution is given by $1 * \xi(a)e(a) = a[\xi(a)e(a)]$.

It follows that

$$e(a) = e(0) - \frac{1-\nu}{B(\nu)}a[\xi(a)e(a)] - \frac{\nu}{B(\nu)}[\xi(a)e(a)].$$

Equivalently, we have

$$e(a)\left[1+\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\xi(a)\right]=e(0).$$

Therefore the equilibrium population of TB Latently infected individuals is given as

$$e(a)=e(0)\left[1+\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\xi(a)\right]^{-1}=e(0)\sigma(a),$$

where

$$\sigma(a)=\sum_{k=0}^{\infty}\left[-\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\xi(a)\right]^{k}=\sum_{k=0}^{\infty}(-1)^{k}\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)^{k}\xi(a)^{k},$$

provided

$$\left|-\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\xi(a)\right|<1.$$

The quantity $\sigma(a)$ gives the probability of remaining infected with TB some time units a after infection. Observe that

$$\int_0^{\infty}\alpha_0(a)e(a)da=e(0)\int_0^{\infty}\alpha_0(a)\sigma(a)da=e(0)B \quad \text{where} \quad B=\int_0^{\infty}\alpha_0(a)\sigma(a)da,$$

and

$$\int_0^{\infty}\gamma(a)e(a)da=e(0)\int_0^{\infty}\gamma(a)\sigma(a)da=e(0)C \quad \text{where} \quad C=\int_0^{\infty}\gamma(a)\sigma(a)da.$$

B and C denote the probability of recovery and the probability of progression of individuals into active infection, respectively. Since individuals can only leave the latent class through recovery, progression or death, the sum of the probabilities is unity; that is,

$$\int_0^{\infty}(\mu+\gamma(a)+\alpha_0(a))\sigma(a)da=\mu\int_0^{\infty}\sigma(a)da+\int_0^{\infty}\gamma(a)\sigma(a)da+\int_0^{\infty}\alpha_0(a)\sigma(a)da,$$

hence, it foolows that

$$\int_0^{\infty}(\mu+\gamma(a)+\alpha_0(a))\sigma(a)da=\mu\int_0^{\infty}\sigma(a)da+B+C=1.$$

Consequently, we have

$$B+C<1, \quad B<1 \quad \text{and} \quad C<1.$$

It follows from (4.12) that

$$e(0)C - \mu I_1 - \alpha_1 I_1 - \delta_1 I_1 I_2 = 0;$$

which implies

$$\beta_1 S I_1 C - \mu I_1 - \alpha_1 I_1 - \delta_1 I_1 I_2 = 0.$$

Therefore, either $I_1 = 0$ or

$$\beta_1 C S - \mu - \alpha_1 - \delta_1 I_2 = 0. \tag{4.15}$$

Similarly, from (4.13) we obtain either $I_2 = 0$ or

$$\beta_2 S - \mu - \alpha_2 - \delta_2 I_1 = 0. \tag{4.16}$$

Consider the following cases,

Case 1 ($I_1 = 0 = I_2$): Since $e(0) = \beta_1 S I_1 = 0$, this leads to $e(a) = e(0)\sigma(a) = 0$. It follows from (4.10) that

$$\Lambda - \mu S = 0, \quad \text{this leads to} \quad S = \frac{\Lambda}{\mu}.$$

Furthermore, (4.14) yields the following

$$J = \frac{\delta_1 + \delta_2}{\mu + \eta} I_1 I_2 = 0,$$

hence the disease-free equilibrium is given by

$$E^0 = (S, e(a), I_1, I_2, J)^T = \left(\frac{\Lambda}{\mu}, 0, 0, 0, 0\right)^T = (S^0, 0, 0, 0, 0)^T, \quad \text{where} \quad S^0 = \frac{\Lambda}{\mu}.$$

Case 2 ($I_1 = 0, I_2 \neq 0$): It follows from (4.13) that

$$\beta_2 S - \mu - \alpha_2 = 0; \quad \text{that is,} \quad S = \frac{\mu + \alpha_2}{\beta_2} = \frac{S^0}{\mathcal{R}_2},$$

where

$$\mathcal{R}_2 = \frac{\Lambda \beta_2}{\mu(\mu + \alpha_2)},$$

denotes the basic reproduction number of HIV. Moreover, (4.10) yields the following

$$\Lambda - \mu S - \beta_2 S I_2 + \alpha_2 I_2 = 0;$$

that is,

$$I_2 = \frac{\Lambda - \mu S}{\beta_2 S - \alpha_2} = \frac{\Lambda - \mu\left(\frac{\mu+\alpha_2}{\beta_2}\right)}{\beta_2\left(\frac{\mu+\alpha_2}{\beta_2}\right) - \alpha_2} = \frac{\mu+\alpha_2}{\beta_2}\left(\frac{\Lambda\beta_2}{\mu(\mu+\alpha_2)} - 1\right) = \frac{\mu+\alpha_2}{\beta_2}(\mathcal{R}_2 - 1).$$

Hence, $I_2 > 0$ if and only if $\mathcal{R}_2 > 1$. Therefore the HIV dominated endemic equilibrium is given by

$$E_2^* = (S, e(a), I_1, I_2, J)^T = \left(\frac{S^0}{\mathcal{R}_2}, 0, 0, \frac{\mu+\alpha_2}{\beta_2}(\mathcal{R}_2 - 1), 0\right)^T, \quad \text{provided} \quad \mathcal{R}_2 > 1.$$

Case 3 ($I_1 \neq 0, I_2 = 0$): It follows from (4.15) that

$$\beta_1 C S - \mu - \alpha_1 = 0, \quad \text{that is} \quad S = \frac{\mu+\alpha_1}{\beta_1 C} = \frac{S^0}{\mathcal{R}_1},$$

where

$$\mathcal{R}_1 = \frac{\beta_1 C \Lambda}{(\mu+\alpha_1)\mu},$$

denotes the basic reproduction number of TB. Moreover, (4.10) yields the following

$$\Lambda - \mu S - \beta_1 S I_1 + \beta_1 B S I_1 + \alpha_1 I_1 = 0;$$

that is

$$I_1 = \frac{\Lambda - \mu S}{(1-B)\beta_1 S - \alpha_1} = \frac{\Lambda - \mu\left(\frac{\mu+\alpha_1}{\beta_1 C}\right)}{(1-B)\beta_1\left(\frac{\mu+\alpha_1}{\beta_1 C}\right) - \alpha_1} = \frac{\beta_1 \Lambda C - \mu(\mu+\alpha_1)}{(1-B)\beta_1(\mu+\alpha_1) - \alpha_1\beta_1 C}.$$

Furthermore

$$I_1 = \frac{\mu(\mu+\alpha_1)\left(\frac{\beta_1\Lambda C}{\mu(\mu+\alpha_1)} - 1\right)}{(\mu+\alpha_1)\left((1-B)\beta_1 - \alpha_1\frac{\beta_1 C\mu\Lambda}{(\mu+\alpha_1)\mu\Lambda}\right)} = \frac{\mu(\mathcal{R}_1 - 1)}{(1-B)\beta_1 - \frac{\mu\alpha_1}{\Lambda}\mathcal{R}_1}.$$

Therefore either

$$\mathcal{R}_1 > 1 \quad \text{and} \quad \mathcal{R}_1 < (1-B)\frac{\beta_1\Lambda}{\mu\alpha_1} < \frac{\beta_1\Lambda}{\mu\alpha_1},$$

or

$$\mathcal{R}_1 < 1 \quad \text{and} \quad \mathcal{R}_1 > (1-B)\frac{\beta_1\Lambda}{\mu\alpha_1}.$$

Therefore the TB dominated endemic equilibrium is given by

$$E_1^* = (S, e(a), I_1, I_2, J)^T = \left(\frac{S^0}{\mathcal{R}_1}, e(0)\sigma(a), \frac{\mu(\mathcal{R}_1 - 1)}{(1-B)\beta_1 - \frac{\mu\alpha_1}{\Lambda}\mathcal{R}_1}, 0, 0\right)^T,$$

provided

$$1 < \mathcal{R}_1 < \frac{\beta_1\Lambda}{\mu\alpha_1} \quad \text{or} \quad (1-B)\frac{\beta_1\Lambda}{\mu\alpha_1} < \mathcal{R}_1 < 1.$$

Case 4 ($I_1 \neq 0, I_2 \neq 0$): It follows from (4.15) that

$$\beta_1 CS - \mu - \alpha_1 - \delta_1 I_2 = 0, \quad \text{which leads to} \quad I_2 = \frac{\mu+\alpha_1}{\delta_1}\left(\frac{\beta_1 CS}{\mu+\alpha_1} - 1\right),$$

that is

$$I_2 = \frac{\mu+\alpha_1}{\delta_1}\left(\frac{\beta_1\Lambda}{\mu(\mu+\alpha_1)}\frac{\mu CS}{\Lambda} - 1\right) = \frac{\mu+\alpha_1}{\delta_1}\left(\frac{S}{S^0}\mathcal{R}_1 - 1\right) > 0.$$

Hence, $I_2 > 0$ provided

$$S > \frac{S^0}{\mathcal{R}_1}.$$

Similarly from (4.16), we obtain

$$I_1 = \frac{\mu+\alpha_2}{\delta_2}\left(\frac{\beta_2\Lambda}{\mu(\mu+\alpha_2)}\frac{\mu S}{\Lambda} - 1\right) = \frac{\mu+\alpha_2}{\delta_2}\left(\frac{S}{S^0}\mathcal{R}_2 - 1\right).$$

Hence, $I_1 > 0$ provided

$$S > \frac{S^0}{\mathcal{R}_2}.$$

From (4.10), we have

$$\Lambda - \mu S - \beta_1 S I_1 - \beta_2 S I_2 + e(0)B + \alpha_1 I_1 + \alpha_2 I_2 = 0,$$

which implies

$$\Lambda - \mu S - \beta_1 S I_1 - \beta_2 S I_2 + \beta_1 S I_1 B + \alpha_1 I_1 + \alpha_2 I_2 = 0. \tag{4.17}$$

Finding the expression of I_2 and I_1 from (4.15) and (4.16), respectively, and substituting them into 4.17 yields

$$\Lambda\delta_1\delta_2 - \mu\delta_1\delta_2 S + \delta_1[(B-1)\beta_1 S + \alpha_1][\beta_2 CS - \mu - \alpha_2] + \delta_2[\alpha_2 - \beta_2 S][\beta_1 S - \mu - \alpha_1] = 0,$$

that is,

$$PS^2 + QS + R = 0,$$

where

$$P = (\delta_1 C(B-1)-\delta_2)\beta_1\beta_2, \quad Q = \delta_1\alpha_1\beta_2 C-\delta_1\beta_1(\mu+\alpha_2)(B-1)+\delta_2\alpha_2\beta_1+\delta_2\beta_2(\mu+\alpha_1)-\mu\delta_1\delta_2,$$

and

$$R = \Lambda\delta_1\delta_2 - \delta_2\alpha_2(\mu+\alpha_1) - \delta_1\alpha_1(\mu+\alpha_2).$$

Since $1 - B > 0$, the following holds

$$-P = -(\delta_1 C(B-1) - \delta_2)\beta_1\beta_2 = (\delta_1 C(1-B) + \delta_2)\beta_1\beta_2 > 0,$$

consequently we have $QS + R = -PS^2 > 0$, which implies $Q\left(S + \frac{R}{Q}\right) > 0$. Therefore, either

$$Q < 0 \quad \text{and} \quad S + \frac{R}{Q} < 0,$$

or

$$Q > 0 \quad \text{and} \quad S + \frac{R}{Q} > 0.$$

Since

$$S + \frac{R}{Q} < 0 \quad \text{leads to} \quad 0 < S < -\frac{R}{Q},$$

it follows from $Q < 0$ that $R > 0$. Similarly,

$$S + \frac{R}{Q} > 0 \quad \text{leads to} \quad S > -\frac{R}{Q} > 0,$$

it follows from $Q > 0$ that $R < 0$. Therefore, either

$$Q < 0 \quad \text{and} \quad R > 0,$$

or

$$Q > 0 \quad \text{and} \quad R < 0.$$

Since $P < 0$, then $PS^2 + QS + R = 0$ yields

$$S^2 + \frac{Q}{P}S + \frac{R}{P} = 0;$$

that is,

$$\left(S + \frac{Q}{P}\right)^2 - \frac{Q^2 - 4RP}{4P^2} = 0,$$

therefore

$$S = -\frac{1}{2P}(Q \pm \sqrt{Q^2 - 4RP}).$$

For $R > 0$, we have $Q^2 - 4RP > 0$ and $\sqrt{Q^2 - 4RP} > 0$, hence from we obtain

$$S_+ = -\frac{1}{2P}(Q + \sqrt{Q^2 - 4RP}) > 0.$$

For $R < 0$, we have $Q^2 - 4RP < Q^2$ and $Q > \pm\sqrt{Q^2 - 4RP}$. Hence,

$$S_+ = -\frac{1}{2P}(Q + \sqrt{Q^2 - 4RP}) > 0 \quad \text{or} \quad S_- = -\frac{1}{2P}(Q - \sqrt{Q^2 - 4RP}) > 0.$$

Finally (4.14) yields the following

$$J = \frac{\delta_1 + \delta_2}{\mu + \eta} I_1 I_2 = \frac{(\delta_1 + \delta_2)(\mu + \alpha_1)(\mu + \alpha_2)}{\delta_1 \delta_2 (\mu + \eta)} \left(\frac{S}{S^0}\mathcal{R}_1 - 1 \right) \left(\frac{S}{S^0}\mathcal{R}_2 - 1 \right) > 0. \tag{4.18}$$

Therefore:

(i) For $R > 0$, the co-epidemic equilibrium is given by

$$E_+^* = (S_+, e(a), I_1, I_2, J)^T = \begin{pmatrix} -\frac{1}{2P}(Q + \sqrt{Q^2 - 4PR}) \\ e(0)\sigma(a) \\ \frac{\mu+\alpha_2}{\delta_2}\left(\frac{S_+}{S^0}\mathcal{R}_2 - 1\right) \\ \frac{\mu+\alpha_1}{\delta_1}\left(\frac{S_+}{S^0}\mathcal{R}_1 - 1\right) \\ \frac{(\delta_1+\delta_2)(\mu+\alpha_1)(\mu+\alpha_2)}{\delta_1\delta_2(\mu+\eta)}\left(\frac{S_+}{S^0}\mathcal{R}_1 - 1\right)\left(\frac{S_+}{S^0}\mathcal{R}_2 - 1\right) \end{pmatrix},$$

provided

$$S_+ > \max\left\{\frac{S^0}{\mathcal{R}_1}, \frac{S^0}{\mathcal{R}_2}\right\}, \quad Q < 0 \quad \text{and} \quad P < 0.$$

(i) For $R < 0$, the co-epidemic equilibrium is given by

$$E_+^* = (S, e(a), I_1, I_2, J)^T = \begin{pmatrix} -\frac{1}{2P}(Q + \sqrt{Q^2 - 4PR}) \\ e(0)\sigma(a) \\ \frac{\mu+\alpha_2}{\delta_2}\left(\frac{S_+}{S^0}\mathcal{R}_2 - 1\right) \\ \frac{\mu+\alpha_1}{\delta_1}\left(\frac{S_+}{S^0}\mathcal{R}_1 - 1\right) \\ \frac{(\delta_1+\delta_2)(\mu+\alpha_1)(\mu+\alpha_2)}{\delta_1\delta_2(\mu+\eta)}\left(\frac{S_+}{S^0}\mathcal{R}_1 - 1\right)\left(\frac{S_+}{S^0}\mathcal{R}_2 - 1\right) \end{pmatrix},$$

or

$$E_-^* = (S_-, e(a), I_1, I_2, J)^T = \begin{pmatrix} -\frac{1}{2P}(Q - \sqrt{Q^2 - 4PR}) \\ e(0)\sigma(a) \\ \frac{\mu+\alpha_2}{\delta_2}\left(\frac{S_-}{S^0}\mathcal{R}_2 - 1\right) \\ \frac{\mu+\alpha_1}{\delta_1}\left(\frac{S_-}{S^0}\mathcal{R}_1 - 1\right) \\ \frac{(\delta_1+\delta_2)(\mu+\alpha_1)(\mu+\alpha_2)}{\delta_1\delta_2(\mu+\eta)}\left(\frac{S_-}{S^0}\mathcal{R}_1 - 1\right)\left(\frac{S_-}{S^0}\mathcal{R}_2 - 1\right) \end{pmatrix},$$

provided

$$\text{either} \quad S_+ > \max\left\{\frac{S^0}{\mathcal{R}_1}, \frac{S^0}{\mathcal{R}_2}\right\} \quad \text{or} \quad S_- > \max\left\{\frac{S^0}{\mathcal{R}_1}, \frac{S^0}{\mathcal{R}_2}\right\}, \quad Q > 0 \quad \text{and} \quad P < 0.$$

4.4 Stability of the disease-free equilibrium

This section focuses of the local asymptotic stability of the disease-free equilibrium point. To do this, we employ the linearization technique around the equilibrium. Let

$$\tilde{S}(t), \tilde{e}(a,t), \tilde{I}_1(t), \tilde{I}_2(t) \quad \text{and} \quad \tilde{J}(t)$$

be perturbations of

$$S(t), e(a,t), I_1(t), I_2(t) \quad \text{and} \quad J(t),$$

respectively, such that

$$\tilde{S}(t) = S(t) - S, \tilde{e}(a,t) = e(a,t) - e(a), \tilde{I}_1(t) = I_1(t) - I_1, \tilde{I}_2(t) = I_2(t) - I_2 \quad \text{and} \quad \tilde{J}(t) = J(t) - J,$$

where $E = (S, e(a), I_1, I_2, J)^T$ is the equilibrium point. The perturbations satisfy the fractional system,

$$\begin{aligned} {}^{CF}D_t^\nu \tilde{S}(t) = &- \tilde{S}(t)(\mu + \beta_1 I_1(t) + \beta_2 I_2(t)) + \int_0^\infty \alpha_0(a)\tilde{e}(a,t)da + (\alpha_1 - \beta_1 S(t)) \\ &\times \tilde{I}_1(t) + (\alpha_2 - \beta_2 S(t))\tilde{I}_2(t), \qquad (4.19) \\ {}^{CF}\partial_t^\nu \tilde{e}(a,t) + {}^{CF}\partial_a^\nu \tilde{e}(a,t) = &-(\mu + \gamma(a) + \alpha_0(a))\tilde{e}(a,t), \qquad (4.20) \end{aligned}$$

$$
{}^{CF}D_t^{\nu}\tilde{I}_1(t) = \int\limits_0^{\infty} \gamma(a)\tilde{e}(a,t)da - (\mu + \alpha_1 - \delta_1 I_2(t))\tilde{I}_1(t) - \delta_1 I_1(t)\tilde{I}_2(t), \tag{4.21}
$$

$$
{}^{CF}D_t^{\nu}\tilde{I}_2(t) = \beta_2\tilde{S}(t)I_2(t) - (\mu + \alpha_2 + \beta_2 S - \delta_2 I_1(t))\tilde{I}_2(t) - \delta_2\tilde{I}_1(t)I_2(t), \tag{4.22}
$$

$$
{}^{CF}D_t^{\nu}\tilde{J}(t) = (\delta_1 + \delta_2)(\tilde{I}_1(t)I_2(t) + I_1(t)\tilde{I}_2(t)) - (\mu + \eta)\tilde{J}(t), \tag{4.23}
$$

after neglecting perturbation terms of order greater than or equal to 2, with boundary condition

$$
\tilde{e}(0,t) = \beta_1(\tilde{S}(t)I_1 + S\tilde{I}_1(t)).
$$

Suppose the solutions of the fractional system are of the form,

$$
\tilde{S}(t) = \frac{B(\nu)\bar{S}}{B(\nu) - (1-\nu)\lambda} \exp\left\{\frac{\nu\lambda}{B(\nu) - (1-\nu)\lambda} t\right\},
$$

$$
\tilde{e}(a,t) = \frac{B(\nu)\bar{e}(a)}{B(\nu) - (1-\nu)\lambda} \exp\left\{\frac{\nu\lambda}{B(\nu) - (1-\nu)\lambda} t\right\},
$$

$$
\tilde{I}_1(t) = \frac{B(\nu)\bar{I}_1}{B(\nu) - (1-\nu)\lambda} \exp\left\{\frac{\nu\lambda}{B(\nu) - (1-\nu)\lambda} t\right\},
$$

$$
\tilde{I}_2(t) = \frac{B(\nu)\bar{I}_2}{B(\nu) - (1-\nu)\lambda} \exp\left\{\frac{\nu\lambda}{B(\nu) - (1-\nu)\lambda} t\right\}
$$

and

$$
\tilde{J}(t) = \frac{B(\nu)\bar{J}}{B(\nu) - (1-\nu)\lambda} \exp\left\{\frac{\nu\lambda}{B(\nu) - (1-\nu)\lambda} t\right\}.
$$

Since the function $f(t) = \frac{B(\nu)f(0)}{B(\nu)-(1-\nu)\lambda} \exp\left\{\frac{\nu\lambda}{B(\nu)-(1-\nu)\lambda} t\right\}$ satisfies the fractional equation ${}^{CF}D_t^{\nu}f(t) = \lambda f(t)$, then it follows that (4.19) - (4.23) can be rewritten as

$$
\lambda\bar{S} = -\bar{S}(\mu + \beta_1 I_1 + \beta_2 I_2) + \int\limits_0^{\infty} \alpha_0(a)\bar{e}(a)da + (\alpha_1 - \beta_1 S)\bar{I}_1 + (\alpha_2 - \beta_2 S)\bar{I}_2, \tag{4.24}
$$

$$
\lambda\bar{e}(a) + {}^{CF}D_a^{\nu}\bar{e}(a) = -(\mu + \gamma(a) + \alpha_0(a))\bar{e}(a), \tag{4.25}
$$

$$
\lambda\bar{I}_1 = \int\limits_0^{\infty} \gamma(a)\bar{e}(a)da - (\mu + \alpha_1 - \delta_1 I_2)\bar{I}_1 - \delta_1 I_1\bar{I}_2, \tag{4.26}
$$

$$
\lambda\bar{I}_2 = \beta_2\bar{S}I_2 - (\mu + \alpha_2 + \beta_2 S - \delta_2 I_1)\bar{I}_2 - \delta_2\bar{I}_1 I_2, \tag{4.27}
$$

$$
\lambda\bar{J} = (\delta_1 + \delta_2)(\bar{I}_1 I_2 + I_1\bar{I}_2) - (\mu + \eta)\bar{J}, \tag{4.28}
$$

with boundary condition

$$
\bar{e}(0) = \beta_1(\bar{S}I_1 + S\bar{I}_1).
$$

Theorem 4.2. *The disease-free equilibrium, E^0, is locally asymptotically stable whenever*

$$1 > \mathcal{R}_1 > \frac{\alpha_1}{(1-B)(\mu+\alpha_1)} \quad \textit{and} \quad \mathcal{R}_2 > \frac{\alpha_2}{\mu+\alpha_2}.$$

The disease-free equilibrium is unstable provided

$$1 < \mathcal{R}_1 < \frac{\alpha_1}{(1-B)(\mu+\alpha_1)} \quad \textit{and} \quad \mathcal{R}_2 > \frac{\alpha_2}{\mu+\alpha_2}.$$

Proof. Substituting the disease-free equilibrium,

$$E^0 = (S^0, 0, 0, 0, 0)^T = \left(\frac{\Lambda}{\mu}, 0, 0, 0, 0\right)^T,$$

into (4.24) - (4.28) leads to

$$\lambda\bar{S} = -\bar{S}\mu + \int_0^\infty \alpha_0(a)\bar{e}(a)da + (\alpha_1 - \beta_1 S^0)\bar{I}_1 + (\alpha_2 - \beta_2 S^0)\bar{I}_2, \tag{4.29}$$

$$\lambda\bar{e}(a) + {}^{CF}D_a^\nu \bar{e}(a) = -(\mu + \gamma(a) + \alpha_0(a))\bar{e}(a), \tag{4.30}$$

$$\lambda\bar{I}_1 = \int_0^\infty \gamma(a)\bar{e}(a)da - (\mu+\alpha_1)\bar{I}_1, \tag{4.31}$$

$$\lambda\bar{I}_2 = -(\mu + \alpha_2 + \beta_2 S^0)\bar{I}_2, \tag{4.32}$$

$$\lambda\bar{J} = -(\mu+\eta)\bar{J}, \tag{4.33}$$

with boundary condition

$$\bar{e}(0) = \beta_1 S^0 \bar{I}_1.$$

It follows from (4.33) that

$$\text{either} \quad \bar{J} = 0 \quad \text{or} \quad \lambda = -(\mu+\eta) < 0.$$

Similarly (4.32) yields

$$\text{either} \quad \bar{I}_2 = 0 \quad \text{or} \quad \lambda = -(\mu + \alpha_2 + \beta_2 S^0) < 0.$$

From (4.30) we obtain the fractional differential equation

$${}^{CF}D_a^\nu \bar{e}(a) = -(\lambda + \mu + \gamma(a) + \alpha_0(a))\bar{e}(a) = -(\lambda + \xi(a))\bar{e}(a),$$

which has the solution $\bar{e}(a) = \bar{e}(0)\sigma_\lambda(a)$, where

$$\sigma_\lambda(a) = \left[1 + \left(\frac{\nu + (1-\nu)a}{B(\nu)}\right)(\lambda + \xi(a))\right]^{-1} = \sum_{k=0}^{\infty}\left[-\left(\frac{\nu + (1-\nu)a}{B(\nu)}\right)(\lambda + \xi(a))\right]^{k},$$

provided

$$\left|-\left(\frac{\nu + (1-\nu)a}{B(\nu)}\right)(\lambda + \xi(a))\right| < 1,$$

or equivalently

$$-\frac{B(\nu)}{\nu + (1-\nu)a} - \xi(a) < \lambda < \frac{B(\nu)}{\nu + (1-\nu)a} - \xi(a).$$

Consider the integrals

$$\int_0^\infty \alpha_0(a)\bar{e}(a)da = \bar{e}(0)\int_0^\infty \alpha_0(a)\sigma_\lambda(a)da = \bar{e}(0)B_\lambda, \quad \text{where} \quad B_\lambda = \int_0^\infty \alpha_0(a)\sigma_\lambda(a)da,$$

and

$$\int_0^\infty \gamma(a)\bar{e}(a)da = \bar{e}(0)\int_0^\infty \gamma(a)\sigma_\lambda(a)da = \bar{e}(0)C_\lambda, \quad \text{where} \quad C_\lambda = \int_0^\infty \gamma(a)\sigma_\lambda(a)da.$$

Hence (4.31) can be rewritten as

$$\lambda\bar{I}_1 = \bar{e}(0)C_\lambda - (\mu + \alpha_1)\bar{I}_1 = \beta_1 S^0\bar{I}_1 C_\lambda - (\mu + \alpha_1)\bar{I}_1 = [\beta_1 S^0 C_\lambda - (\mu + \alpha_1)]\bar{I}_1,$$

and hence $\bar{I}_1 = 0$ or

$$\lambda = \beta_1 S^0 C_\lambda - (\mu + \alpha_1) = (\mu + \alpha_1)\left(\frac{\beta_1 S^0}{(\mu + \alpha_1)}C_\lambda - 1\right) = (\mu + \alpha_1)\left(\frac{C_\lambda}{C}\mathcal{R}_1 - 1\right). \tag{4.34}$$

The following cases will be considered to solve (4.34).

4.4.1 Case 1 ($\lambda \in \mathbb{R}$):

Since

$$\begin{aligned}\frac{d}{d\lambda}\sigma_\lambda(a) &= \frac{d}{d\lambda}\left[1 + \left(\frac{\nu + (1-\nu)a}{B(\nu)}\right)(\lambda + \xi(a))\right]^{-1} \\ &= -\left(\frac{\nu + (1-\nu)a}{B(\nu)}\right)\left[1 + \left(\frac{\nu + (1-\nu)a}{B(\nu)}\right)(\lambda + \xi(a))\right]^{-2}\end{aligned}$$

$$= -\left(\frac{\nu + (1-\nu)a}{B(\nu)}\right)\sigma_\lambda^2(a) < 0,$$

it follows that

$$\frac{d}{d\lambda}C_\lambda = \int_0^\infty \gamma(a)\frac{d}{d\lambda}\sigma_\lambda(a)da = -\int_0^\infty \gamma(a)\left(\frac{\nu + (1-\nu)a}{B(\nu)}\right)\sigma_\lambda^2(a)da = -||K_{\gamma,\lambda}||_1 < 0,$$

where

$$K_{\gamma,\lambda}(a) = \gamma(a)\left(\frac{\nu + (1-\nu)a}{B(\nu)}\right)\sigma_\lambda^2(a) > 0.$$

Therefore C_λ is a decreasing function of λ. It follows that for $\lambda < 0$, we have $C = C_0 < C_\lambda$, and hence the following holds

$$\frac{C_\lambda}{C}\mathcal{R}_1 - 1 < 0;$$

that is,

$$\mathcal{R}_1 < \frac{C}{C_\lambda} < 1.$$

However, for $\lambda > 0$, we have $C = C_0 > C_\lambda$, and hence

$$\frac{C_\lambda}{C}\mathcal{R}_1 - 1 > 0;$$

that is,

$$\mathcal{R}_1 > \frac{C}{C_\lambda} > 1.$$

It follows from (4.29) that

$$\begin{aligned}\lambda\bar{S} &= -\bar{S}\mu + \bar{e}(0)B_\lambda + (\alpha_1 - \beta_1 S^0)\bar{I}_1 + (\alpha_2 - \beta_2 S^0)\bar{I}_2\\ &= -\bar{S}\mu + \beta_1 S^0\bar{I}_1 B_\lambda + (\alpha_1 - \beta_1 S^0)\bar{I}_1 + (\alpha_2 - \beta_2 S^0)\bar{I}_2;\end{aligned}$$

that is,

$$(\lambda + \mu)\bar{S} = (\alpha_1 - \beta_1(1 - B_\lambda)S^0)\bar{I}_1 + (\alpha_2 - \beta_2 S^0)\bar{I}_2,$$

which yields the characteristic equation

$$F(\lambda) = 1, \tag{4.35}$$

where

$$F(\lambda) = \frac{(\lambda+\mu)\bar{S} - (\alpha_1 - \beta_1(1-B_\lambda)S^0)\bar{I}_1}{(\alpha_2 - \beta_2 S^0)\bar{I}_2}.$$

Consider the derivative below

$$\begin{aligned} D_\lambda[F(\lambda)] &= \frac{D_\lambda[\lambda+\mu]\bar{S} - D_\lambda[\alpha_1 - \beta_1(1-B_\lambda)S^0]\bar{I}_1}{(\alpha_2 - \beta_2 S^0)\bar{I}_2} \\ &= \frac{\bar{S} - \beta_1 D_\lambda[B_\lambda]S^0\bar{I}_1}{(\alpha_2 - \beta_2 S^0)\bar{I}_2}. \end{aligned}$$

Since

$$-D_\lambda[B_\lambda] = -\int\limits_0^\infty \alpha_0(a) D_\lambda \sigma_\lambda(a)da = \int\limits_0^\infty \alpha_0(a)\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\sigma_\lambda^2(a)da = ||H_{\alpha_0,\lambda}||_1 > 0,$$

where

$$H_{\alpha_0,\lambda}(a) = \alpha_0(a)\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\sigma_\lambda^2(a) > 0,$$

it follows that

$$D_\lambda[F(\lambda)] < 0$$

if and only if

$$\alpha_2 - \beta_2 S^0 < 0.$$

Therefore $F(\lambda)$ is a decreasing function of λ provided $\alpha_2 - \beta_2 S^0 < 0$. Since

$$\alpha_2 - \beta_2 S^0 = \mu + \alpha_2 - \beta_2 S^0 - \mu = (\mu+\alpha_2)\left(1 - \frac{\beta_2 S^0}{\mu+\alpha_2}\right) - \mu = (\mu+\alpha_2)\left(1 - \mathcal{R}_2\right) - \mu < 0;$$

that is,

$$\mathcal{R}_2 > \frac{\alpha_2}{\mu+\alpha_2}.$$

We consider the following sub-cases to discuss the solution of $F(\lambda)$, for $\lambda < 0$ and $\lambda > 0$.

Subcase 1 ($\lambda < 0$): It follows that

$$F(\lambda) = 1 > F(0) = \frac{\mu\bar{S} - (\alpha_1 - \beta_1(1-B)S^0)\bar{I}_1}{(\alpha_2 - \beta_2 S^0)\bar{I}_2},$$

which leads to

$$\mu\bar{S} - (\alpha_1 - \beta_1(1-B)S^0)\bar{I}_1 > (\alpha_2 - \beta_2 S^0)\bar{I}_2.$$

Equivalently, we have

$$-(\alpha_1 - \beta_1(1-B)S^0)\bar{I}_1 > (\alpha_2 - \beta_2 S^0)\bar{I}_2 - \mu\bar{S},$$

and hence

$$\alpha_1 - \beta_1(1-B)S^0 < 0.$$

This yields

$$(\mu + \alpha_1 - \beta_1(1-B)S^0 - \mu)\bar{I}_1 = \left[(\mu+\alpha_1)\left(1 - (1-B)\frac{\beta_1 S^0}{\mu+\alpha_1}\right) - \mu\right]\bar{I}_1 > 0,$$

which implies

$$(\mu + \alpha_1 - \beta_1(1-B)S^0 - \mu)\bar{I}_1 = \left[(\mu+\alpha_1)\left(1 - (1-B)\frac{\mathcal{R}_1}{C}\right) - \mu\right]\bar{I}_1 > 0;$$

that is,

$$\mathcal{R}_1 > \frac{\alpha_1 C}{(1-B)(\mu+\alpha_1)} > \frac{\alpha_1 C}{(\mu+\alpha_1)}.$$

Hence the disease-free equilibrium, E^0, is locally asymptotically stable provided

$$\mathcal{R}_1 > \frac{\alpha_1 C}{\mu+\alpha_1} \quad \text{and} \quad \mathcal{R}_2 > \frac{\alpha_2}{\mu+\alpha_2};$$

that is,

$$|\arg(\lambda)| = 0 < \frac{\nu\pi}{2} \quad \text{for all} \quad \nu \in (0,1).$$

Subcase 2 ($\lambda > 0$): It follows that

$$F(0) = \frac{\mu\bar{S} - (\alpha_1 - \beta_1(1-B)S^0)\bar{I}_1}{(\alpha_2 - \beta_2 S^0)\bar{I}_2} < F(\lambda) = 1,$$

which leads to

$$\mu\bar{S} - (\alpha_1 - \beta_1(1-B)S^0)\bar{I}_1 < (\alpha_2 - \beta_2 S^0)\bar{I}_2 < 0,$$

and hence,

$$0 < \mu\bar{S} < (\alpha_1 - \beta_1(1-B)S^0)\bar{I}_1;$$

that is,

$$0 < \mu\bar{S} < (\alpha_1 - \beta_1(1-B)S^0)\bar{I}_1.$$

Therefore,

$$(\alpha_1 - \beta_1(1-B)S^0)\bar{I}_1 > 0.$$

This yields

$$(\mu+\alpha_1-\beta_1(1-B)S^0-\mu)\bar{I}_1=\left[(\mu+\alpha_1)\left(1-(1-B)\frac{\beta_1 S^0}{\mu+\alpha_1}\right)-\mu\right]\bar{I}_1>0,$$

that is,

$$(\mu+\alpha_1)(1-(1-B)\frac{\mathcal{R}_1}{C})-\mu<0,$$

and hence

$$\mathcal{R}_1<\frac{\alpha_1 C}{(1-B)(\mu+\alpha_1)}<\frac{\alpha_1}{(1-B)(\mu+\alpha_1)}.$$

Hence the disease-free equilibrium, E^0, is unstable provided

$$\mathcal{R}_1<\frac{\alpha_1}{(1-B)(\mu+\alpha_1)}\quad\text{and}\quad\mathcal{R}_2>\frac{\alpha_2 C}{\mu+\alpha_2},$$

that is

$$|\arg(\lambda)|=\pi>\frac{\nu\pi}{2}\quad\text{for all}\quad\nu\in(0,1).$$

4.4.2 Case 2 ($\lambda\in\mathbb{C}$):

Let $\lambda=x+\iota y$. It follows from (4.34) that

$$x+\iota y=(\mu+\alpha_1)\left(\mathcal{R}_1\frac{C_{xy}}{C}-1\right),\quad\text{where}\quad C_{xy}=\int_0^\infty\gamma(a)\sigma_{xy}(a)da,$$

with

$$\begin{aligned}\sigma_{xy}(a)&=\left[1+\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)(x+\iota y+\xi(a))\right]^{-1}\\&=\left[1+(x+\xi(a))\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)+\iota y\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\right]^{-1},\end{aligned}$$

which leads to

$$\sigma_{xy}(a)=\frac{1+(x+\xi(a))\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)-\iota y\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)}{\left[1+(x+\xi(a))\left(\frac{\nu+(1-\nu)a}{M(\nu)}\right)\right]^2+\left[y\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\right]^2},$$

$$
\begin{aligned}
=&\frac{1+(x+\xi(a))\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)}{\left[1+(x+\xi(a))\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\right]^2+\left[y\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\right]^2}-\\
&\iota\frac{y\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)}{\left[1+(x+\xi(a))\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\right]^2+\left[y\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\right]^2}\\
=&E_{xy}(a)-\iota E^*_{xy}(a),
\end{aligned}
$$

where

$$
E_{xy}(a)=\frac{1+(x+\xi(a))\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)}{\left[1+(x+\xi(a))\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\right]^2+\left[y\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\right]^2},
$$

and

$$
E^*_{xy}(a)=\frac{y\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)}{\left[1+(x+\xi(a))\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\right]^2+\left[y\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\right]^2}.
$$

Hence, we have

$$
C_{xy}=\int\limits_0^\infty\gamma(a)(E_{xy}(a)-\iota E^*_{xy}(a))da=\int\limits_0^\infty\gamma(a)E_{xy}(a)da-\iota\int\limits_0^\infty\gamma(a)E^*_{xy}(a)da=G_{xy}-\iota G^*_{xy},
$$

which yields

$$
x+\iota y=(\mu+\alpha_1)\left(\frac{\mathcal{R}_1}{C}[G_{xy}-\iota G^*_{xy}]-1\right)=(\mu+\alpha_1)\left(\frac{\mathcal{R}_1}{C}G_{xy}-1\right)-\iota(\mu+\alpha_1)\frac{\mathcal{R}_1}{C}G^*_{xy},
$$

Which implies,

$$
x=(\mu+\alpha_1)\left(\frac{\mathcal{R}_1}{C}G_{xy}-1\right)\quad\text{and}\quad y=-(\mu+\alpha_1)\frac{\mathcal{R}_1}{C}G^*_{xy},
$$

it follows that

$$
x-(\mu+\alpha_1)\frac{\mathcal{R}_1}{C}G_{xy}+(\mu+\alpha_1)=0;
$$

that is,

$$
x-(\mu+\alpha_1)\frac{\mathcal{R}_1}{C}\int\limits_0^\infty\gamma(a)E_{xy}(a)da+(\mu+\alpha_1)=0.
$$

Since

$$E_{xy}(a) = \frac{1+\xi(a)\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)}{\left[1+(x+\xi(a))\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\right]^2+\left[y\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\right]^2} + \frac{x\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)}{\left[1+(x+\xi(a))\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\right]^2+\left[y\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\right]^2}.$$

Setting

$$U_{\gamma,xy}(a) = \frac{\gamma(a)\left[1+\xi(a)\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\right]}{\left[1+(x+\xi(a))\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\right]^2+\left[y\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\right]^2}$$

and

$$V_{\gamma,xy}(a) = \frac{\gamma(a)\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)}{\left[1+(x+\xi(a))\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\right]^2+\left[y\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\right]^2}$$

leads to

$$x-(\mu+\alpha_1)\frac{\mathcal{R}_1}{C}\left(||U_{\gamma,xy}||_1+x||V_{\gamma,xy}||_1\right)+(\mu+\alpha_1)=0,$$

which implies

$$x\left(1-(\mu+\alpha_1)\frac{\mathcal{R}_1}{C}||V_{\gamma,xy}||_1\right)=(\mu+\alpha_1)\left(\frac{\mathcal{R}_1}{C}||U_{\gamma,xy}||_1-1\right). \tag{4.36}$$

This yields the following:

Sub-Case 1 ($\frac{\mathcal{R}_1}{C}||U_{\gamma,xy}||_1-1>0$):

That is,

$$\mathcal{R}_1>\frac{C}{||U_{\gamma,xy}||_1}.$$

From (4.36), we have

$$x\left(1-(\mu+\alpha_1)\frac{\mathcal{R}_1}{C}||V_{\gamma,xy}||_1\frac{\mathcal{R}_1}{C}\right)=(\mu+\alpha_1)\left(\frac{\mathcal{R}_1}{C}||U_{\gamma,xy}||_1-1\right)>0,$$

and hence, either

$$x < 0 \quad \text{and} \quad 1 - (\mu + \alpha_1)\frac{\mathcal{R}_1}{C}||V_{\gamma,xy}||_1 < 0$$

or

$$x > 0 \quad \text{and} \quad 1 - (\mu + \alpha_1)\frac{\mathcal{R}_1}{C}||V_{\gamma,xy}||_1 > 0,$$

which yield, either

$$x < 0 \quad \text{and} \quad \mathcal{R}_1 > \frac{C}{(\mu + \alpha_1)||V_{\gamma,xy}||_1},$$

or

$$x > 0 \quad \text{and} \quad \mathcal{R}_1 < \frac{C}{(\mu + \alpha_1)||V_{\gamma,xy}||_1}.$$

Therefore, the disease-free equilibrium is locally asymptotically stable whenever

$$x < 0 \quad \text{and} \quad \mathcal{R}_1 > \max\left\{\frac{C}{||U_{\gamma,xy}||_1}, \frac{C}{(\mu + \alpha_1)||V_{\gamma,xy}||_1}\right\},$$

and the disease-free equilibrium is unstable whenever

$$x > 0 \quad \text{and} \quad \frac{C}{||U_{\gamma,xy}||_1} < \mathcal{R}_1 < \frac{C}{(\mu + \alpha_1)||V_{\gamma,xy}||_1}.$$

Sub-Case 2 ($\frac{\mathcal{R}_1}{C}||U_{\gamma,xy}||_1 - 1 < 0$):

That is,

$$\mathcal{R}_1 < \frac{C}{||U_{\gamma,xy}||_1}.$$

From (4.36), we have

$$x\left(1 - (\mu + \alpha_1)\frac{\mathcal{R}_1}{C}||V_{\gamma,xy}||_1\frac{\mathcal{R}_1}{C}\right) = (\mu + \alpha_1)\left(\frac{\mathcal{R}_1}{C}||U_{\gamma,xy}||_1 - 1\right) < 0,$$

and hence, either

$$x < 0 \quad \text{and} \quad 1 - (\mu + \alpha_1)\frac{\mathcal{R}_1}{C}||V_{\gamma,xy}||_1 > 0$$

or

$$x > 0 \quad \text{and} \quad 1 - (\mu + \alpha_1)\frac{\mathcal{R}_1}{C}||V_{\gamma,xy}||_1 < 0,$$

which yield, either

$$x < 0 \quad \text{and} \quad \mathcal{R}_1 < \frac{C}{(\mu + \alpha_1)||V_{\gamma,xy}||_1},$$

or

$$x > 0 \quad \text{and} \quad \mathcal{R}_1 > \frac{C}{(\mu+\alpha_1)||V_{\gamma,xy}||_1}.$$

Therefore, the disease-free equilibrium is locally asymptotically stable whenever

$$x < 0 \quad \text{and} \quad \mathcal{R}_1 < \min\left\{\frac{C}{||U_{\gamma,xy}||_1}, \frac{C}{(\mu+\alpha_1)||V_{\gamma,xy}||_1}\right\},$$

and the disease-free equilibrium is unstable whenever

$$x > 0 \quad \text{and} \quad \frac{C}{||U_{\gamma,xy}||_1} > \mathcal{R}_1 > \frac{C}{(\mu+\alpha_1)||V_{\gamma,xy}||_1}.$$

Using the following integral

$$\begin{aligned} B_{xy} &= \int_0^\infty \alpha_0(a)(E_{xy}(a) - \iota E^*_{xy}(a))da \\ &= \int_0^\infty \alpha_0(a)E_{xy}(a)da - \iota\int_0^\infty \alpha_0(a)E^*_{xy}(a)da \\ &= W_{xy} - \iota W^*_{xy}, \end{aligned}$$

into the characteristic equation (4.35) leads to

$$\begin{aligned} F(x+\iota y) &= \frac{(x+\iota y+\mu)\bar{S} - (\alpha_1 - \beta_1(1-[W_{xy}-\iota W^*_{xy}])S^0)\bar{I}_1}{(\alpha_2-\beta_2 S^0)\bar{I}_2} \\ &= \frac{[(x+\mu)\bar{S} - (\alpha_1-\beta_1(1-W_{xy})S^0)\bar{I}_1] + \iota[y\bar{S} + \beta_1 W^*_{xy}S^0\bar{I}_1]}{(\alpha_2-\beta_2 S^0)\bar{I}_2} \\ &= \frac{(x+\mu)\bar{S} - (\alpha_1-\beta_1(1-W^*_{xy})S^0)\bar{I}_1}{(\alpha_2-\beta_2 S^0)\bar{I}_2} + \iota\frac{y\bar{S}+\beta_1 W^*_{xy}S^0\bar{I}_1}{(\alpha_2-\beta_2 S^0)\bar{I}_2} = 1, \end{aligned}$$

and hence

$$\Re\{F(\lambda)\} = \frac{(x+\mu)\bar{S} - (\alpha_1-\beta_1(1-W_{xy})S^0)\bar{I}_1}{(\alpha_2-\beta_2 S^0)\bar{I}_2} = 1$$

and

$$\Im\{F(\lambda)\} = \frac{y\bar{S}+\beta_1 W^*_{xy}S^0\bar{I}_1}{(\alpha_2-\beta_2 S^0)\bar{I}_2} = 0.$$

From $\Re\{F(\lambda)\} = 1$, we have

$$(x+\mu)\bar{S} - (\alpha_1-\beta_1(1-W_{xy})S^0)\bar{I}_1 = (\alpha_2-\beta_2 S^0)\bar{I}_2,$$

which implies

$$(\alpha_2-\beta_2 S^0)\bar{I}_2 + (\alpha_1-\beta_1(1-W_{xy})S^0)\bar{I}_1 = (x+\mu)\bar{S}.$$

Assuming $x < -\mu < 0$, yields

$$(\alpha_1 - \beta_1(1 - W_{xy})S^0)\bar{I}_1 + (\alpha_2 - \beta_2 S^0)\bar{I}_2 = (x + \mu)\bar{S} < 0,$$

and hence

$$(\alpha_1 - \beta_1(1 - W_{xy})S^0)\bar{I}_1 < -(\alpha_2 - \beta_2 S^0)\bar{I}_2.$$

Assuming

$$\alpha_1 - \beta_1(1 - W_{xy})S^0 > 0,$$

yields

$$\alpha_2 - \beta_2 S^0 < 0.$$

Therefore the following holds

$$W_{xy} > 1 - \frac{\alpha_1}{\beta_1 S^0},$$

which leads to

$$||U_{\alpha_0,xy}||_1 + x||V_{\alpha_0,xy}||_1 > 1 - \frac{\alpha_1}{\beta_1 S^0} = 1 - \frac{\alpha_1 C}{(\mu + \alpha_1)\mathcal{R}_1}, \tag{4.37}$$

where

$$U_{\alpha_0,xy}(a) = \frac{\alpha_0(a)\left[1 + \xi(a)\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\right]}{\left[1 + (x + \xi(a))\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\right]^2 + \left[y\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\right]^2}$$

and

$$V_{\alpha_0,xy}(a) = \frac{\alpha_0(a)\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)}{\left[1 + (x + \xi(a))\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\right]^2 + \left[y\left(\frac{\nu+(1-\nu)a}{B(\nu)}\right)\right]^2}.$$

Hence,

(i)

$$0 > ||U_{\alpha_0,xy}||_1 + x||V_{\alpha_0,xy}||_1 > 1 - \frac{\alpha_1 C}{(\mu + \alpha_1)\mathcal{R}_1}.$$

(ii)

$$||U_{\alpha_0,xy}||_1 + x||V_{\alpha_0,xy}||_1 > 1 - \frac{\alpha_1 C}{(\mu + \alpha_1)\mathcal{R}_1} > 0.$$

(iii)

$$||U_{\alpha_0,xy}||_1 + x||V_{\alpha_0,xy}||_1 > 1 - \frac{\alpha_1 C}{(\mu+\alpha_1)\mathcal{R}_1}.$$

From (i), we have

$$x < -\frac{||U_{\alpha_0,xy}||_1}{||V_{\alpha_0,xy}||_1} < 0 \quad \text{and} \quad \mathcal{R}_1 < \frac{\alpha_1 C}{\mu+\alpha_1}.$$

From (ii), we have

$$x > -\frac{||U_{\alpha_0,xy}||_1}{||V_{\alpha_0,xy}||_1} \quad \text{and} \quad \mathcal{R}_1 > \frac{\alpha_1 C}{\mu+\alpha_1}.$$

From (iii), we have

$$x > -\frac{||U_{\alpha_0,xy}||_1}{||V_{\alpha_0,xy}||_1} \quad \text{and} \quad \mathcal{R}_1 < \frac{\alpha_1 C}{\mu+\alpha_1}.$$

Therefore, the disease-free equilibrium is locally asymptotically stable provided (i) and the disease-free equilibrium is unstable provided (ii) or (iii). □

The local asymptotic stability of the disease-free equilibrium is determined by the reproduction numbers of HIV and TB in both Case 1 and Case 2.

Chapter 5

Conclusions

A Caputo fractional model for the spread of HIV infection within-host through two transmission routes and cell types was investigated in Chapter 3. The boundedness of the solutions of (3.1) - (3.7) was established and the positive invariance of the state space of (3.1) - (3.7) was proven provided

$$\frac{\Lambda_i}{(\Lambda_1 + \Lambda_2)^2} > \frac{\beta_i + \kappa_i}{c_3^2}, \quad \text{for all} \quad i = 1, 2.$$

This ensured that the cell populations and the viral population are not only finite, but are always positively defined. In Theorem 3.2 the existence and uniqueness of solutions of (3.1) - (3.7) were proven. Thus the populations are continuously defined for all time and are uniquely determined by the initial populations. The basic reproduction numbers, $\mathcal{R}_1$ and $\mathcal{R}_2$ of HIV through each cell type are derived. Furthermore, it was also proven that the reproduction number through each cell type i is composed of the reproduction number of HIV through cell-to-cell transmission routes, $\mathcal{R}_i^{CC}$, and cell-to-virus transmission routes, $\mathcal{R}_i^{CV}$, for all $i = 1, 2$. We aimed to study the impact of HIV latent transmission through two routes and cell types. The effects of age-structure are included in the probabilities, ξ_1 and ξ_2, of latently infected cells transitioning to productively infected cells, which directly affect the reproduction number of HIV through each cell type $\mathcal{R}_1$ and $\mathcal{R}_2$, respectively. This illustrates that the reproduction of HIV within-host is facilitated by progression of the virus through each transmission route. The existence of equilibria was discussed under certain conditions on the basic reproduction numbers. Specifically, the disease-free equilibrium always exists whenever the productively infected cells are absent. Stability analysis for a system of Caputo fractional differential equations given by (3.1) - (3.7) was conducted and the findings the analysis show that the local asymptotic stability of the disease-free equilibrium is given by

$$\mathcal{R}_1 < 1 \quad \text{and} \quad \mathcal{R}_2 < 1.$$

That is, the disease will be eliminated from the host whenever the reproduction numbers through each cell type are both less than 1. Furthermore, the disease-free equilibrium was proven to be unstable whenever

$$\mathcal{R}_1 > 1 \quad \text{and} \quad \mathcal{R}_2 < 1, \quad \text{or} \quad \mathcal{R}_1 < 1 \quad \text{and} \quad \mathcal{R}_2 > 1.$$

Hence, the disease persists whenever the reproduction numbers through one cell type is less than 1 and the reproduction numbers through the other cell type is greater than 1. The asymptotic behavior of the system suggests that the latent reservoir and viral population that persist at relatively low levels may be suppressed and eradicated from the host. This can be achieved through the use of various treatment strategies aimed generating an extremely slow decay of the latent reservoir due to prolonged therapy. Incorporating treatment into the model enables investigation into the asymptotic effects of different therapies on the dynamics of HIV within-host.

A Caputo-Fabrizio fractional model for a co-epidemic of HIV and TB was investigated in Chapter 4. The boundedness of the solutions of (4.1) - (4.5) was established and the state space was proven to be positively invariant provided (4.7), (4.8) and (4.9) hold. In Theorem 4.1 the existence and uniqueness of solutions of (4.1) - (4.5) were established. The basic reproduction numbers $\mathcal{R}_1$ and $\mathcal{R}_2$, of TB and HIV, respectively were computed. The model formulated by [Xiaoyan, 2013] considered the transition of only TB infectives into the co-infection class. To account for the contribution of HIV to co-infection, we proposed an extension of the model to include the transition of HIV infectives into the co-infection class. We observed that the conditions on the reproduction number of HIV and TB, for the local asymptotic stability of the disease-free equilibrium of the extended fractional system are different to those obtained for the classical system.

The effects of age-structure are included in the probability of members of the latently infected TB class to transition into the active TB class and the probability of members of the latently infected class to recover from TB, denoted by C and B, respectively; were the probability C directly affects the reproduction number of TB. Stability analysis yielded two characteristic equations (4.15) and (4.17), from which we conclude that the disease-free equilibrium is locally asymptotically stable whenever

$$1 > \mathcal{R}_1 > \frac{\alpha_1 C}{\mu + \alpha_1} \quad \text{and} \quad \mathcal{R}_2 > \frac{\alpha_2}{\mu + \alpha_2}.$$

Hence, both diseases can be eradicated from the host population provided the reproduction number of TB is less than 1. Furthermore, the disease-free equilibrium was unstable provided

$$1 < \mathcal{R}_1 < \frac{\alpha_1 C}{\mu + \alpha_1} \quad \text{and} \quad \mathcal{R}_2 > \frac{\alpha_2}{\mu + \alpha_2}.$$

We observed that the condition on reproduction number of HIV is the same regardless of the stability of the disease-free equilibrium, hence the reproduction number of TB is a key factor in determining the progression or eradication of both diseases from the host population. Furthermore, the probability of treatment of TB infectives directly impacts the reproduction of TB, which can be used to investigate the asymptotic behavior of the co-epidemic due to application of effective treatment for TB.

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