MATHEMATICAL MODEL DEVELOPMENT TO

CONTROL THE OUTBREAK OF CASSAVA MOSAIC

DISEASE IN STOCHASTIC EPIDEMICS

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การพัฒนาแบบจำลองทางคณิตศาสตร์เพื่อควบคุมการแพร่ระบาดของโรคใบด่างมันสำปะหลังภายใต้ความไม่แน่นอนของการระบาด

นายนัทธ์ดนัย จันลาวงศ์

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ของโรคใบด่างมันสำปะหลังภายใต้ความไม่แน่นอนของการระบาด (MATHEMATICAL
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โรคใบด่างมันสำปะหลังเป็นโรคระบาดในพืช ซึ่งลดขนาดหัวและสัดส่วนแป้งของมัน
สำปะหลังจากต้นน้ำในห่วงโซ่อุปทานมันสำปะหลัง ส่งผลต่อการลดลงของยอดขายพืชผลมัน
สำปะหลัง เป้าหมายของงานวิจัยนี้คือเพื่อพัฒนาแบบจำลองทางคณิตศาสตร์ซึ่งแสดงพลวัตการ
ระบาดของโรคใบด่างมันสำปะหลัง โดยมีสาเหตุการระบาดมาจากแมลงหวี่ขาวหรือการปลูกด้วย
ท่อนพันธุ์ที่ติดเชื้อ พลวัตของประชากรมันสำปะหลังและแมลงหวี่ขาวสามารถศึกษาได้จากการใช้
แบบจำลองดังกล่าว โดยมีสถานะของพืช 4 สถานะ คือ สถานะทนทานโรค สถานะเสี่ยงติดเชื้อ
สถานะแฝงเชื้อ และสถานะติดเชื้อโดยแสดงอาการ และมีสถานะของแมลงหวี่ขาว 2 สถานะ คือ
สถานะเสี่ยงติดเชื้อ และสถานะติดเชื้อ แบบจำลองทางคณิตศาสตร์ถูกใช้ในการวิเคราะห์พฤติกรรม
การระบาดของโรคใบด่างมันสำปะหลังและนโยบายที่เหมาะสมก็สามารถถูกกำหนดได้จาก
แบบจำลองดังกล่าว

ความรุนแรงของการแพร่ระบาดโรคใบด่างมันสำปะหลังถูกตรวจสอบได้จากค่าระดับการ
ติดเชื้อพื้นฐาน (R_0) ซึ่งคำนวณจากวิธีการเดอะเน็กซ์เจเนเรชั่น พบว่าเกิดเสถียรภาพกำกับเฉพาะที่
ณ จุดเสถียรภาพปลอดโรคเมื่อ $R_0 < 1$ โดยใช้เกณฑ์ของเราธ์-เฮอร์วิทซ์ ขณะที่การตรวจสอบการมี
เสถียรภาพวงกว้าง ณ จุดเสถียรภาพปลอดโรคและ ณ จุดเสถียรภาพการแพร่ระบาดสามารถ
ตรวจสอบได้โดยทฤษฎีเลียปูนอฟและลาซาล ผลการวิเคราะห์ชี้ว่า ณ จุดเสถียรภาพปลอดโรคมี
เสถียรภาพวงกว้างและ $R_0 \leq 1$ ส่งผลให้โรคระบาดถูกควบคุมได้ อย่างไรก็ตาม โรคระบาดจะ
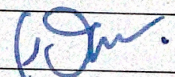ยังคงอยู่หาก ณ จุดเสถียรภาพการแพร่ระบาดมีเสถียรภาพวงกว้างและ $R_0 > 1$

การวิเคราะห์ความไวถูกใช้เพื่อตรวจสอบพารามิเตอร์ที่เป็นสาเหตุของการแพร่ระบาด โดย
พารามิเตอร์ที่มีค่าความไวต่อค่า R_0 มากที่สุดจะบ่งบอกว่าเป็นสาเหตุสำคัญของการแพร่ระบาด
ผลลัพธ์เชิงตัวเลขแสดงให้เห็นว่าการลดจำนวนแมลงหวี่ขาวโดยการฉีดพ่นยาฆ่าแมลง การถอน
ทำลายต้นที่ติดเชื้อ การเลือกท่อนพันธุ์ที่ไม่ติดเชื้อมาปลูก และการปลูกท่อนพันธุ์ทนทานโรค ช่วย
ในการควบคุมโรคและลดความรุนแรงในการระบาดได้ อย่างไรก็ตาม ยังไม่มีวิธีการคำนวณความ
คุ้มค่าด้านต้นทุนในการควบคุมการแพร่ระบาดอย่างชัดเจน

นโยบายที่มีความคุ้มค่าด้านต้นทุนมากที่สุดถูกคำนวณได้จากการใช้ทฤษฎีระบบควบคุม
แบบเหมาะสมที่สุดและค่าเฉลี่ยอัตราส่วนต้นทุนประสิทธิผล จากผลการทดลองแนะนำว่าการใช้

วิธีควบคุมร่วมกันระหว่างการปลูกด้วยพันธุ์ทนทาน การฉีดพ่นยาฆ่าแมลง และการถอนทำลายต้น
ที่ติดเชื้อเป็นนโยบายที่มีความคุ้มค่าด้านต้นทุนสูงสุดโดยมีค่าเฉลี่ยอัตราส่วนต้นทุนประสิทธิผล
1.643 การจำลองสถานการณ์เชิงตัวเลขชี้ว่าการควบคุมการแพร่ระบาดของแมลงหวี่ขาวไปสู่มัน
สำปะหลังและจากมันสำปะหลังไปสู่แมลงหวี่ขาวเป็นนโยบายที่สำคัญที่สุด
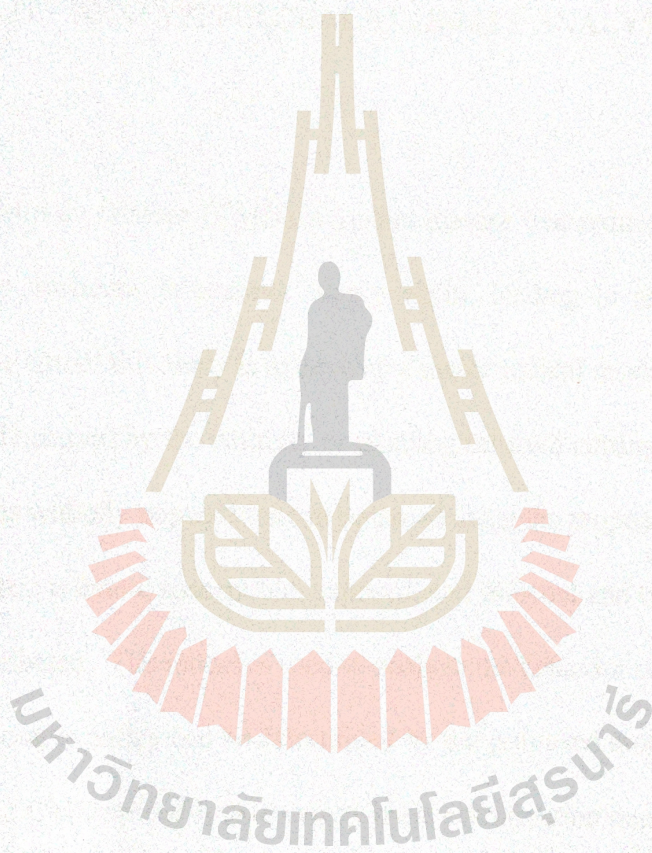
สาขาวิชา <u>วิศวกรรมอุตสาหการ</u>   ลายมือชื่อนักศึกษา _____
ปีการศึกษา 2563   ลายมือชื่ออาจารย์ที่ปรึกษา _____

NATDANAI CHANLAWONG : MATHEMATICAL MODEL
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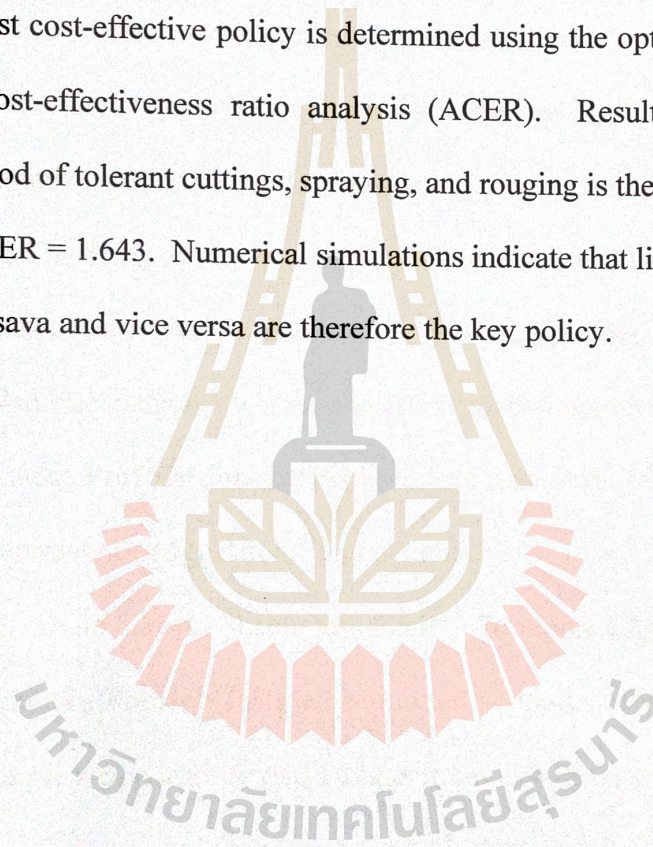ASST. PROF. PHONGCHAI JITTAMAI, Ph.D., 149 PP.

CASSAVA MOSAIC DISEASE (CMD)/BASIC REPRODUCTION NUMBER
LOCAL STABILITY ANALYSIS/GLOBAL STABILITY ANALYSIS/OPTIMAL
CONTROL;

Cassava Mosaic Disease (CMD) is a plant disease that reduces tuber size and
starch percentage upstream in cassava supply chain, leading to sales decrease of
cassava crop. The aim of this study is to develop a mathematical model that represents
dynamics of CMD caused by the whitefly or planting infected cuttings. Dynamics of
the cassava and the whitefly populations can be traced using the proposed model. There
are four plant states: tolerant, susceptible, exposed, and infected and two vector states:
susceptible and infected. The model is used to analyze the behavior of CMD outbreak
and the optimal control policy can be determined by the proposed model.

Severity of CMD spread is assessed by basic reproduction number (R_0), which
is calculated by using the next-generation method. The locally-asymptotically-stable
disease-free equilibrium point is established when $R_0 < 1$, using the Routh-Hurwitz
criteria. The globally-asymptotically-stable disease-free and the endemic equilibrium
points are established using Lyapunov-LaSalle's Theorem. Results indicate that
disease-free equilibrium point is globally-asymptotically-stable and $R_0 \leq 1$, implying
that the disease can be controlled. However, the disease will persist if the endemic
equilibrium point is globally-asymptotically-stable and $R_0 > 1$.

Sensitivity analysis is used to evaluate all parameters for cause of disease spread. A parameter with the highest absolute value of R_0 signifies the critical cause of outbreak. Numerical results show that reducing the number of whitefly by spraying pesticide, rouging infected cassavas, selecting non-virus cuttings, or promoting tolerant cuttings helps containing the disease and reducing the severity of the outbreak. However, there is no clear cost-effective approach to control disease spread.

The most cost-effective policy is determined using the optimal control theory and average cost-effectiveness ratio analysis (ACER). Results suggest that the combined method of tolerant cuttings, spraying, and rouging is the most cost-effective policy with ACER = 1.643. Numerical simulations indicate that limiting transmission of whitefly-cassava and vice versa are therefore the key policy.

School of <u>Industrial Engineering</u>   Student's Signature _____

Academic Year 2020   Advisor's Signature _____

ACKNOWLEDGMENTS

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CHAPTER I

INTRODUCTION

1.1   Background

Manihot Esculenta is a kind of tuber crops, commonly called cassava or tapioca in English and manioc in French. Cassava has been grown in many areas around the world, especially in the tropics. According to a bank of Thailand annual report (2017), global production was approximated 270 million tons with 30% from the African, where Nigeria is the world's largest producer. Cassava yields in Thailand is about 30 million tons per year which account for 9% of global production. According to Khandare and Choomsook (2019), an average the total export value of cassava of Thailand was 94,845.33 million baths during the period from 2010 to 2018.

In 2018 to 2019, the cassava production in Thailand decreased sharply due to cassava mosaic disease (CMD). CMD is a plant disease that reduces tuber size and starch percentage upstream in the cassava supply chain, reducing sales of the cassava crop. This leads to downstream economic impacts since cassava is a major industrial raw material.

CMD was found in the African continent in 1894 in Tanzania. It was first reported in Uganda in 1920, resulting in great economic loss. There was no outbreak reported of CMD for many years until the outbreak appeared again in Uganda and Kenya in the late 1990.

An CMD outbreak hit Southeast Asia in 2016, mainly in Cambodia and Vietnam (Wang et al., 2016). This disease was spread to Thailand through imported virus-infected cassava cuttings in 2018 and the outbreak was found in major cassava growing areas, such as Nakhon Ratchasima, Sa Kaeo, and Buriram provinces. The timeline of global CMD outbreak is shown in Figure 1.1.
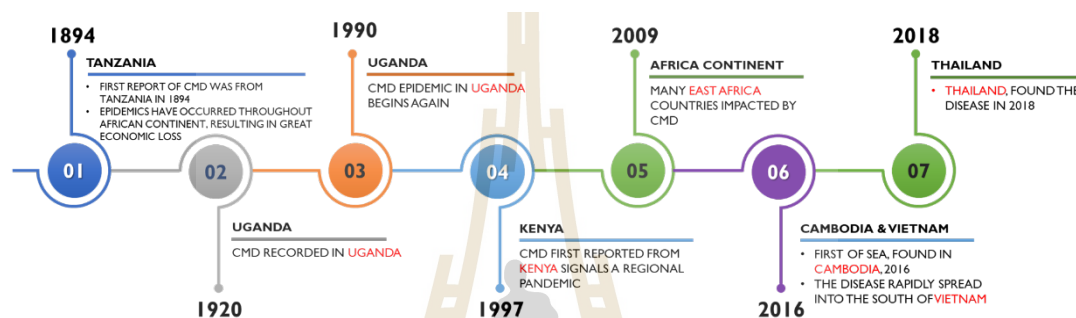
Figure 1.1 Timeline of global CMD outbreak. Source: Wang et al. (2016), Macfadyen et al. (2018)

CMD has caused epidemics in numerous plantations worldwide when proper control measures were not taken (Banito et al., 2010). The financial losses due to CMD in the African continent were estimated $1.2 – 2.3 billion in 1997 (Thresh et al., 1997), increasing to $1.9 – 2.7 billion in 2009 (Patil and Fauquet, 2009). Thottappilly et al. (2003) identified 23 virus species that cause diseases in cassava:

- ten species from genus *Begomovirus*, *Geminiviridae* family
- two species from genus *Ipomovirus*, *Potyviridae* family
- three species from genus *Potexvirus*, *Flexiviridae* family
- two species from genus *Nepovirus*, *Comoviridae* family
- one specie from genus *Oryzavirus*, *Reoviridae* family

- two species from genus *Ourmiavirus*

- one specie from genus *Nucleorhabdovirus*, *Rhabdoviridae* family

- one specie from genus *Cavemovirus*, *Caulimoviridae* family

- A further one type that is still in the identification stage.

The genus *Begomovirus* is the most virulent family due to its strong genetic diversity. It has caused significant damage in Africa and parts of Asia. Without proper study and control, this family could trigger a worldwide pandemic. CMD is spread in two ways: by the introduction of infected cuttings or by the whitefly (*Bemisia tabaci*). After acquiring the virus from an infected plant, the whitefly becomes infective in a three-hour period. The hatching or latent period of the virus in the whitefly vector is approximately eight hours and the time for virus transmission to a healthy cassava leaf is at least 10 minutes. If an infected cutting is introduced, the symptoms of CMD will appear within three months. If infection is through the whitefly vector, symptoms will appear in 2-3 weeks. They begin with of distortion and crinkling of leaves, followed by the color changing to mosaic. This resembles polished stone, as shown in Figure 1.2(a). Leaves become pale yellow and the whole plant is shorter than a healthy plant, as seen in Figure 1.2(b).

Figure 1.2 (a) Cassava leaves symptom caused by CMD and **(b)** infected
cassava in a farm

Cassava is propagated by transplanting stems. CMD may proliferate rapidly if
the farmer does not check whether the transplanted stem is virus-free. An infected stem
is a potential source of inoculum for the whitefly. The progression of the outbreak
depends on the replanting rate and the population of whitefly. Whitefly populations can
increase rapidly when temperatures are between 27 and 32 $°C$ and conditions are dry.
However, outbreaks are more serious when infected but symptomless stems are
transplanted. Whitefly generally does not migrate far from its habitat. If there are a
great number of whiteflies in the area but the plantation is virus-free, no infection will
occur. The CMD outbreak process is shown in Figure 1.3.
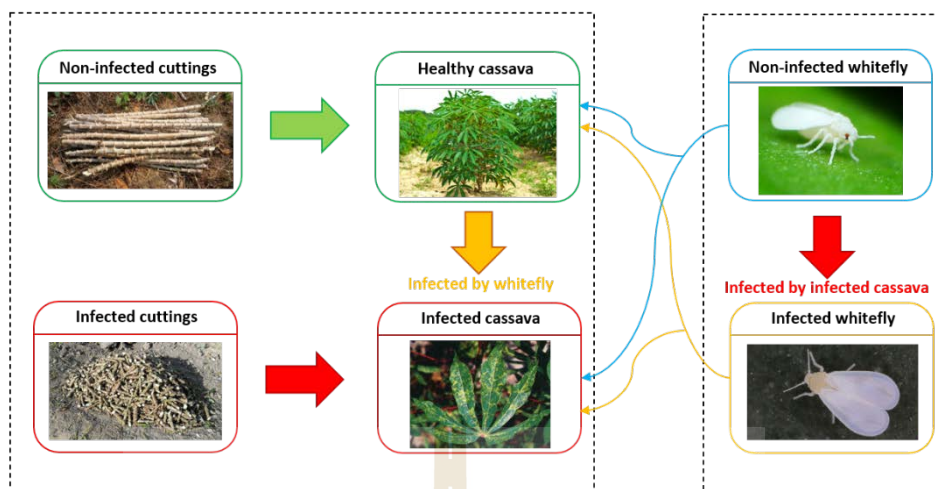
Figure 1.3 CMD outbreak flow

1.1.1 Outbreak prevention and control of CMD

CMD control involves (1) eliminating infected cassava from the plantation area, (2) promoting the use of virus-free cuttings, (3) using tolerant varieties, or (4) killing infected whitefly (Thresh et al., 1997, Legg, 1999). The first approach is widely used, but reduces the crop yield. The government of Uganda promoted the use of virus-free cuttings in all plantation areas and enacted laws to punish those who released cassava infected with CMD. This was shown to be highly effective in disease control (Jameson, 1964). However, a shift in enforcement policy by a new government led to repeated epidemics of CMD up to the present. The third approach was developed in 1971 by the international institute of tropical agriculture (IITA), which created CMD-tolerant cassava varieties. However, tolerant varieties become vulnerable to evolved species of virus after approximately 20 years. At present, there is no reliable approach to eliminating the CMD but the best is to limit the outbreak area.

1.2   Problem Definition

CMD epidemics negatively impact the overall global economy. Thailand, as the world's largest cassava exporter, is exposed to the same risks. In 2016, 2017, and 2018, Thailand's earning from exports of cassava products were \$3,294,210, \$3,048,070, and \$3,179,190, respectively.

In 2018, the outbreak was spread into Thailand by farmers who imported and planted virus-infected cassava stems. When whiteflies acquired the virus from the infected plants, they spread the outbreak to Thailand. Currently, the only way of containing the spread is either to remove the infected cassava plants or use pesticide spray to kill the whitefly. However, this imposed financial losses on the farmers, due to lower cassava yields. The Thai ministry of agriculture and cooperatives decided to pay compensation to farmers with no clear policy for controlling and containing plant diseases (\$40 per 400 m^2, with a limit of 12,000 m^2 per farmer). This allows the outbreak to spread rapidly, causing serious economic losses.

However, it is possible to apply methodologies from human epidemiology. This involves: (1) collecting of relevant statistical data, (2) compiling and analyzing of the data, and (3) interpretating of the data. The results are forwarded to planning and prevention units, which select measures for countering the spread of disease. Comprehensive data collection and analysis are equally essential in detecting and preventing the spread of plant diseases. Appropriate plant prevention measures may strengthen the economy and support farmers' incomes.

1.3 Framework of This Study

Research's approach combines the fundamental principles of epidemiology, systems engineering, and operations research. The predicted outcome is to develop systems for plant endemic control. This yields the optimal policy, used to control the CMD outbreak. The conceptual framework underpinning this research is illustrated in Figure 1.4.
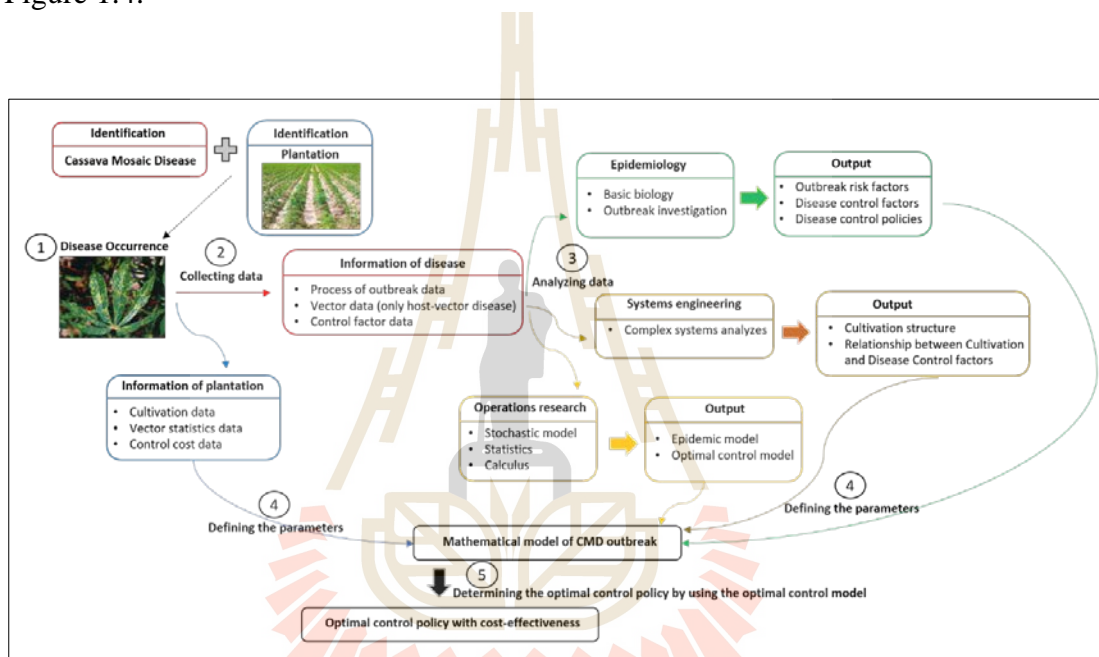
Figure 1.4 Framework of research

1.4 Systems Engineering

Incorporating a concept of systems engineering to epidemiology study allows us to envision a bigger picture that may reflect the clearer analysis of cause and effect of the CMD outbreak. The important task in systems engineering is to define and connect all relevant sub-systems as well as to provide methods to fulfill objectives of the defined system (Kossiakoff et al., 2011).

In order to clearly empathize epidemiology system of the CMD, it is essential to understand the cassava cultivation process, which can be categorized into 6 activities as follows:

(1) Selection of suitable land for cassava cultivation

(2) Cassava stem preparation

(3) Planting cassavas

(4) Weeding the cassava plantation

(5) Fertilizing the cassava plantation

(6) Harvesting cassava tubers

The main objective of planting cassava is to obtain tubers that meet expectation of the consumers. Incorporating requirements from the demand side as input information together with connecting all cassava cultivation process into a system express flows of information, products, and finance. They help us visualize the effect of the outbreak as well as find the better ways to contain the spread of disease by selecting appropriate control policy. The system flow of cassava cultivation is illustrated in Figure 1.5.
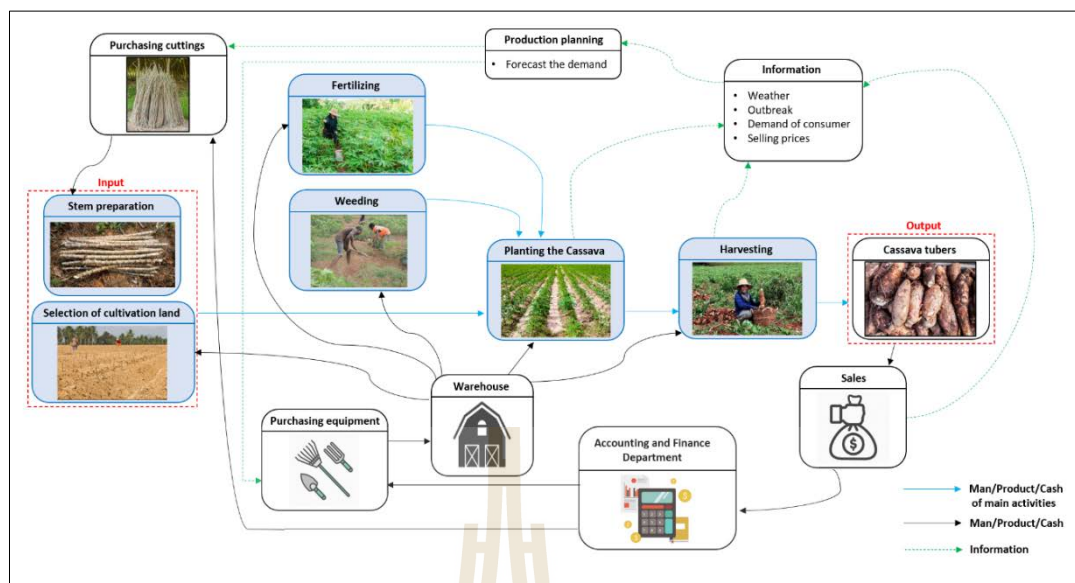
Figure 1.5 Structure of cultivation systems shows relationship between

activities and flows of information, product, and finance

1.5 Epidemiology

Epidemiology is the study and analysis of the distribution (who, when, and where), the frequency and the determinants of disease conditions in any defined population, such as people, animals, or plants (Charlton, 1996). Any outbreak was generally started by some factors and any disease has some certain parameters to contain the epidemic. Systematic study among different population groups at different time periods is required to unveil these parameters. Epidemiology is useful for disease surveillance, investigation the cause of disease, evaluation methods of treatment, as well as creating preventive measures.

This research incorporates epidemiology to study the process of CMD outbreak in order to identify risk factors of the outbreak and determine key factors to control the

spread, as well as to conduce to the establishment of appropriate policies to contain epidemic of CMD.

A CMD outbreak can be spread in two ways (Bock and Woods, 1983, Legg, 1999):

(1) by whitefly transmission, and

(2) by planting of infected cuttings.

From the works of Thresh and Otim-Nape (1994), Bock (1994), and Legg and Thresh (2000), the authors reported that CMD outbreaks can be controlled in four ways:

(1) by removing infected cassava from the plantation,

(2) by promoting the use of virus-free cuttings,

(3) by using tolerant varieties, or

(4) by killing infected whitefly in the plantation area.

1.6   Operations Research

Operations research (OR) applies mathematical techniques in decision-making process of various operations in the organizations. OR is a quantitative method to determine solutions that helps management of any organizations. (Rardin, 1998). Study of this research focuses on severity of the CMD and prediction of outbreak patterns to monitor and control the epidemic. Generally, outbreak patterns are simulated as various Markov models such as *SIR*, *SEIR*, and *SI* models (Markov, 1971). The Markov model is typically used to represent any systems with stochastic transition stages. It is assumed that future states depend only on the current state, not on events that occurred before current stage. The prediction of future stages depends on transition probability of current stage to stages that follow.

OR tools are used to formulate the structure of the cassava cultivation system and important factors of spread and control into a mathematical model. This research studies the dynamics of CMD outbreak caused by two factors: whitefly transmission and planting of infected cuttings. It can be controlled by four factors: spraying insecticide, rouging infected plants, selecting uninfected cuttings, and promoting tolerant cuttings.

1.7   Gap of This Study

The main objective of this research is to construct a mathematical model for CMD outbreak prediction and prevention. All relevant parameters were set with reference to real world, set by applying the principles of epidemiology, systems engineering, and operations research. Unfortunately, data collection in Thailand has been divided among different agencies and cooperation has been poor. It is therefore difficult to use the data to predict and prevent plant disease outbreaks.

There are quite a number of studies in the literature that focus on mathematical model development for the spread of cassava mosaic disease virus in Africa such as Holt et al., 1997, Kinene et al., 2015, Bokil et al., 2019, and Magoyo et al., 2019. The planting conditions reviewed in these studies are similar to what is done in Thailand. Therefore, all parameter values and ranges are also assumed to be the same as those in the reviewed literature.

To develop a model that represents the dynamics of CMD outbreak. State variables of cassava and whitefly populations are divided based on the dynamics of CMD outbreak and the control mechanism. Holt et al., Kinene et al., and Bokil et al., formulated mathematical models for vector-host dynamics using a non-tolerant cassava

state. Magoyo et al.'s model focused on the effect of promoting the use of tolerant cuttings in an outbreak area, which was not found in earlier models. However, latent class was not studied in Magoyo et al.'s work.

1.7.1 Latent cassava

Latent cassava is an infected cassava but asymptomatic. In practice, symptoms of CMD take 2-3 weeks to appear (Fargette et al. (1994)). Thus, during this time period latent cassava will spread virus. Jittamai et al. (2021) extended Bokil et al.'s model by adding latent state in order to analyze the comparative contribution of whitefly transmission and planting of infected cuttings. They concluded that the severity of CMD outbreak is high due to asymptomatic cassava, which cannot be easily detected and removed from the plantation area. However, tolerant cassava was not used in Jittamai et al.'s work to control this disease spread.

Promoting tolerant cuttings may limit the severity of CMD spread due to the latent cassava in the plantation area. Therefore, this study extended Jittmai et al.'s work by adding a tolerant state to study the severity of CMD outbreak and to determine the most cost-effectiveness policy. States and descriptions of cassava and whitefly populations assumed in this study are listed in Table 1.1.

Table 1.1 States and descriptions of cassava and whitefly.

State	Description
Tolerant cassava S_T	Cassava plants that resist CMD (tolerant cassava)
Susceptible cassava S_H	Cassava plants that are susceptible to infection with CMD (healthy cassava)
Exposed cassava E_H	Cassava plants that exposed to CMD (infected but asymptomatic)
Infected cassava I_H	Cassava plants with CMD symptoms
Uninfected whitefly S_V	Susceptible whitefly vector (uninfected whitefly)
Infected whitefly I_V	Infected whitefly vector

1.8 Objectives of The Research

The main objective of this research is to develop an epidemic model based on CMD outbreak and cultivation system in Nakhon Ratchasima province, Thailand, which has the largest cassava growing plantation in Thailand. The model results can be

used as guidelines for reducing the severity of CMD spread and maximizing incomes, yields, and profits. The following objectives will be fulfilled:

- Analyze all relevant factors contributed to CMD outbreak and assess factors that help control the spread.

- Develop a mathematical model to analyze the dynamics of CMD outbreaks with consideration latent and tolerant states.

- Select of optimal policy that maximizes economic benefit that yields the minimum number of cassava plants infected.

1.9   Organization of The Research

The rest of the research is organized as follows. Chapter II reviews related works of epidemic and optimal control models used to determine optimal policies to control the outbreak. Chapter III shows CMD outbreak model formulation. Chapter IV presents an optimal control policy. Chapter V provides discussion and recommendation of the future works.

CHAPTER II

MODEL DERIVATION

2.1 Models and Notations

An epidemic model is used to study the dynamics of CMD outbreak. It isolates infection factors that have a major impact in an outbreak. The output may be used to formulate optimal strategies for the outbreak. The most important concepts of epidemic models can be demonstrated using *SIR* model.

The basic model consists of three different compartments: *Susceptible (S)*, *Infected (I)*, and *Recovered* or *Removed (R)* in a population. In the model, all these state variables are differentiable functions in time $t \geq 0$. The definition of state variables is as follows.

- *Susceptible population (in large population is denoted S):* Susceptible population in the large population that has not been infected but it is at risk of becoming infected. When it has contracted an exposed population or an infected population, it will become to exposed population.

- *Infected (in large population is denoted I):* Infected population has been infected and show symptomatic. It can infect susceptible population.

- *Recovered or Removed (in large population is denoted R):* This population has been recovered or removed (or died) from the disease.

2.1.1   *SIR* model

The first compartmental model was presented in 1927 by Kermack and McKendrick (Kermack and McKendrick, 1927), and it has played a major role in mathematical epidemiology. The model includes three state variables S, I, and R. The model, which is a system of ordinary differential equations (*ODEs*) with three state variables (as shown in Figure 2.1).

Definition 2.1: (Ordinary differential equations; *ODEs*) Consider a dynamical system which satisfies

$$\frac{dx}{dt} = f(x, t) \qquad \text{for all } t \geq 0. \qquad (2.1)$$

$$x(t_0) = x_0 \qquad \text{for all } t_0 \geq 0. \qquad (2.2)$$

where $x \in \mathbb{R}^n$, f is a given nonlinear continuous function in t where $t \in \mathbb{R}^+$. Assume that $f(x, t)$ satisfies the standard conditions for the existence and the uniqueness of solutions. The nonlinear system (2.1) is said to be autonomous if $f(x, t)$ does not depend explicitly on time, i.e., if the system can be written as

$$\frac{dx}{dt} = f(x). \qquad (2.3)$$

The system is called non-autonomous (Allen, 2007).
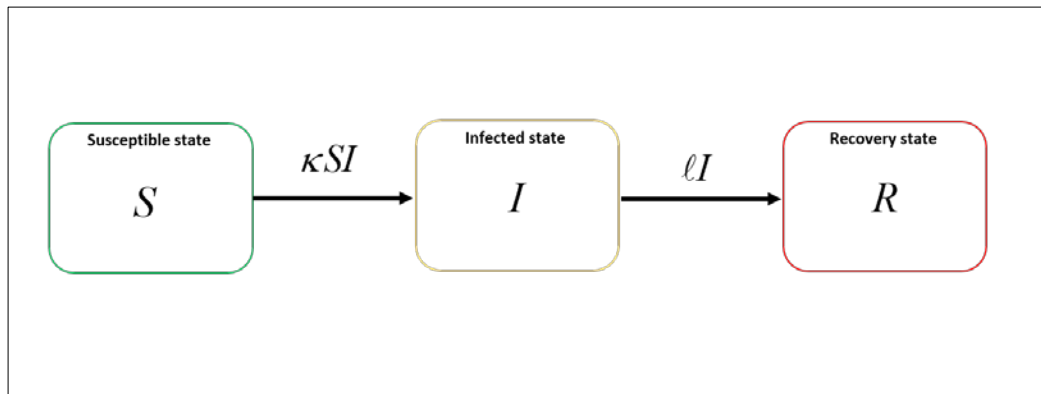
Figure 2.1 Flow diagram of *SIR* model

ODEs of *SIR* model are

$$\frac{dS}{dt} = -\kappa SI, \tag{2.4}$$

$$\frac{dI}{dt} = \kappa SI - \ell I, \tag{2.5}$$

$$\frac{dR}{dt} = \ell I, \tag{2.6}$$

where κ is the rate of infection or the contact rate, ℓ is the rate of recovery and $N = S + I + R$, where N is the total population. In their study, the total population was fixed, while κ and ℓ were constants. The success of the model was the beginning of developments in mathematical modelling of cassava mosaic virus diseases.

2.1.2 *SEIR* Model

As discussed above, an improved version of *SIR* model will be more realistic (Jeger et al., 1998, Kinene et al., 2016, Jittamai et al., 2021). A system is a *SEIR* model, which includes four state variables $S, E, I,$ and R.

- Exposed (in large population is denoted *E*): Exposed population has been infected but not show symptomatic (latent stage). It can spread a disease to susceptible population.

The flow of the *SEIR* model is shown in Figure 2.2
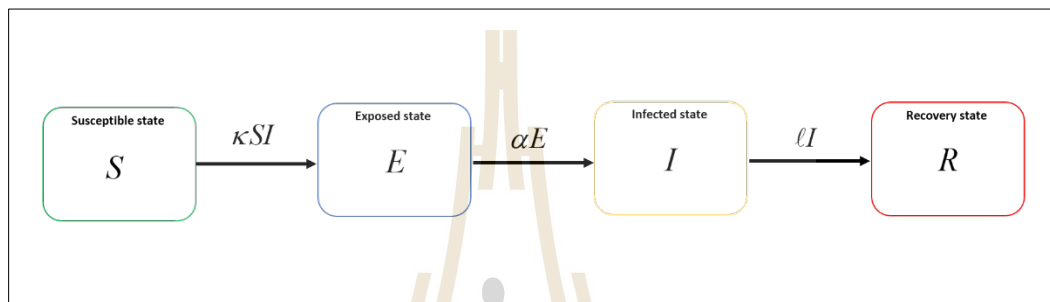
Figure 2.2 Flow diagram of *SEIR* model

ODEs from Figure 2.2 become

$$\frac{dS}{dt} = -\kappa SI, \tag{2.7}$$

$$\frac{dE}{dt} = \kappa SI - \alpha E, \tag{2.8}$$

$$\frac{dI}{dt} = \alpha E - \ell I, \tag{2.9}$$

$$\frac{dR}{dt} = \ell I, \tag{2.10}$$

where α is the rate of development to show symptomatic. Since a latent state is not show symptomatic. It can rapidly spread virus to healthy population and increase the severity level of the outbreak. The *SEIR* model is used to study the dynamics of disease spread with more realistic. The CMD model of this research is developed based on the *SEIR* model.

2.2   Methodology of Mathematical Model Development

Research contribution helps to investigate a most cost-effectiveness policy for disease limitation. It should help farmers by increasing cassava production and profits. A CMD outbreak model can be constructed by following three steps:

(1)   *Determine infection and control factors.* These factors contribute to a CMD outbreak and estimate the prevention of the outbreak.

(2)   *Formulate a mathematical model.* A CMD outbreak model is constructed by formulating infection factors as parameters. This yields *ODEs* of the system, which can be used to calculate the rate of changes of the population from any state to the other state.

(3)   *Analyze the stability of the system.* The realistic of the dynamics of the outbreak is proved by analyzing the stability of equilibrium point of the system.

Definition 2.2: The equilibrium point is a constant solution to ODEs. The equilibrium point is obtained by zeroing the right-hand side of Equation (2.3) (Kinene et al., 2016).

Definition 2.3: A state $\overline{x}$ is an equilibrium point of the system if $f(\overline{x}) = 0$. Intuitively and somewhat crudely speaking. Suppose that an equilibrium point is stable if all solutions which start near $\overline{x}$ (meaning that the initial conditions are in a neighborhood of $\overline{x}$) remain mean $\overline{x}$ for all time (Allen, 2007).

Definition 2.4: The equilibrium $\overline{x}$ is stable if all solutions starting near $\overline{x}$ tend towards $\overline{x}$ as $t \to \infty$ (Allen, 2007).

The CMD outbreak model admits two equilibrium points are the disease-free equilibrium point and the endemic equilibrium point.

Definition 2.5: The disease-free equilibrium point (*DFE*) is a steady-state solution when there is no disease in a population (Allen, 2007).

Definition 2.6: The endemic equilibrium point (*EE*) is the steady-state solutions when the disease persists in the population (Allen, 2007).

Basic reproduction number (R_0) is one of the most important concerns about any infectious disease is its ability to invade a population. Therefore, R_0 is used to prove the stability of the *DFE* or the *EE* of the system.

Definition 2.7: (Basic reproduction number; R_0) The value of R_0 is the number of secondary infections caused by one infectious individual during the individual's infectious period. If $R_0 < 1$, the disease cannot invade the population, but if $R_0 > 1$, the invasion is always possible (Hethcote, 2000).

The decision flow of the mathematical model analyzing as shown in Figure 2.3
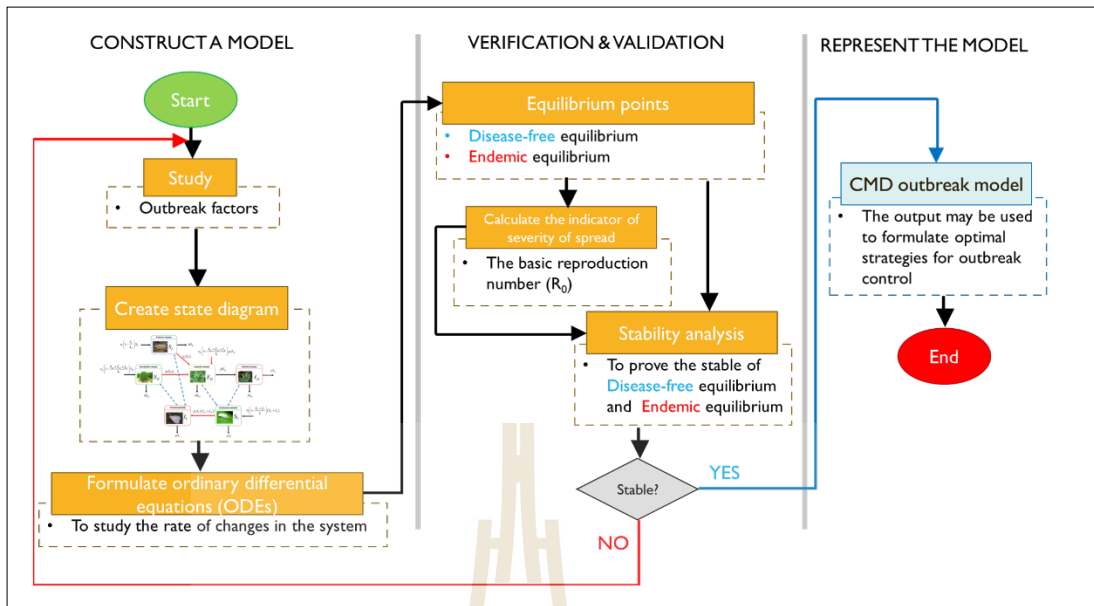
Figure 2.3 Decision flow of the mathematical model

This thesis presents the stability analysis of the system at the *DFE* and the *EE* by using the Routh-Hurwitz criterion and Lyapunov theory. The local stability of the *DFE* is proved by Routh-Hurwitz criterion. The system is locally-asymptomatically-stable if $R_0 < 1$ and unstable if $R_0 > 1$. The global stability of the *DFE* and *EE* are proved by Lyapunov's method. When $R_0 \leq 1$, the *DFE* is globally-asymptotically-stable. If $R_0 > 1$ then the *EE* is globally-asymptotically-stable.

2.3   Basic Reproduction Number

Definition 2.8: The Jacobian matrix J is a matrix formed by the first-order partial derivatives of scalar functions with respect to a set of independent variables. If all partial derivatives of $f : \Omega \subset \mathbb{R}^n \to \mathbb{R}^m$ exist at $\overline{x} \in \Omega$, then the Jacobian matrix of f at $\overline{x}$ is

$$J_{\overline{x}}(f) = \begin{bmatrix} \dfrac{\partial f_1}{\partial x_1}(\overline{x}) & \dfrac{\partial f_1}{\partial x_2}(\overline{x}) & \cdots & \dfrac{\partial f_1}{\partial x_n}(\overline{x}) \\ \dfrac{\partial f_2}{\partial x_1}(\overline{x}) & \dfrac{\partial f_2}{\partial x_2}(\overline{x}) & \cdots & \dfrac{\partial f_2}{\partial x_n}(\overline{x}) \\ \vdots & \vdots & \ddots & \vdots \\ \dfrac{\partial f_m}{\partial x_1}(\overline{x}) & \dfrac{\partial f_m}{\partial x_2}(\overline{x}) & \cdots & \dfrac{\partial f_m}{\partial x_n}(\overline{x}) \end{bmatrix}$$

(Gradshteyn and Ryzhik, 2000).

The Jacobian method used for an epidemic model yields a biologically reasonable R_0. However, for more complex compartmental models, especially those with more infected compartments, the method is hard to apply as it relies on the algebraic Routh-Hurwitz conditions for the stability of the system. R_0 can be derived from the spectral radius of the next-generation matrix proposed by Diekmann et al. (1990). It was also determined by using an *ODE* compartmental model from the next-generation matrix proposed by van den Driessche and Watmough (2002).

Let $x = (x_1, x_2, \ldots, x_3)^T$ be the number of individuals in each compartment, where the first $m < n$ compartments contain infected individuals. Assume that the *DFE* x_0 exists and is stable in the absence of disease, and that the linearized equations for $x_1, \ldots, x_m$ at the *DFE* decouple from equations of other equilibrium points. Consider these equations written in the form $\frac{dx_i}{dt} = F_i(x) - V_i(x)$ for $i = 1, 2, \ldots, m$. In this splitting, $F_i(x)$ is the rate of appearance of new infections in compartment i, and $V_i(x)$ is the rate of other transitions between compartment i and other infected compartments. It is assumed that F_i and $V_i(x) \in C^2$, and $F_i = 0$ if $i \in [m + 1, n]$.

Now define $\boldsymbol{F} = \left[\frac{\partial F_i(x_0)}{\partial x_j}\right]$ and $\boldsymbol{V} = \left[\frac{\partial V_i(x_0)}{\partial x_j}\right]$ for $1 < i, j < m$. From the biology meaning, $\boldsymbol{F}$ and $\boldsymbol{V}$ are entrywise non-negative and are non-singular M-matrix

(Berman and Plemmons, 1970), so $\boldsymbol{V}^{-1}$ is entrywise non-negative. Let $\psi(0)$ be the number of initially infected individuals. Then $\boldsymbol{FV}^{-1}\psi(0)$ is an entrywise non-negative vector giving the expected number of new infections. Matrix $\boldsymbol{FV}^{-1}$ has (i, j) entry equal to the expected number of secondary infections in compartment i produced by an infected individual introduced in compartment j. Thus $\boldsymbol{FV}^{-1}$ is the next-generation matrix and

$$R_0 = \rho(\boldsymbol{FV}^{-1}),$$

where ρ denotes the spectral radius of a matrix $\boldsymbol{FV}^{-1}$. The R_0 is the dominant (or maximum) eigenvalue of $\boldsymbol{FV}^{-1}$.

2.4   Stability Analysis of The System

2.4.1   Routh Hurwitz criterion

An equilibrium point can be classified by checking at the signs of eigenvalues of linearization of the equations. By evaluating the Jacobian matrix at each equilibrium point of the system, resulting eigenvalues and equilibrium point can be categorized. The behavior of the system in the neighborhood of each equilibrium point can be qualitatively determined by investigating eigenvectors associated with each eigenvalue.

The equilibrium point is hyperbolic if none of eigenvalues have zero real part. If all eigenvalues have negative real part, the equilibrium is stable. If at least one has a positive real part, the equilibrium is unstable. If at least one eigenvalue has negative real part and at least one has positive real part, the equilibrium is a saddle point.

Important criteria that give necessary and sufficient conditions for all of the roots of the characteristic polynomial (with real coefficients) to lie in the left half of the complex plane are known as the Routh-Hurwitz criterion. The name refers to E. J. Routh and A. Hurwitz, who contributed to the formulation of these criteria. In 1875, Routh, a British mathematician, developed an algorithm to determine the number of roots that lie in the right half of the complex plane (Gantmacher, 1964). In 1895, Hurwitz, a German mathematician, verified the determinant criteria for roots to lie in the left half of the complex plane. If the roots of the characteristic polynomial lie in the left half of the complex plane, then any solution to the linear, homogeneous differential equation converges to zero. The Routh-Hurwitz criteria for differential equations are analogous to the Jury conditions for difference equations. The Routh-Hurwitz criteria are used in Chapter III to determine local asymptotic stability of an equilibrium for nonlinear systems of differential equations.

Definition 2.9: Given the polynomial,

$$P(\lambda) = \lambda^n + a_1\lambda^{n-1} + \cdots + a_{n-1}\lambda + a_n,$$

where the coefficients a_i are real constants, $i = 1, \ldots, n$. Define the n Hurwitz matrices using the coefficients a_i of the characteristic polynomial:

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

and

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

where $a_j = 0$ $if\ j > n$. All of the roots of the polynomial $P(\lambda)$ are negative or have

negative real part if the determinants of all Hurwitz matrices are positive:

$$det\ H_j > 0, \quad j = 1,2,\dots,n.$$

When $n = 2$, the Routh-Hurwitz criteria simplify to $H_1 = a_1 > 0$ and

$$det\ H_2 = det \begin{pmatrix} a_1 & 1 \\ a_3 & a_2 \end{pmatrix} = a_1 a_2 > 0 \text{ or } a_1 > 0 \text{ and } a_2 > 0.$$

For polynomials of degree $n = 2, 3, 4$ and 5, the Routh-Hurwitz criteria are summarized.

Routh-Hurwitz criteria for $n = 2, 3, 4$ and 5.

$n = 2$: $a_1 > 0$ and $a_2 > 0$.

$n = 3$: $a_1 > 0$ and $a_3 > 0$, and $a_1 a_2 > a_3$.

$n = 4$: $a_1 > 0$, $a_3 > 0$, $a_4 > 0$, and $a_1 a_2 a_3 > a_3{}^2 + a_1{}^2 a_4$.

$n = 5$: $a_i > 0$ for $i = 1,2,3,4,5$, $a_1 a_2 a_3 > a_3{}^2 + a_1{}^2 a_4$

and $(a_1 a_4 - a_5)(a_1 a_2 a_3 - a_3{}^2 - a_1{}^2 a_4) > a_5(a_1 a_2 - a_3)^2 + a_1 a_5{}^2$

(Allen, 2007).

2.4.2 Lyapunov Theory

Aleksandr Mikhailovich Lyapunov was a Russian mathematician. He

developed the stability theory of the dynamical system, known as Lyapunov function,

which is an important to stability theory of dynamical systems and control theory. For

certain classes of *ODEs*, the existence of Lyapunov functions is a necessary and

sufficient condition for stability.

The autonomous system (Equation (2.1)) is investigated the globally asymptotically stable by using the Lyapunov function. Lyapunov functions are scalar functions that used to prove the stability of an equilibrium of *ODEs*.

Definition 2.10: Let U be an open subset of $\mathbb{R}^n$ containing the origin. A real-valued $C^{-1}(U)$ function V, $V: U \to \mathbb{R}$, $[x \in U, V(x) \in \mathbb{R}]$ is said to be positive definite on the set U if the following two conditions hold:

(1) $V(\overline{x}) = 0$.

(2) $V(x) > 0$ for all $x \in U$ with $x \neq \overline{x}$.

The function V is said to be negative definite if $-V$ is positive definite (Malisoff and Mazenc, 2009).

Definition 2.11: A positive definite function V in an open neighborhood of the origin is said to be a Lyapunov function for the autonomous differential system,

$$\frac{dx}{dt} = f(x), \text{ if } \frac{dV(x)}{dt} \leq 0 \text{ for all } x \in U - \overline{x}.$$

If $\frac{dV(x)}{dt} < 0$ for all $x \in U - \overline{x}$, the function V is called a strict Lyapunov function (Malisoff and Mazenc, 2009).

2.5   Optimal Control Theory

Optimal control theory is a powerful mathematical tool that can be used to make decisions involving complex biological situations. For example, what percentage of the population should be vaccinated as time evolves in a given epidemic model to minimize the number of infected and the cost of implementing the vaccination strategy? The desired outcome, or goal, depends on the particular situation.

The behavior of the underlying dynamical system is described by state variables. Assume that there is a way to steer the state by acting upon it with suitable control functions. The control enters the system of *ODEs* and affects the dynamics of the state system. The goal is to adjust the control in order to maximize (or minimize) a given objective functional.

In the control of single *ODE*, denote the control variables as $u(t)$ and the state variable as $x(t)$. Given a control function, $u(t)$, the state, $x(t)$, is defined as a solution to an *ODE*

$$\frac{dx}{dt} = g\big(t, x(t), u(t)\big), \tag{2.11}$$

with a given initial condition

$$x(0) = x_0. \tag{2.12}$$

Note the rate of change of the state is dependent on the control variable $u(t)$. The goal is expressed by the objective functional,

$$J(u) = \int_0^{t_f} f\big(t, x(t), u(t)\big)dt. \tag{2.13}$$

The challenge is seeking to find $u^*(t)$ that achieves the maximum (or minimum) of our objective function, i.e., $J(u^*) = max_{u \in \mathbf{u}} J(u)$, where $\mathbf{u}$ is the set of possible control. Taking $\mathbf{u}$ to be a subset of piecewise-continuous functions. The objective functional is subject to Equations (2.11) and (2.12). Both the state and control variables usually affect the goal.

The control that maximizes or minimizes the objective function is denoted by $u^*(t)$. Substituting $u^*(t)$ into the state differential equation (2.11) results in obtaining the corresponding optimal state, $x^*(t)$. Thus $\big(u^*(t), x^*(t)\big)$ is the optimal pair.

If $\left(u^*(t), x^*(t)\right)$ is an optimal pair, then these conditions hold. Pontryagin et al. (1962) introduced the idea of adjoint functions to append the differential equations to the objective function. These adjoint functions have a similar purpose as Lagrange multiplies in multivariate calculus, which append constraints to the function of several variables to be maximized or minimized. Refer to Lenhart and Workman (2007) for an introduction into optimal control theory.

Assuming h and g are both continuously differentiable in their arguments, the first order necessary conditions in the simplest form are given by Pontryagin's maximum principle (Pontryagin et al., 1962).

Definition 2.12: If $u^*(t)$ and $x^*(t)$ are optimal for problems (2.11) to (2.13), then there exists a piecewise differentiable adjoint variable $\lambda(t)$ such that

$$H\left(t, x^*(t), u(t), \lambda(t)\right) \leq H\left(t, x^*(t), u^*(t), \lambda(t)\right),$$

for all $u \in \boldsymbol{u}$ at each time t, where the Hamiltonian, H, is

$$H = h\left(t, x(t), u(t)\right) + \lambda(t)g\left(t, x(t), u(t)\right),$$

and

$$\frac{d\lambda(t)}{dt} = -\frac{\partial H\left(t, x^*(t), u^*(t), \lambda(t)\right)}{\partial x},$$

$$\lambda\left(t_f\right) = 0$$

(Naidu, 2003).

Note the final time condition on the adjoint variable is called the transversality condition. Pontryagin maximum principle changes the problem of finding the control that maximizes the objective function subject to the state ODE and initial condition to

the problem of optimizing the Hamiltonian pointwise. Another way to think of the Hamiltonian is

$$H = h\big(t, x(t), u(t)\big) + \lambda(t) g\big(t, x(t), u(t)\big)$$

$$= \text{(integrand)+(adjoint)} \times \text{(right hand side of } ODE).$$

The necessary conditions can be generated by maximizing H with respect to $u(t)$ at $u^*(t)$. From Lenhart and Workman (2007), they can be described as follows:

$$\frac{\partial H}{\partial u} = 0 \qquad \Rightarrow h_u + \lambda g_u = 0 \qquad \text{(Optimality equation),}$$

$$\frac{d\lambda}{dt} = \frac{\partial H}{\partial x} \qquad \Rightarrow \frac{d\lambda}{dt} = -(h_x + g_x) \qquad \text{(Adjoint equation), and}$$

$$\lambda\big(t_f\big) = 0 \qquad \text{(Transversality condition).}$$

Considering second order conditions. For each $t \in \big(0, t_f\big)$, for a maximization problem,

$$\frac{\partial^2 H}{\partial u^2} \leq 0 \text{ at } u^*(t)$$

must hold (from concavity), and for a minimization problem

$$\frac{\partial^2 H}{\partial u^2} \geq 0 \text{ at } u^*(t)$$

must hold (from convexity) (Lenhart and Workman, 2007).

Pontryagin maximum principle can be extended to multiple states and controls and consequently corresponding adjoint variables are introduced. For example, if it had n state variables,

$$x_1(t) = g_1\big(t, x_1(t), \dots, x_n(t), u(t)\big)$$

$$\vdots$$

$$x_n(t) = g_n\big(t, x_1(t), \dots, x_n(t), u(t)\big)$$

with corresponding initial conditions, then adjoint functions, $\lambda_1(t), \dots, \lambda_n(t)$ were introduced. Thus, the objective function becomes,

$$\max_u \int_o^{t_f} h\big(t, x_1(t), \dots, x_n(t), u(t)\big)dt.$$

Similarly, the Hamiltonian is

$$H = h\big(t, x_1(t), \dots, x_n(t), u(t)\big) \quad +\lambda_1(t)g_1\big(t, x_1(t), \dots, x_n(t), u(t)\big)$$

$$+ \cdots$$

$$+\lambda_n(t)g_n\big(t, x_1(t), \dots, x_n(t), u(t)\big).$$

According the appropriate optimality equations, adjoint equations, and transversality conditions are generated. For example, the i -th adjoint *ODE* is

$$\lambda_i = -\frac{\partial H}{\partial x_i}. \tag{2.14}$$

In short, for the simplest case it was started with two unknowns, $u^*(t)$ and $x^*(t)$, and then introduced an adjoint variable, $\lambda(t)$. Thus, it must to solve for three unknowns. Then the optimality equation was attained from setting

$$\left.\frac{\partial H}{\partial u}\right|_{u=u^*} = 0 \tag{2.15}$$

and solving for $u^*(t)$, which will be characterized in terms of $x^*(t)$ and $\lambda(t)$. Note that many real-world application problems require bounds on the control, like

$$a \leq u(t) \leq b$$

and that Pontryagin maximum principle still holds.

The optimality system is comprised of the state, the adjoint *ODEs*, and the control characterization. Often solutions of optimality system cannot be solved explicitly but can be approximated numerically.

2.6 Cost-Effectiveness Analysis

Cost-effectiveness analysis is one of important tools that is vital to examine both costs and outcomes of one or more interventions. It compares an intervention to another intervention by estimating how much it costs to gain outcomes, i.e., gained of yields or incomes. There are three types of cost-effectiveness ratios.

2.6.1 Average cost-effectiveness ratio (ACER)

This deals with a single intervention and evaluates the intervention against its baseline option. It is calculated by dividing the net cost of the intervention by the total number of health outcomes prevented by the intervention. ACER formula is given by

$$\text{ACER} = \frac{\text{Total cost of intervention}}{\text{Outcome gained}}. \tag{2.16}$$

2.6.2 Marginal cost-effectiveness ratio (MCER)

This deals with assessment of the specific changes in cost and effect when a program is expended or contracted. MCER formula is given by

$$\text{MCER} = \frac{\text{Change in costs of intervention}}{\text{Change in outcome gained}}. \tag{2.17}$$

2.6.3 Incremental cost-effectiveness ratio (ICER)

This provides the means of comparing the differences between costs and health outcomes of two alternative intervention strategies that compete for the same resources and it is generally described as additional cost per additional health outcome. ICER formula is given by

$$\text{ICER} = \frac{\text{Cost of intervention - cost of alternative intervention}}{\text{Outcome of intervention - outcome of alternative intervention}}. \qquad (2.18)$$

2.7 Literature Review

An epidemic model has become an important tool for breaking down and analyzing the spread of infectious diseases. It helps to develop a better understanding and facilitate predictions. The model is also used to test the plausibility of epidemiology explanations. Another application is forecasting the possible effects of changes system dynamics, and to predict structural changes through early warning signals. Thereby making it possible to control an emerging disease outbreak. In this section, previous epidemic models are reviewed.

2.7.1 Models and Notation

In this section, the basic definition and notation of CMD outbreak mathematical models are established. The five different compartments of a cassava (or host) population of CMD outbreak models are Susceptible tolerant cassava (S_T), Susceptible cassava (S_H), Exposed cassava (E_H), and Infected (I_H). The two compartments of a whitefly (or vector) population of CMD outbreak models are Uninfected whitefly (S_V) and Infected whitefly (I_V). State variables are differentiable functions in time $t \geq 0$. The definitions of state variables are

- Susceptible tolerant cassava (in a cassava population is denoted S_T): Tolerant cassava in the cassava population that has not been infected. Although it is cassava tolerant varieties, it is at risk of becoming infected. When it has contracted the infected whitefly, it will transfer to exposed cassava.

- Susceptible cassava (in a cassava population is denoted S_H): Susceptible cassava in the cassava population that has not been infected. When it has contacted infected whiteflies. It becomes exposed cassava.

- Exposed cassava (in a cassava population is denoted E_H): Exposed cassava in the cassava population that has been infected but not show symptomatic. It can spread a disease to the uninfected whitefly. It becomes infected state (show symptomatic) in next period time.

- Infected cassava (in a cassava population is denoted I_H): Infected cassava in the cassava population that has been infected and show symptomatic. It can spread a CMD virus to uninfected whitefly.

- Uninfected whitefly (in a whitefly population is denoted S_V): Uninfected whitefly in the whitefly population. It becomes to an infected whitefly after it received CMD virus from exposed or infected cassavas.

- Infected whitefly (in a whitefly population is denoted I_V): Infected whitefly in the whitefly population. It can spread a CMD virus to tolerant and susceptible cassavas.

Parameter values and ranges that used in this research are defined based on the previous works due to the lack of data collection system in Thailand. Parameters are listed in Table 2.1.

Table 2.1 Parameters of CMD outbreak

Parameter	Description	Reference
h	harvesting rate of cassavas	Holt et al. (1997)
β	CMD latent rate	Wagaba et al. (2013)
γ	rouging rate of symptomatic cassava	Kinene et al. (2015)
r_H	replanting rate of non-tolerant cassava	Kinene et al. (2015)
r_T	replanting rate of tolerant cassava	Magoyo et al. (2019)
k_1	maximum plant of non-tolerant cuttings capacity (m^{-2})	Magoyo et al. (2019)
k_2	maximum plant of tolerant cuttings capacity (m^{-2})	Magoyo et al. (2019)
a	Average number of cassava plants visited by uninfected whitefly	Jittamai et al. (2021)
Λ	birth rate of whitefly (*vector·day^{-1}*)	Jeger et al. (2004)
μ	natural death rate of whitefly (*vector·day^{-1}*)	Kinene et al. (2015)
L	maximum whitefly density (m^{-2})	Bokil et al. (2019)
p_1	probability of susceptible cassava plants receiving virus from infected whitefly	Bokil et al. (2019)
p_2	probability of tolerant cassava plants receiving virus from infected whitefly	Magoyo et al. (2019)
p_3	probability of planting infected cassava cuttings	Holt et al. (1997)
p_4	probability of uninfected whitefly receiving virus from exposed (latent) or symptomatic	Bokil et al. (2019)

2.7.2 Holt et al.'s model

Most models of CMD are extended from the work of Holt et al. *SI* model for an outbreak of African cassava mosaic virus (ACMV) was developed to describe

the dynamics of infected cassava and infected whitefly, which is driven by whitefly transmission. Authors derived a strategy in which cassava yields are maximized by reducing whitefly population. However, this approach is not cost-effective, so farmers are advised to select uninfected cuttings for planting to prevent a collapse of healthy cassava population. This is an economical strategy that is capable of controlling an outbreak.

Epidemic model of ACMV was developed in which the dynamics within a locality, of susceptible and infected cassava, and of infected and uninfected whitefly vectors, were specified. Infections of ACMV of Holt et al.'s model are driven either by contact between infected cassava or uninfected vectors and between infected vectors and susceptible cassava.

Let S_H and I_H be the abundances (m^{-2}) of healthy and diseased plants, respectively, S_V and I_V be the abundances (m^{-2}) of uninfected and infected vectors, respectively. The dynamics of ACMV is illustrated in Figure 2.4.
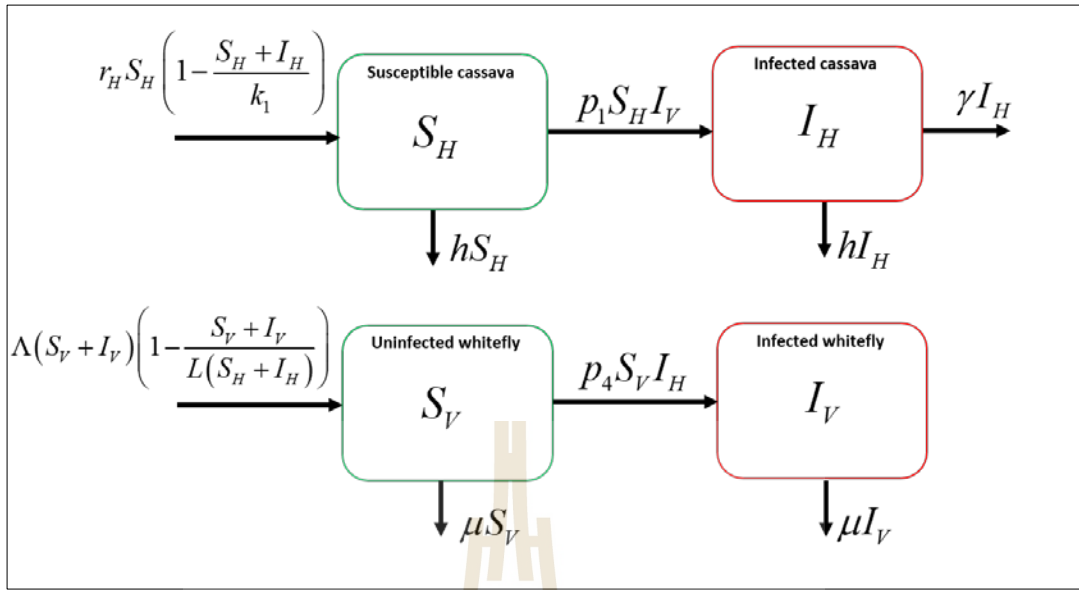
Figure 2.4 State diagram of Holt et al. model. Source: Holt et al., 1997

ODEs of the model are

$$\frac{dS_H}{dt} = r_H S_H \left(1 - \frac{S_H + I_H}{k_1}\right) - p_1 S_H I_V - h S_H, \tag{2.19}$$

$$\frac{dI_H}{dt} = p_1 S_H I_V - h I_H - \gamma I_H, \tag{2.20}$$

$$\frac{dS_V}{dt} = \Lambda(S_V + I_V)\left(1 - \frac{S_V + I_V}{L(S_H + I_H)}\right) - p_4 S_V I_H - \mu S_V, \tag{2.21}$$

$$\frac{dI_V}{dt} = p_4 S_V I_H - \mu I_V. \tag{2.22}$$

Parameters of cassava population are described as follows. k_1 is the maximum plant density (m^{-2}), r_H is the rate of replanting healthy plants, h is the rate at which cassava plants are removed and harvested for their tuberous roots, assumed to occur at a constant rate (day^{-1}), γ is the loss rate of plants due to the effects of ACMV infection but can also represent the rate of removal of diseased plants in rouging operations (day^{-1}).

Parameters of whitefly population are described as follows. *L* is the maximum abundance of vectors (*plant⁻¹*), Λ is the vector birth rate, and μ is the death rate of vectors.

Pathogen parameters are described as follows. p_1 is the rate of inoculation of susceptible plants (*vector⁻¹·day⁻¹*) and p_4 is the rate of virus acquisition by uninfected vectors (*plant⁻¹·day⁻¹*).

2.7.3 Evolution of CMD outbreak model

The dynamics of CMD is driven by both whitefly transmission and planting of infected cuttings. The works that using a single factor (whitefly transmission) as are as the following:

(1) *Zhang et al. (2001)* developed *SI* model in which two viruses, ACMV and east African cassava mosaic virus (EACMV), are carried by whitefly into the plantation area. They used a simulation technique to clarify the relationship between cassava production and the severity of outbreak from two viruses. They summarized that by this mechanism, a virus that was nonviable alone could invade and persist in a chronic epidemic of another virus.

(2) *Jeger et al. (2004)* developed *SEI* model based on Holt et el.'s work by adding a latent state. They improved a better understanding of the severity of ACMV outbreak and the use of rouging strategy. Numerical simulation suggested that rouging would usually only be needed for propagative viruses at very high population densities.

(3) *Lawrence et al. (2010)* adapted *SI* model of Holt et al.'s model by modifying it to incorporate the spatial dynamics of the spread of the disease. This means the whitefly vector can be equally likely to fly in any direction. This movement, the characteristic short distance flight patterns of whiteflies, can be represented

mathematically by diffusion. They used numerical simulation to study the effectiveness of using tolerant varieties and windbreaks to control the disease spread. The model suggested that the use of windbreaks and ACMD tolerant strains of cassava will have the most beneficial impact on cassava yield.

(4) *Hebert (2014)* developed *SEI* model of an outbreak of cassava mosaic virus (CMV) to study the effect of whitefly transmission on cassava yield. Numerical simulation suggested that with whitefly aggregation, increasing complexity of whitefly movement, and using tolerant varieties, there is a reduction in the probability that the disease becomes established in the host plant.

(5) *Kinene et al. (2015)* developed *SEI* model including a latent state into the model to study the dynamics of cassava brown streak disease (CBSD) outbreaks. The model is used to determine the most cost-effectiveness from killing whitefly and rouging infected cassava policies by applying the optimal control theory and Pontryagin maximum principle. The model suggested that rouging method is the most cost-effective policy.

The models that took account of whitefly transmission and disease cuttings are as the following:

(1) *Bokil et al. (2019)* developed *SI* model of ACMV outbreaks. Infections in the model are driven both by virus cuttings and whitefly transmission. They then applied an optimal control theory and Pontryagin maximum principle to investigate the effect of rouging and spraying to maximize uninfected plants. The model suggested that a strategy combining rouging and spraying performed better than those that apply a single control mechanism.

(2) *Magoyo et al. (2019)* developed *SI* model of CMV outbreak took account of tolerant cassava state. The objective of Magoyo et al.'s work is to investigate the effect of spraying, rouging, selecting non-virus cuttings, and promoting tolerant cuttings on disease control.

As can be observed, a latent stage is missing from works of Bokil et al. and Magoyo et al. Since the symptoms take 2 - 3 weeks to appear (Fargette et al., 1994), then during this period the asymptomatic cassava may spread the disease. Thus, this gap should be fulfilled.

This thesis aspires to fill the gap from works of Kinene et al., Bokil et al., and Magoyo et al. The mathematical model of this research is developed by adding the latent stage into Magoyo et al.'s model. Next, the review presents the mathematical model of three works.

2.7.4 Kinene et al.'s model

Kinene et al. developed the *SEIR* model for the dynamics of the disease in the cassava plants and *SI* for the dynamics in whitefly vectors. The total cassava population N is subdivided into the following sub-populations: cassava plants that are susceptible to infection with CBSD S_H, those exposed to CBSD E_H, and cassava plants with CBSD symptoms I_H. The total whitefly vector population N_V is sub-divided into susceptible whitefly vector population S_V and infectious whitefly vector population I_V. Namely, $N_V = S_V + I_V$, the transmission dynamics of CBSD is summarized in the compartmental diagram shown in Figure 2.5.
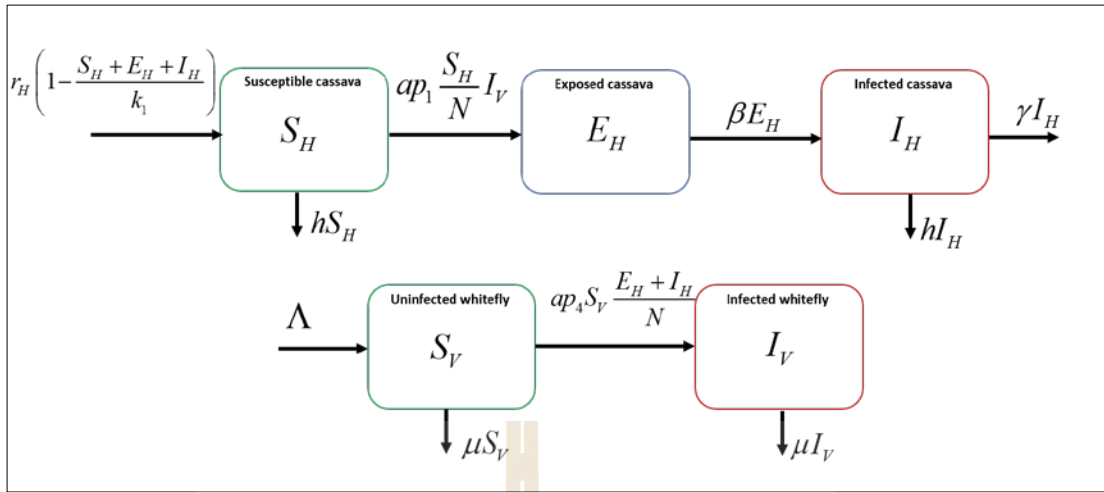
Figure 2.5 State diagram of Kinene et al. model. Source: Kinene et al., 2015

ODEs of the model are

$$\frac{dS_H}{dt} = r_H\left(1 - \frac{N}{K}\right) - ap_1\frac{S_H}{N}I_V - hS_H, \tag{2.23}$$

$$\frac{dE_H}{dt} = ap_1\frac{S_H}{N}I_V - \beta E_H - hE_H, \tag{2.24}$$

$$\frac{dI_H}{dt} = \beta E_H - \gamma I_H - hI_H, \tag{2.25}$$

$$\frac{dS_V}{dt} = \Lambda - ap_4 S_V\frac{E_H + I_H}{N} - \mu S_V, \tag{2.26}$$

$$\frac{dI_V}{dt} = ap_4 S_V\frac{E_H + I_H}{N} - \mu I_V, \tag{2.27}$$

It is assumed that healthy cassava plants are planted or replanted at a rate r_H. They are either harvested at a rate h or move to the exposed class after acquiring CBSD through contact with the infectious whitefly vector at a rate ap_1, where p_1 is the probability that a healthy plant will be inoculated by the virus during a single visit by an infected whitefly vector, a is the number of plants visited either by an infected whitefly or uninfected whitefly per day. Exposed cassava plants are either harvested at

a rate h or move to the infectious class at a rate β. Infected cassava plants are assumed to be harvested or removed from the garden and burnt at a rate γ.

Susceptible whitefly vectors are recruited at a rate Λ. They either die naturally at a rate μ or move to the infectious class after acquiring CBSD from the infected cassava plants at a rate ap_4, where p_4 is the probability that a non-infectious vector will acquire the virus from an infected cassava plant during a single visit. The infected whitefly vectors also die naturally at a rate μ. Kinene et al. assumed that farmers plant only healthy varieties of cassava in a garden of carrying capacity k_1, no death of cassava plants before harvesting and the vectors are assumed to remain infectious once they acquire the virus.

They took account of latent stage into the model, however, the transmission by disease cuttings was not establish to study the dynamics of disease outbreak.

2.7.5 Bokil et al.'s model

The model was developed to study the dynamics of ACMV. The infection of this system is driven both by planting or replanting by infected cuttings and whitefly transmission. Let S_H and I_H be the healthy and infected plants, respectively. The total plant population is denoted as $N = S_H + I_H$. The vector population is divided into uninfected S_V and infected vectors I_V with no latent period. The total vector population is denoted $N_V = S_V + I_V$.

Growth rates of healthy and infected plants are occurred by logistic growth equations, $r_H S_H \left(1 - \frac{N}{k_1}\right)$ and $r_H p_3 I_H \left(1 - \frac{N}{k_1}\right)$, respectively. The planting rate is density-dependent to ensure that plant density does not exceed the carrying capacity of the field, k_1. The growth rate of the vector population is also density-dependent.

The vector population density depends on plant density with maximum vector density per plant given by $L(S_H + I_H)$. Infected and healthy plants are harvested at the same per capita rate h. Additionally, infected plants may be removed from the field at a rate γ (rouging). Uninfected and infected vectors die at the same per capita rate of μ, where μ is natural mortality. The inoculation rate of healthy plants by infective vectors is $p_1 S_H I_V$ and the acquisition rate of uninfected vectors feeding on infected plants $p_4 S_V I_H$. The dynamics of ACMV is illustrated in Figure 2.6.
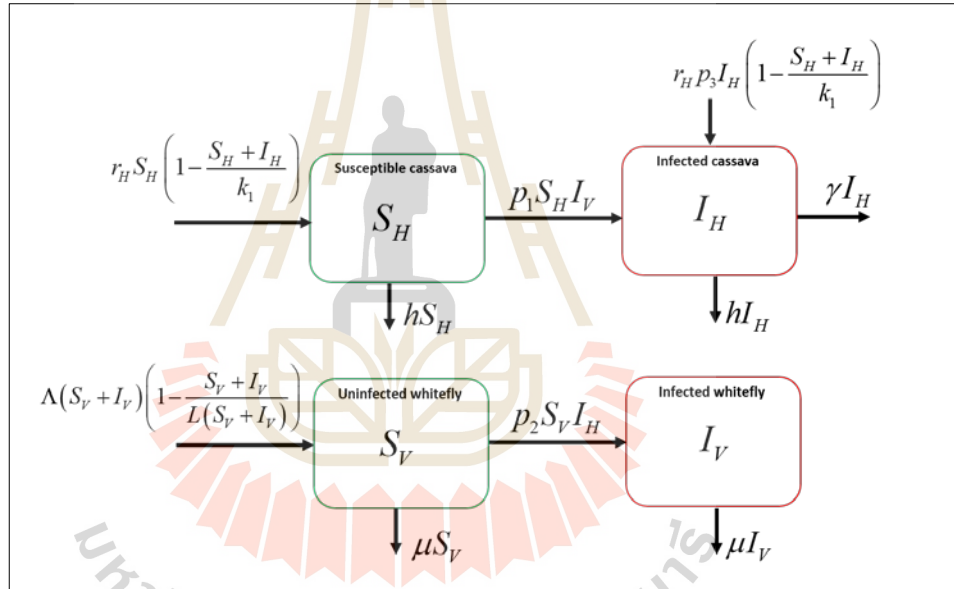
Figure 2.6 State diagram of Bokil et al. model. Source: Bokil et al., 2019

The *ODEs* of the model are

$$\frac{dS_H}{dt} = r_H S_H \left(1 - \frac{S_H + I_H}{k_1}\right) - p_1 S_H I_V - h S_H, \tag{2.28}$$

$$\frac{dI_H}{dt} = r_H p_3 I_H \left(1 - \frac{N}{k_1}\right) + p_1 S_H I_V - (h + \gamma)I, \tag{2.29}$$

$$\frac{dS_V}{dt} = \Lambda(S_V + I_V)\left(1 - \frac{S_V + I_V}{L(S_H + I_H)}\right) - p_4 S_V I_H - \mu S_V, \tag{2.30}$$

$$\frac{dI_V}{dt} = p_4 S_V I_H - \mu I_V. \tag{2.31}$$

However, a tolerant state was missing from this model. Magoyo et al. extended the model by adding tolerant cassava state.

2.7.6 Magoyo et al.'s model

The model was developed for an outbreak of CMV. The population of cassava is divided into three states: tolerant cassava (S_T) and susceptible cassava (S_H), and infected cassava (I_H). The population of whitefly is divided into two states: uninfected whitefly (S_V) and infected whitefly (I_V). The dynamics of CMV is illustrated in Figure 2.7.
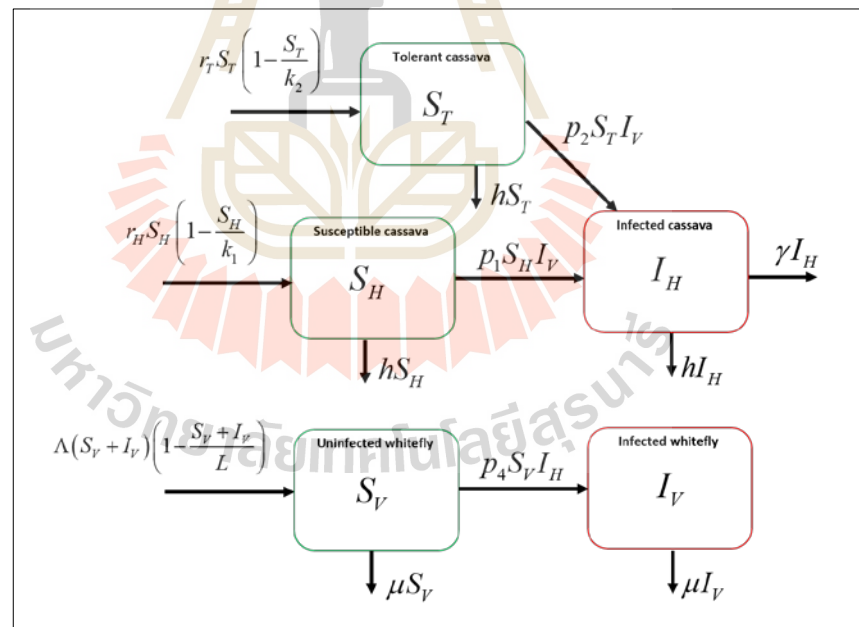
Figure 2.7 State diagram of Magoyo et al. model. Source: Magoyo et al., 2019

Tolerant cassava is replanted at rate r_T and susceptible cassava is replanted at rate r_H. Infections of cassava from whitefly are given by $p_2 S_T I_V$ (S_T to I_H)

and by $p_1 S_H I_V$ (S_H to I_V). Tolerant, susceptible, and infected cassava are harvested at rates h. I_H decrease due to the effect of CMV at rate γ. k_2 represents the maximum plants for tolerant cassava which can be planted. k_1 represents the maximum plants for non-tolerant cassavas (S_H and I_H) which can be planted.

Uninfected vector is recruited by birth at a rate Λ and catch infection following contact with infected cassava at a rate p_4. L is the maximum number of vectors in a plantation area. Infected vector is recruited when susceptible vector catch infection following contact with I_H at a rate p_4 and μ is a death rate of whitefly.

ODEs of the model are

$$\frac{dS_T}{dt} = r_T S_T \left(1 - \frac{S_T}{k_2}\right) - p_2 S_T I_V - h S_T, \tag{2.32}$$

$$\frac{dS_H}{dt} = r_H S_H \left(1 - \frac{S_H}{k_1}\right) - p_1 S_H I_V - h S_H, \tag{2.33}$$

$$\frac{dI_H}{dt} = p_1 S_H I_V + p_2 S_T I_V - h I_H - \gamma I_H, \tag{2.34}$$

$$\frac{dS_V}{dt} = \Lambda(S_V + I_V)\left(1 - \frac{S_V + I_V}{L}\right) - p_4 S_V I_H - \mu S_V, \tag{2.35}$$

$$\frac{dI_V}{dt} = p_4 S_V I_H - \mu I_V. \tag{2.36}$$

2.8   Gap of Literatures

Mathematical model of this thesis is developed for an outbreak of CMD caused by whitefly transmission and disease cuttings, following works of Bokil et al. The model added latent cassava state, which was missing from Magoyo et al. work to investigate the comparative contribution of using of four control methods (spraying, rouging, selecting non-infected cuttings, and promoting tolerant cuttings).

Growth rates of cassava and whitefly populations using the logistic growth equations. Cassava population assumes four states of cassava: tolerant, susceptible, exposed, and infected. Whitefly population assumed two states: uninfected and infected. The difference among the model of this research and other models are listed in Table 2.2.

Parameter values and ranges that used in this research are defined based on the previous works due to the lack of data collection system in Thailand. Table 2.3 lists the related works that used the parameters in the same values, while parameter values and ranges of this thesis are listed in Chapter III.

The model admits two equilibrium points: the *DFE* and *EE* points. Locally and globally asymptotically stable of the system are analyzed using basic reproduction number (R_0) and calculated using next-generation method. If $R_0 < 1$, the *DFE* point is locally-asymptotically-stable, proved by the Routh-Hurwitz criteria. If $R_0 \leq 1$, the *DFE* point is globally-asymptotically-stable, while $R_0 > 1$, the *EE* point is globally-asymptotically-stable, proved by Lyapunov's method.

Finally, optimal control theory and cost-effectiveness analysis are applied to investigate the cost-effectiveness of control policy. Optimal control theory may help stakeholders, including cassava farmers and government agencies, develop optimal policies for control of CMD outbreaks. This should increase yields, income, and profits.

Table 2.2 Gap of literatures

Works	Infection		State variables						Growth rate				Local stability		Global stability		Optimal control
									Cassava		Whitefly						
	Whitefly	Cuttings	S_T	S_H	E_H	I_H	S_V	I_V	Constant	Logistic growth	Constant	Logistic growth	DFE	EE	DFE	EE	
This research	✓	✓	✓	✓	✓	✓	✓	✓		✓		✓	✓		✓	✓	✓
Holt et al. (1997)	✓			✓		✓	✓	✓		✓		✓					
Jeger et al. (2004)	✓			✓	✓	✓	✓	✓	✓		✓						
Lawrence and Wallace (2011)	✓			✓		✓	✓	✓		✓		✓					
Hebert (2014)	✓			✓	✓	✓	✓	✓	✓		✓		✓	✓			
Kinene et al. (2015)	✓			✓	✓	✓	✓	✓	✓		✓		✓		✓		✓
Bokil et al. (2019)	✓	✓		✓		✓	✓	✓		✓		✓	✓	✓	✓	✓	✓
Magoyo et al. (2019)	✓		✓	✓		✓	✓	✓		✓		✓			✓	✓	
Jittamai et al. (2021)	✓	✓		✓	✓	✓	✓	✓		✓	✓		✓		✓	✓	

Table 2.3 List of parameters used to study from related works

(in the same values and ranges)

Related works	Parameters														
	h	β	γ	r_H	r_T	k_1	k_2	a	Λ	μ	L	p_1	p_2	p_3	p_4
This research	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓
Holt et al. (1997)	✓			✓		✓			✓	✓	✓	✓			✓
Jeger et al. (2004)	✓			✓		✓			✓	✓	✓	✓			✓
Lawrence et al. (2010)	✓			✓		✓			✓	✓	✓	✓			✓
Hebert (2014)				✓						✓		✓			✓
Kinene et al. (2015)	✓	✓	✓	✓		✓		✓	✓	✓		✓			✓
Bokil et al. (2019)	✓		✓	✓		✓			✓	✓	✓	✓			✓
Magoyo et al. (2019)	✓		✓	✓	✓	✓	✓		✓	✓	✓	✓	✓		✓
Jittamai et al. (2021)	✓	✓	✓	✓		✓		✓	✓	✓		✓		✓	✓

CHAPTER III

CMD OUTBREAK MODEL FORMULATION – WITH

TOLERANT AND LATENT

3.1 Infection and Control Factors

The model development can be first done by defining infection and control factors from previous literature that are related to CMD outbreaks. Cassava (*Manihot esculenta*, Crantz) is grown as a staple food crop in many parts of the Africa and the Southeast Asia. The main disease affecting the crop is cassava mosaic disease (CMD), caused by cassava mosaic *begomoviruses* (CMBs) that are transmitted by the whitefly (*Bemisia tabaci*, Gennadius) (Dubern, 1994) and planting with infected cuttings (Bock, 1994).

There are four approaches that are commonly used to control CMD, spraying pesticide, rouging infected cassavas, planting with non-virus cuttings and tolerant varieties. Kinene et al. (2015) and Bokil et al. (2019) applied spraying pesticide and rouging infected plant methods to control disease in their models. Magoyo et al. (2019) studied the dynamics of CMD outbreaks by using tolerant varieties.

Survey from the literature to determine major factors that cause and approach to control disease can be summarized in Figure 3.1.
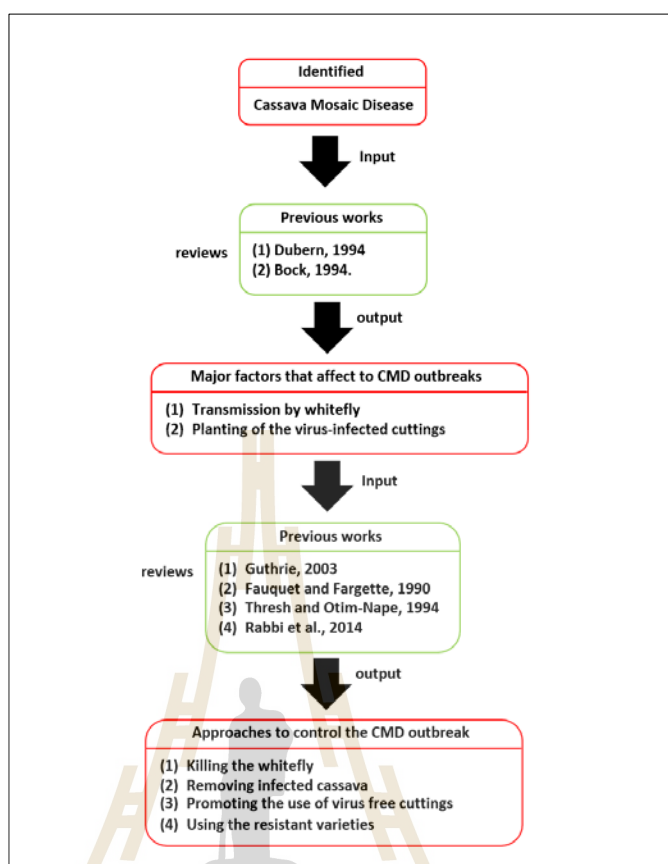
Figure 3.1 Survey of causes and approaches to control CMD

Table 3.1 Relationship between infection and control factors of CMD outbreak

Transmission	Infection factors		Control factors			
	Whitefly	Infected cuttings	Spraying	Rouging	Selecting uninfected cuttings	Promoting tolerant cuttings
Whitefly-cassava	✓		✓	✓		
Cassava-whitefly	✓	✓	✓	✓	✓	✓

Table 3.1 lists the relationship between infection and control factors. Whitefly is the major caused of disease transmission. To reduce severity of CMD spreads from the whitefly can be done by insecticide spraying and rouging infected plants from a plantation area. In addition, cassava-whitefly transmission is also caused by planting

with infected cuttings. Severity of cassava-whitefly transmission outbreak can be reduced by using at least these four approaches: spraying, rouging, selecting uninfected cuttings to plant, and promoting tolerant cuttings. An optimal policy is established by identifying crucial parameters that contribute to severity of CMD spread and determine control policy that is cost-effective. This can be done by sensitivity analysis and optimal control theory.

3.2 Mathematical Model Formulation

The CMD outbreak model is driven by virus cuttings and by transmission of whitefly. The model tracks the dynamics of the cassava population and the whitefly population. A state diagram of the CMD control system is shown in Figure 3.2.
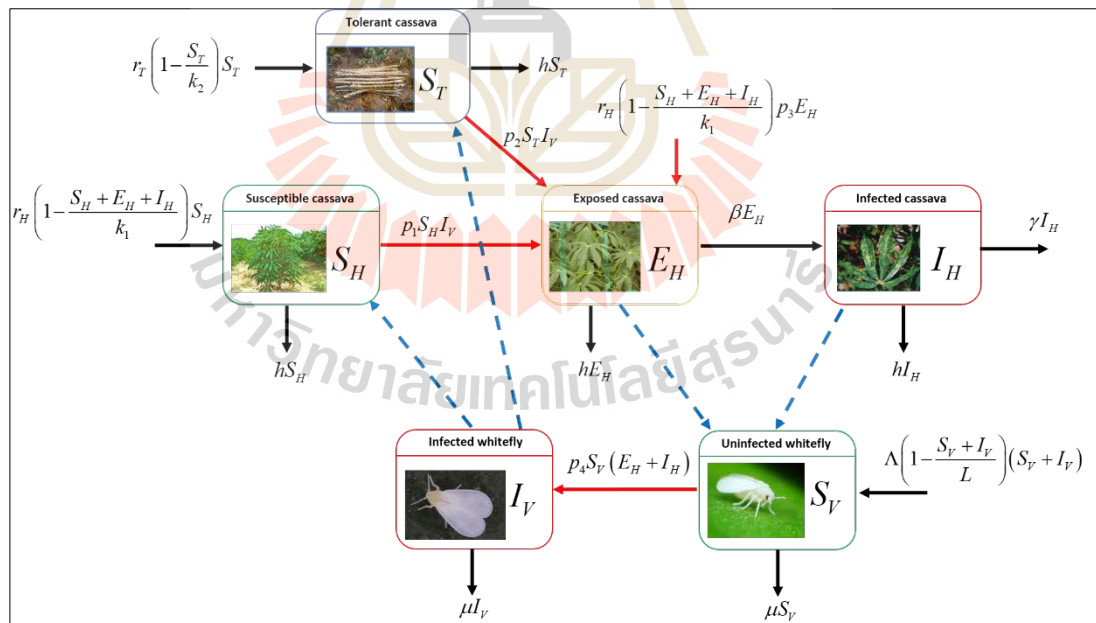
Figure 3.2 State diagram of the CMD outbreak system

The model tracks the dynamics of the cassava population and the whitefly population.

- Total non-tolerant cassava population at time t, denoted by N_H, where $N_H = S_H + E_H + I_H$.

- Tolerant population at time t, denoted by N_T, where $N_T = S_T$.

- Total cassava population at time t, denoted by N, where $N = N_H + N_T = S_T + S_H + E_H + I_H$.

- Total population of whitefly at time t, denoted by N_V, where $N_V = S_V + I_V$.

The transmission of CMD from an initial state to a next state are governed by parameters in Table 3.2. The dynamics of CMD outbreak is driven by

- *Whitefly transmission.* An infection by infected whitefly, given by $p_1 S_H I_V$ (whitefly-non-tolerant cassava transmission), $p_2 S_T I_V$ (cassava-whitefly transmission), and $p_4 S_V (E_H + I_H)$ (whitefly-tolerant cassava transmission).

- *Promote infected cuttings.* Virus infection by planting of infected cuttings, denoted by $r_H \left(1 - \frac{S_H + E_H + I_H}{k_1}\right) p_3 E_H$.

The size of the cassava population in a CMD outbreak is increased by replanting into the plantation area. Let r_H be the replating rate of non-tolerant cassava S_H, E_H, and I_H. The non-tolerant cassava growth of this model is governed by logistic growth terms $r_H \left(1 - \frac{S_H + E_H + I_H}{k_1}\right) S_H$ and $r_H \left(1 - \frac{S_H + E_H + I_H}{k_1}\right) p_3 E_H$, which is inspired from the work of Bokil et al. Let r_T be the replating rate of tolerant cassava S_T, the growth of this state is increased by $r_T \left(1 - \frac{S_T}{k_2}\right) S_T$, where k_1 is the maximum non-

tolerant cassava plants capacity and k_2 is the maximum tolerant cassava plant. They are removed from the system by constant harvesting h and rouging γ.

The change from S_T to E_H and from S_H to E_H reflect the number of plants infected after planting. The change from E_H to I_H reflects the number of infected cuttings that begin to show CMD symptoms.

The whitefly population is driven by two factors: birth rate Λ and death rate μ. The number of the whitefly population is increased by $\Lambda \left(1 - \frac{S_V + I_V}{L}\right)(S_V + I_V)$. Transmission within the population is reflected in a change from S_V state to I_V state, as whitefly visit and acquire the virus from infected plants.

Values and ranges of the parameters were set with reference to previous studies or estimations of CMD outbreaks. Parameters in CMD outbreaks represented disease spread factors are listed in Table 3.2.

Table 3.2 Parameter values and ranges to analyze the outbreak

Parameter	Value	Range	Reference
h	0.003	[0.002,0.004]	Holt et al. (1997)
β	0.008	[0.008,0.05]	Wagaba et al. (2013)
γ	0.03	[0,0.033]	Kinene et al. (2015)
r_H	0.05	[0.025,0.1]	Kinene et al. (2015)
r_T	0.025	[0.025,0.2]	Magoyo et al. (2019)
k_1	0.2	(0, 1]	Magoyo et al. (2019)
k_2	0.5	(0, 1]	Magoyo et al. (2019)
Λ	0.2	[0.1,0.3]	Jeger et al. (2004)
μ	0.0142	[0.0142,0.0166]	Kinene et al. (2015)
L	200	(0, 2500]	Bokil et al. (2019)
p_1	0.008	[0,1.0]	Bokil et al. (2019)

Table 3.2 Parameter values and ranges to analyze the outbreak (Continued)

Parameter	Value	Range	Reference
p_2	0.001	[0,1.0]	Magoyo et al. (2019)
p_3	0.1	[0,1.0]	Holt et al. (1997)
p_4	0.008	[0,1.0]	Bokil et al. (2019)

3.2.1 Ordinary differential equations

Ordinary differential equations (*ODEs*) are constructed by parameters and values that are given in Table 3.3

$$\frac{dS_T}{dt} = r_T \left(1 - \frac{S_T}{k_2}\right) S_T - p_2 S_T I_V - h S_T, \tag{3.1}$$

$$\frac{dS_H}{dt} = r_H \left(1 - \frac{S_H + E_H + I_H}{k_1}\right) S_H - p_1 S_H I_V - h S_H, \tag{3.2}$$

$$\frac{dE_H}{dt} = r_H \left(1 - \frac{S_H + E_H + I_H}{k_1}\right) p_3 E_H + p_1 S_H I_V + p_2 S_T I_V - (\beta + h) E_H, \tag{3.3}$$

$$\frac{dI_H}{dt} = \beta E_H - (\gamma + h) I_H, \tag{3.4}$$

$$\frac{dS_V}{dt} = \Lambda \left(1 - \frac{S_V + I_V}{L}\right)(S_V + I_V) - p_4 S_V (E_H + I_H) - \mu S_V, \tag{3.5}$$

$$\frac{dI_V}{dt} = p_4 S_V (E_H + I_H) - \mu I_V, \tag{3.6}$$

with the initial conditions

$$S_T(0), S_H(0), E_H(0), I_H(0), S_V(0), I_V(0) > 0. \tag{3.7}$$

Equations (3.8) and (3.9) give the total cassava population and the total whitefly population:

$$\frac{dN}{dt} = r_H \left(1 - \frac{S_H + E_H + I_H}{k_1}\right)(S_H + p_3 E_H) + r_T \left(1 - \frac{S_T}{k_2}\right) S_T - h N, \tag{3.8}$$

$$\frac{dN_V}{dt} = \Lambda\left(1 - \frac{S_V + I_V}{L}\right)(S_V + I_V) - \mu(S_V + I_V). \qquad (3.9)$$

3.2.2 Basic assumptions of the model

The following are assumptions for mathematical model.

- All model parameters are positive.

- A growth rate of the cassava population is positive, i.e., $r_H - h > 0$ and $r_T - h > 0$, where r_H and r_T are the replanting rate of non-tolerant and tolerant cassava, respectively, and h is harvesting rate.

- The increase of cassava population is calculated by the logistic growth equations, $r_H\left(1 - \frac{S_H + E_H + I_H}{k_1}\right)S_H$, $r_H\left(1 - \frac{S_H + E_H + I_H}{k_1}\right)p_3 E_H$, and $r_T\left(1 - \frac{S_T}{k_2}\right)S_T$.

- A growth rate of the whitefly population is positive, i.e., $\Lambda - \mu > 0$, where Λ is the whitefly birth rate and μ is the natural whitefly death rate.

- The increase of whitefly population is calculated by the logistic growth equation, $\Lambda\left(1 - \frac{S_V + I_V}{L}\right)(S_V + I_V)$.

- The growth rate of the whitefly density is greater than the growth rate of the cassava, $(\Lambda - \mu) > (r_H - h)$.

3.2.3 Basic properties of the model

To confirm the biological validity of the model, it must prove that solutions to *ODEs* are positive and bounded for all time values. Furthermore, the cassava population and the whitefly population must remain finite since they are

bounded by the plantation area. In this section, the positivity and boundedness of these solutions are discussed.

3.2.3.1 Positivity

Theorem 3.1: *In the model, if the initial conditions satisfy with Equation (3.7) then for all $t \geq 0$, all solutions of ODEs in Equations (3.1) to (3.6) will remain positive in $\mathbb{R}_+^6$.*

Proof: Since all of parameters used in the system are positive. Theorem 3.1 can be proved by placing lower bounds on each of equations given in the model.

- *Positivity of $S_T(t)$ for all $t \geq 0$*

    From Equation (3.1),

    $$\frac{dS_T}{dt} = r_T \left(1 - \frac{S_T}{k_2}\right) S_T - p_2 S_T I_V - h S_T \geq -p_2 S_T I_V - h S_T.$$

The integration of the inequality is

$$S_T(t) \geq S_T(0) e^{-ht - \int_0^t p_2 I_V(s)ds}, \qquad \text{for all } t \geq 0. \qquad (3.10)$$

Thus, $S_T(t) > 0$ for all $t \geq 0$.

- *Positivity of $S_H(t)$ for all $t \geq 0$*

    From Equation (3.2),

    $$\frac{dS_H}{dt} = r_H \left(1 - \frac{S_H + E_H + I_H}{k_1}\right) S_H - p_1 S_H I_V - h S_H \geq -p_1 S_H I_V - h S_H.$$

The integration of the inequality is

$$S_H(t) \geq S_H(0) e^{-ht - \int_0^t p_1 I_V(s)ds} \qquad \text{for all } t \geq 0. \qquad (3.11)$$

This means that $S_H(t) > 0$ for all $t \geq 0$.

- *Positivity of $E_H(t)$ for all $t \geq 0$*

  From Equation (3.3),

$$\frac{dE_H}{dt} = r_H \left(1 - \frac{S_H + E_H + I_H}{k_1}\right) p_3 E_H + p_1 S_H I_V + p_2 S_T I_V - (\beta + h)E_H$$

$$\geq -(\beta + h)E_H.$$

The integration of the inequality is

$$E_H(t) \geq E_H(0)e^{-(\beta+h)t} \qquad \text{for all } t \geq 0. \qquad (3.12)$$

Hence, $E_H(t) > 0$ for all $t \geq 0$.

- *Positivity of $I_H(t)$ for all $t \geq 0$*

  From Equation (3.4),

$$\frac{dI_H}{dt} = \beta E_H - hI_H \geq -hI_H$$

It then follows that

$$I_H(t) \geq I_H(0)e^{-ht} > 0, \qquad \text{for all } t \geq 0. \qquad (3.13)$$

Therefore, $I_H(t_1) > 0$ for all $t \geq 0$.

- *Positivity of $S_V(t)$ for all $t \geq 0$*

  From Equation (3.5),

$$\frac{dS_V}{dt} = \Lambda \left(1 - \frac{S_V + I_V}{L}\right)(S_V + I_V) - p_4 S_V(E_H + I_H) - \mu S_V$$

$$\geq -p_4 S_V(E_H + I_H) - \mu S_V.$$

A comparison argument shows that

$$S_V(t) \geq S_V(0)e^{-\mu t - \int_0^t p_4(E_H(s) + I_H(s))ds}, \qquad \text{for all } t \geq 0. \qquad (3.14)$$

Hence, $S_V(t) > 0$ for all $t \geq 0$.

- *Positivity of $I_V(t)$ for all $t \geq 0$*

    From Equation (3.6),

$$\frac{dI_V}{dt} = p_4 S_V(E_H + I_H) - \mu I_V \geq -\mu I_V,$$

It then follows that

$$I_V(t) \geq I_V(0)e^{-\mu t} > 0, \qquad\qquad \text{for all } t \geq 0. \qquad (3.15)$$

Therefore, $I_V(t) > 0$ for all $t \geq 0$.

This can be concluded that the solutions of the model are positive in $\mathbb{R}_+^6$. □

3.2.3.2 Boundedness

The boundedness of the system is showed with the initial condition (3.7). Let $\Omega = \Omega_C \times \Omega_V \subset \mathbb{R}_+^4 \times \mathbb{R}_+^2$ be any solution of the system with positive initial condition, where

$$\Omega_C = \{S_T(t), S_H(t), E_H(t), I_H(t) \in \mathbb{R}_+^4\} \text{ and } \Omega_V = \{S_V(t), I_V(t) \in \mathbb{R}_+^2\}.$$

Therefore, all the solutions of the system start in

$$\mathbb{R}_+^6 = \left\{ S_T, S_H, E_H, I_H, S_V, I_V \left| \begin{matrix} S_T(0) > 0, S_H(0) > 0, E_H(0) > 0, \\ I_H(0) > 0, S_V(0) > 0, I_V(0) > 0 \end{matrix} \right. \right\} \qquad \text{for } t \geq 0.$$

Theorem 3.2: *All solutions of the ODEs in Equations (3.1) to (3.6) with positive initial conditions (3.7) are ultimately bounded.*

Proof: From **Theorem 3.1**, the solutions to these *ODEs* are positive for all $t \geq 0$.

- *Boundedness of $N(t)$ for all $t \geq 0$*

Since $N = N_H + N_T$, we have

$$\frac{dN}{dt} = \frac{dN_H}{dt} + \frac{dN_T}{dt}.$$

First, we consider N_H for all $t \geq 0$. From Equation (3.8),

$$\frac{dN}{dt} = r_H \left(1 - \frac{S_H + E_H + I_H}{k_1}\right)(S_H + p_3 E_H) + r_T \left(1 - \frac{S_T}{k_2}\right) S_T - hN.$$

As can be observed, the solution is bounded by logistic growth

$$\frac{dN_H}{dt} \leq r_H \left(1 - \frac{N_H}{k_2}\right) N_H.$$

The integration of the inequality is

$$N_H(t) \leq \frac{N_H(0)k_1}{N_H(0) + \left(k_1 - N_H(0)\right)e^{-r_H t}}$$

(assuming $N_H(0) > 0$), which implies that $lim_{t \to \infty} N_H(t) \leq k_1$.

Next, we consider N_T for all $t \geq 0$. From Equation (3.8), the solution is also bounded by logistic growth

$$\frac{dN_T}{dt} \leq r_T \left(1 - \frac{N_T}{k_2}\right) N_T.$$

The integration of the inequality is

$$N_T(t) \leq \frac{N_T(0)k_2}{N_T(0) + \left(k_2 - N_T(0)\right)e^{-r_T t}}$$

(assuming $N_T(0) > 0$), which implies that $lim_{t \to \infty} N_T(t) \leq k_2$.

This gives the feasible solution set of the cassava entering the region:

$$\Omega_C = \left\{ S_T, S_H, E_H, I_H \in \mathbb{R}_+^4 \, \middle| \, N(t) \le k_1 + k_2 \right\} \qquad \text{for all } t \ge 0.$$

- *Boundedness of $N_V(t)$ for all $t \ge 0$*

Let $N_V = S_V + I_V$. From Equation (3.9),

$$\frac{dN_V}{dt} = \Lambda \left(1 - \frac{N_V}{L} \right) N_V - \mu N_V.$$

As can be observed, the solution is bounded by logistic growth

$$\frac{dN_V}{dt} \le \Lambda \left(1 - \frac{N_V}{L} \right) N_V.$$

The integration of the inequality is

$$N_V(t) \le \frac{N_V(0)L}{N_V(0) + \left(L - N_V(0) \right) e^{-\Lambda t}},$$

(assuming $N_V(0) > 0$), which implies that $lim_{t \to \infty} N_V(t) \le L$. Thus, the feasible solution set for the CMD system is given by

$$\Omega_V = \left\{ S_V, I_V \in \mathbb{R}_+^2 \, \middle| \, N_V \le L \right\} \qquad \text{for all } t \ge 0.$$

The solutions of the system in $\mathbb{R}_+^6$ are confined to the region Ω. Here

$$\Omega = \left\{ S_T, S_H, E_H, I_H, S_V, I_V \in \mathbb{R}_+^6 \, | \, N \le k_1 + k_2, N_V \le L \right\} \qquad \text{for all } t \ge 0.$$

Hence, all solutions of the system (3.1) to (3.6) with initial conditions (3.7) remain positive invariant in the region Ω for all $t \ge 0$. □

3.3   Stability Analysis of the System

In this section, local and global stability of the feasible equilibrium of CMD system is established.

3.3.1   Disease-free equilibrium point

In the absence of CMD in the cassava population, the system in Equations (3.1) to (3.6) admits a trivial equilibrium also known as the disease-free equilibrium (DFE), denoted by $E_0 = (S_T^*, S_H^*, E_H^*, I_H^*, S_V^*, I_V^*)$ and given by

$$E_0 = (S_T^*, S_H^*, E_H^*, I_H^*, S_V^*, I_V^*) = \left(\frac{(r_T - h)k_2}{r_T}, \frac{(r_H - h)k_1}{r_H}, 0, 0, \frac{(\Lambda - \mu)L}{\Lambda}, 0\right) \qquad (3.16)$$

3.3.2   Endemic equilibrium point

The endemic equilibrium point (EE) of the system is denoted by $E_1 = \left(\overline{S_T}, \overline{S_H}, \overline{E_H}, \overline{I_H}, \overline{S_V}, \overline{I_V}\right)$. The EE is determined by setting the right-hand sides of Equations (3.1) to (3.6) to zero. Therefore,

$$\overline{S_T} = \frac{(r_T - h - p_2\overline{I_V})k_2}{r_T},$$

$$\overline{S_H} = \frac{(\gamma + h)(r_H - h - p_1\overline{I_V}) - r_H\overline{E_H}(\beta + \gamma + h)}{r_H(\gamma + h)},$$

$$\overline{E_H} = \frac{(\gamma + h)\overline{I_V}\left(r_T p_1 k_1(r_H - h - p_1\overline{I_V}) + r_H p_2 k_2(r_T - h - p_2\overline{I_V})\right)}{r_T r_H\left(h^2 + h(\beta + \gamma + p_1\overline{I_V}(1 - p_3) - p_3 h) + (\beta + \gamma(1 - p_3))p_1\overline{I_V} + \gamma(\beta - p_3 h)\right)},$$

$$\overline{I_H} = \frac{\beta}{\gamma + h}\overline{E_H},$$

$$\overline{S_V} = \frac{\mu(\gamma + h)\overline{I_V}}{p_4\overline{E_H}(\beta + \gamma + h)},$$

$$\overline{I_V} = \frac{(\Lambda - \mu)(\beta + \gamma + h)p_4 L\overline{E_H}}{\Lambda\left(\mu(\gamma + h) + p_4\overline{E_H}(\beta + \gamma + h)\right)}.$$

3.3.3 Reproduction number

R_0 is one of the most useful threshold parameters in epidemiology. It is defined as the expected number of secondary cases produced by a single infection in a completely susceptible population. It is used as an indicator of the stability of E_0 and E_1, where E_1 is the symbol of the *EE*. The *DFE* E_0 is asymptotically stable if $R_0 < 1$, as the disease cannot invade the population and unstable if $R_0 > 1$. E_1 is asymptotically stable if $R_0 > 1$. R_0 is calculated by using the next-generation method, which is similar to the works of Tumwiine et al. (2008) and Bhunu and Garira (2009).

The appearance of new infections is represented by vector F and the transfer of existing infections by vector V. Let x_j be an infection state for $j = 1,2,3$, i.e., $x_1 = E_H$, $x_2 = I_H$, $x_3 = I_V$. F describes new infection arising in state x_j and V represents the transfer of existing infection to state x_j.

The Jacobian matrices generated by differentiating F and V with respect to the relevant subset of variables are calculated at E_0. This yields the matrices $\boldsymbol{F}$ and $\boldsymbol{V}$. The (j, k) entry of the matrix $\boldsymbol{F}$ is the rate at which infected individuals in compartment k produce new infections in compartment j. The (j, k) entry of the matrix $\boldsymbol{V}$ represents the transfer of existing infection. R_0 is computed from the spectral radius of $\boldsymbol{F}\boldsymbol{V}^{-1}$ at *DFE*. $\boldsymbol{F}\boldsymbol{V}^{-1}$ is called the next generation matrix and is set as follows:

$$R_0 = \rho(FV^{-1}),$$

where $\rho(M)$ denotes the spectral radius of a matrix M. The spectral radius of $\boldsymbol{F}\boldsymbol{V}^{-1}$ is equal to the dominant (or maximum) eigenvalue of $\boldsymbol{F}\boldsymbol{V}^{-1}$.

In this model, the vectors F and V can be derived from Equations (3.1) to (3.6):

$$F = \begin{bmatrix} p_1 S_H I_V + p_2 S_T I_V + r_H \left(1 - \frac{S_H + E_H + I_H}{k_1}\right) p_3 E_H \\ 0 \\ p_4 S_V (E_H + I_H) \end{bmatrix} \text{ and } V = \begin{bmatrix} (\beta + h) E_H \\ (\gamma + h) I_H - \beta E_H \\ \mu I_V \end{bmatrix}.$$

The Jacobians of F and V with respect to the infectious classes are defined by $\boldsymbol{F} = \left[\frac{\partial F_j(E_0)}{\partial x_k}\right]$ and $\boldsymbol{V} = \left[\frac{\partial V_j(E_0)}{\partial x_k}\right]$,

$$\boldsymbol{F} = \begin{bmatrix} r_H \left(1 - \frac{S_H^*}{k_1}\right) p_3 & 0 & p_1 S_H^* + p_2 S_T^* \\ 0 & 0 & 0 \\ p_4 S_V^* & p_4 S_V^* & 0 \end{bmatrix} \text{ and } \boldsymbol{V} = \begin{bmatrix} \beta + h & 0 & 0 \\ -\beta & (\gamma + h) & 0 \\ 0 & 0 & \mu \end{bmatrix},$$

respectively.

Therefore, the next generation matrix $\boldsymbol{FV}^{-1}$ is

$$\boldsymbol{FV}^{-1}(E_0) = \begin{bmatrix} \frac{p_3 h}{\beta + h} & 0 & \frac{p_1 k_1 (r_H - h)}{r_H \mu} + \frac{p_2 k_2 (r_T - h)}{r_T \mu} \\ 0 & 0 & 0 \\ \frac{p_4 L(\Lambda - \mu)(\beta + \gamma + h)}{\Lambda(\beta + h)(\gamma + h)} & \frac{p_4 L(\Lambda - \mu)}{\Lambda(\gamma + h)} & 0 \end{bmatrix} \quad (3.17)$$

Hence, R_0 is the dominant eigenvalue of Matrix (3.17).

$$R_0 = \max\left(\frac{p_3 h}{2(\beta + h)} \pm \sqrt{\left(\frac{p_3 h}{2(\beta + h)}\right)^2 + \frac{p_4 L(\Lambda - \mu)(\beta + \gamma + h)}{\Lambda \mu (\beta + h)(\gamma + h)}\left(\frac{p_1 k_1 (r_H - h)}{r_H} + \frac{p_2 k_2 (r_T - h)}{r_T}\right)}\right)$$

$$= \frac{p_3 h}{2(\beta + h)} + \sqrt{\left(\frac{p_3 h}{2(\beta + h)}\right)^2 + \frac{p_4 L(\Lambda - \mu)(\beta + \gamma + h)}{\Lambda \mu (\beta + h)(\gamma + h)}\left(\frac{p_1 k_1 (r_H - h)}{r_H} + \frac{p_2 k_2 (r_T - h)}{r_T}\right)} \quad (3.18)$$

3.3.4 Local stability analysis of disease-free equilibrium point

Theorem 3.3: *The DFE point, E_0, of Equations (3.1) to (3.6) is locally-asymptotically-stable in Ω if $R_0 < 1$ and unstable if $R_0 > 1$.*

Proof: The local stability is determined based on the eigenvalue λ of the Jacobian. The E_0 is locally-asymptotically-stable if the real parts of λ are all negative. The Jacobian matrix at E_0 is given by

$$J(E_0) = \begin{bmatrix} -(r_T - h) & 0 & 0 & 0 & 0 & -\frac{p_2 k_2 (r_T - h)}{r_T} \\ 0 & -(r_H - h) & -(r_H - h) & -(r_H - h) & 0 & -\frac{p_1 k_1 (r_H - h)}{r_H} \\ 0 & 0 & p_3 h - (\beta + h) & 0 & 0 & \frac{p_1 k_1 (r_H - h)}{r_H} + \frac{p_2 k_2 (r_T - h)}{r_T} \\ 0 & 0 & \beta & -(\gamma + h) & 0 & 0 \\ 0 & 0 & -\frac{p_4 L(\Lambda - \mu)}{\Lambda} & -\frac{p_4 L(\Lambda - \mu)}{\Lambda} & -(\Lambda - \mu) & \Lambda - 2\mu \\ 0 & 0 & \frac{p_4 L(\Lambda - \mu)}{\Lambda} & \frac{p_4 L(\Lambda - \mu)}{\Lambda} & 0 & -\mu \end{bmatrix} \qquad (3.19)$$

The characteristic equation of (3.19) is

$$\big(\lambda + (r_T - h)\big)\big(\lambda + (r_H - h)\big)\big(\lambda + (\Lambda - \mu)\big)(\lambda^3 + a_1 \lambda^2 + a_2 \lambda + a_3) = 0, \qquad (3.20)$$

where

$$a_1 = \beta + \gamma + \mu + h(2 - p_3),$$

$$a_2 = (\beta + h - p_3 h)(\gamma + h + \mu) + (\gamma + h)\mu - \frac{p_4 L(\Lambda - \mu)}{\Lambda}\left(\frac{p_1 k_1 (r_H - h)}{r_H} + \frac{p_2 k_2 (r_T - h)}{r_T}\right), \qquad (3.21)$$

$$a_3 = \mu(\gamma + h)(\beta + h - p_3 h) - \frac{p_4 L(\Lambda - \mu)(\beta + \gamma + h)}{\Lambda}\left(\frac{p_1 k_1 (r_H - h)}{r_H} + \frac{p_2 k_2 (r_T - h)}{r_T}\right).$$

The eigenvalues are calculated under the model assumptions $r_T > h$, $r_H > h$ and $\Lambda > \mu$. It is clear that the first three eigenvalues of this system are negative: $-(r_T - h)$, $-(r_H - h)$ and $-(\Lambda - \mu)$.

The polynomial from (3.21) is considered

$$\lambda^3 + a_1 \lambda^2 + a_2 \lambda + a_3 = 0.$$

As $0 \le p_3 \le 1$, yields

$$a_1 = \beta + \gamma + \mu + h(2 - p_3) > 0.$$

If $R_0 = \dfrac{p_3 h}{2(\beta+h)} + \sqrt{\left(\dfrac{p_3 h}{2(\beta+h)}\right)^2 + \dfrac{p_4 L(\Lambda-\mu)(\beta+\gamma+h)}{\Lambda\mu(\beta+h)(\gamma+h)}\left(\dfrac{p_1 k_1(r_H-h)}{r_H} + \dfrac{p_2 k_2(r_T-h)}{r_T}\right)} < 1,$

It can be rewritten as

$$R_0 < \frac{p_3 h}{2(\beta+h)} + \sqrt{\left(\frac{2(\beta+h)-p_3 h}{2(\beta+h)}\right)^2}$$

$$\frac{p_4 L(\Lambda - \mu)(\beta + \gamma + h)}{\Lambda\mu(\beta + h)(\gamma + h)}\left(\frac{p_1 k_1(r_H - h)}{r_H} + \frac{p_2 k_2(r_T - h)}{r_T}\right) < \frac{\beta + h - p_3 h}{\beta + h}.$$

Therefore,

$$a_3 = \mu(\gamma + h)(\beta + h - p_3 h) - \frac{p_4 L(\Lambda-\mu)(\beta+\gamma+h)}{\Lambda}\left(\frac{p_1 k_1(r_H-h)}{r_H} + \frac{p_2 k_2(r_T-h)}{r_T}\right) > 0.$$

Finally, $a_1 a_2 - a_3 > 0$ is considered

$$a_1 a_2 - a_3 = \big(\beta + \gamma + \mu + h(2 - p_3)\big)\bigg((\beta + h - p_3 h)(\gamma + h + \mu) + (\gamma + h)\mu$$

$$- \frac{p_4 L(\Lambda - \mu)}{\Lambda}\left(\frac{p_1 k_1(r_H - h)}{r_H} + \frac{p_2 k_2(r_T - h)}{r_T}\right)\bigg) - \mu(\gamma + h)(\beta + h - p_3 h)$$

$$+ \frac{p_4 L(\Lambda - \mu)(\beta + \gamma + h)}{\Lambda}\left(\frac{p_1 k_1(r_H - h)}{r_H} + \frac{p_2 k_2(r_T - h)}{r_T}\right).$$

It can be rewritten as

$$a_1 a_2 - a_3 = (\gamma + h + \mu)(\gamma + h)\mu + \frac{p_4 L(\Lambda - \mu)(\beta + \gamma + h)}{\Lambda}\left(\frac{p_1 k_1(r_H - h)}{r_H} + \frac{p_2 k_2(r_T - h)}{r_T}\right)$$

$$+ \big(\beta + \gamma + \mu + h(2 - p_3)\big)\bigg((\beta + h - p_3 h)(\gamma + h + \mu) - \frac{p_4 L(\Lambda - \mu)}{\Lambda}\left(\frac{p_1 k_1(r_H - h)}{r_H} + \frac{p_2 k_2(r_T - h)}{r_T}\right)\bigg)$$

$$= G_1 + G_2 + a_3,$$

where

$$G_1 = \frac{\beta + \gamma + h}{\beta + \gamma + \mu + h(2 - p_3)}\left((\gamma + h + \mu)(\gamma + h)\mu + \frac{p_4 L(\Lambda - \mu)(\beta + \gamma + h)}{\Lambda}\left(\frac{p_1 k_1(r_H - h)}{r_H} + \frac{p_2 k_2(r_T - h)}{r_T}\right)\right)$$

$$G_2 = \big((\gamma + h)(\beta + \gamma + h) + \mu\beta\big)(\beta + h - p_3 h).$$

It is clear $G_1 > 0$, $G_2 > 0$, and $a_3 > 0$ since $R_0 < 1$, $r_T > h$, $r_H > h$, $\Lambda > \mu$, and $0 \le p_3 \le 1$.

This means that $a_1 a_2 - a_3 > 0$. Using the Routh-Hurwitz criteria for the polynomial of degree three ($a_1 > 0$, $a_3 > 0$, and $a_1 a_2 - a_3 > 0$), the remaining λ of the disease-free equilibrium system have negative real parts.

Therefore, E_0 will be locally-asymptotically-stable if $R_0 < 1$. When $R_0 > 1$, E_0 is unstable and the disease will persist. $\qquad\square$

3.3.5 Global stability analysis of disease-free equilibrium point

The global stability of *DFE* is discussed using the Lyapunov's method and Lasalle theorem to obtain the control condition under which disease can be eradicated.

Theorem 3.4: *If $R_0 \le 1$ then E_0 is globally-asymptotically-stable, by assuming that:*

$$\mu = p_1 S_H^* + p_2 S_T^* \tag{3.22}$$

Proof: Let V be the Lyapunov function, where

$$V:\{(S_T, S_H, E_H, I_H, S_V, I_V) \in \Omega : S_T, S_H, S_V > 0\} \to \mathbb{R}_6^+.$$

The Lyapunov function V for Equations (3.1) to (3.6) is defined as

$$V(S_T, S_H, E_H, I_H, S_V, I_V) = \left(S_T - S_T^* - S_T^* \ln\frac{S_T}{S_T^*}\right) + \left(S_H - S_H^* - S_H^* \ln\frac{S_H}{S_H^*}\right) + E_H + I_H$$

$$+ \left(S_V - S_V^* - S_V^* \ln\frac{S_V}{S_V^*}\right) + I_V.$$

When V is C^1, a proper positive definite function, and E_0 is the global minimum of V on Ω, yields

$$V(S_T^*, S_H^*, E_H^*, I_H^*, S_V^*, I_V^*) = 0.$$

The time derivative of V computed along solutions of Equations (3.1) to (3.6) is

$$\frac{dV}{dt} = \left(1 - \frac{S_T^*}{S_T}\right)\frac{dS_T}{dt} + \left(1 - \frac{S_H^*}{S_H}\right)\frac{dS_H}{dt} + \frac{dE_H}{dt} + \frac{dI_H}{dt} + \left(1 - \frac{S_V^*}{S_V}\right)\frac{dS_V}{dt} + \frac{dI_V}{dt} \qquad (3.23)$$

Substituting the *ODEs* (3.1) to (3.6) into Equation (3.23) yields

$$\frac{dV}{dt} = \left(1 - \frac{S_T^*}{S_T}\right)\left(r_T\left(1 - \frac{S_T}{k_2}\right)S_T - p_2 S_T I_V - h S_T\right) + \left(1 - \frac{S_H^*}{S_H}\right)\left(r_H\left(1 - \frac{S_H + E_H + I_H}{k_1}\right)S_H - p_1 S_H I_V - h S_H\right)$$

$$+ \left(r_H\left(1 - \frac{S_H + E_H + I_H}{k_1}\right)p_3 E_H + p_1 S_H I_V + p_2 S_T I_V - (\beta + h)E_H\right) + (\beta E_H - (\gamma + h)I_H)$$

$$+ \left(1 - \frac{S_V^*}{S_V}\right)\left(\Lambda\left(1 - \frac{S_V + I_V}{L}\right)(S_V + I_V) - p_4 S_V(E_H + I_H) - \mu S_V\right) + (p_4 S_V(E_H + I_H) - \mu I_V),$$

this simplifies to

$$\frac{dV}{dt} = \left(r_T\left(1 - \frac{S_T^*}{k_2}\right)S_T - h S_T\right)\left(1 - \frac{S_T^*}{S_T}\right) + \left(r_H\left(1 - \frac{S_H^*}{k_1}\right)S_H - h S_H\right)\left(1 - \frac{S_H^*}{S_H}\right)$$

$$+ r_H\left(1 - \frac{S_H^*}{k_1}\right)p_3 E_H - h E_H - (\gamma + h)I_H + \Lambda\left(1 - \frac{S_V^*}{L}\right)S_V^*\left(1 - \frac{S_V^*}{S_V}\right) + \mu S_V^*\left(1 - \frac{S_V}{S_V^*}\right)$$

$$+ p_4 S_V^*(E_H + I_H) - (p_1 S_H^* + p_2 S_T^* - \mu)I_V, \qquad (3.24)$$

Since $E_H + I_H = N_H - S_H$, $N_H = S_H^* = \frac{(r_H - h)k_1}{r_H}$, $S_T^* = \frac{(r_T - h)k_2}{r_T}$, $N_V = S_V^* = \frac{(\Lambda - \mu)L}{\Lambda}$ and the conditions (3.22) where $N_H = S_H + E_H + I_H$ is the non-tolerant cassava population, Equation (3.24) can be rewritten as

$$\frac{dV}{dt} = hp_3 E_H - hE_H - (\gamma + h)I_H + \mu S_V^* \left(2 - \frac{S_V^*}{S_V} - \frac{S_V}{S_V^*} \right) + G_3(S_H^* - S_H), \qquad (3.25)$$

where $G_3 = p_4 S_V^*$. Therefore, Equation (3.25) becomes

$$\frac{dV}{dt} = -\mu \frac{(S_V - S_V^*)^2}{S_V} + hE_H(p_3 - 1) - (\gamma + h)I_H + G_3(S_H^* - S_H) \leq 0. \qquad (3.26)$$

All terms in Equation (3.26) are always non-positive since $\lim_{t \to \infty} S_H(t) \geq S_H^*$ (Equation 3.11) and $0 \leq p_3 \leq 1$ (Table 2.4). Note that $\frac{dV}{dt} = 0$ if and only if $S_T = S_T^*$, $S_H = S_H^*$, $E_H = E_H^*$, $I_H = I_H^*$, and $S_V = S_V^*$.

Therefore, the largest invariant compact invariant set in $\left\{ (S_T, S_H, E_H, I_H, S_V, I_V) \in \Omega : \frac{dV}{dt} = 0 \right\}$ is the singleton, i.e., $E_0 = (S_T^*, S_H^*, E_H^*, I_H^*, S_V^*, I_V^*)$. Thus, $\frac{dV}{dt} \leq 0$. By LaSalle's theorem, any solution approaches to E_0 as $t \to \infty$. This implies that E_0 is globally-asymptotically-stable in Ω. $\qquad \square$

3.3.6 Global stability analysis of endemic equilibrium point

Theorem 3.5: *If $R_0 > 1$ then E_1 is globally-asymptotically-stable.*

Proof: Theorem 3.5 can be proved by the Lyapunov functions of Cai and Li (2010) and Chen and Junyuan (2016). Let W be the Lyapunov function, where

$$W : \{ (S_T, S_H, E_H, I_H, S_V, I_V) \in \Omega : S_T, S_H, E_H, I_H, S_V, I_V > 0 \} \to \mathbb{R}_6^+.$$

and

$$f : (0, \infty) \ni \omega \to \omega - 1 - \ln \omega.$$

As can be observed, $f(\omega) \geq 0$ and $f(\omega) = 0$ if and only if $\omega = 1$.

The Lyapunov function W for Equations (3.1) to (3.6) is defined as

$$W(S_T, S_H, E_H, I_H, S_V, I_V) = c_1 W_1(S_T) + c_2 W_2(S_H) + c_3 W_3(E_H)$$
$$+ c_4 W_4(I_H) + c_5 W_5(S_V) + c_6 W_6(I_V), \qquad (3.27)$$

where

$$W_1(S_T) = f\left(\frac{S_T}{\overline{S_T}}\right), W_2(S_H) = f\left(\frac{S_H}{\overline{S_H}}\right), W_3(E_H) = f\left(\frac{E_H}{\overline{E_H}}\right),$$

$$W_4(I_H) = f\left(\frac{I_H}{\overline{I_H}}\right), W_5(S_V) = f\left(\frac{S_V}{\overline{S_V}}\right), W_6(I_V) = f\left(\frac{I_V}{\overline{I_V}}\right),$$

$$c_1 = \frac{1}{p_2 \overline{I_V}}, c_2 = \frac{1}{p_1 \overline{I_V}}, c_3 = \frac{\overline{E_H}}{(p_1 \overline{S_H} + p_2 \overline{S_T}) \overline{I_V}},$$

$$c_4 = \frac{\overline{I_H}}{\beta \overline{E_H}}, c_5 = \frac{1}{p_4 (\overline{E_H} + \overline{I_H})}, c_6 = \frac{\overline{I_V}}{p_4 \overline{S_V} (\overline{E_H} + \overline{I_H})}.$$

When W is C^1, a proper positive definite function, and E_1 is the global minimum of W on Ω, we obtain

$$W(S_T^*, S_H^*, E_H^*, I_H^*, S_V^*, I_V^*) = 0.$$

For simplicity of notations, we denote

$$x = \frac{S_T}{\overline{S_T}}, y = \frac{S_H}{\overline{S_H}}, z = \frac{E_H}{\overline{E_H}}, q = \frac{I_H}{\overline{I_H}}, r = \frac{S_V}{\overline{S_V}}, u = \frac{I_V}{\overline{I_V}}, w = \frac{p_1 S_H + p_2 S_T}{p_1 \overline{S_H} + p_2 \overline{S_T}}, v = \frac{E_H + I_H}{\overline{E_H} + \overline{I_H}}.$$

For clarity, we first calculate the derivatives of $W_1, W_2, W_3, W_4, W_5,$ and W_6 one by one (Equations (3.28) to (3.33)).

We first consider the derivative of W_1

$$\frac{dW_1}{dt} = \frac{1}{\overline{S_T}}\left(1 - \frac{\overline{S_T}}{S_T}\right)\left(r_T\left(1 - \frac{N_T}{k_2}\right)S_T - p_2 S_T I_V - hS_T\right).$$

Since $r_T\left(1 - \frac{N_T}{k_2}\right) = p_2\overline{I_V} + h$ and $c_1 = \frac{1}{p_2\overline{I_V}}$, we have

$$\frac{dW_1}{dt} = \frac{1}{\overline{S_T}}\left(1 - \frac{\overline{S_T}}{S_T}\right)\left(p_2 S_T\overline{I_V} + hS_T - p_2 S_T I_V - hS_T\right)$$

$$= \frac{1}{c_1}\left(\frac{S_T}{\overline{S_T}} - 1\right)\left(1 - \frac{I_V}{\overline{I_V}}\right)$$

$$= \frac{1}{c_1}(x - 1 - xu + u). \tag{3.28}$$

Next, we consider the derivative of W_2

$$\frac{dW_2}{dt} = \frac{1}{\overline{S_H}}\left(1 - \frac{\overline{S_H}}{S_H}\right)\left(r_H\left(1 - \frac{N_H}{k_1}\right)S_H - p_1 S_H I_V - hS_H\right).$$

Since $r_H\left(1 - \frac{N_H}{k_1}\right) = p_1\overline{I_V} + h$ and $c_2 = \frac{1}{p_1\overline{I_V}}$, we have

$$\frac{dW_2}{dt} = \frac{1}{\overline{S_H}}\left(1 - \frac{\overline{S_H}}{S_H}\right)\left(p_1 S_H\overline{I_V} + hS_H - p_1 S_H I_V - hS_H\right)$$

$$= \frac{1}{c_2}\left(\frac{S_H}{\overline{S_H}} - 1\right)\left(1 - \frac{I_V}{\overline{I_V}}\right)$$

$$= \frac{1}{c_2}(y - 1 - yu + u). \tag{3.29}$$

We next consider the derivative of W_3

$$\frac{dW_3}{dt} = \frac{1}{\overline{E_H}}\left(1 - \frac{\overline{E_H}}{E_H}\right)\left(r_H\left(1 - \frac{N_H}{k_1}\right)p_3 E_H + p_1 S_H I_V + p_2 S_T I_V - (\beta + h)E_H\right).$$

Since $(\beta + h)\overline{E_H} = r_H\left(1 - \frac{N_H}{k_1}\right)p_3\overline{E_H} + p_1\overline{S_H I_V} + p_2\overline{S_T I_V}$ and $c_3 = \frac{\overline{E_H}}{(p_1\overline{S_H} + p_2\overline{S_T})\overline{I_V}}$, we have

$$\frac{dW_3}{dt} = \frac{1}{\overline{E_H}}\left(1 - \frac{\overline{E_H}}{E_H}\right)\left(r_H\left(1 - \frac{N_H}{k_1}\right)p_3 E_H + p_1 S_H I_V + p_2 S_T I_V\right.$$

$$\left. - \frac{E_H}{\overline{E_H}}\left(r_H\left(1 - \frac{N_H}{k_1}\right)p_3\overline{E_H} + p_1\overline{S_H I_V} + p_2\overline{S_T I_V}\right)\right)$$

$$= \frac{1}{c_3}\left(1 - \frac{\overline{E_H}}{E_H}\right)\left(\frac{(p_2 S_T + p_1 S_H)}{(p_2\overline{S_T} + p_1\overline{S_H})}\frac{I_V}{\overline{I_V}} - \frac{E_H}{\overline{E_H}}\right)$$

$$= \frac{1}{c_3}\left(wu - \frac{wu}{z} - z + 1\right). \tag{3.30}$$

We now consider $\frac{dW_4}{dt}$, since $(\gamma + h)\overline{I_H} = \beta\overline{E_H}$ and $c_4 = \frac{\overline{I_H}}{\beta\overline{E_H}}$, we get

$$\frac{dW_4}{dt} = \frac{1}{\overline{I_H}}\left(1 - \frac{\overline{I_H}}{I_H}\right)(\beta E_H - (\gamma + h)I_H).$$

$$= \frac{1}{\overline{I_H}}\left(1 - \frac{\overline{I_H}}{I_H}\right)\left(\beta E_H - \frac{I_H}{\overline{I_H}}\beta\overline{E_H}\right)$$

$$= \frac{1}{c_4}\left(1 - \frac{\overline{I_H}}{I_H}\right)\left(\frac{E_H}{\overline{E_H}} - \frac{I_H}{\overline{I_H}}\right)$$

$$= \frac{1}{c_4}\left(z - \frac{z}{q} - q + 1\right). \tag{3.31}$$

We then consider $\frac{dW_5}{dt}$, since $\mu\overline{S_V} = \Lambda\left(1 - \frac{N_V}{L}\right)N_V - p_4\overline{S_V}\left(\overline{E_H} + \overline{I_H}\right)$ and $c_5 = \frac{1}{p_4\left(\overline{E_H} + \overline{I_H}\right)}$, we obtain

$$\frac{dW_5}{dt} = \frac{1}{\overline{S_V}}\left(1 - \frac{\overline{S_V}}{S_V}\right)\left(\Lambda\left(1 - \frac{N_V}{L}\right)N_V - p_4 S_V(E_H + I_H) - \mu S_V\right).$$

$$= \frac{1}{\overline{S_V}}\left(1 - \frac{\overline{S_V}}{S_V}\right)\left(\Lambda\left(1 - \frac{N_V}{L}\right)N_V - p_4 S_V(E_H + I_H)\right.$$

$$\left. - \frac{S_V}{\overline{S_V}}\left(\Lambda\left(1 - \frac{N_V}{L}\right)N_V - p_4\overline{S_V}\left(\overline{E_H} + \overline{I_H}\right)\right)\right)$$

$$= \frac{1}{\overline{S_V}}\left(1 - \frac{\overline{S_V}}{S_V}\right)\Lambda\left(1 - \frac{N_V}{L}\right)N_V\left(1 - \frac{S_V}{\overline{S_V}}\right) + \frac{1}{c_5}\left(\frac{S_V}{\overline{S_V}} - 1\right)\left(1 - \frac{E_H + I_H}{\overline{E_H} + \overline{I_H}}\right)$$

$$= -\Lambda\left(1 - \frac{N_V}{L}\right)N_V\frac{(S_V + \overline{S_V})^2}{S_V\overline{S_V}^2} + \frac{1}{c_5}(r - 1 - rv + v). \tag{3.32}$$

Next, we consider the derivative of W_6

$$\frac{dW_6}{dt} = \frac{1}{\overline{I_V}}\left(1 - \frac{\overline{I_V}}{I_V}\right)(p_4 S_V(E_H + I_H) - \mu I_V).$$

Since $\mu\overline{I_V} = p_4\overline{S_V}(\overline{E_H} + \overline{I_H})$ and $c_6 = \frac{\overline{I_V}}{p_4\overline{S_V}(\overline{E_H}+\overline{I_H})}$, we have

$$\frac{dW_6}{dt} = \frac{1}{\overline{I_V}}\left(1 - \frac{\overline{I_V}}{I_V}\right)\left(p_4 S_V(E_H + I_H) - \frac{I_V}{\overline{I_V}}p_4\overline{S_V}(\overline{E_H} + \overline{I_H})\right)$$

$$= \frac{1}{c_6}\left(1 - \frac{\overline{I_V}}{I_V}\right)\left(\frac{S_V(E_H+I_H)}{\overline{S_V}(\overline{E_H}+\overline{I_H})} - \frac{I_V}{\overline{I_V}}\right)$$

$$= \frac{1}{c_6}\left(rv - \frac{rv}{u} - u + 1\right). \tag{3.33}$$

Lyapunov-Lasalle's Theorem indicates that the E_1 is globally-asymptotically-stable in Ω when $\frac{dW}{dt} \leq 0$. The time derivative of W computed along solutions of Equations (3.1) to (3.6) is

$$\frac{dW}{dt} = c_1\frac{dW_1}{dt} + c_2\frac{dW_2}{dt} + c_3\frac{dW_3}{dt} + c_4\frac{dW_4}{dt} + c_5\frac{dW_5}{dt} + c_6\frac{dW_6}{dt} \tag{3.34}$$

Finally, Equation (3.34) is substituted by Equations (3.28) to (3.33). Therefore, the derivative of W becomes

$$\frac{dW}{dt} = -\frac{\left(S_V + \overline{S_V}\right)^2}{S_V\overline{S_V}^2}\Lambda\left(1 - \frac{N_V}{L}\right)\frac{N_V}{p_4(\overline{E_H} + \overline{I_H})}$$

$$+ \left(r + u + v + wu + x + y - q - xu - yu - \frac{z}{q} - \frac{rv}{u} - \frac{wu}{z}\right)$$

$$\leq 0. \tag{3.35}$$

The equality of Equation (3.35) satisfies if and only if $S_T = \overline{S_T}$, $S_H = \overline{S_H}$, $E_H = \overline{E_H}$, $I_H = \overline{I_H}$, $S_V = \overline{S_V}$, and $I_V = \overline{I_V}$. By Lyapunov-Lasalle's Theorem, any solution tends to E_1 as $t \to \infty$. This implies that E_1 is globally-asymptotically-stable in Ω. □

3.4 Summary

So far, the *DFE* point is globally-asymptotically-stable and that the disease can be controlled as long as the threshold $R_0 \leq 1$ and the *EE* point is globally-asymptotically-stable when $R_0 > 1$ and the disease will persist. From an epidemiological view, the goal of policy is to control CMD outbreaks by maintaining $R_0 \leq 1$ and maximizing the uninfected population. However, an agricultural viewpoint would instead focus on maximizing the economic returns. Therefore, it needs to identify the strategy that is the most cost-effectiveness.

In Chapter IV, optimal control policy is established. Sensitivity analysis is used to identify the parameters that is the most significant to maintain the stability of the CMD system.

CHAPTER IV

OPTIMAL CONTROL POLICY

4.1   CMD Outbreak Model - With Control Methods

This chapter aims to determine the optimal policy that maximizes economic benefit by including control variables to CMD outbreak model. Currently, there are four strategies to control the spread of disease (Thresh and Otim-Nape, 1994; Rabbi et al., 2014) as listed in Table 4.1.

Table 4.1 Control strategies and related variables

Control strategy	Variable or term
Spraying pesticide to damage whiteflies	u_1
Rouging infected cassava plants	u_2
Selecting non-infected cuttings to plant	u_3
Promoting tolerant cuttings	$r_T \left(1 - \dfrac{S_T}{k_2}\right) S_T$

4.1.1   CMD control model

Figure 4.1 shows a state diagram of CMD control model
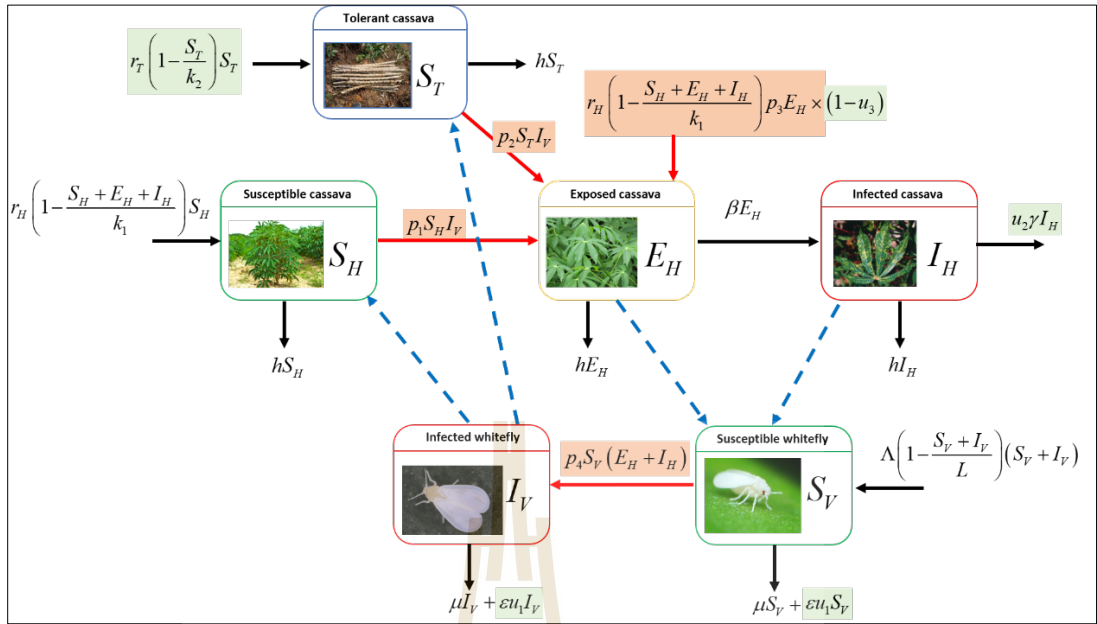
Figure 4.1 State diagram of CMD outbreak model – with four control methods

State diagram with control methods become Equations (4.1) to (4.6):

$$\frac{dS_T}{dt} = r_T \left(1 - \frac{S_T}{k_2}\right) S_T - p_2 S_T I_V - h S_T, \tag{4.1}$$

$$\frac{dS_H}{dt} = r_H \left(1 - \frac{S_H + E_H + I_H}{k_1}\right) S_H - p_1 S_H I_V - h S_H, \tag{4.2}$$

$$\frac{dE_H}{dt} = r_H \left(1 - \frac{S_H + E_H + I_H}{k_1}\right) p_3 (1 - u_3) E_H + p_1 S_H I_V + p_2 S_T I_V$$

$$- (\beta + h) E_H, \tag{4.3}$$

$$\frac{dI_H}{dt} = \beta E_H - (\gamma u_2 + h) I_H, \tag{4.4}$$

$$\frac{dS_V}{dt} = \Lambda \left(1 - \frac{S_V + I_V}{L}\right) (S_V + I_V) - p_4 S_V (E_H + I_H) - (\varepsilon u_1 + \mu) S_V, \tag{4.5}$$

$$\frac{dI_V}{dt} = p_4 S_V (E_H + I_H) - (\varepsilon u_1 + \mu) I_V. \tag{4.6}$$

In this model, CMD spread can be controlled by reducing the following four infection terms:

(1) $p_1 S_H I_V$ represents infection number of non-tolerant cassavas by whitefly.

(2) $p_2 S_T I_V$ represents infection number of tolerant cassavas by whitefly.

(3) $r_H \left(1 - \frac{S_H + E_H + I_H}{k_1}\right) p_3 E_H$ represents infection number by replanting of infected cuttings.

(4) $p_4 S_V (E_H + I_H)$ represents infection number of the whitefly after acquiring CMD from infected cassavas.

As can be observed, these infection terms can be controlled and increased yields by decreasing the number of E_H, I_H, S_V, and I_V. Thus, control factors u_1, u_2, u_3 and $r_T \left(1 - \frac{S_T}{k_2}\right) S_T$ play important role in controlling disease spreads.

Spraying of insecticide is represented in term of εu_1, where ε is an efficiency rate of pesticide spray and $u_1 \in [0,1]$ is a control variable of spraying. The goal of this method is to decrease the whitefly population (S_V and I_V) in terms $p_1 S_H I_V$, $p_2 S_T I_V$, and $p_4 S_V (E_H + I_H)$, leading to the decrease of exposed cassava (E_H).

Uprooting of infected cuttings is represented in term of γu_2, where γ is an efficiency rate of rouging and $u_2 \in [0,1]$ is a control variable of rouging. The infected cassava (I_H) will be reduced by directly removing infected plants out of a plantation area, leading to the decrease of cassava-whitefly transmission as shown in the term of $p_4 S_V (E_H + I_H)$.

Selecting non-infected cuttings is represented in term of $p_3(1 - u_3)$, where $u_3 \in [0,1]$ is a control variable of selecting non-infected cuttings. This method reduces the number of E_H in terms of $r_H \left(1 - \frac{S_H + E_H + I_H}{k_1}\right) p_3 E_H$ and $p_4 S_V(E_H + I_H)$.

Planting with tolerant cuttings is represented in term of $r_T \left(1 - \frac{S_T}{k_2}\right) S_T$. This method reduces cassava-whitefly transmission (term $p_4 S_V(E_H + I_H)$) by using the same technique as the herd immunity effect ($p_2 < p_1$).

4.2 Sensitivity Analysis

Sensitivity analysis plays an important role to study variation of the CMD spread severity caused by CMD outbreak parameters as descried in Table 3.2. Result of sensitivity analysis leads to the source of CMD spread, where the parameter with the highest value of R_0 is the cause of the outbreak. Hence, prevention strategies could be designed to cope the spread of the outbreak. The sensitivity analysis is the normalized forward sensitivity index of R_0 as defined in Equation (4.7).

Definition 4.1: The normalized forward sensitivity index of R_0, which is differentiable with respect to a given parameter, is defined by

$$\text{Sensitivity index (S.I.)} = \frac{\partial R_0}{\partial (\text{parameter})} \times \frac{\text{parameter}}{R_0} \tag{4.7}$$

(Wang et al. 2019).

Results of S.I. can be done by substituting parameter values appear in Table 3.2 into Equation (4.7). Table 4.2 lists the S.I. of R_0.

Table 4.2 Sensitivity indices of R_0

Parameter	Sensitivity index
h	-0.1770
β	-0.2670
γ	-0.0890
r_H	+0.0304
r_T	+0.0030
k_1	+0.4767
k_2	+0.0223
Λ	+0.0381
μ	-0.5371
L	+0.4990
p_1	+0.4767
p_2	+0.0223
p_3	+0.0020
p_4	+0.4990

Table 4.2 shows sensitivity indices of R_0, where the natural whitefly death rate, μ, has the highest sensitive value (S.I. = -0.5371). One simple approach that contributes to an increase of whitefly death rate is spraying pesticide. This strategy is effective in controlling the whitefly but it has high costs of pesticide and operation. According to Kinene et al. (2016), massive spraying gives farmers more yields but it is not cost-effective. Bokil et al. (2019) suggested that combined strategy of rouging and spraying performs better than applying a single method. Therefore, the aim of this study is to determine which combination of these four controlling methods, as described in Table 4.1, is the most cost-effectiveness. Eight policies are proposed in this study for optimal control are listed in Table 4.3.

Table 4.3 Policies and related control variable for optimal control

Policies	Description	Control variables			
		$S_T(t)$	u_1	u_2	u_3
A-1	Tolerant cuttings and spraying insecticide	✓	✓		
A-2	Tolerant, spraying and rouging infected plants	✓	✓	✓	
A-3	Tolerant, spraying and selecting non-virus cuttings	✓	✓		✓
A-4	Tolerant, spraying, rouging, and selecting	✓	✓	✓	✓
B-1	Spraying		✓		
B-2	Spraying and rouging		✓	✓	
B-3	Spraying and selecting		✓		✓
B-4	Spraying, rouging, and selecting		✓	✓	✓

4.3   Optimal Control Theory

The mathematical formulation for optimal control is constructed to minimize the operation costs of each control method.

4.3.1   Objective function

The objective function is given by

$$J(u_1, u_2, u_3) = \int_0^{t_f} (A_0 I_H + A_1 u_1^2 + A_2 u_2^2 + A_3 u_3^2) dt, \qquad (4.8)$$

where t_f is a final time, subjected to Equations (4.1) to (4.6). A_0 represents the weight constant of the infected cassava I_H. The quantities of A_1, A_2, and A_3 represent the cost per unit of each control variable u_1, u_2, and u_3, respectively. The costs of control methods are described below.

(1) $A_1 u_1{}^2$ represents control cost by spraying pesticide to the whitefly.

(2) $A_2 u_2{}^2$ represents control cost by uprooting infected plants.

(3) $A_3 u_3{}^2$ represents control cost by selecting non-virus cuttings.

4.3.2   The existence of optimal control

The Lagrangian for the optimal control of Equations (4.1) to (4.6) is

$$L(I_H, u_1, u_2, u_3) = (A_0 I_H + A_1 u_1^2 + A_2 u_2^2 + A_3 u_3^2), \qquad (4.9)$$

Theorem 4.1: *There exists an optimal control u_1^*, u_2^*, and u_3^* so that*

$$J(u_1^*, u_2^*, u_3^*) = \text{minimize}\{J(u_1, u_2, u_3), (u_1, u_2, u_3) \in \boldsymbol{u}\}. \qquad (4.10)$$

Proof: Theorem 4.1 can be proved by checking the following conditions:

(1) The corresponding set of controls and the state variables are nonempty.

(2) The control set $\boldsymbol{u}$ is convex and closed.

(3) The right-hand side of state system is bounded by the linear function in state and control variables.

(4) The integrand of the objective function is convex on $\boldsymbol{u}$.

(5) There exist nonnegative constants ϕ_1 and ϕ_2 and $\theta > 1$ satisfying the following expression:

$$L(x, u_1, u_2, u_3) \geq \phi_2 + \phi_1(|u_1|^2 + |u_2|^2 + |u_3|^2)^{\frac{\theta}{2}},$$

where x is any state variables of the CMD model.

Checking the following conditions:

According to theorem of Lukes (1982), the existence of system in Equations (4.1) to (4.6) are defined by bounded coefficients, which are nonempty. Thus, the control set is convex and closed.

Note that the state system is linear in u_1, u_2, and u_3. Therefore, the right-hand side of the system is bounded by the linear function.

Since the solutions to the system of Equations (4.1) to (4.6) are bounded, the control function is convex in $\boldsymbol{u}$.

Let $\overline{\phi_2} = \min (I_H)$ and $\phi_1 = \min(A_1, A_2, A_3)$ and $\theta = 2$, then the Lagrangian L can be rewritten as

$$L(x, u_1, u_2, u_3) = A_0 I_H + A_1 u_1^2 + A_2 u_2^2 + A_3 u_3^2$$

$$\geq A_0 \overline{\phi_2} + \phi_1 (|u_1|^2 + |u_2|^2 + |u_3|^2)^{\frac{\theta}{2}}$$

$$= \phi_2 + \phi_1 (|u_1|^2 + |u_2|^2 + |u_3|^2)^{\frac{\theta}{2}}.$$

All conditions are satisfied and consequently there exists an optimal control for the system of Equations (4.1) to (4.6). □

4.3.3 Characterization of the optimal control

The optimal control of CMD outbreaks can be derived through the use of Pontryagin maximum principle (Pontryagin et al., 1962).

Theorem 4.2: *There exist the adjoint variables λ_i, $i = 1, 2, 3, 4, 5, 6$, under the control of CMD outbreaks that satisfy the following:*

$$\frac{d\lambda_1}{dt} = -\frac{\partial H}{\partial S_T} = -\lambda_1 \left(r_T \left(1 - \frac{2S_T}{k_2} \right) - (p_2 I_V + h) \right) - \lambda_3 p_2 I_V \tag{4.11}$$

$$\frac{d\lambda_2}{dt} = -\frac{\partial H}{\partial S_H} = -\lambda_2 \left(r_H \left(1 - \frac{2S_H + E_H + I_H}{k_1} \right) - (p_1 I_V + h) \right)$$
$$+ \lambda_3 \left(\frac{r_H p_3 (1 - u_3) E_H}{k_1} - p_2 I_V \right) \tag{4.12}$$

$$\frac{d\lambda_3}{dt} = -\frac{\partial H}{\partial E_H} = \lambda_2 \frac{r_H S_H}{k_1} - \lambda_3 \left(r_H \left(1 - \frac{S_H + 2E_H + I_H}{k_1} \right) p_3 (1 - u_3) - (\beta + h) \right)$$
$$- \lambda_4 \beta + (\lambda_5 - \lambda_6) p_4 S_V \tag{4.13}$$

$$\frac{d\lambda_4}{dt} = -\frac{\partial H}{\partial I_H} = -A_0 + \lambda_2 \frac{r_H S_H}{k_1} + \lambda_3 \frac{r_H p_3 (1 - u_3) E_H}{k_1} + \lambda_4 (\gamma u_2 + h) + (\lambda_5 - \lambda_6) p_4 S_V \tag{4.14}$$

$$\frac{d\lambda_5}{dt} = -\frac{\partial H}{\partial S_H} = -\lambda_5\left(\Lambda\left(1 - \frac{2(S_V + I_V)}{L}\right) - (p_4(E_H + I_H) + \varepsilon u_1 + \mu)\right) - \lambda_6 p_4(E_H + I_H) \quad (4.15)$$

$$\frac{d\lambda_6}{dt} = -\frac{\partial H}{\partial I_V} = (\lambda_2 - \lambda_3)p_1 S_H + (\lambda_1 - \lambda_3)p_2 S_T - \lambda_5\Lambda\left(1 - \frac{2(S_V + I_V)}{L}\right) + \lambda_6(\varepsilon u_1 + \mu) \quad (4.16)$$

with the transversality conditions

$$\lambda_i(t_f) = 0, \qquad i = 1, 2, 3, 4, 5, 6. \tag{4.17}$$

Furthermore, the optimal control variables u_1^*, u_2^*, and u_3^* are given by

$$u_1^* = \text{maximize}\left\{0, \text{minimize}\left\{1, \frac{\varepsilon(\lambda_5 S_V + \lambda_6 I_V)}{2A_1}\right\}\right\} \tag{4.18}$$

$$u_2^* = \text{maximize}\left\{0, \text{minimize}\left\{1, \frac{\lambda_4 \gamma I_H}{2A_2}\right\}\right\} \tag{4.19}$$

$$u_3^* = \text{maximize}\left\{0, \text{minimize}\left\{1, \frac{\lambda_3}{2A_3}r_H\left(1 - \frac{S_H + E_H + I_H}{k_1}\right)p_3 E_H\right\}\right\} \tag{4.20}$$

Proof: The Hamiltonian for the optimal control of CMD outbreaks is defined as follows:

$$\begin{aligned}
H = \ & L(x, u_1, u_2, u_3) \\
& + \lambda_1\left(r_T\left(1 - \frac{S_T}{k_2}\right)S_T - p_2 S_T I_V - hS_T\right) \\
& + \lambda_2\left(r_H\left(1 - \frac{S_H + E_H + I_H}{k_1}\right)S_H - p_1 S_H I_V - hS_H\right) \\
& + \lambda_3\left(r_H\left(1 - \frac{S_H + E_H + I_H}{k_1}\right)p_3(1 - u_3)E_H + p_1 S_H I_V + p_2 S_T I_V - (\beta + h)E_H\right) \\
& + \lambda_4(\beta E_H - (\gamma u_2 + h)I_H) \\
& + \lambda_5\left(\Lambda\left(1 - \frac{S_V + I_V}{L}\right)(S_V + I_V) - p_4 S_V(E_H + I_H) - (\varepsilon u_1 + \mu)S_V\right) \\
& + \lambda_6(p_2 S_V(E_H + I_H) - (\varepsilon u_1 + \mu)I_V)
\end{aligned}$$

The adjoint system is obtained as follows:

$$\frac{d\lambda_1}{dt} = -\lambda_1\left(r_T\left(1 - \frac{2S_T}{k_2}\right) - (p_2 I_V + h)\right) - \lambda_3 p_2 I_V$$

$$\frac{d\lambda_2}{dt} = -\lambda_2\left(r_H\left(1 - \frac{2S_H + E_H + I_H}{k_1}\right) - (p_1 I_V + h)\right) + \lambda_3\left(\frac{r_H p_3(1 - u_3)E_H}{k_1} - p_1 I_V\right)$$

$$\frac{d\lambda_3}{dt} = \lambda_2\frac{r_H S_H}{k_1} - \lambda_3\left(r_H\left(1 - \frac{S_H + 2E_H + I_H}{k_1}\right)p_3(1 - u_3) - (\beta + h)\right) - \lambda_4\beta$$

$$+(\lambda_5 - \lambda_6)p_4 S_V$$

$$\frac{d\lambda_4}{dt} = -A_0 + \lambda_2\frac{r_H S_H}{k_1} + \lambda_3\frac{r_H p_3(1 - u_3)E_H}{k_1} + \lambda_4(\gamma u_2 + h) + (\lambda_5 - \lambda_6)p_4 S_V$$

$$\frac{d\lambda_5}{dt} = -\lambda_5\left(\Lambda\left(1 - \frac{2(S_V + I_V)}{L}\right) - (p_4(E_H + I_H) + \varepsilon u_1 + \mu)\right) - \lambda_6 p_4(E_H + I_H)$$

$$\frac{d\lambda_6}{dt} = (\lambda_2 - \lambda_3)p_1 S_H + (\lambda_1 - \lambda_3)p_2 S_T - \lambda_5\Lambda\left(1 - \frac{2(S_V + I_V)}{L}\right) + \lambda_6(\varepsilon u_1 + \mu),$$

with transversality conditions (4.17).

The optimal condition characterization given by (4.18) to (4.20) is determined by solving the following partial differential equations:

$$\frac{\partial H}{\partial u_1} = 2A_1 u_1 - \varepsilon(\lambda_5 S_V + \lambda_6 I_V) = 0 \qquad \text{for } u_1^*,$$

$$\frac{\partial H}{\partial u_2} = 2A_2 u_2 - \lambda_4\gamma I_H \qquad \text{for } u_2^*,$$

$$\frac{\partial H}{\partial u_3} = 2A_3 u_3 - \lambda_3 r_H\left(1 - \frac{S_H + E_H + I_H}{k_1}\right)p_3 E_H \qquad \text{for } u_3^*.$$

By standard control arguments involving bounds on the control, then

$$u_m^* = \begin{cases} 0 & \text{if } u_m^* \leq 0, \\ u_m^* & \text{if } u_m^* < 1, \\ 1 & \text{if } u_m^* \geq 1, \end{cases}$$

for $m = 1, 2, 3$ and where

$$u_1^* = \frac{\varepsilon(\lambda_5 S_V + \lambda_6 I_V)}{2A_1},$$

$$u_2^* = \frac{\lambda_4 \gamma I_H}{2A_2},$$

$$u_3^* = \frac{\lambda_3}{2A_3} r_H \left(1 - \frac{S_H + E_H + I_H}{k_1}\right) p_3 E_H.$$

This completes the proof. $\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad$ □

4.4   Numerical Simulation

The optimal policy is determined using data obtained from Holt et al. (1997), Jeger et al. (2004), Wagaba et al. (2013), Kinene et al. (2015), Bokil et al. (2019), and Magoyo et al. (2019). The solutions in this system are calculated using MATLAB.

4.4.1   Data settings

The units of all parameters are per day. The parameters used for all simulations are described below.

Weight constant   : $A_0 = 1.000$,

Costs   : $A_1 = \$0.003$, $A_2 = \$0.001$, and $A_3 = \$0.001$,

Efficiency parameters   : $\gamma = 0.03$ and $\varepsilon = 0.2$,

Range of time   : $t \in [0,300]$,

Initial conditions

(With tolerant cuttings)   : $S_T(0) = 0.20$, $S_H(0) = 0.20$, $E_H(0) = 0.10$,

$\qquad\qquad\qquad\qquad\qquad\qquad I_H(0) = 0$, $S_V(0) = 100$, and $I_V(0) = 50$,

Initial conditions

(Without tolerant cuttings)   : $S_T(0) = 0$, $S_H(0) = 0.20$, $E_H(0) = 0.10$,

$$I_H(0) = 0, \ S_V(0) = 100, \text{ and } I_V(0) = 50,$$

and the rest of all parameters used in this study is shown in Table 3.2.

4.4.2   Algorithm of optimal control

The number of cassava population and the control costs are determined using the fourth-order Runge-Kutta method as defined in Definition 4.2.

Definition 4.2: Let x be states of *ODEs* and $[t_0, t_f]$ be any time interval in T. Optimal control values are determined using the following iterations.

(1)   Setting all variables. Let $\vec{x} = x(t)$ be state variables at different time t, $\vec{u_m} = u_m(t)$ be control parameters for $t \in [t_n, t_{n+1}]$, and $\vec{\lambda} = \lambda(t)$ be adjoint parameters for $t \in [t_{n+1}, t_n]$, where $n = 0, 1, \dots, T\text{-}1$ and $m = 1, 2, 3$.

(2)   Calculating state variables.   Use initial conditions $x = x(t_0)$ and values of $\vec{u_m}$ to solve $\vec{x}$ forward in time $[t_0, t_f]$.

(3)   Calculating adjoint variables. Use the adjoint condition $\lambda_{T+1} = \lambda(t_f) = 0$ and values of $\vec{x}$ and $\vec{u_m}$ to solve $\vec{\lambda}$ backward in time $[t_f, t_0]$.

(4)   Calculating control variables.   Update values of $\vec{u_m}$ by using new values of $\vec{x}$ and $\vec{\lambda}$ into the characterization Equations (4.18) to (4.20).

(5)   Checking convergence of control variables. If $\vec{u_m} \in [0,1]$, the optimal control variables are converged, otherwise repeat to the whole iteration.

4.4.3 The cost-effectiveness analysis

According to Okosun et al. (2011) and Okosun et al. (2013), the most cost-effective policy is calculated using the average cost-effectiveness ratio (ACER). ACER is a ratio of total control cost to the increase number of healthy cassava tubers and is a measurement of economic value of an intervention as shown in Equation (4.21).

$$\text{ACER} = \frac{\text{The total cost produced by the intervention}}{\text{The increase number of healthy cassava per population}}. \tag{4.21}$$

4.5 Results

This section determines which policy is the most cost-effective one. This can be done by calculating the number of cassava tubers and the total control costs according to Equations (4.1) to (4.6) in order to compute ACER values of eight policies.

4.5.1 Policy A: Promoting of tolerant cassava cuttings

In this scenario, tolerant (S_T) and susceptible (S_H) cuttings are initially planted at 40% of the maximum plantation capacity. Initial conditions were $S_T(0) = 0.20$, $S_H(0) = 0.20$, $E_H(0) = 0.10$, $I_H(0) = 0$, $S_V(0) = 100$, and $I_V(0) = 50$.
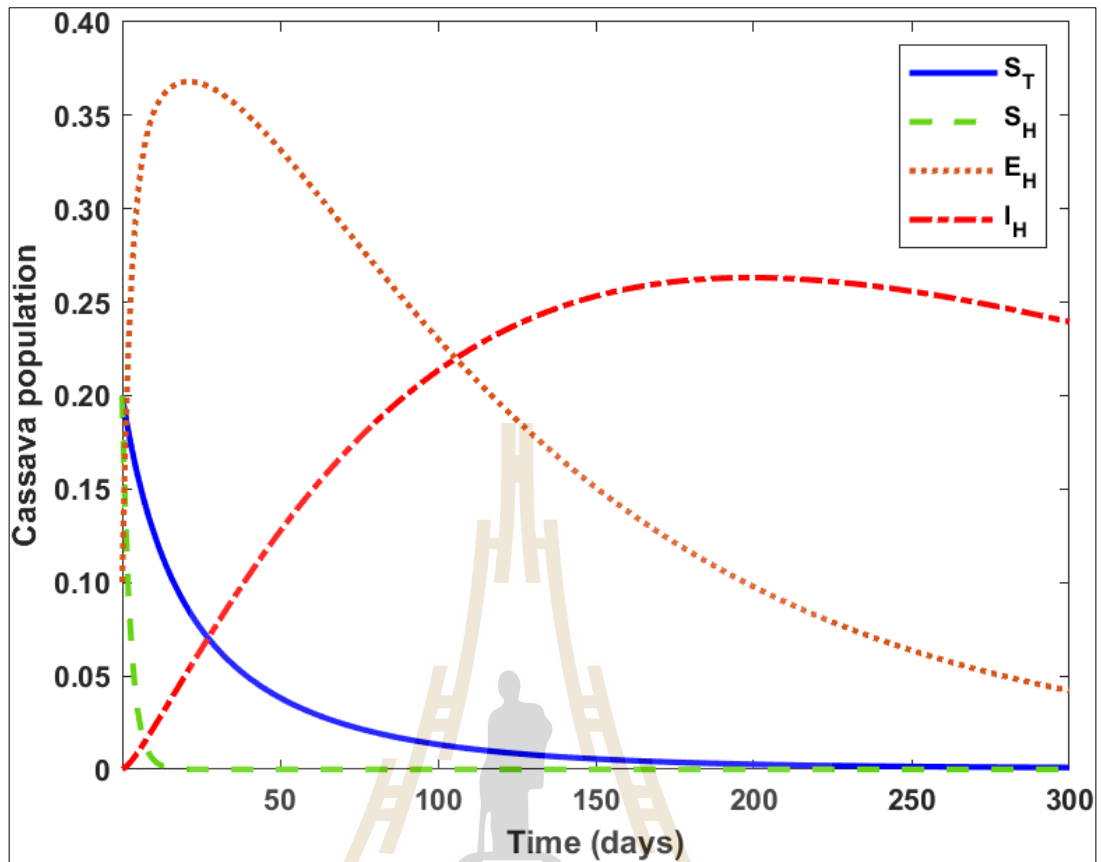
Figure 4.2   Cassava population with promoting of tolerant cassava cuttings

Figure 4.2 shows the number of cassava population when using only promoting tolerant cuttings method. Namely, no control method is applied in this policy (u_1, u_2, and $u_3 = 0$). Exposed and infected cassava plants outnumbered healthy cassava plants (tolerant and susceptible) at day 3. This is due to the fact that the infected cassavas were still in the plantation and the infected whitefly were not killed. At the end of numerical simulation, the number of healthy cassavas remaining at the harvest time is approximately 5% of the initial planting assuming that a daily harvest rate, h, equals to 0.003.

(1) Policy A-1: spraying and promoting tolerant cuttings

In this scenario, spraying and promoting tolerant cuttings were applied. Therefore, control variable for spraying method, $u_1 \in [0,1]$ and the rest of control variables were not applied (u_2 and $u_3 = 0$).
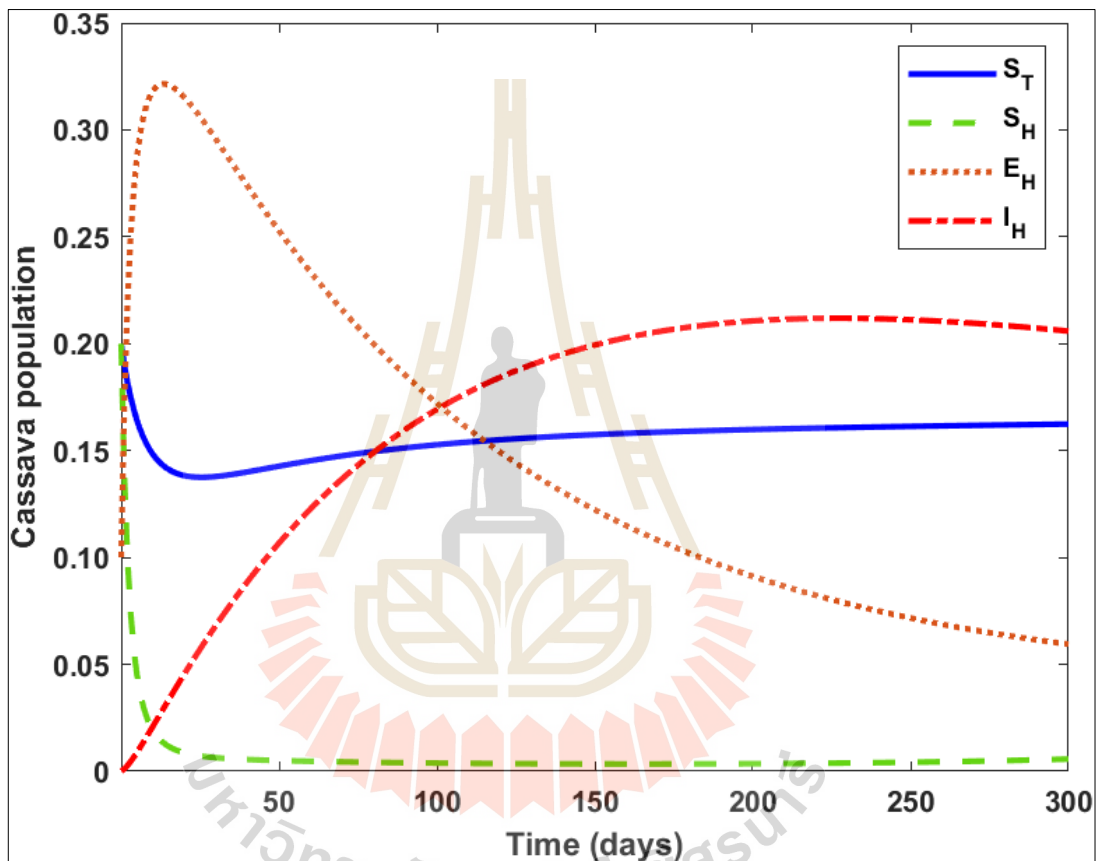
Figure 4.3   Cassava population with promoting of tolerant cassava cuttings and spraying insecticide (Policy A-1)
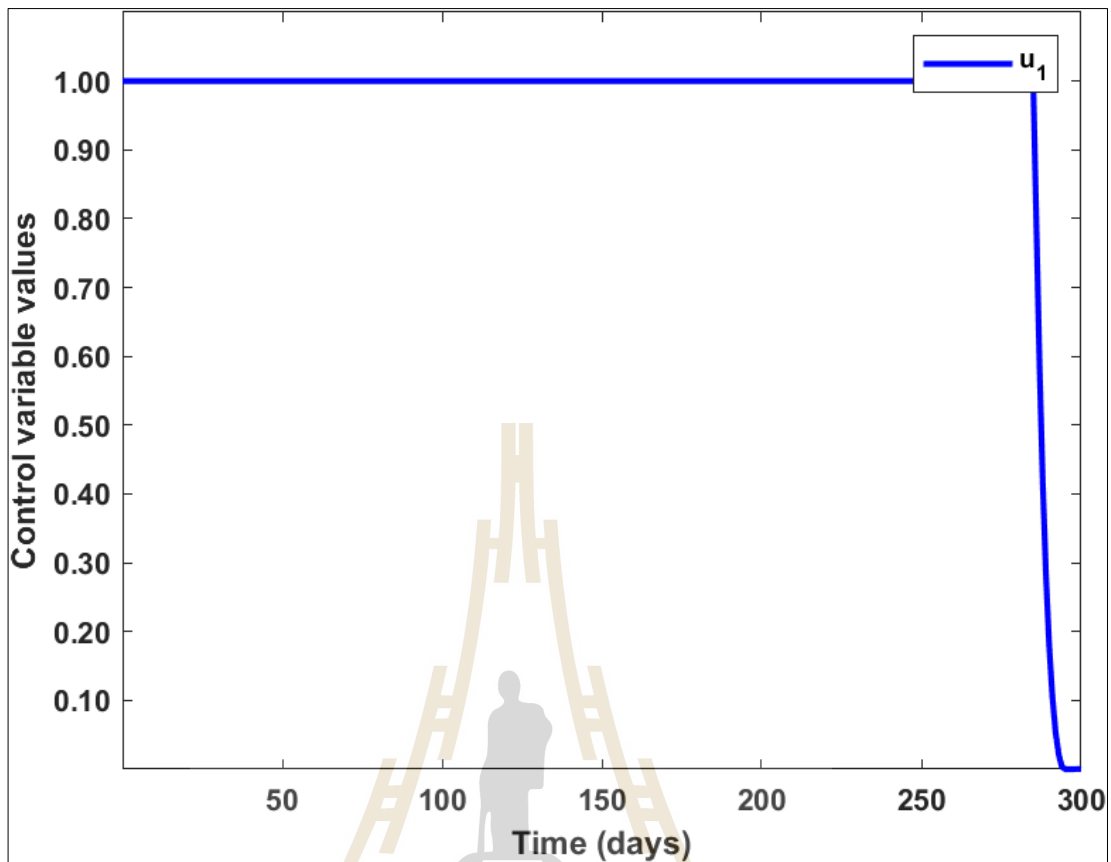
Figure 4.4 Control profile for Policy A-1 $u_1 \in [0,1], u_2, u_3 = 0$

Figure 4.3 shows dynamics of cassava population using tolerant cuttings and spraying methods. Infected cassavas (exposed and infected) outnumbered healthy plants on day 3. This is because infected cassavas were not removed from the plantation. There were only 14.50% healthy tubers remaining in the plantation at the harvest time, on day 300. Figure 4.4 shows that u_1 remains at the upper bound for 285 consecutive days and then decreases to the lower bound on the harvest day. This means that spraying was done continuously for the whole planting period to prevent the spread. Therefore, this method was the least cost-effective one.

(2) Policy A-2: spraying, rouging, and promoting tolerant cuttings

In this scenario, spraying, rouging and promoting tolerant cuttings were applied. Therefore, control variables for spraying method, $u_1 \in [0,1]$ and for rouging method, $u_2 \in [0,1]$. Selecting non-infected cuttings method was not applied in this policy hence, $u_3 = 0$.

Figure 4.5   Cassava population with promoting of tolerant cassava cuttings, spraying insecticide, and rouging infected cassavas (Policy A-2)

Figure 4.6   Control profile for Policy A-2 $u_1, u_2 \in [0,1], u_3 = 0$

Figure 4.5 shows numerical results of dynamics of cassava population when Policy A-2 was applied. Removing infected cassavas by rouging method together with spraying method helped increasing healthy cassava yields to 17.49%. Figure 4.6 shows control variables u_1 and u_2 of Policy A-2. u_1 remains at the upper bound for 287 consecutive days and then reduces to lower bound on the harvest day. u_2 raises to the upper bound on the day 2 and remains at the upper bound for 296 consecutive days and then decreases to the lower bound on the harvest day.

(3) Policy A-3: spraying, selecting, and promoting tolerant cuttings

In this scenario, spraying, selecting and promoting tolerant cuttings were applied. Therefore, control variables for spraying method, $u_1 \in [0,1]$ and for selecting method, $u_3 \in [0,1]$. Rouging method was not applied in this policy hence, $u_2 = 0$.
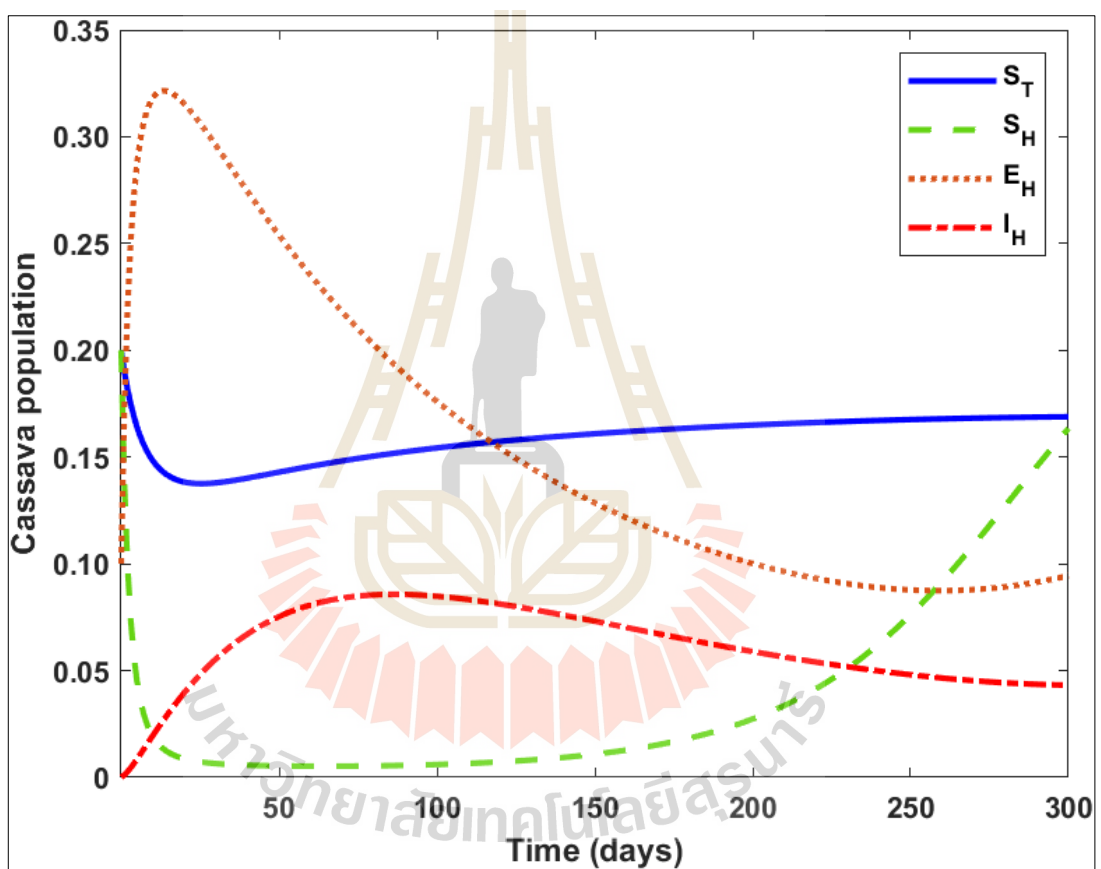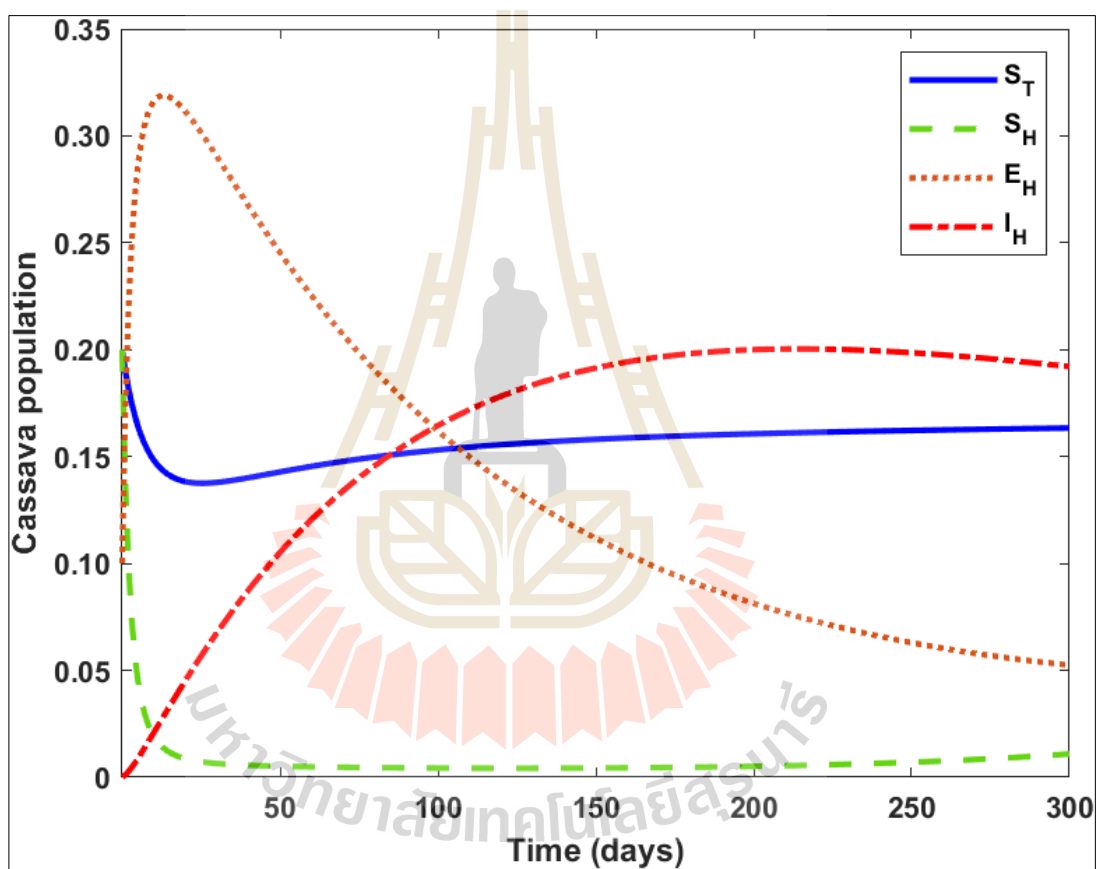

Figure 4.7 Cassava population with promoting of tolerant cassava cuttings, spraying insecticide, and selecting non-infected cuttings (Policy A-3)
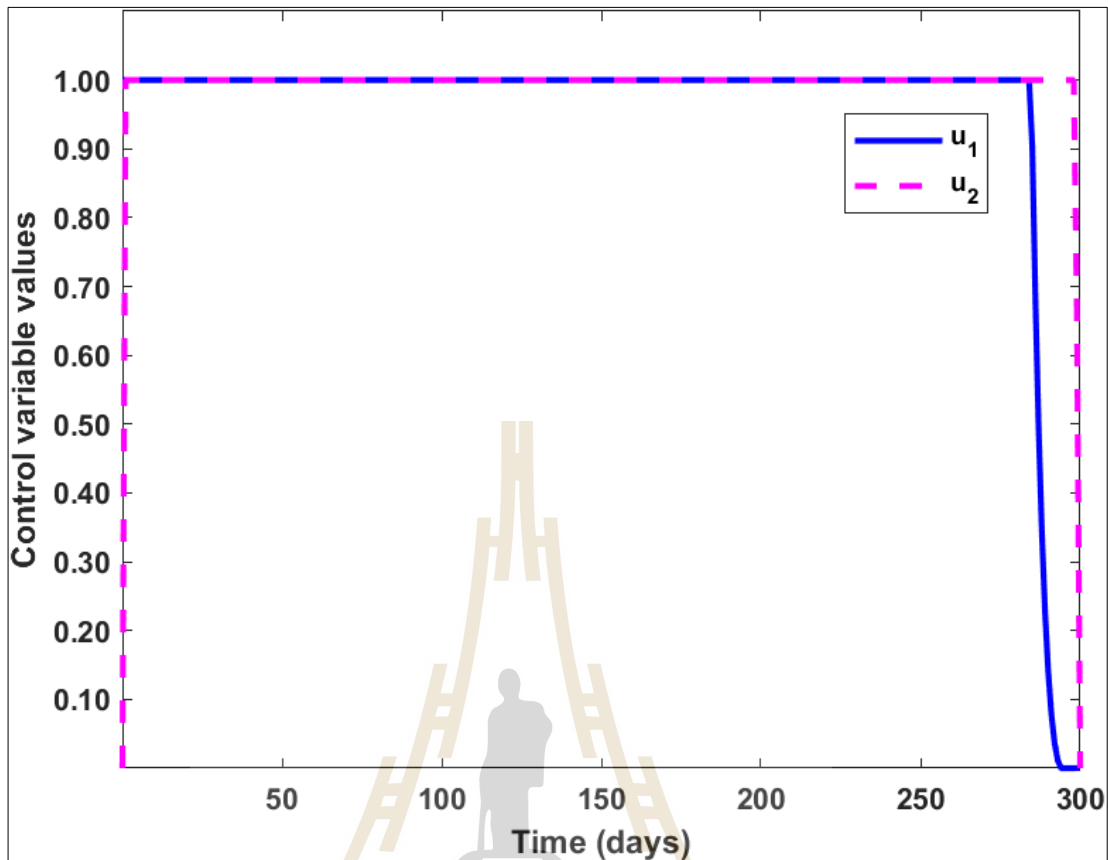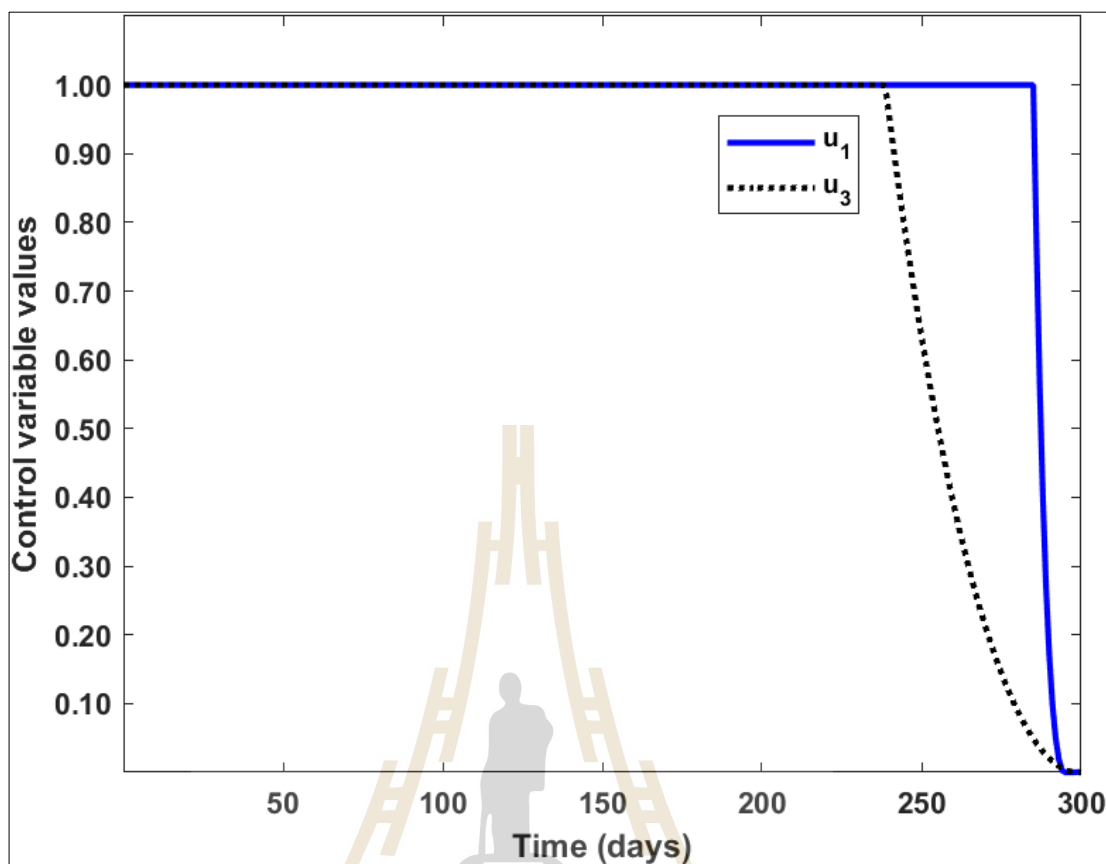
Figure 4.8 Control profile for Policy A-3 $u_1, u_3 \in [0,1], u_2 = 0$

Figure 4.7 shows dynamics of cassava population when Policy A-3 was applied. There were only 14.68% healthy cassava tubers remaining in the plantation on day 300 because infected cassavas were not removed from the plantation. Figure 4.8 shows control variables u_1 and u_3. u_1 remains at the upper bound for 284 consecutive days and then reduces to the lower bound on the harvest day. u_3 remains at the upper bound for 237 consecutive days and then decreases to the lower bound on day 300.

(4) Policy A-4: spraying, rouging, selecting, and promoting tolerant

cuttings

In this scenario, all control methods were applied. Therefore, control variables for spraying, rouging, and selecting methods, u_1, u_2, and $u_3 \in [0,1]$.
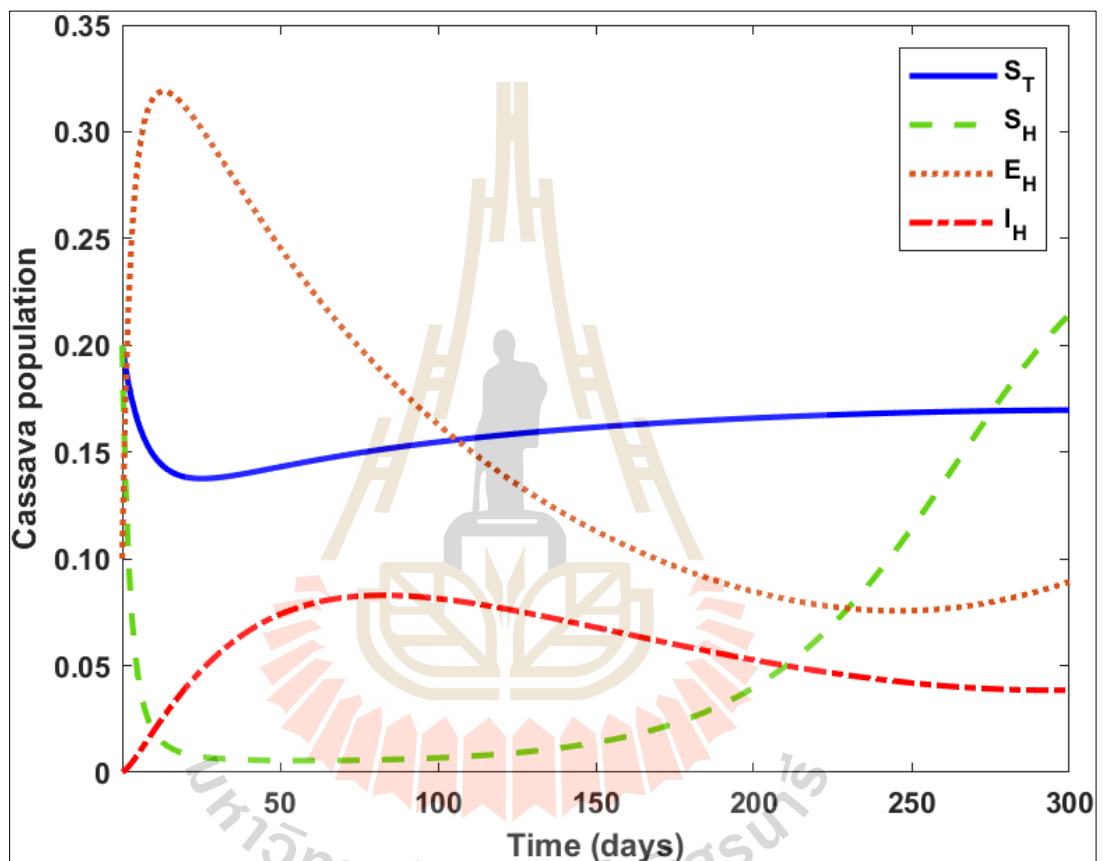
Figure 4.9 Cassava population with promoting of tolerant cassava cuttings,

spraying insecticide, rouging infected cassavas, and

selecting non-infected cuttings (Policy A-4)
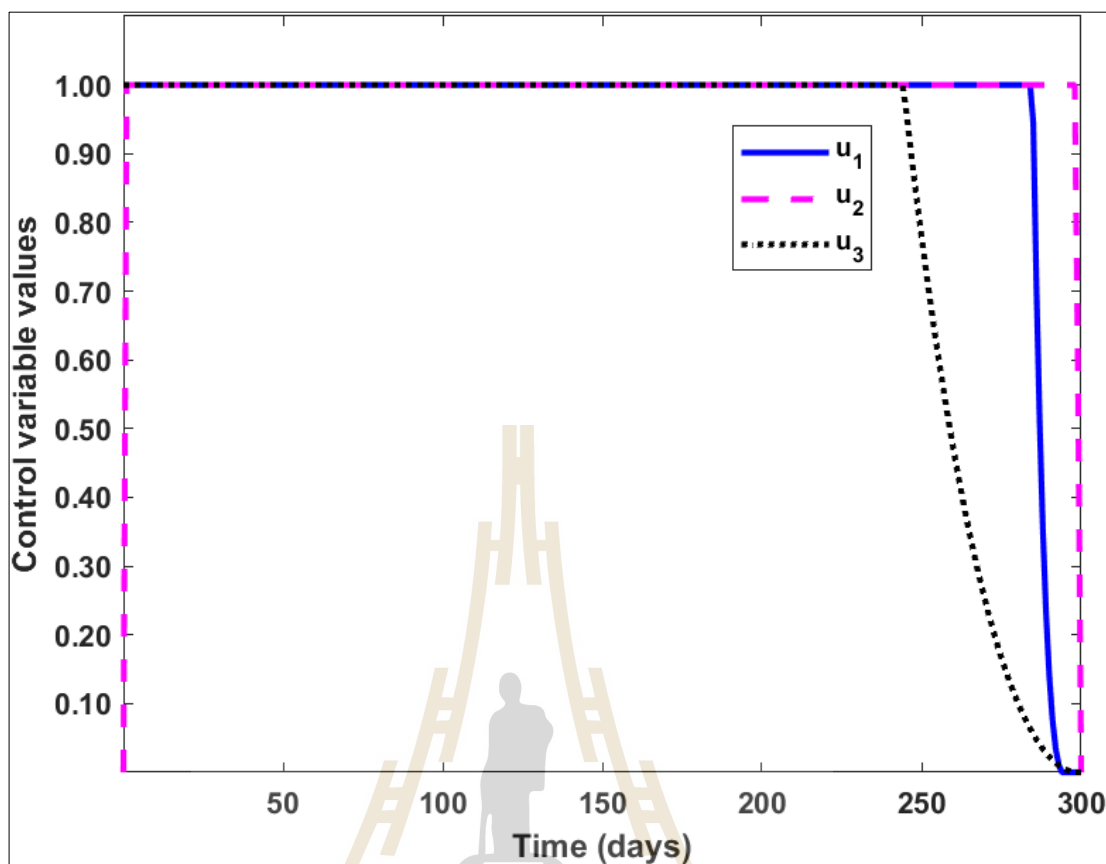
Figure 4.10 Control profile for Policy A-4 $u_1, u_2, u_3 \in [0,1]$

Figure 4.9 shows dynamics of cassava population when all methods were applied. Controlling the number of infected cassavas by rouging and selecting methods together with spraying helped increasing healthy cassava yields to 18.77%. Spraying pesticide while removing infected cassavas by rouging method was proved to be an effective approach to improve yields. However, this policy is still not cost-effective one. Figure 4.10 shows control variables u_1, u_2, and u_3 of Policy A-4. u_1 remains at the upper bound for 283 consecutive days and then decreases to the lower bound on the harvest day. u_2 remains at the upper bound from day 2 to 298 and then

decreases to lower bound on day 300. u_3 remains at the upper bound for 244 consecutive days and then decreases to the lower bound on the harvest day.

4.5.2   Policy B: Without tolerant cassava cuttings

In this scenario, susceptible (S_H) cuttings were initially planted at 20% of the maximum plantation capacity and tolerant (S_T) cuttings were not used. Therefore, initial conditions were $S_T(0) = 0$, $S_H(0) = 0.20$, $E_H(0) = 0.10$, $I_H(0) = 0$, $S_V(0) = 100$, and $I_V(0) = 50$.
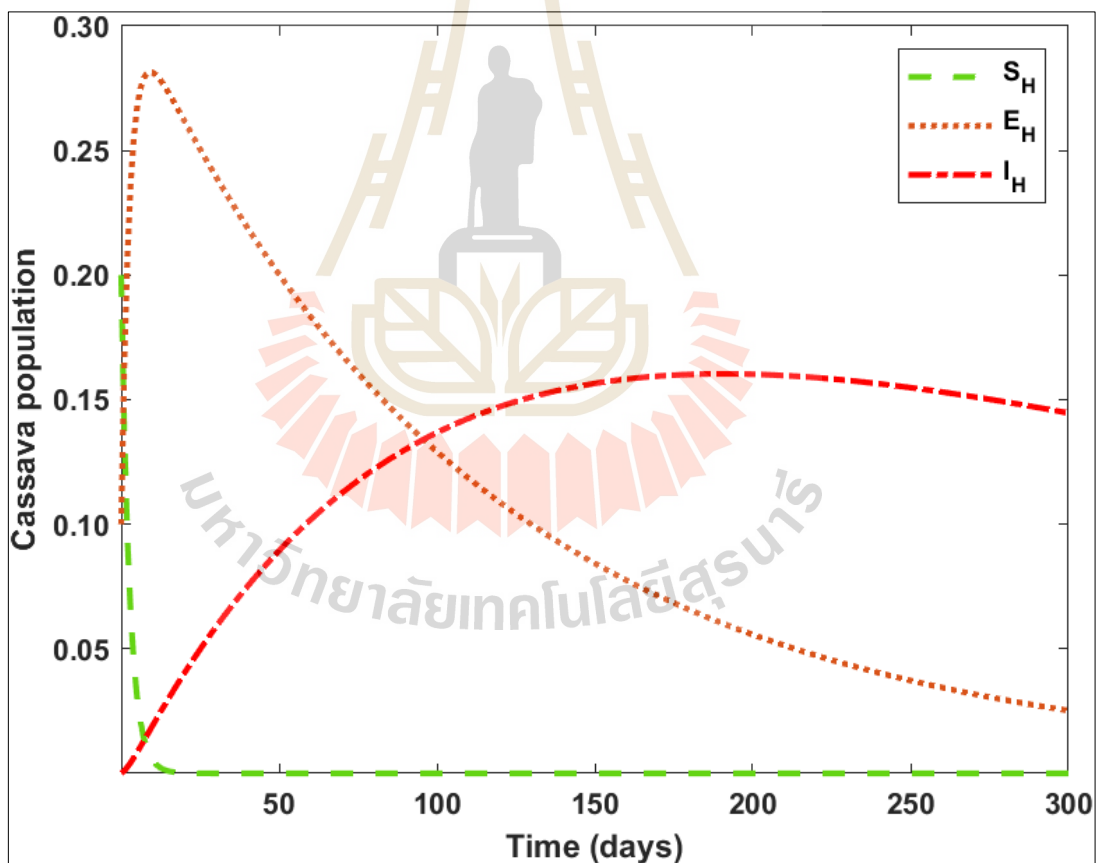
Figure 4.11 Cassava population with no control strategy

Figure 4.11 shows dynamics of cassava population (S_H, E_H, and I_H) when promoting tolerant cuttings method was not applied ($S_T = 0$). By the time of harvest on day 300, 16.99% of infected cassava tubers remained in the plantation. The number of healthy cassavas remaining at the harvest day was approximately 0.13%.

(1) Policy B-1: spraying

In this scenario, spraying method was applied. Therefore, control variable for spraying method, $u_1 \in [0,1]$ and the rest of control variables were not applied, u_2 and $u_3 = 0$.
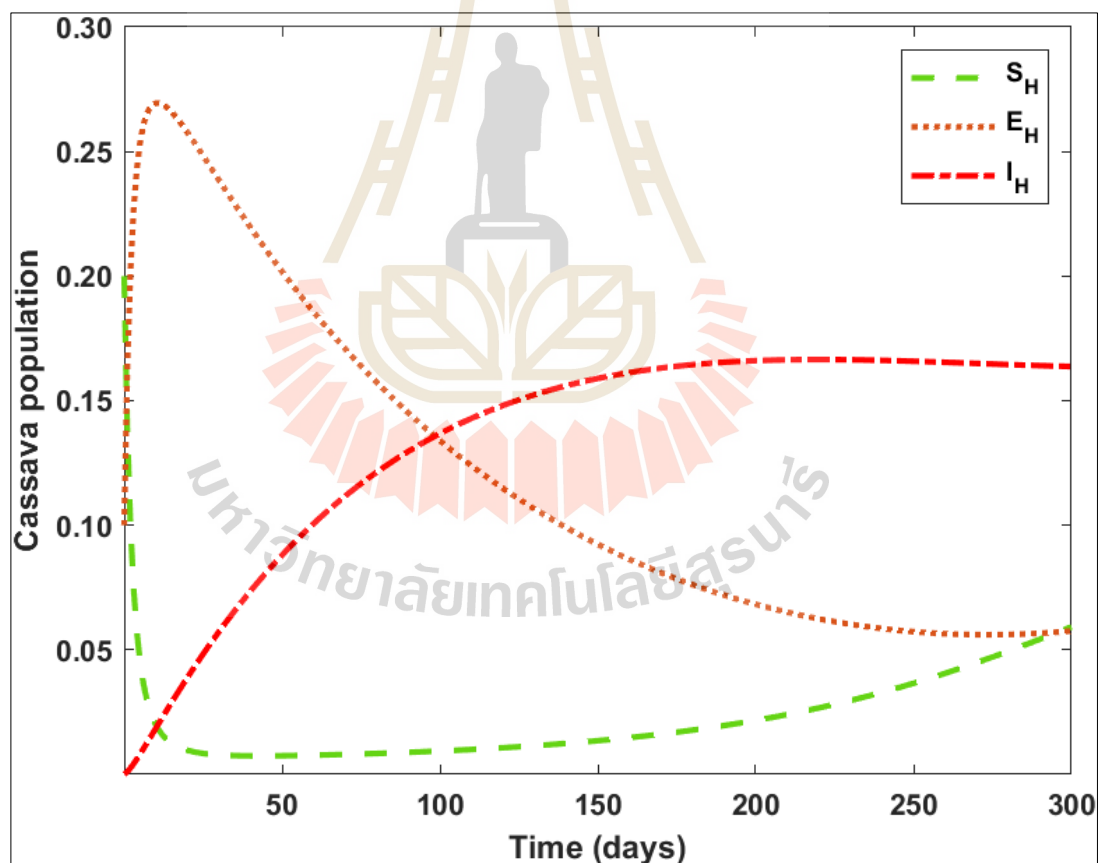
Figure 4.12 Cassava population with spraying insecticide method (Policy B-1)
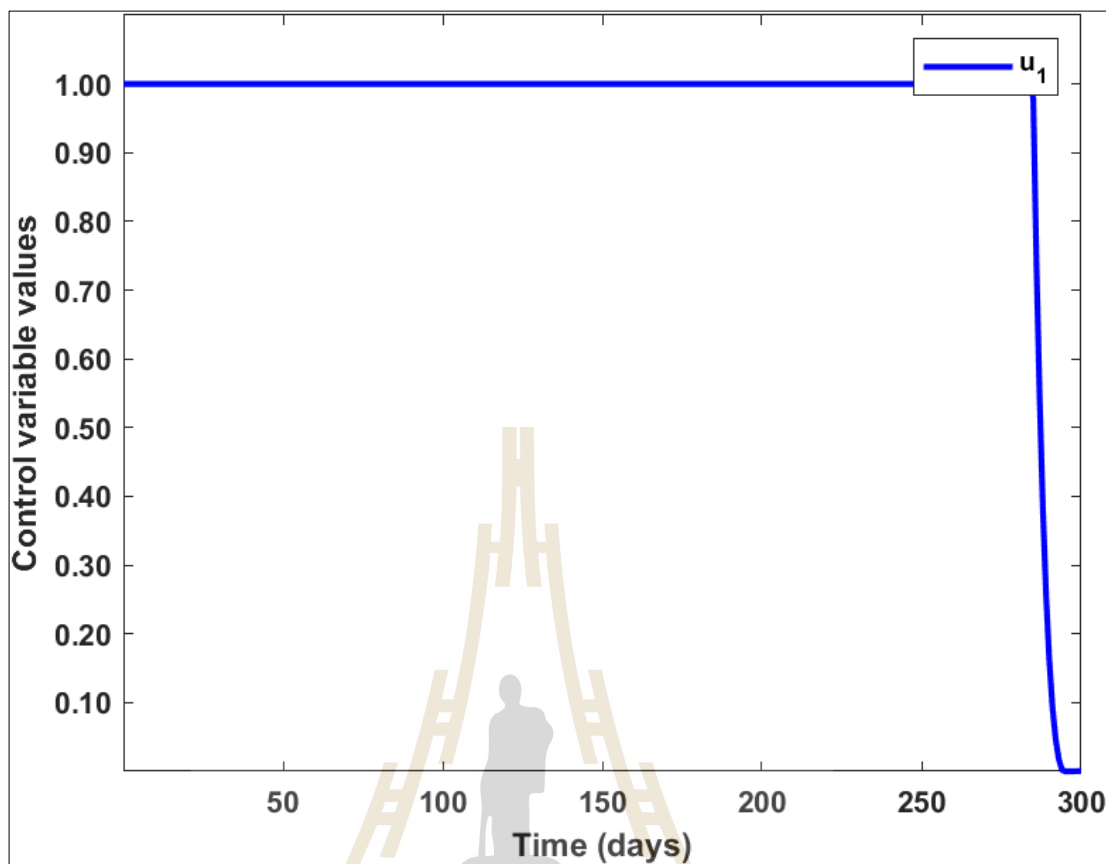
Figure 4.13 Control profile for Policy B-1 $u_1 \in [0,1], u_2, u_3 = 0$

Figures 4.12 and 4.13 show dynamics of cassava population and control variable u_1 when Policy B-1 was applied. At the harvest day, 1.97% of healthy cassava tubers remained in the plantation. u_1 remains at the upper bound for 284 consecutive days and then reduces to the lower bound at the lower bound.

(2) Policy B-2: spraying, rouging

In this scenario, spraying and rouging methods were applied. Therefore, control variables for spraying method, $u_1 \in [0,1]$ and for rouging method, $u_2 \in [0,1]$. Selecting non-infected method was not applied thus $u_3 = 0$.
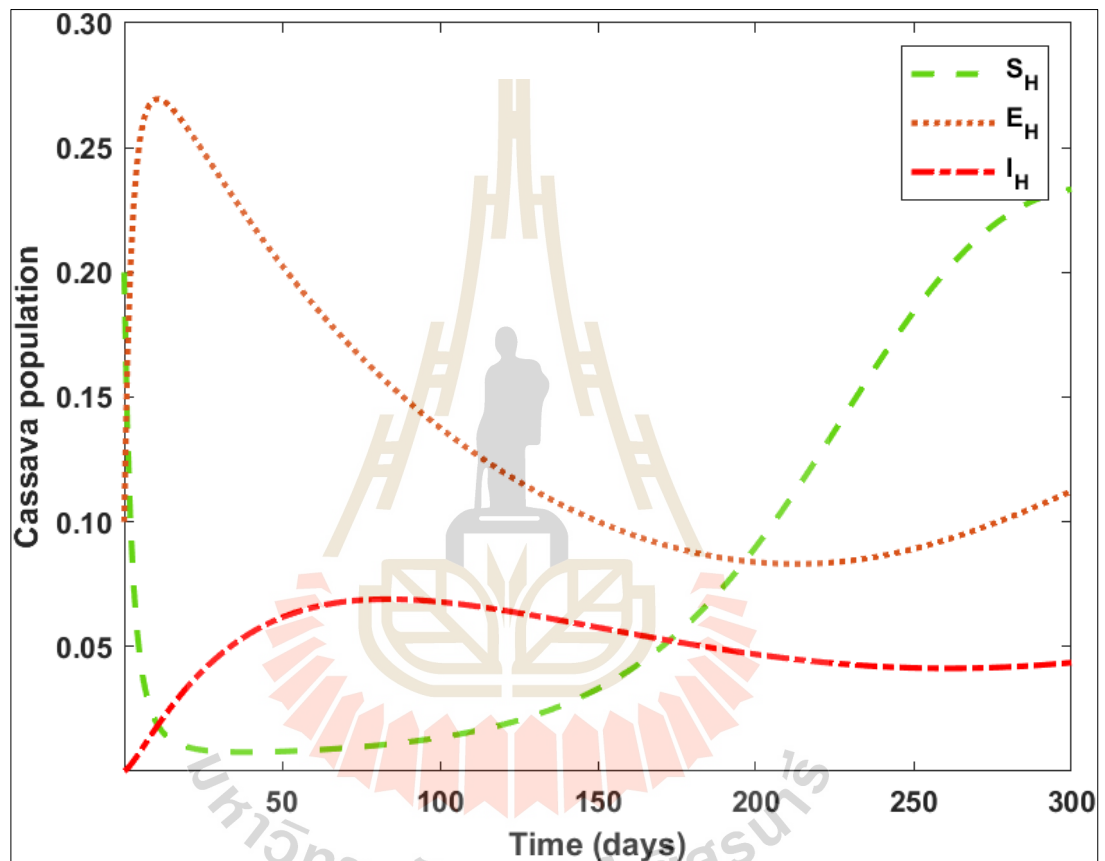
Figure 4.14 Cassava population with spraying insecticide and rouging infected cassavas (Policy B-2)
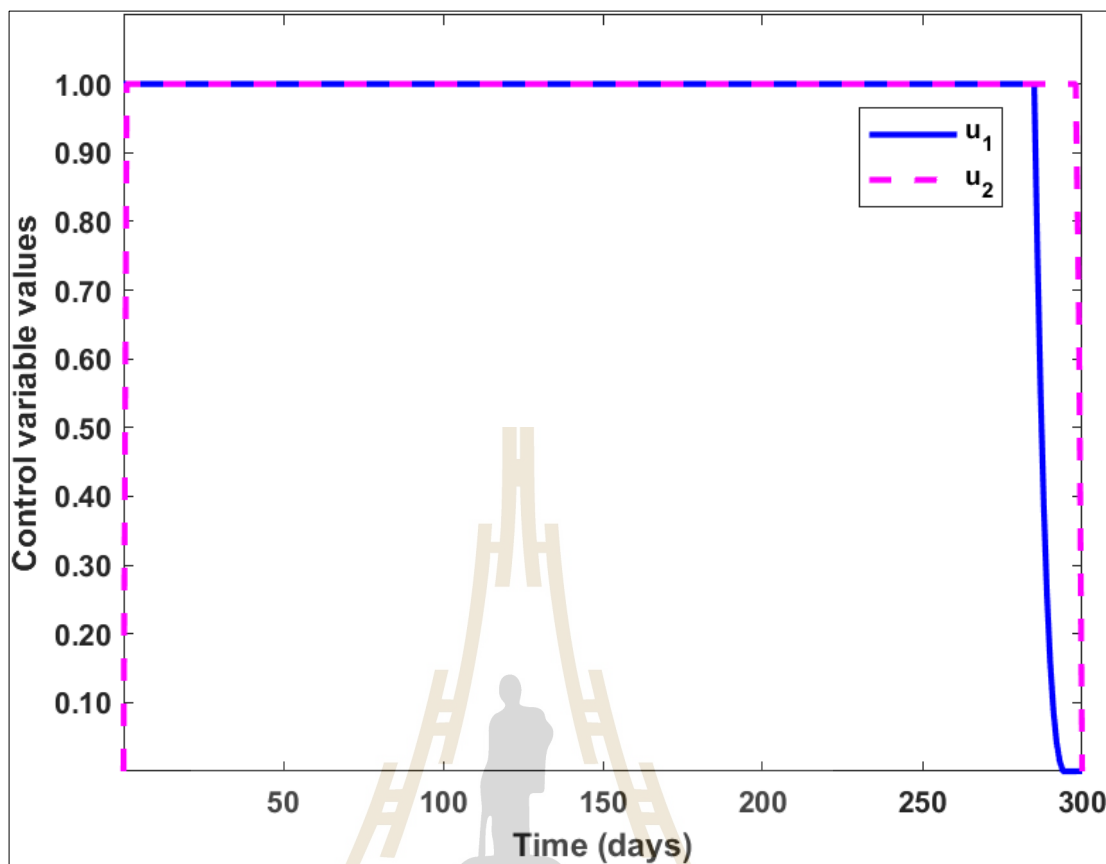
Figure 4.15 Control profile for Policy B-2 $u_1, u_2 \in [0,1], u_3 = 0$

Figure 4.14 shows dynamics of cassava population when Policy B-2 was applied. Removing infected cassavas by rouging method together with spraying method helped increasing healthy cassava tubers to 6.92% on the harvest day. Figure 4.15 shows control variables, u_1 and u_2 of Policy B-1. u_1 remains at the upper bound for 285 consecutive days and then reduces to the lower bound on the harvest day. u_2 remains at the upper bound from day 2 to 298 and then decreases to the lower bound on the harvest day.

(3) Policy B-3: spraying, selecting

In this scenario, spraying and selecting methods were applied. Thus, control variables for spraying method, $u_1 \in [0,1]$ and for selecting method, $u_3 \in [0,1]$. Rouging method was not applied thus $u_2 = 0$.
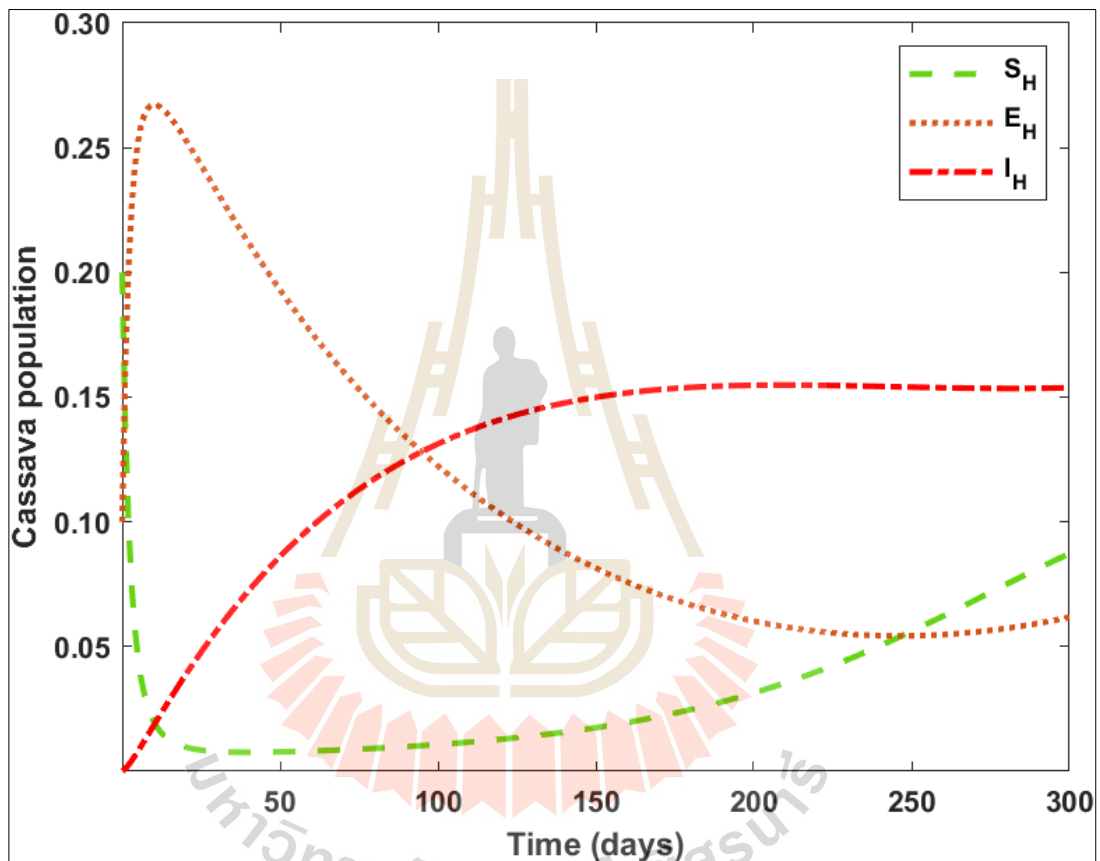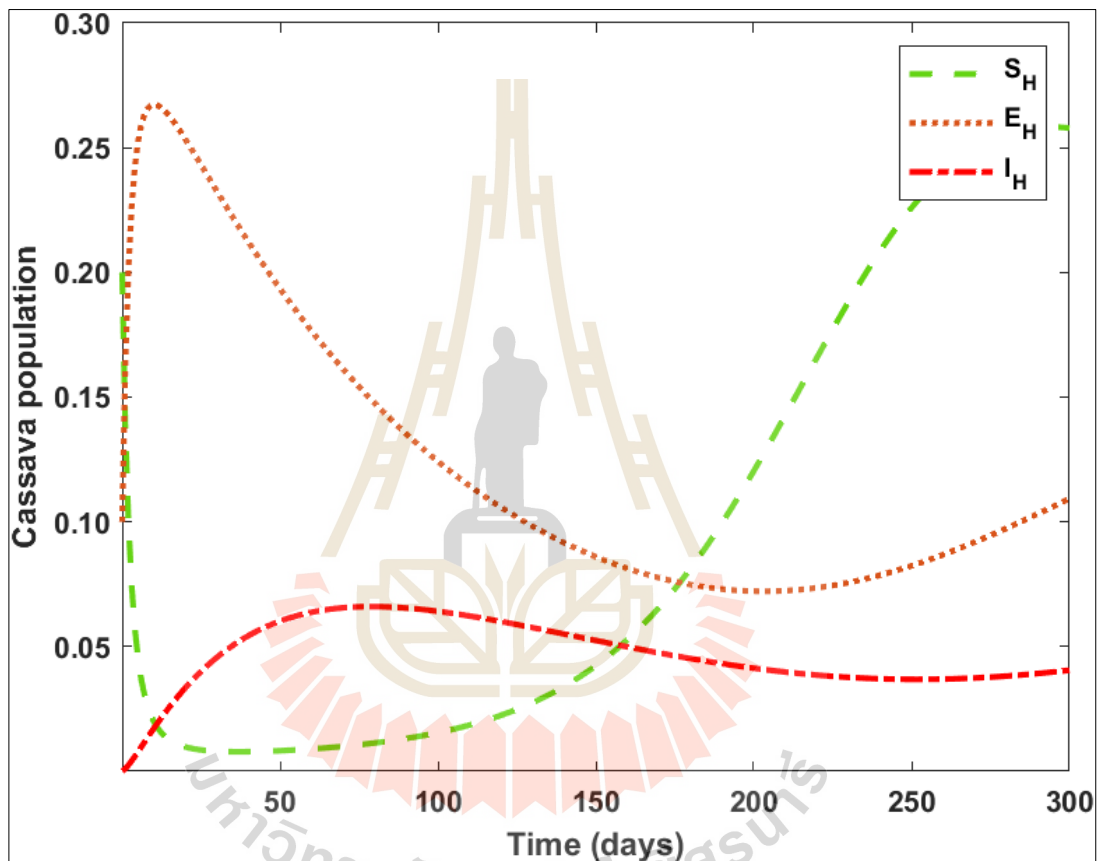
Figure 4.16 Cassava population with spraying insecticide, and selecting non-infected cuttings methods (Policy B-3)

Figure 4.17 Control profile for Policy B-3 $u_1, u_3 \in [0,1], u_2 = 0$

Figure 4.16 shows dynamics of cassava population when Policy B-3 was applied, 2.70% of healthy cassava tubers and 21.55% of infected cassava tubers remained in the plantation area on the harvest day. Figure 4.17 shows control variables when Policy B-3 was applied. u_1 remains at the upper bound for 285 consecutive days and then reduces to the lower bound on the harvest day. u_3 remains at the upper bound for 235 consecutive days and then decreases to the lower bound on the harvest day.

Figure 4.19 Control profile for Policy B-4 $u_1, u_2, u_3 \in [0,1]$

      Figure 4.18 shows dynamics of cassava population when Policy B-4 was applied. By the time of harvest on day 300, 8.39% of healthy cassava yields remained in the plantation. Figure 4.19 shows dynamics of control variables u_1, u_2, and u_3. u_1 remains at the upper bound for 285 consecutive days and then decreases to the lower bound on the harvest day. u_2 remains at the upper bound from day 2 to 298 and then decreases to the lower bound on the harvest day. u_3 remains at the upper bound for 233 consecutive days and then decreases to the lower bound on the harvest day.

4.5.3 Cost-effectiveness analysis

ACER values of eight policies are listed in Table 4.4.

Table 4.4 ACER of control policies

Policies	Total costs	Healthy cassava ratios	ACER values	Ranking
A-2	$1.156	0.703	1.643	1
A-4	$1.410	0.746	1.888	2
B-2	$1.157	0.600	1.929	3
B-4	$1.402	0.633	2.216	4
A-1	$0.859	0.384	2.235	5
A-3	$1.108	0.412	2.686	6
B-3	$1.106	0.288	3.836	7
B-1	$0.858	0.211	4.064	8

Table 4.4 ranks all eight policies according to ACER values. It can be seen from the above table that Policy A-2 is the most cost-effective policy. Controlling the increase of infected cassavas by tolerant cuttings and rouging methods together with spraying pesticide helped reducing the number of infected plants and the number of whitefly simultaneously. Policy B-1 is the least cost-effective one. Spraying pesticide without removing infected plants was proved to be both the most expensive and the least effective method.

4.6 Discussion

Sensitivity analysis results show that R_0 was the most sensitive to the existence of whitefly. Spraying pesticide is the most effective method. The more spraying applied in the plantation, the more effective it is to reduce the number of whitefly. However, it leads to high costs of labor and pesticide as shown by ACER value of Policy B-1 equals to 4.064 in Table 4.4, which is the highest value and not cost-effective.

The existence of infected cassavas was another factor to spread CMD virus. Thus, the combined method of rouging and spraying, Policy B-2 performs better than using a single control, Policy B-1. ACER value of Policy B-2 equals 1.929, which is much lower than that of Policy B-1.

Using three methods simultaneously shows improvement in increased yields. Policy A-2, which combines spraying, rouging, and tolerant cuttings, gives the lowest ACER value of 1.643, which is more cost-effectiveness than Policy B-2.

However, when applying four methods altogether in Policy A-4, its yield is only 5.75% higher than that of Policy A-2, however, the increased control cost of Policy A-4 is 18% higher than that of Policy A-2. Hence, the use of spraying, rouging, and tolerant cuttings is sufficient to control CMD outbreak with optimal cost-effectiveness goal.

CHAPTER V

CONCLUSION AND RECOMMENDATIONS

5.1   Conclusion

This research developed CMD outbreak model caused by whitefly transmission and infected cuttings. The severity of CMD outbreak is increased when infected cassavas are not uprooted out of the plantation. Infected cassavas can be categorized in two forms, symptomatic and asymptomatic. Asymptomatic or latent cassavas are infected but it takes a couple weeks to show the symptom. Without a clear understanding of this state, it could lead to serious outbreak that is difficult to control. There is no study of latent state in the literature. The proposed model is extended from models of Bokil et al. and Magoyo et al. by adding a latent state to study the relationship between latent cassavas and the severity of CMD spread. The model is used to indicate factors that affect CMD outbreak the most by using sensitivity analysis. Testing model with sensitivity analysis suggests that the existence of whitefly is the most crucial factor that affects the severity of CMD outbreak.

Currently, disease spread can be controlled by four methods: spraying pesticide, rouging infected cassavas, selecting non-infected cuttings to plant, and promoting tolerant cuttings. Spraying pesticide is the most effective method to reduce the number of whitefly but this approach requires high labor costs. Using all four methods simultaneously are proved to be the most effective way to control the outbreak giving higher yields of healthy cassavas than applying only three control approaches but this policy requires high investment costs. The optimal control policy in terms of maximum

number of healthy cassava yields and minimum costs is Policy A-2 that applies spraying, rouging, and tolerant cuttings

5.2 Recommendation for Future Works

This study used principles of epidemiology, systems engineering, and systems engineering to develop a model that represented dynamics of CMD. The model was developed based on CMD outbreak and cultivation system in Nakhon Ratchasima province, Thailand, which has the largest cassava growing plantation in Thailand. The model was used to determine the optimal policy to control this disease spread, which should increase cassava production and profits.

Since CMD was detected in Thailand in 2018, which was the emerging infectious disease. There are no data collection for CMD outbreak in Thailand. Therefore, parameters values and ranges are assumed from the previous work to construct the model. In order to represent the real outbreak scenario in Thailand, it is recommended to collect the data of CMD outbreak and cassava cultivation. This could lead to optimal policy determination that fits to solve outbreak in the real case.

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APPENNDIX A

PAPER PUBLICATION
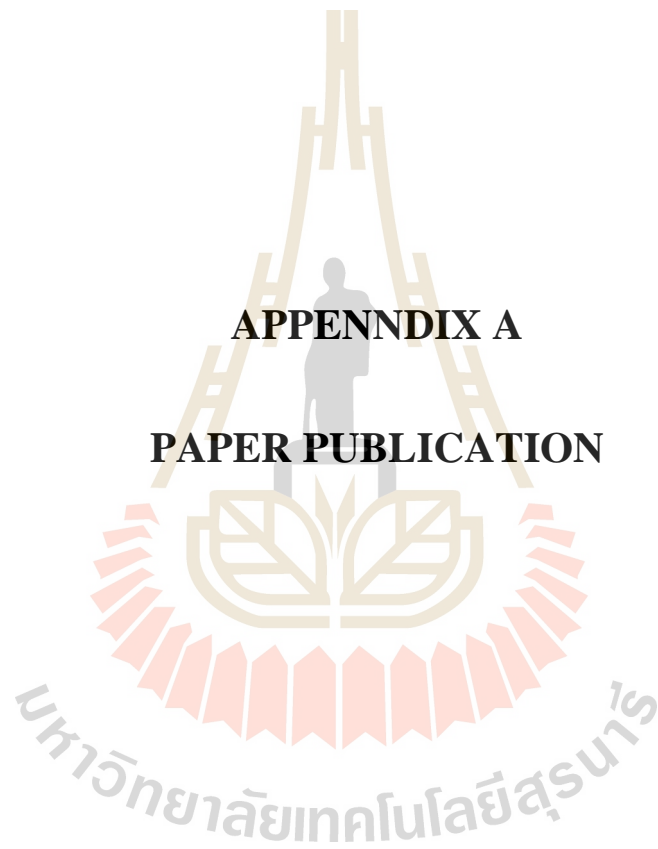
Research article

Reproduction number and sensitivity analysis of cassava mosaic disease spread for policy design

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Abstract: We develop a mathematical model for the dynamics of Cassava Mosaic Disease (CMD), which is driven by both planting of infected cuttings and whitefly transmission. We use the model to analyze the dynamics of a CMD outbreak and to identify the most cost-effective policy for controlling it. The model uses the reproduction number $\mathscr{R}_0$ as a threshold, calculated using the Next-Generation Method. A locally-asymptotically-stable disease-free equilibrium is established when $\mathscr{R}_0 < 1$, proved by the Routh-Hurwitz criterion. The globally-asymptotically-stable disease-free and endemic-equilibrium points are obtained using Lyapunov's method and LaSalle's invariance principle. Our results indicate that the disease-free equilibrium point is globally-asymptotically-stable when $\mathscr{R}_0 \leq 1$, while the endemic-equilibrium point is globally-asymptotically-stable when $\mathscr{R}_0 > 1$. Our sensitivity analysis shows that $\mathscr{R}_0$ is most sensitive to the density of whitefly. Numerical simulations confirmed the effectiveness of whitefly control for limiting an outbreak while minimizing costs.

Keywords: cassava mosaic disease (CMD); reproduction number; local stability; global stability; sensitivity analysis

1. Introduction

Cassava Mosaic Disease (CMD) is a plant disease that reduces tuber size and starch percentage upstream in the cassava supply chain, reducing sales of the cassava crop [1]. This leads to downstream economic impacts since cassava is a major industrial raw material. The financial losses due to CMD in the African continent were estimated at \$1.2–2.3 billion in 1997 [2], increasing to \$1.9–2.7 billion

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in 2009 [3]. A CMD outbreak can be controlled in four ways: (1) by removing infected cassava from the plantation, (2) by promoting the use of virus-free cuttings, (3) by using resistant varieties, or (4) by killing infected whitefly in the plantation area [4–6]. These methods incur huge planning effort and expense. However, there is no clear approach to mapping the major spread factors for appropriate control planning. In this study, we analyzed the CMD spread factors and proposed an epidemic model to isolate those factors that have a major impact in an outbreak. The output may be used to formulate optimal strategies for outbreak control.

Using such an epidemic model, the authors of [7] showed how tomato yields in India suffered from whitefly-vectored Tomato Leaf Curl Geminivirus (TLCV). The most effective disease-control strategy was to distribute netting treated with persistent insecticide. This significantly controlled spread by decreasing vector immigration to the plantation and increasing vector mortality. The authors of [8] studied the outbreak of Huanglongbing disease (HLB) caused by psyllid bacteria, which seriously impacts citrus greening. They tested different intervention strategies over a short time-frame and showed that the best insecticide intervention was to spray over an optimal number of days.

Most epidemic models in the literature are based on the pioneering work in [9]. The models identify the major factors that contribute to the outbreak by applying differential equations. This yields the basic reproduction number ($\mathscr{R}_0$), used to indicate the severity of spread [10–12]. Analysis of the sensitivity of $\mathscr{R}_0$ determines which parameters have the greatest impact on disease control and should be targeted by prevention policies [13, 14].

Most viral crop plant diseases radiate in vectors [15, 16]. The models must therefore represent the dynamics of plant-virus epidemics in order to reveal relationships between vectors and infected plant numbers [17–19]. In 1994, African cassava mosaic virus (ACMV) caused widespread loss of production. The authors in [20] incorporated vector-population dynamics into their statistical model to empirically derive plant-virus relationships. In [21], an epidemiological model of ACMV was introduced to describe the dynamics of infected cassava and infective whitefly. The authors derived a strategy in which cassava yields are maximized by reducing the whitefly population. However, this approach is not cost-effective, so farmers are advised to select uninfected cuttings for planting to prevent a collapse of the healthy cassava population. This is an economical strategy that is capable of controlling an outbreak. The authors [22] developed a mathematical model for the spread of Cassava Brown Streak Disease (CBSD) caused by whitefly, using an approach similar to that in [21]. They simulated two control policies: uprooting and burning of infected cassava, and killing of whitefly in the plantation. They concluded that the optimal policy was uprooting and burning.

In previous works [21, 22], the same authors formulated a mathematical model for vector-host dynamics using a single spread factor (whitefly). However, CMD infection requires both whitefly (*Bemisia tabaci*) transmission and the presence of virus-infected cuttings [23, 24]. Outbreaks have spread beyond the African continent to countries in Asia including India and Sri Lanka following imports of virus-infected cuttings. The CMD model must incorporate this route when devising optimal strategies for outbreak control. The mathematical model developed in [25] for an outbreak of ACMV took account of diseased cuttings, following [21]. The model suggested that a strategy combining rouging and spraying performed better than those that apply a single control mechanism.

When infection levels are high, symptomatic cassava can be readily detected and removed from the plantation. However, the symptoms take five weeks to appear [20], and during this period the asymptomatic cassava may spread the disease. Our goal was to develop a better understanding of the

relationship between asymptomatic plants and the severity of CMD spread. Our model added a latent state to that in [25], in an effort to analyze the comparative contribution of whitefly transmission and planting of infected cuttings. We applied sensitivity analysis to identify the most important parameters in determining the severity of an outbreak.

The rest of this paper is organized as follows. Section 2 discusses CMD, the construction of our model, and the most important parameters in CMD spread. In section 3 we introduce the positivity and boundedness of solutions to initial conditions. Section 4 concerns the stability of the disease-free and endemic-equilibrium points, and introduces the threshold parameter ($\mathscr{R}_0$), obtained using the Next-Generation method. The sensitivity analysis described in section 5 identified the most sensitive parameter with respect to $\mathscr{R}_0$, key to improving the design of CMD-control policies. We conducted numerical simulations to explore the behavior of the system with and without control policies. The simulation is introduced in section 6, and the results reported in section 7. Section 8 presents a summary and our conclusions.

2. Construction of CMD outbreak model

Few mathematical models of viral cassava disease (East African Cassava Mosaic Virus (EACMV), ACMV, or CBSD) [21,22,26] have analyzed how the disease spreads within a plantation. To understand the dynamics of an outbreak, we used ordinary differential equations (ODEs).

The dynamics of ACMV spread were analyzed in [21] and [25], and the "SI-type epidemic model" was developed, which categorizes plants as infected or uninfected. In [26], an epidemic model was developed in which two viruses, ACMV and EACMV, are carried by whitefly into the plantation. The model was based on the "m-group SI-type epidemic model" of [27], which incorporates four plant states: uninfected, infected by ACMV, infected by EACMV, or infected by both. The authors of [22] developed an epidemic model based on the SEIR-type model of [28], and used it to explore the dynamics of CBSD. It assumed four states: healthy, latent, exposed, and rouging. The latent stage, which was missing from earlier models, increases the transmission rate from infected plants to whitefly and vice versa. Our proposed model takes account of the spread of CMD by both by planting and whitefly transmission. The design process is comprised of three steps:

(1) The dynamics are based on infection by transplanting and by whitefly transmission [23, 24]. Defining these factors as parameters yields the ODEs, which we use to calculate equilibrium points and to establish the stability of the outbreak. The Next-Generation method is used to construct $\mathscr{R}_0$.

(2) The local stability of the disease-free equilibrium is proved by the Routh-Hurwitz criterion. The system is locally asymptotically stable if $\mathscr{R}_0 < 1$ and unstable if $\mathscr{R}_0 > 1$. Global stability of the disease-free equilibrium and the endemic equilibrium point are proved by Lyapunov's method and LaSalle's invariance principle. When $\mathscr{R}_0 \leq 1$, the disease-free equilibrium is globally asymptotically stable. If $\mathscr{R}_0 > 1$ then the endemic equilibrium is globally asymptotically stable.

(3) The use of sensitivity analysis to determine the parameters that most strongly affect the outbreak, and the use of these parameters to simulate outbreak control by addressing risk factors.

2.1. Parameters

In our model, the parameters in the CMD outbreak represent disease spread factors. The values and ranges of the parameters were set with reference to previous studies or by analysis of CMD outbreaks. The parameters are listed in Table 1.

Table 1. Parameters for outbreak analysis.

Symbol	Description	Value	Range	Source
h	harvesting rate of cassava plants	0.003	[0.002, 0.004]	[21]
β	CMD latent rate	0.008	[0.008, 0.05]	[29]
γ	rouging rate of symptomatic cassava	0.03	[0.03, 0.1]	[22]
K	^{a}maximum plantation capacity (m^2)	15,000	[10,000, 20,000]	estimated
r	replanting rate of cassava	0.025	[0.025, 0.1]	[21]
a	average number of cassava plants visited by uninfected whitefly	200	[50, 300]	estimated
Λ	constant birth rate of whitefly	0.2	[0.1, 0.3]	[30]
μ	natural death rate of whitefly	0.0142	[0.0142, 0.06]	[22]
p_1	probability of transmission to healthy cassava plants from infected whitefly	0.0033	[0, 1.0]	[22]
p_2	probability of transmission to uninfected whitefly from latent or symptomatic cassava	0.0033	[0, 1.0]	[22]
p_3	probability of planting infected cassava cuttings	0.1	[0, 1.0]	[21]

*Note: ^{a}assuming 1 plant per m^2. The unit of h, β, γ, r and a is per *day*, and the unit of Λ is *#vector* per *day* and μ is per *day*.

2.2. Ordinary differential equations

The model tracks the dynamics of the cassava and whitefly populations. Cassava may be uninfected X, latent Y (infected but asymptomatic), or infected and symptomatic Z. Whitefly may be infected R or uninfected Q. The total cassava population N is therefore $N = X + Y + Z$ at time t. Similarly, the total whitefly population N_V is $N_V = Q + R$.

The transmission dynamics of CMD from an initial state to a second state are governed by the parameters in Table 1. Infection by whitefly is given by $ap_1\frac{X}{N}R$. Infection of whitefly from infected plants is given by $ap_2Q\frac{Y+Z}{N}$. CMD infection by planting of infected cuttings is $r\left(1 - \frac{N}{K}\right)p_3Y$. This term was not used in previous works.

$$\frac{dX}{dt} = r\left(1 - \frac{N}{K}\right)X - ap_1\frac{X}{N}R - hX, \tag{2.1}$$

$$\frac{dY}{dt} = r\left(1 - \frac{N}{K}\right)p_3Y + ap_1\frac{X}{N}R - (\beta + h)Y, \tag{2.2}$$

$$\frac{dZ}{dt} = \beta Y - (\gamma + h)Z, \tag{2.3}$$

$$\frac{dQ}{dt} = \Lambda - ap_2Q\frac{Y+Z}{N} - \mu Q, \tag{2.4}$$

$$\frac{dR}{dt} = ap_2 Q \frac{Y+Z}{N} - \mu R. \tag{2.5}$$

The size of the cassava population is increased by replanting into the plantation area. $r\left(1 - \frac{N}{K}\right)X$ in Eq (2.1) and $r\left(1 - \frac{N}{K}\right)p_3 Y$ in Eq (2.2) represent the replanting terms of healthy and latent cassavas. Cassavas are removed from the system by constant harvesting (h) and rouging (γ). The change from state X (non-infected) to Y reflects the plants that become infected after planting. The change from Y to Z reflects the number of infected cuttings that begin to show CMD symptoms during the period.

The whitefly population is driven by two factors: birth rate (Λ) and death rate (μ). Transmission within the population causes a change from state Q to state R, as whitefly visit infected plants and acquire the virus. Equations (2.6) and (2.7) give the total cassava and whitefly populations:

$$\frac{dN}{dt} = r\left(1 - \frac{N}{K}\right)(X + p_3 Y) - \gamma Z - hN, \tag{2.6}$$

$$\frac{dN_V}{dt} = \Lambda - \mu N_V. \tag{2.7}$$

The model makes the following assumptions:

(1) All model parameters are positive.

(2) The growth rate of the cassava population is positive, i.e., $r - h > 0$, where r is the replanting rate and h is the harvesting rate.

(3) The cassava population increases by one of the logistic growth equations, $r\left(1 - \frac{N}{K}\right)X$ or $r\left(1 - \frac{N}{K}\right)p_3 Y$.

(4) The whitefly birth rate (Λ) is constant.

3. Basic properties of the model

To confirm the biological validity of the model, we must prove that solutions to the ODEs are positive and bounded for all time values. Furthermore, the cassava and whitefly populations must remain finite since they are bounded by the plantation area. In the next section we analyze our model and demonstrate the positivity and boundedness of the system of ODEs.

3.1. Positivity

Theorem 3.1. *Let $t \geq 0$. In the model, if the initial conditions satisfy*

$$X(0), Y(0), Z(0), Q(0), R(0) > 0, \tag{3.1}$$

then $X(t), Y(t), Z(t), Q(t),$ and $R(t)$ will remain positive in $\mathbb{R}_+^5$.

Proof. Let us consider $Y(t)$ for all $t \geq 0$.

From Eq (2.2), we have

$$\frac{dY}{dt} = r\left(1 - \frac{N}{K}\right)p_3 Y + ap_1 \frac{X}{N}R - (\beta + h)Y \geq r\left(1 - \frac{N}{K}\right)p_3 Y - (\beta + h)Y.$$

The integration of the inequality is

$$Y(t) \geq Y(0)e^{-\left(\beta+h-r\left(1-\frac{N}{K}\right)p_3\right)t} > 0, \qquad \text{for all } t \geq 0. \tag{3.2}$$

From the initial conditions (3.1), we have $Y(t) > 0$ for all $t \geq 0$.

   Next, we consider $Z(t)$ for all $t \geq 0$. From Eq (2.3),

$$\frac{dZ}{dt} = \beta Y - (\gamma+h)Z \geq -(\gamma+h)Z.$$

A comparison argument shows that

$$Z(t) \geq Z(0)e^{-(\gamma+h)t} > 0, \qquad \text{for all } t \geq 0. \tag{3.3}$$

Since $Z(0) > 0$, we conclude that $Z(t)$ is always positive for all $t \geq 0$.

   We prove that $Q(t) > 0$ for all $t \geq 0$ by contradiction. Let t_1 be the first point that satisfies $Q(t_1) = 0$. Equation (2.4) yields

$$\left.\frac{dQ}{dt}\right|_{t=t_1} = \Lambda > 0. \tag{3.4}$$

This means that $Q(t) < 0$ for $t \in (t_1 - \theta, t_1)$, where θ is an arbitrarily small positive constant. This leads to a contradiction. Hence, $Q(t) > 0$ for all $t \geq 0$.

   Next, we prove that $R(t)$ is positive for all $t \geq 0$. From Eq (2.5),

$$\frac{dR}{dt} = ap_2 Q \frac{Y+Z}{N} - \mu R \geq -\mu R,$$

it then follows that

$$R(t) \geq R(0)e^{-\mu t} > 0, \qquad \text{for all } t \geq 0. \tag{3.5}$$

Since $R(0) > 0$, we know that $R(t)$ remains positive for all $t \geq 0$.

   Finally, we prove that $X(t) > 0$ for all $t \geq 0$. From Eq (2.1), we have

$$\frac{dX}{dt} = r\left(1-\frac{N}{K}\right)X - ap_1\frac{X}{N}R - hX \geq -ap_1\frac{X}{N}R - hX.$$

The integration of the inequality is

$$X(t) \geq X(0)e^{-ht-\int_0^t \frac{ap_1 R(s)}{N}ds} > 0, \qquad \text{for all } 0 \leq t \leq t_1. \tag{3.6}$$

From the initial conditions (3.1), we have $X(t) > 0$ for all $t \geq 0$.

   We conclude that the solutions of the model are positive in $\mathbb{R}_+^5$. $\qquad\square$

3.2. Boundedness

   We show the boundedness of the system with the initial conditions (3.1).

Theorem 3.2. *All solutions of the system (2.1) to (2.5) with positive initial conditions (3.1) are ultimately bounded.*

Proof. From Theorem 3.1, the solutions to the system are positive for all $t \geq 0$. Since $N = X + Y + Z$. From Eq (2.6), we have

$$\frac{dN}{dt} = r(X + p_3Y)\left(1 - \frac{N}{K}\right) - \gamma Z - hN.$$

As can be observed, the solution is bounded by logistic growth

$$\frac{dN}{dt} \leq r\left(1 - \frac{N}{K}\right)N.$$

The integration of the inequality is

$$N(t) \leq \frac{N(0)K}{N(0) + (K - N(0))e^{-rt}}$$

(assuming $N(0) > 0$), and hence $\lim_{t \to \infty} N(t) \leq K$. This gives the feasible solution set of the cassava entering the region:

$$\Omega_H = \{X, Y, Z \in \mathbb{R}_+^3 \mid N \leq K\} \qquad \text{for all } t \geq 0.$$

Next, note that $N_V = Q + R$. From Eq (2.7),

$$\frac{dN_V}{dt} = \Lambda - \mu N_V.$$

The integration of the equation is

$$N_V(t) = \frac{\Lambda + (N_V(0)\mu - \Lambda)e^{-\mu t}}{\mu}$$

(assuming $N_V(0) > 0$), which implies that $\lim_{t \to \infty} N_V(t) = \frac{\Lambda}{\mu}$. Thus, the feasible solution set for the CMD system is given by

$$\Omega_V = \left\{Q, R \in \mathbb{R}_+^2 \mid N_V \leq \frac{\Lambda}{\mu}\right\} \qquad \text{for all } t \geq 0.$$

The solutions of the system in $\mathbb{R}_+^5$ are confined to the region Ω. Here

$$\Omega = \left\{(X, Y, Z, Q, R) \in \mathbb{R}_+^5 \mid N \leq K, N_V \leq \frac{\Lambda}{\mu}\right\} \qquad \text{for all } t \geq 0.$$

Therefore, all solutions of the system (2.1) to (2.5) with initial conditions (3.1) remain positive invariant in the region Ω for all $t \geq 0$. $\qquad\qquad\square$

4. Equilibrium points and stability analysis

To ensure that disease eradication is independent of the initial size of the susceptible population, locally- and globally-stable disease-free equilibria and endemic equilibria are established when the region Ω is positivity invariant.

4.1. Equilibrium points

Our model admits two equilibrium points: a disease-free equilibrium point (DFE) and an endemic equilibrium point (EE). The notation of DFE is

$$E_0 = (X^*, Y^*, Z^*, Q^*, R^*) = \left(\frac{(r-h)K}{r}, 0, 0, \frac{\Lambda}{\mu}, 0 \right).$$

The EE is denoted $E_1 = (\bar{X}, \bar{Y}, \bar{Z}, \bar{Q}, \bar{R})$, where

$$\bar{X} = \frac{rN(K(\gamma + h) - (\beta + \gamma + h)\bar{Y}) - K(\gamma + h)(ap_1\bar{R} + hN)}{r(\gamma + h)N},$$

$$\bar{Y} = \frac{ap_1K\bar{R}(\gamma + h)((r-h)N - ap_1\bar{R})}{rN((\gamma + h)(\beta + h - hp_3)N + ap_1\bar{R}(\beta + \gamma + h - p_3(\gamma + h)))},$$

$$\bar{Z} = \frac{\beta}{\gamma + h}\bar{Y},$$

$$\bar{Q} = \frac{\Lambda(\gamma + h)N}{ap_2(\beta + \gamma + h)\bar{Y} + \mu(\gamma + h)N},$$

$$\bar{R} = \frac{a\Lambda p_2(\beta + \gamma + h)\bar{Y}}{\mu(ap_2(\beta + \gamma + h)\bar{Y} + \mu(\gamma + h)N)}.$$

4.2. Basic reproduction number

The basic reproduction number ($\mathscr{R}_0$) is the one of the most useful threshold parameters in epidemiology. It is defined as the expected number of secondary cases produced by a single infection in a completely susceptible population. It is used as an indicator of the stability of E_0 and E_1. The DFE E_0 is asymptotically stable if $\mathscr{R}_0 < 1$, as the disease cannot invade the population, but unstable if $\mathscr{R}_0 > 1$. E_1 is asymptotically stable if $\mathscr{R}_0 > 1$. We use the Next-Generation method, following [31, 32], to determine $\mathscr{R}_0$.

The appearance of new infections is represented by the vector F and the transfer of existing infections by the vector V. Let x_j be an infection state for $j = 1, 2, 3$, i.e., $x_1 = Y, x_2 = Z, x_3 = R$. F describes new infections arising in state x_j and V represents the transfer of existing infections to state x_j.

The Jacobian matrices generated by differentiating F and V with respect to the relevant subset of variables are calculated at E_0. This yields the matrices $\mathbb{F}$ and $\mathbb{V}$. The (j, k) entry of the matrix $\mathbb{F}$ is the rate at which infected individuals in compartment k produce new infections in compartment j. The (j, k) entry of the matrix $\mathbb{V}$ represents the transfer of existing infection.

$\mathscr{R}_0$ is computed from the spectral radius of $\mathbb{F}\mathbb{V}^{-1}$ at DFE. $\mathbb{F}\mathbb{V}^{-1}$ is called the Next Generation Matrix [10] and is set as follows:

$$\mathscr{R}_0 = \rho(\mathbb{F}\mathbb{V}^{-1}),$$

where $\rho(\mathscr{M})$ denotes the spectral radius of a matrix $\mathscr{M}$. The spectral radius of $\mathbb{F}\mathbb{V}^{-1}$ is equal to the dominant (or maximum) eigenvalue of $\mathbb{F}\mathbb{V}^{-1}$.

In our model, the vectors F and V can be derived from Eqs (2.1)–(2.5):

$$F = \begin{bmatrix} r\left(1 - \frac{N}{K}\right)p_3Y + ap_1\frac{X}{N}R \\ 0 \\ ap_2Q\frac{Y+Z}{N} \end{bmatrix} \quad \text{and} \quad V = \begin{bmatrix} (\beta + h)Y \\ (\gamma + h)Z - \beta Y \\ \mu R \end{bmatrix}.$$

The Jacobians of F and V with respect to the infectious classes are calculated as $\mathbb{F} = \left[\frac{\partial F_j(E_0)}{\partial x_k}\right]$ and $\mathbb{V} = \left[\frac{\partial V_j(E_0)}{\partial x_k}\right]$, for $j = 1, 2, 3$ and $k = 1, 2, 3$. We then have

$$\mathbb{F} = \begin{bmatrix} r\left(1 - \frac{X^*}{K}\right)p_3 & 0 & ap_1 \\ 0 & 0 & 0 \\ \frac{ap_2 Q^*}{X^*} & \frac{ap_2 Q^*}{X^*} & 0 \end{bmatrix} \quad \text{and} \quad \mathbb{V} = \begin{bmatrix} \beta + h & 0 & 0 \\ -\beta & \gamma + h & 0 \\ 0 & 0 & \mu \end{bmatrix}.$$

Therefore, the Next Generation Matrix $\mathbb{F}\mathbb{V}^{-1}$ is

$$\mathbb{F}\mathbb{V}^{-1}(E_0) = \begin{bmatrix} \frac{hp_3}{(\beta+h)} & 0 & \frac{ap_1}{\mu} \\ 0 & 0 & 0 \\ \frac{ra\Lambda p_2(\beta+\gamma+h)}{\mu K(r-h)(\beta+h)(\gamma+h)} & \frac{ra\Lambda p_2}{\mu K(r-h)(\gamma+h)} & 0 \end{bmatrix}. \tag{4.1}$$

Hence, $\mathscr{R}_0$ is the dominant eigenvalue of Matrix (4.1).

$$\mathscr{R}_0 = \max\left(\frac{hp_3}{2(\beta+h)} \pm \sqrt{\left(\frac{hp_3}{2(\beta+h)}\right)^2 + \frac{ra^2\Lambda p_1 p_2(\beta+\gamma+h)}{\mu^2 K(r-h)(\gamma+h)(\beta+h)}}\right)$$

$$= \frac{hp_3}{2(\beta+h)} + \sqrt{\left(\frac{hp_3}{2(\beta+h)}\right)^2 + \frac{ra^2\Lambda p_1 p_2(\beta+\gamma+h)}{\mu^2 K(r-h)(\gamma+h)(\beta+h)}}. \tag{4.2}$$

4.3. Local stability analysis of disease-free equilibrium point

Theorem 4.1. *Under the hypotheses $r - h > 0$ and $0 \leq p_3 \leq 1$, if $\mathscr{R}_0 < 1$ then E_0 is locally asymptotically stable; otherwise it will be unstable.*

Proof. The local asymptotic stability is determined based on the eigenvalue (λ) of the Jacobian at E_0. The E_0 is locally asymptotically stable if the real parts of λ are all negative. The Jacobian matrix at E_0 is given by

$$J(E_0) = \begin{bmatrix} -(r-h) & -(r-h) & -(r-h) & 0 & -ap_1 \\ 0 & hp_3 - (\beta+h) & 0 & 0 & ap_1 \\ 0 & \beta & -(\gamma+h) & 0 & 0 \\ 0 & -\frac{ra\Lambda p_2}{\mu K(r-h)} & -\frac{ra\Lambda p_2}{\mu K(r-h)} & -\mu & 0 \\ 0 & \frac{ra\Lambda p_2}{\mu K(r-h)} & \frac{ra\Lambda p_2}{\mu K(r-h)} & 0 & -\mu \end{bmatrix}. \tag{4.3}$$

The characteristic equation is given by

$$(\lambda + \mu)(\lambda + (r-h))\left(\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3\right) = 0, \tag{4.4}$$

with coefficients

$$a_1 = \beta + \gamma + \mu + h(2 - p_3),$$
$$a_2 = (\beta + h - hp_3)(\gamma + h + \mu) + (\gamma + h)\mu - \frac{ra^2\Lambda p_1 p_2}{\mu K(r-h)},$$

and

$$a_3 = \mu(\gamma + h)(\beta + h - hp_3) - \frac{ra^2\Lambda p_1 p_2(\beta + \gamma + h)}{\mu K(r-h)}.$$

Under the model assumption $r > h$, it is clear that the first two eigenvalues of this system are negative, $-\mu$ and $-(r - h)$, respectively.

We now consider the cubic equation from (4.4)

$$\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0.$$

As $0 \le p_3 \le 1$, we obtain

$$a_1 = \beta + \gamma + \mu + h(2 - p_3) > 0.$$

We can observe that if $\mathscr{R}_0 = \frac{hp_3}{2(\beta+h)} + \sqrt{\left(\frac{hp_3}{2(\beta+h)}\right)^2 + \frac{ra^2\Lambda p_1 p_2(\beta+\gamma+h)}{\mu^2 K(r-h)(\gamma+h)(\beta+h)}} < 1$, then

$$\frac{ra^2\Lambda p_1 p_2(\beta + \gamma + h)}{\mu^2 K(r - h)(\gamma + h)} < \beta + h - hp_3.$$

Therefore, we obtain

$$a_3 = \mu(\gamma + h)(\beta + h - hp_3) - \frac{ra^2\Lambda p_1 p_2(\beta + \gamma + h)}{\mu K(r - h)} > 0.$$

Finally, we consider

$$a_1 a_2 - a_3 = (\beta + \gamma + \mu + h(2 - p_3))\left((\beta + h - hp_3)(\gamma + h + \mu) + (\gamma + h)\mu - \frac{ra^2\Lambda p_1 p_2}{\mu K(r - h)}\right)$$
$$- \mu(\gamma + h)(\beta + h - hp_3) + \frac{ra^2\Lambda p_1 p_2(\beta + \gamma + h)}{\mu K(r - h)}. \tag{4.5}$$

Under hypotheses $\mathscr{R}_0 < 1$, $r > h$, and $0 \le p_3 \le 1$, we obtain

$$a_1 a_2 - a_3 = (\gamma + \mu + h)(\gamma + h)\mu + \frac{ra^2\Lambda p_1 p_2(\beta + \gamma + h)}{\mu K(r - h)}$$
$$+ (\beta + \gamma + \mu + h(2 - p_3))\left((\beta + h - hp_3)(\gamma + h + \mu) - \frac{ra^2\Lambda p_1 p_2}{\mu K(r - h)}\right)$$
$$= G_1 + G_2 + a_3,$$

with coefficients

$$G_1 = \frac{(\beta + \gamma + h)}{(\beta + \gamma + \mu + h(2 - p_3))}\left((\gamma + \mu + h)(\gamma + h)\mu + \frac{ra^2\Lambda p_1 p_2(\beta + h - hp_3)}{\mu K(r - h)}\right) > 0,$$
$$G_2 = ((\gamma + h)(\beta + \gamma + h) + \mu\beta)(\beta + h - hp_3) > 0.$$

This means that $a_1 a_2 - a_3 > 0$ whenever $\mathscr{R}_0 < 1$, $r > h$, and $0 \le p_3 \le 1$.

The Routh-Hurwitz criterion for the third order polynomial indicated that the remaining eigenvalues of the disease-free equilibrium system have negative real parts when $a_1 > 0, a_3 > 0$, and $a_1 a_2 > a_3$. □

Therefore, E_0 will be locally asymptotically stable if $\mathscr{R}_0 < 1$. When $\mathscr{R}_0 > 1$, E_0 is unstable and the disease will persist.

4.4. Global stability analysis

The global stability of the DFE and the EE are established using Lyapunov's method and LaSalle's invariance principle to obtain the control condition under which disease can be eradicated.

Theorem 4.2. *(1) If $\mathcal{R}_0 \leq 1$, then the disease-free equilibrium point E_0 is globally asymptotically stable in Ω. (2) If $\mathcal{R}_0 > 1$, then the endemic equilibrium point E_1 is globally asymptotically stable in Ω.*

Proof. Theorems 4.2 (1) and 4.2 (2) can be proved by using a Lyapunov function. We adopt the Lyapunov function used in [33, 34].

First, we prove Theorem 4.2 (1) by assuming that:

$$\mu = \frac{ap_1}{N}X^*. \tag{4.6}$$

We define the Lyapunov function

$$L_1 : \{(X, Y, Z, Q, R) \in \Omega \mid X, Q > 0\} \rightarrow \mathbb{R}_5^+$$

by

$$L_1(X, Y, Z, Q, R) = \left(X - X^* - X^* \ln \frac{X}{X^*}\right) + Y + Z + \left(Q - Q^* - Q^* \ln \frac{Q}{Q^*}\right) + R. \tag{4.7}$$

When L_1 is C^1, a proper positive definite function, and E_0 is the global minimum of L_1 on Ω, we obtain

$$L_1(X^*, Y^*, Z^*, Q^*, R^*) = 0.$$

The time derivative of L_1 computed along solutions of Eqs (2.1)–(2.5) is

$$\frac{dL_1}{dt} = \frac{dX}{dt}\left(1 - \frac{X^*}{X}\right) + \frac{dY}{dt} + \frac{dZ}{dt} + \frac{dQ}{dt}\left(1 - \frac{Q^*}{Q}\right) + \frac{dR}{dt}. \tag{4.8}$$

Substituting the ODEs (2.1) to (2.5) into Eq (4.8) yields

$$\frac{dL_1}{dt} = \left(r\left(1 - \frac{N}{K}\right)X - ap_1\frac{X}{N}R - hX\right)\left(1 - \frac{X^*}{X}\right) + \left(r\left(1 - \frac{N}{K}\right)p_3Y + ap_1\frac{X}{N}R - (\beta + h)Y\right)$$
$$+ (\beta Y - (\gamma + h)Z) + \left(\Lambda - ap_2Q\frac{Y+Z}{N} - \mu Q\right)\left(1 - \frac{Q^*}{Q}\right) + \left(ap_2Q\frac{Y+Z}{N} - \mu R\right),$$

this simplifies to

$$\frac{dL_1}{dt} = \left(r\left(1 - \frac{N}{K}\right)X - hX\right)\left(1 - \frac{X^*}{X}\right) + r\left(1 - \frac{N}{K}\right)p_3Y - hY - (\gamma + h)Z$$
$$+ \Lambda\left(1 - \frac{Q^*}{Q}\right) + \mu Q^*\left(1 - \frac{Q}{Q^*}\right) + \frac{ap_2}{N}Q^*(Y + Z) + \left(\frac{ap_1}{N}X^* - \mu\right)R. \tag{4.9}$$

Since $Y + Z = N - X$, $N = X^* = \frac{(r-h)K}{r}$, $N_V = Q^* = \frac{\Lambda}{\mu}$, and observing the condition in Eq (4.6), Equation (4.9) can be rewritten as

$$\frac{dL_1}{dt} = hp_3 Y - hY - (\gamma + h)Z + \Lambda\left(1 - \frac{Q^*}{Q}\right) + \Lambda\left(1 - \frac{Q}{Q^*}\right) + G_3(X^* - X), \qquad (4.10)$$

where $G_3 = \frac{ap_2}{N}Q^*$. Therefore, Eq (4.10) becomes

$$\frac{dL_1}{dt} = \Lambda\left(2 - \frac{Q^*}{Q} - \frac{Q}{Q^*}\right) - (\gamma + h)Z + G_3(X^* - X) + h(p_3 - 1)Y$$

$$= -\Lambda\frac{(Q - Q^*)^2}{QQ^*} - (\gamma + h)Z + G_3(X^* - X) + h(p_3 - 1)Y.$$

$$\leq 0. \qquad (4.11)$$

All terms in Eq (4.11) are always non-positive since $\lim_{t\to\infty} X(t) \geq X^*$ (Eq (3.6)) and $0 \leq p_3 \leq 1$ (Table 1). Note that $\frac{dL_1}{dt} = 0$ if and only if $X = X^*$, $Q = Q^*$, $Y = 0$, and $Z = 0$.

Therefore, the largest invariant compact invariant set in $\left\{(X, Y, Z, Q, R) \in \Omega \mid \frac{dL_1}{dt} = 0\right\}$ is the singleton, i.e., $E_0 = (X^*, Y^*, Z^*, Q^*, R^*)$. Thus, $\frac{dL_1(t)}{dt} \leq 0$. This implies that E_0 is globally asymptotically stable in Ω.

We next prove Theorem 4.2 (2). We define the Lyapunov function

$$L_2 : \{(X, Y, Z, Q, R) \in \Omega \mid X, Y, Z, Q, R > 0\} \to \mathbb{R}_5^+$$

by

$$L_2(X, Y, Z, Q, R) = \frac{N}{ap_1\bar{X}\bar{R}}\left(X - \bar{X} - \bar{X}\ln\frac{X}{\bar{X}}\right) + \frac{N}{ap_1\bar{X}\bar{R}}\left(Y - \bar{Y} - \bar{Y}\ln\frac{Y}{\bar{Y}}\right) + \frac{1}{\beta\bar{Y}}\left(Z - \bar{Z} - \bar{Z}\ln\frac{Z}{\bar{Z}}\right)$$

$$+ \frac{N}{ap_2\bar{Q}(\bar{Y}+\bar{Z})}\left(Q - \bar{Q} - \bar{Q}\ln\frac{Q}{\bar{Q}}\right) + \frac{N}{ap_2\bar{Q}(\bar{Y}+\bar{Z})}\left(R - \bar{R} - \bar{R}\ln\frac{R}{\bar{R}}\right), \qquad (4.12)$$

When L_2 is C^1, a proper positive definite function, and E_1 is the global minimum of L_2 on Ω, we obtain

$$L_2(\bar{X}, \bar{Y}, \bar{Z}, \bar{Q}, \bar{R}) = 0.$$

The time derivative of L_2 computed along solutions of Eqs (2.1)–(2.5) is

$$\frac{dL_2}{dt} = \frac{N}{ap_1\bar{X}\bar{R}}\left(1 - \frac{\bar{X}}{X}\right)\frac{dX}{dt} + \frac{N}{ap_1\bar{X}\bar{R}}\left(1 - \frac{\bar{Y}}{Y}\right)\frac{dY}{dt} + \frac{1}{\beta\bar{Y}}\left(1 - \frac{\bar{Z}}{Z}\right)\frac{dZ}{dt}$$

$$+ \frac{N}{ap_2\bar{Q}(\bar{Y}+\bar{Z})}\left(1 - \frac{\bar{Q}}{Q}\right)\frac{dQ}{dt} + \frac{N}{ap_2\bar{Q}(\bar{Y}+\bar{Z})}\left(1 - \frac{\bar{R}}{R}\right)\frac{dR}{dt}. \qquad (4.13)$$

Under Eqs (2.1)–(2.5), if the system meets E_1,

$$r\left(1 - \frac{N}{K}\right) = \frac{ap_1\bar{R}}{N} + h,$$

$$(\beta + h)\bar{Y} = r\left(1 - \frac{N}{K}\right)p_3\bar{Y} + ap_1\frac{\bar{X}}{N}\bar{R},$$

$$(\gamma + h)\bar{Z} = \beta\bar{Y},$$

$$\mu\bar{Q} = \Lambda - ap_2\bar{Q}\frac{\bar{Y} + \bar{Z}}{N},$$

$$\mu\bar{R} = ap_2\bar{Q}\frac{\bar{Y} + \bar{Z}}{N}.$$

We rewrite this to obtain

$$\frac{dL_2}{dt} = \frac{N}{ap_1\bar{X}\bar{R}}\left(1 - \frac{\bar{X}}{X}\right)\left(ap_1\frac{X}{N}\bar{R} - ap_1\frac{X}{N}R\right) + \frac{N}{ap_1\bar{X}\bar{R}}\left(1 - \frac{\bar{Y}}{Y}\right)\left(ap_1\frac{X}{N}R - ap_1\bar{R}\frac{\bar{X}}{N}\frac{Y}{\bar{Y}}\right)$$

$$+ \frac{1}{\beta\bar{Y}}\left(1 - \frac{\bar{Z}}{Z}\right)\left(\beta Y - \beta\bar{Y}\frac{Z}{\bar{Z}}\right) + \frac{N}{ap_2\bar{Q}(\bar{Y} + \bar{Z})}\left(1 - \frac{\bar{Q}}{Q}\right)\left(\Lambda - ap_2Q\frac{Y+Z}{N} - \frac{Q}{\bar{Q}}\left(\Lambda - ap_2\bar{Q}\frac{\bar{Y} + \bar{Z}}{N}\right)\right)$$

$$+ \frac{N}{ap_2\bar{Q}(\bar{Y} + \bar{Z})}\left(1 - \frac{\bar{R}}{R}\right)\left(ap_2Q\frac{Y+Z}{N} - ap_2\bar{Q}\frac{\bar{Y} + \bar{Z}}{N}\frac{R}{\bar{R}}\right). \tag{4.14}$$

The derivative of L_2 then becomes

$$\frac{dL_2}{dt} = -\frac{N}{ap_2\bar{Q}(\bar{Y} + \bar{Z})}\frac{\Lambda(\bar{Q} - Q)^2}{Q\bar{Q}} + 1 + \frac{X}{\bar{X}} + \frac{Q}{\bar{Q}} + \frac{Y+Z}{\bar{Y} + \bar{Z}} - \frac{Z}{\bar{Z}} - \frac{Y\bar{Z}}{\bar{Y}Z} - \frac{XR\bar{Y}}{\bar{X}\bar{R}Y} - \frac{Q\bar{R}(Y+Z)}{\bar{Q}R(\bar{Y} + \bar{Z})}$$

$$\leq 0. \tag{4.15}$$

Using the arithmetic–geometric means inequality, we can see that $\frac{dL_2}{dt} \leq 0$. Note that, $\frac{dL_2}{dt} = 0$ only if $X = \bar{X}$, $Y = \bar{Y}$, $Z = \bar{Z}$, $Q = \bar{Q}$, and $R = \bar{R}$.

Therefore, the largest compact invariant set in $\left\{(X, Y, Z, Q, R) \in \Omega \mid \frac{dL_2}{dt} = 0\right\}$ is the singleton $E_1 = (\bar{X}, \bar{Y}, \bar{Z}, \bar{Q}, \bar{R})$. Thus, $\frac{dL_2}{dt} \leq 0$. This implies that E_1 is globally-asymptotically-stable in Ω. □

We have established that the disease-free equilibrium point E_0 is globally asymptotically stable and that the disease can be controlled as long as the threshold $\mathscr{R}_0 \leq 1$. If $\mathscr{R}_0 > 1$ the endemic equilibrium point E_1 is globally-asymptotically-stable and the disease will persist. From an epidemiological point of view the goal of policy is to control CMD outbreaks by reducing $\mathscr{R}_0$ to below one and maximizing the uninfected population. However, an agricultural viewpoint would instead focus on maximizing the economic returns. We therefore need to identify the strategy that maximizes profits. To do this we first identify the parameter that plays the greatest role in the stability of $\mathscr{R}_0$.

5. Sensitivity analysis

Sensitivity analysis is used to assess the relative impact of different factors on the stability of a model under data uncertainty. The analysis is also able to determine which parameters play critical roles. We perform the analysis by calculating the sensitivity indices of the basic reproduction number, $\mathscr{R}_0$ to the parameters in the model using both local and global methods.

5.1. Local sensitivity analysis

The local sensitivity analysis is based on the normalized forward sensitivity index $\mathscr{R}_0$. The sensitivity index of $\mathscr{R}_0$ with respect to the parameters in our model are derived as follows [35]:

$$\Gamma_P^{\mathscr{R}_0} = \frac{\partial \mathscr{R}_0}{\partial P} \times \frac{P}{\mathscr{R}_0}. \tag{5.1}$$

Here, P is a parameter value from Table 2, while the value of $\mathscr{R}_0$ is computed from Eq (4.2). We analyze the sensitivity of $\mathscr{R}_0$ by substituting the parameter values into Eq (5.1). For example, the sensitivity index $\mathscr{R}_0$ with respect to h is

$$\Gamma_h^{\mathscr{R}_0} = \frac{\partial \mathscr{R}_0}{\partial h} \times \frac{h}{\mathscr{R}_0} = -0.0713.$$

Table 2 lists the sensitivity indices of $\mathscr{R}_0$ obtained using Maple.

Table 2. Sensitivity Indices of $\mathscr{R}_0$ (Definition from Table 1).

Parameter	Parameter Value	Sensitivity Index
h	0.003	-0.0713
β	0.008	-0.2693
γ	0.03	-0.0881
K	$15,000$	-0.4965
r	0.025	-0.0677
a	200	$+0.9929$
Λ	0.2	$+0.4965$
μ	0.0142	-0.9929
p_1	0.0033	$+0.4965$
p_2	0.0033	$+0.4965$
p_3	0.1	$+0.0071$

We first consider the pathogen parameters p_1, p_2 and p_3. Our model limits the severity of an outbreak by controlling three infection terms:

(1) Transmission by whitefly, $ap_1 \frac{X}{N}R$.

(2) Infection of whitefly by CMD virus from infected cassava, $ap_2 Q \frac{Y+Z}{N}$.

(3) CMD spread by replanting of infected cuttings, $r\left(1 - \frac{N}{K}\right)p_3 Y$.

Whitefly-cassava transmission (p_1) and cassava-whitefly transmission (p_2) were given the same probability, and these parameters had the highest sensitivity index magnitude of $+0.4965$ (Table 2). This suggested that the most important determinants of the severity of a CMD outbreak are transmission by whitefly to cassava and transmission to whitefly from infected plants.

The model also assigned a probability to CMD spread by planting of infected cuttings (p_3). As can be seen from Table 2, this was the parameter with the lowest sensitivity index magnitude of $+0.0071$. Replanting of infected cuttings does increase the number of plants exposed to the virus, but contributes less to the spread than does whitefly transmission. Control of the whitefly population is therefore the key policy goal.

We next analyzed the parameters that determine the whitefly population. The whitefly death rate ($\mu = -0.9929$) and the average number of cassava plants visited ($a = +0.9929$) turn out to be significant. The birth rate of whitefly also affects the stability of the system ($\Lambda = +0.4965$). As μ is negative, the whitefly population will decrease as μ increases. However, the sensitivity index values of a and Λ are positive, so that $\mathscr{R}_0$ will increase as these parameters increase. The significance of μ, a and Λ in determining $\mathscr{R}_0$ (Table 2) suggests that whitefly elimination is the optimal approach.

5.2. Uncertainty and global sensitivity analysis

Global sensitivity analysis is used to examine the model which responses to parameter variation within a wider range in the parameter space. The parameter values and ranges are listed in Table 1. Partial rank correlation coefficient (PRCC) between the $\mathscr{R}_0$ and each parameter for the model are derived as in references [36–38]. We computed the PRCC by setting of input parameter values sampled using the Latin Hypercube Sampling (LHS) method. Table 3 shows the results of PRCC and P-value from 1000 independent simulations.

Table 3. PRCC between $\mathscr{R}_0$ and each parameter.

Parameter	PRCCs	P-values
h	-0.0075	0.8136
β	-0.1415	0.0000
γ	-0.0055	0.8624
K	-0.1298	0.0000
r	-0.0012	0.9704
$^{**}a$	$+0.4684$	0.0000
Λ	$+0.1449$	0.0000
$^{**}\mu$	-0.4312	0.0000
$^{**}p_1$	$+0.4049$	0.0000
$^{**}p_2$	$+0.4358$	0.0000
p_3	$+0.0286$	0.3671

Parameters with absolute maximum PRCC values as well as corresponding lowest P-values are the most critical factor in disease spread. As shown in Table 3, we noticed that the parameter a has the most effect on $\mathscr{R}_0$, followed in decreasing order by p_2 (cassava-whitefly transmission), μ (death rate of whitefly), and p_1 (whitefly-cassava transmission). The most important parameters for $\mathscr{R}_0$ from the global sensitivity analysis match those from the local sensitivity analysis, i.e., a, p_2, μ, and p_1. These results allow us to considerably reduce $\mathscr{R}_0$ by decreasing the whitefly population.

Local and global sensitivity analysis are used to examine the impact of parameters on $\mathscr{R}_0$. We found that killing whitefly is the optimal policy. In practice, whitefly density in plantation area is also a factor that affects to the severity of CMD outbreaks. We therefore investigated the sensitivity of $\mathscr{R}_0$ in Eq (4.2) to vary the different sizes of the plantation area (K).

Figure 1a shows that the sensitivity of $\mathscr{R}_0$ to a increases as a increases and K decreases. Figure 1b shows that the sensitivity of $\mathscr{R}_0$ to Λ increases as Λ increases and K decreases, which means that $\mathscr{R}_0$ is more sensitive to the whitefly birth rate if the plantation area is small. In contrast, the sensitivity of $\mathscr{R}_0$ to μ increases as μ and K decrease. This means that CMD outbreaks are more severe when K is small, and a whitefly elimination policy will fail to eliminate the disease. A cost-effective control strategy must therefore take account of the plantation area. To determine the most cost-effective policy, we conducted numerical simulations.
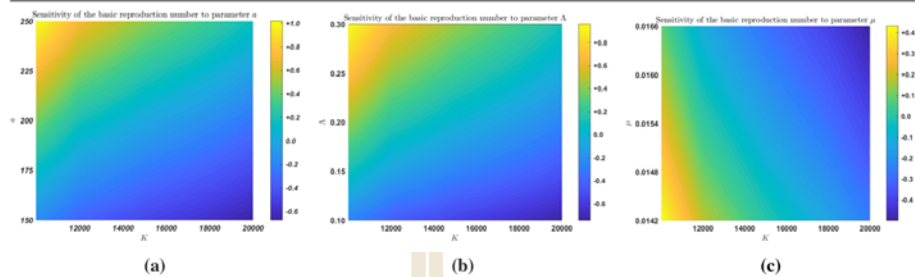
5084

Figure 1. (a) sensitivity of $\mathscr{R}_0$ to a as K increases from 10,000 to 20,000 and a increases from 150 to 250. (b) sensitivity of $\mathscr{R}_0$ to Λ as K increases from 10,000 to 20,000 and Λ increases from 0.1 to 0.3. (c) sensitivity of $\mathscr{R}_0$ to μ as K increases from 10,000 to 20,000 and μ increases from 0.0142 to 0.0166.

6. Numerical simulations

To determine the effectiveness of a control policy, it is necessary to assess the number of whitefly in the plantation. Equations (2.4) and (2.5) are modified by introducing two control parameters: $\epsilon \in [0, 1]$, the efficacy of pesticide spray in controlling whitefly, and g, the resulting whitefly death rate. Adding terms $(\mu + g\epsilon)$ to Eqs (2.4) and (2.5) produces Eqs (6.1) and (6.2). These take account of deaths of uninfected and infected whitefly from natural causes and from pesticide spraying.

$$\frac{dQ}{dt} = \Lambda - ap_2 Q \frac{Y + Z}{N} - (\mu + g\epsilon)Q, \tag{6.1}$$

$$\frac{dR}{dt} = ap_2 Q \frac{Y + Z}{N} - (\mu + g\epsilon)R. \tag{6.2}$$

6.1. Simulation of CMD outbreak dynamics without control

We used Eqs (2.1)–(2.3), (6.1) and (6.2) to represent the dynamics of a CMD outbreak when no control is applied ($g\epsilon = 0$) and to determine the resulting cassava yield. We used two plantation capacity scenarios (K) to simulate the dynamics of such a CMD outbreak: (1) $K = 15,000$ and (2) $K = 10,000$. The other parameters were given the values in Table 1. Figures 2–5 assume a 300 d growing season, no control policy, and initial conditions $X(0) = 9,000$, $Y(0) = 1,000$, $Z(0) = 0$, $Q(0) = 900$, and $R(0) = 100$.

6.1.1. Scenario 1: maximum plantation capacity 15,000 m^2

Figure 2 shows the number of infected whitefly increasing to a maximum at D 17, then decreasing. Figure 3 shows the numbers of healthy, latent, and symptomatic cassava. Latent and asymptomatic plants outnumbered healthy plants at D 19, or 2 d after the whitefly infection peak. Comparing Figure 2 with 3, the number of infected plants tracked the whitefly population. The impact was mainly on the rate of latent cassava, which exceeded the number of healthy cassava. The harvest of 1,173 tubers from an initial planting of 9,000 gave a daily rate of $h = 0.003$.

5085
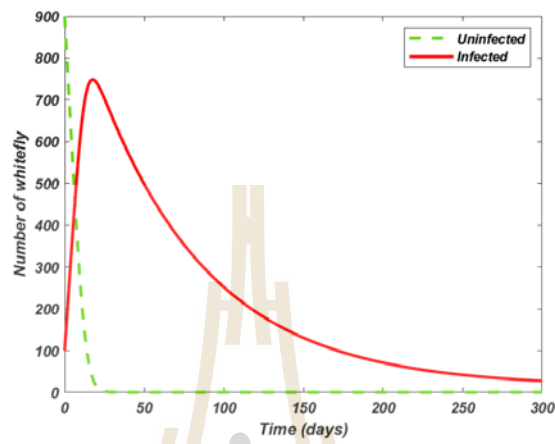
Figure 2. Whitefly population without control, Scenario 1.
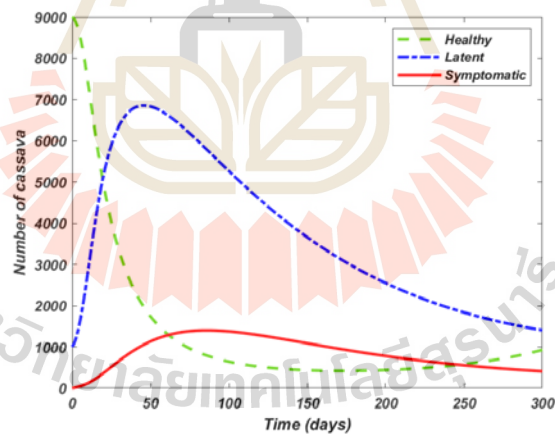
Figure 3. Cassava population without control, Scenario 1.

5086
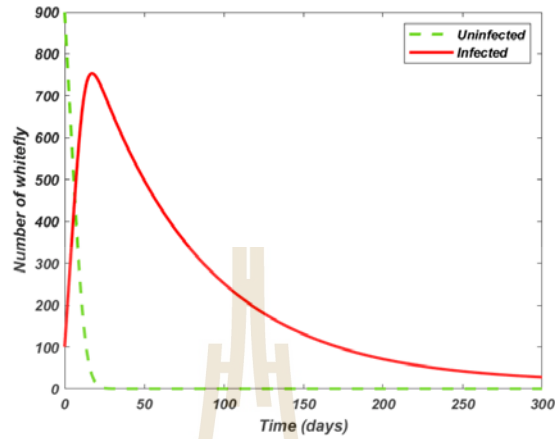
Figure 4. Whitefly population without control, Scenario 2.

6.1.2. Scenario 2: maximum plantation capacity 10,000 m^2

The numerical results in Figure 5 show that latent and symptomatic plants outnumbered healthy plants at D 17, lagging the trend in infected whitefly. Infected whitefly reached a maximum at D 17 (Figure 4), then decreased. By the time of harvest at D 300, 714 tubers out of 9,000 remained healthy. In the smaller plantation, this increased whitefly density and CMD spread.
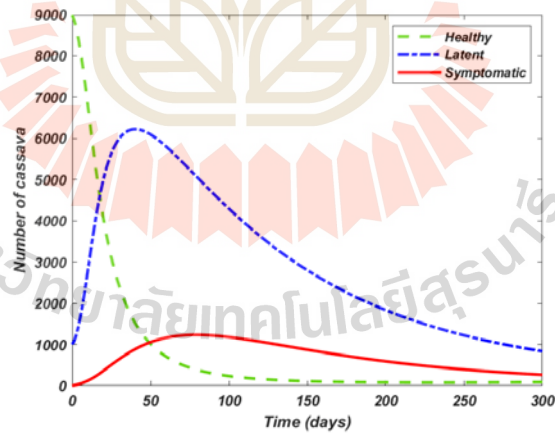
Figure 5. Cassava population without control, Scenario 2.

6.2. Simulations and cost-effectiveness analysis

Our sensitivity analysis showed that the rapidity of CMD spread was driven primarily by the whitefly population. A simple approach to CMD control is to spray pesticide. However, this may not be economical as more efficient pesticide is also more costly. It is therefore necessary to analyze the cost-effectiveness of spraying as well as its effectiveness.

Table 4. Operating cost of spray pesticide policy.

Operating cost	Cost per unit	Unit per week per 15,000 m^2	Total cost per week	
			$K = 15,000$	$K = 10,000$
(1) Labor	$10/labor/7,500 m^2	2 labors	$20	$13.333
(2) Pesticide spray				
Type I $\epsilon = 0.05$	$10/kg.	2 kg.	$20	$13.333
Type II $\epsilon = 0.10$	$20/kg.	2 kg.	$40	$26.667
Type III $\epsilon = 0.15$	$50/kg.	2 kg.	$100	$66.667

We simulated the three control strategies shown in Table 4, representing pesticide sprays with effectiveness of 5%, 10% and 15%. A whitefly control target (g) of 5% per day was set. We then determined the cost-effectiveness of using each spray. Table 4 shows the operating costs. Two kilograms of pesticide are sprayed once a week, requiring two laborers at a cost of $10 each per 7,500 m^2. The operating costs are shown in the final column. The Cost-Effectiveness Ratio (CER) of [39] is then applied. CER is the ratio of total control costs to yield loss averted, and is used to measure the economic value of an intervention (Eq (6.3)).

$$\text{CER} = \frac{\text{total control costs}}{\text{yield loss averted}}. \tag{6.3}$$

The optimal policy minimizes the CER.

Figure 6. Infected whitefly with control strategy in Scenario 1.
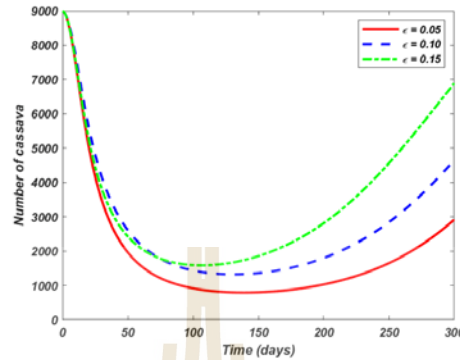
Figure 7. Healthy cassava with control strategy in Scenario 1.
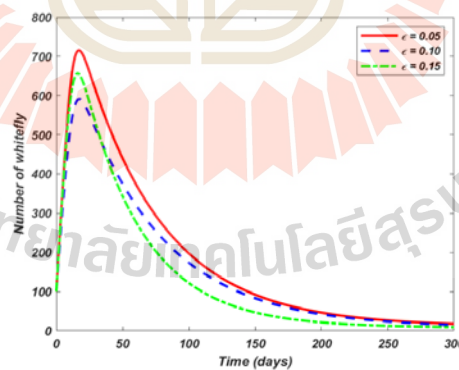
6.2.1. Scenario 1: maximum plantation capacity 15,000 m^2

The simulation used the parameter values given in Table 1. The numerical results in Figures 6 and 7 show that, when the three control strategies were applied, the increase in the healthy cassava population and decrease in the infected whitefly population tracked the efficiency of the pesticide spray. This gave a yield of 1173 tubers when no control strategy was applied. Infection of 518, 1221 and 1851 tubers were averted when Type I, II and III sprays were used. This represents a significant increase in profit. We then used CER to compare the cost-effectiveness of the three control strategies.

The CERs were calculated from Eq (6.3):

$$\text{CER(I)} = \frac{1,600}{518}, \quad \text{CER(II)} = \frac{2,400}{1,221}, \quad \text{and} \quad \text{CER(III)} = \frac{4,800}{1,851}.$$

Table 5 compares the cost-effectiveness. The sixth column gives the CER of each approach for $K = 15,000$, where a smaller number represents a more desirable outcome. As can be seen, the Type II spray yielded the greatest overall economic benefit. This result provides policymakers with a useful tool for optimizing their control strategies.

Table 5. CER of control policies for K of 15,000 m^2 (Sce.1) and 10,000 m^2 (Sce.2).

Pesticide spray	Yields infection averted		Total cost		CER	
	Sce.1	Sce.2	Sce.1	Sce.2	Sce.1	Sce.2
Type I	518	154	$1600	$1067	3.088	6.942
Type II	1,221	449	$2400	$1600	1.965	3.567
Type III	1851	777	$4800	$3200	2.593	4.121

6.2.2. Scenario 2: maximum plantation capacity 10,000 m^2

We next simulated the strategy with plantation capacity $K = 10,000$, using the same parameters. The results are shown in Figures 8 and 9. The harvests of healthy tubers were 714 with no control, 868

with Type I spray, 1163 with Type II, and 1491 with Type III. Equation (6.3) was used to identify the most cost-effective policy.
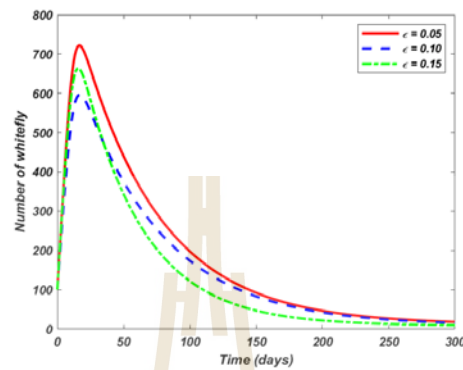
Figure 8. Infected whitefly with control strategy in Scenario 2.
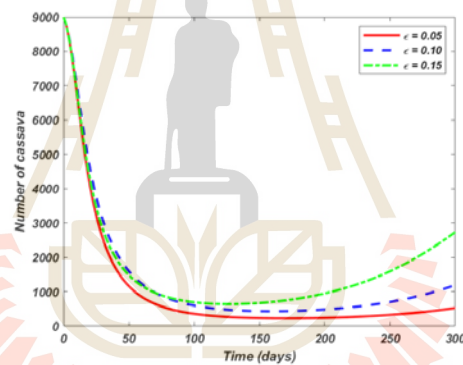
Figure 9. Healthy cassava with control strategy in Scenario 2.

The final column of Table 5 confirms that Type II spraying yielded the greatest economic benefit. However, this strategy was less cost-effective when applied to the smaller plantation as the whitefly density was higher.

7. Discussion

In this study, we modeled control of a CMD outbreak driven both by whitefly transmission and planting of infected cuttings. From an epidemiological perspective, $\mathscr{R}_0 < 1$ is a sufficient condition for eradication of the disease from a cassava population. The Routh-Hurwitz criterion confirmed that E_0 was locally-asymptotically-stable when $\mathscr{R}_0 < 1$, becoming unstable when $\mathscr{R}_0 > 1$. E_0 was globally-

asymptotically-stable if $\mathcal{R}_0 \leq 1$, while E_1 was globally-asymptotically-stable if $\mathcal{R}_0 > 1$, as confirmed by application of Lyapunov's method and LaSalle's invariance principle.

Our goal was to clarify the vectors that determine the severity of a CMD outbreak. To achieve this, we modeled increases in latent cassava due to whitefly transmission and due to planting of infected cuttings. By identifying the parameters that most affect the stability of the system, we hoped to optimize policy design. A sensitivity analysis determined that the most critical factor in disease spread was the presence of whitefly. We then sought to identify the most cost-effective pesticide for whitefly elimination. Numerical simulations showed that an increase in the death rate of whitefly through spraying was associated with a reduction in the CMD infection rate, and that the efficacy of the pesticide was key to control of the whitefly population. However, the increase in yield had to be offset against the cost of spraying.

We compared the cost-effectiveness of three pesticide sprays to determine the optimal balance between input cost and yield. The CER showed that Type II spraying was the most cost-effective in both scenarios, and particularly in Scenario 2. Whitefly population control was more costly in a smaller plantation, where the whitefly density was higher and CMD spread more rapidly.

The effects of rouging of infected plants should be investigated further, as should the effect of combining pesticide treatment with replanting. This may make spraying less efficient, thereby encouraging spread of CMD. Development of resistant strains is an alternative approach. However, it is typically costly and time consuming, and may also reduce the population of beneficial insects. Mathematical models may be used to compare such strategies to identify those that are most cost-effective in the real world.

8. Conclusions

We developed a mathematical model to clarify the dynamics of CMD spread. The normalized forward sensitivity index of the reproduction number was used to compare the relative contribution of different factors to a CMD outbreak. We found that the two most important were the death rate of whitefly and the number of cassava plants visited. We also identified the most cost-effective policy for reducing the whitefly population using numerical simulations. CER was used to compare the economic effectiveness of three spraying strategies in farms of different sizes. The results may help stakeholders, including cassava farmers and government agencies, develop optimal policies for control of CMD outbreaks. This should increase yields, income, and profits.

Acknowledgments

Conflict of interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

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APPENNDIX B

MATLAB CODE
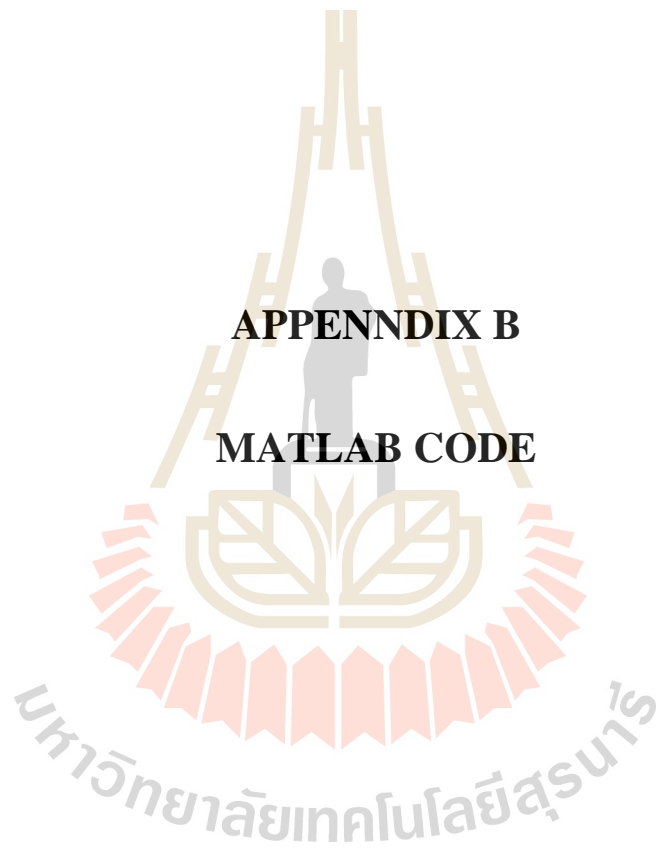
```matlab
%The CMD outbreak model - With tolerant and latent
clc;
clear all;

test = -1;

%Step size
    a = 1;
    a2 = a/2;
    T = 300;
    t = linspace(0,T,T+1);

%State variables
    S_T = zeros(1,T+1);
    S_H = zeros(1,T+1);
    E_H = zeros(1,T+1);
    I_H = zeros(1,T+1);
    S_V = zeros(1,T+1);
    I_V = zeros(1,T+1);

%Control variables
    u1 = zeros(1,T+1);
    u2 = zeros(1,T+1);
    u3 = zeros(1,T+1);

%Adjoint system
    L1 = zeros(1,T+1);
    L2 = zeros(1,T+1);
    L3 = zeros(1,T+1);
    L4 = zeros(1,T+1);
    L5 = zeros(1,T+1);
    L6 = zeros(1,T+1);

%Parameters of the model
    %Host parameters
    h = 0.003; beta = 0.008; r_H = 0.05; r_R = 0.025;
    k_1 = 0.5; k_2 = 0.2;
    %k_1 = 0.7; k_2 = 0.2; %(without tolerant cuttings)

    %Vector parameters
    Lambda = 0.2; mu = 0.0142; L = 200;

    %Pathogen parameters
    p1 = 0.008;
    p2 = 0.001;
```

```
    p3 = 0.1;
    p4 = 0.008;

%Efficiently parameters
gamma = 0.03;
epsilon = 0.2;

%Controls variables
    %u1=0;
    %u2=0;
    %u3=0;

%Control costs and Weight constant
    A0 = 1.000; A1 = 0.003; A2 = 0.001; A3 = 0.001; A4 = 0.001;

%Initial values
    %S_T(1) = 0; %(without tolerant cuttings)
    S_T(1) = 0.2;
    S_H(1) = 0.2;
    E_H(1) = 0.1;
    I_H(1) = 0;
    S_V(1) = 100;
    I_V(1) = 50;

%Final conditions
    L1(T+1) = 0;
    L2(T+1) = 0;
    L3(T+1) = 0;
    L4(T+1) = 0;
    L5(T+1) = 0;
    L6(T+1) = 0;

while(test < 0)
    %ODEs
    fS_T = @(S_T,S_H,E_H,I_H,S_V,I_V,u1,u2,u3) r_R*(1 - S_T/k_2)*S_T -
p2*S_T*I_V - h*S_T;
    fS_H = @(S_T,S_H,E_H,I_H,S_V,I_V,u1,u2,u3) r_H*(1-(S_H+E_H+I_H)/k_1)*S_H -
p1*S_H*I_V - h*S_H;
    fE_H = @(S_T,S_H,E_H,I_H,S_V,I_V,u1,u2,u3) r_H*(1-(S_H+E_H+I_H)/k_1)*p3*(1-
u3)*E_H + p2*S_T*I_V + p1*S_H*I_V - (beta + h)*E_H;
    fI_H = @(S_T,S_H,E_H,I_H,S_V,I_V,u1,u2,u3) beta*E_H - (gamma*u2 + h)*I_H;
    fS_V = @(S_T,S_H,E_H,I_H,S_V,I_V,u1,u2,u3) Lambda*(1-(S_V+I_V)/L)*(S_V+I_V)
- p4*S_V*(E_H+I_H) - (epsilon*u1 + mu)*S_V;
    fI_V = @(S_T,S_H,E_H,I_H,S_V,I_V,u1,u2,u3) p4*S_V*(E_H+I_H) - (epsilon*u1 +
mu)*I_V;
    %Adioint equations
```

```matlab
    fL1 = @(S_T,S_H,E_H,I_H,S_V,I_V,u1,u2,u3,L1,L2,L3,L4,L5,L6) -L1*(r_R*(1-
(2*S_T/k_2)) - (p2*I_V + h)) - L3*p2*I_V;
    fL2 = @(S_T,S_H,E_H,I_H,S_V,I_V,u1,u2,u3,L1,L2,L3,L4,L5,L6) -L2*(r_H*(1-
(2*S_H+E_H+I_H)/k_1) - (p1*I_V + h)) + L3*((r_H*p3*(1-u3)*E_H/k_1) - p1*I_V);
    fL3 = @(S_T,S_H,E_H,I_H,S_V,I_V,u1,u2,u3,L1,L2,L3,L4,L5,L6) L2*r_H*S_H/k_1
- L3*(r_H*(1-((S_H + 2*E_H + I_H)/k_1))*p3*(1-u3) - (beta + h)) - L4*beta + (L5-
L6)*p4*S_V;
    fL4 = @(S_T,S_H,E_H,I_H,S_V,I_V,u1,u2,u3,L1,L2,L3,L4,L5,L6) -A0 +
L2*(r_H*S_H/k_1) + L3*r_H*p3*(1-u3)*E_H/k_1 + L4*(gamma*u2 + h) + (L5-
L6)*p4*S_V;
    fL5 = @(S_T,S_H,E_H,I_H,S_V,I_V,u1,u2,u3,L1,L2,L3,L4,L5,L6) -L5*(Lambda*(1-
(2*(S_V+I_V)/L)) - (p4*(E_H+I_H) + epsilon*u1 + mu)) - L6*p4*(E_H+I_H);
    fL6 = @(S_T,S_H,E_H,I_H,S_V,I_V,u1,u2,u3,L1,L2,L3,L4,L5,L6) (L1 -
L3)*p2*S_T + (L2 - L3)*p1*S_H - L5*Lambda*(1-(2*(S_V+I_V)/L)) + L6*(epsilon*u1 +
mu);
 for i = 1:T
    %k1
    k1S_T = fS_T(S_T(i)            ,S_H(i)               ,E_H(i)
,I_H(i)           ,S_V(i)             ,I_V(i)               ,u1(i)
,u2(i)         ,u3(i));
    k1S_H = fS_H(S_T(i)            ,S_H(i)               ,E_H(i)
,I_H(i)           ,S_V(i)             ,I_V(i)               ,u1(i)
,u2(i)         ,u3(i));
    k1E_H = fE_H(S_T(i)            ,S_H(i)               ,E_H(i)
,I_H(i)           ,S_V(i)             ,I_V(i)               ,u1(i)
,u2(i)         ,u3(i));
    k1I_H = fI_H(S_T(i)            ,S_H(i)               ,E_H(i)
,I_H(i)           ,S_V(i)             ,I_V(i)               ,u1(i)
,u2(i)         ,u3(i));
    k1S_V = fS_V(S_T(i)            ,S_H(i)               ,E_H(i)
,I_H(i)           ,S_V(i)             ,I_V(i)               ,u1(i)
,u2(i)         ,u3(i));
    k1I_V = fI_V(S_T(i)            ,S_H(i)               ,E_H(i)
,I_H(i)           ,S_V(i)             ,I_V(i)               ,u1(i)
,u2(i)         ,u3(i));
    %k2
    k2S_T = fS_T(S_T(i)+a2*k1S_T    ,S_H(i)+a2*k1S_H      ,E_H(i)+a2*k1E_H
,I_H(i)+a2*k1I_H      ,S_V(i)+a2*k1S_V      ,I_V(i)+a2*k1I_V      ,u1(i)+a2
,u2(i)+a2      ,u3(i)+a2);
    k2S_H = fS_H(S_T(i)+a2*k1S_T    ,S_H(i)+a2*k1S_H      ,E_H(i)+a2*k1E_H
,I_H(i)+a2*k1I_H      ,S_V(i)+a2*k1S_V      ,I_V(i)+a2*k1I_V      ,u1(i)+a2
,u2(i)+a2      ,u3(i)+a2);
    k2E_H = fE_H(S_T(i)+a2*k1S_T    ,S_H(i)+a2*k1S_H      ,E_H(i)+a2*k1E_H
,I_H(i)+a2*k1I_H      ,S_V(i)+a2*k1S_V      ,I_V(i)+a2*k1I_V      ,u1(i)+a2
,u2(i)+a2      ,u3(i)+a2);
```

```
    k2I_H = fI_H(S_T(i)+a2*k1S_T      ,S_H(i)+a2*k1S_H      ,E_H(i)+a2*k1E_H
,I_H(i)+a2*k1I_H    ,S_V(i)+a2*k1S_V     ,I_V(i)+a2*k1I_V     ,u1(i)+a2
,u2(i)+a2    ,u3(i)+a2);
    k2S_V = fS_V(S_T(i)+a2*k1S_T      ,S_H(i)+a2*k1S_H      ,E_H(i)+a2*k1E_H
,I_H(i)+a2*k1I_H    ,S_V(i)+a2*k1S_V     ,I_V(i)+a2*k1I_V     ,u1(i)+a2
,u2(i)+a2    ,u3(i)+a2);
    k2I_V = fI_V(S_T(i)+a2*k1S_T      ,S_H(i)+a2*k1S_H      ,E_H(i)+a2*k1E_H
,I_H(i)+a2*k1I_H    ,S_V(i)+a2*k1S_V     ,I_V(i)+a2*k1I_V     ,u1(i)+a2
,u2(i)+a2    ,u3(i)+a2);
    %k3
    k3S_T = fS_T(S_T(i)+a2*k2S_T      ,S_H(i)+a2*k2S_H      ,E_H(i)+a2*k2E_H
,I_H(i)+a2*k2I_H    ,S_V(i)+a2*k2S_V     ,I_V(i)+a2*k2I_V     ,u1(i)+a2
,u2(i)+a2    ,u3(i)+a2);
    k3S_H = fS_H(S_T(i)+a2*k2S_T      ,S_H(i)+a2*k2S_H      ,E_H(i)+a2*k2E_H
,I_H(i)+a2*k2I_H    ,S_V(i)+a2*k2S_V     ,I_V(i)+a2*k2I_V     ,u1(i)+a2
,u2(i)+a2    ,u3(i)+a2);
    k3E_H = fE_H(S_T(i)+a2*k2S_T      ,S_H(i)+a2*k2S_H      ,E_H(i)+a2*k2E_H
,I_H(i)+a2*k2I_H    ,S_V(i)+a2*k2S_V     ,I_V(i)+a2*k2I_V     ,u1(i)+a2
,u2(i)+a2    ,u3(i)+a2);
    k3I_H = fI_H(S_T(i)+a2*k2S_T      ,S_H(i)+a2*k2S_H      ,E_H(i)+a2*k2E_H
,I_H(i)+a2*k2I_H    ,S_V(i)+a2*k2S_V     ,I_V(i)+a2*k2I_V     ,u1(i)+a2
,u2(i)+a2    ,u3(i)+a2);
    k3S_V = fS_V(S_T(i)+a2*k2S_T      ,S_H(i)+a2*k2S_H      ,E_H(i)+a2*k2E_H
,I_H(i)+a2*k2I_H    ,S_V(i)+a2*k2S_V     ,I_V(i)+a2*k2I_V     ,u1(i)+a2
,u2(i)+a2    ,u3(i)+a2);
    k3I_V = fI_V(S_T(i)+a2*k2S_T      ,S_H(i)+a2*k2S_H      ,E_H(i)+a2*k2E_H
,I_H(i)+a2*k2I_H    ,S_V(i)+a2*k2S_V     ,I_V(i)+a2*k2I_V     ,u1(i)+a2
,u2(i)+a2    ,u3(i)+a2);
    %k4
    k4S_T = fS_T(S_T(i)+a*k3S_T      ,S_H(i)+a*k3S_H      ,E_H(i)+a*k3E_H
,I_H(i)+a*k3I_H    ,S_V(i)+a*k3S_V      ,I_V(i)+a*k3I_V     ,u1(i)+a
,u2(i)+a    ,u3(i)+a);
    k4S_H = fS_H(S_T(i)+a*k3S_T      ,S_H(i)+a*k3S_H      ,E_H(i)+a*k3E_H
,I_H(i)+a*k3I_H    ,S_V(i)+a*k3S_V      ,I_V(i)+a*k3I_V     ,u1(i)+a
,u2(i)+a    ,u3(i)+a);
    k4E_H = fE_H(S_T(i)+a*k3S_T      ,S_H(i)+a*k3S_H      ,E_H(i)+a*k3E_H
,I_H(i)+a*k3I_H    ,S_V(i)+a*k3S_V      ,I_V(i)+a*k3I_V     ,u1(i)+a
,u2(i)+a    ,u3(i)+a);
    k4I_H = fI_H(S_T(i)+a*k3S_T      ,S_H(i)+a*k3S_H      ,E_H(i)+a*k3E_H
,I_H(i)+a*k3I_H    ,S_V(i)+a*k3S_V      ,I_V(i)+a*k3I_V     ,u1(i)+a
,u2(i)+a    ,u3(i)+a);
    k4S_V = fS_V(S_T(i)+a*k3S_T      ,S_H(i)+a*k3S_H      ,E_H(i)+a*k3E_H
,I_H(i)+a*k3I_H    ,S_V(i)+a*k3S_V      ,I_V(i)+a*k3I_V     ,u1(i)+a
,u2(i)+a    ,u3(i)+a);
```

```matlab
    k4I_V = fI_V(S_T(i)+a*k3S_T      ,S_H(i)+a*k3S_H      ,E_H(i)+a*k3E_H
,I_H(i)+a*k3I_H      ,S_V(i)+a*k3S_V      ,I_V(i)+a*k3I_V      ,u1(i)+a
,u2(i)+a      ,u3(i)+a);

    %Update states
    S_T(i+1) = S_T(i) + (a/6)*(k1S_T + 2*k2S_T + 2*k3S_T + k4S_T);
    S_H(i+1) = S_H(i) + (a/6)*(k1S_H + 2*k2S_H + 2*k3S_H + k4S_H);
    E_H(i+1) = E_H(i) + (a/6)*(k1E_H + 2*k2E_H + 2*k3E_H + k4E_H);
    I_H(i+1) = I_H(i) + (a/6)*(k1I_H + 2*k2I_H + 2*k3I_H + k4I_H);
    S_V(i+1) = S_V(i) + (a/6)*(k1S_V + 2*k2S_V + 2*k3S_V + k4S_V);
    I_V(i+1) = I_V(i) + (a/6)*(k1I_V + 2*k2I_V + 2*k3I_V + k4I_V);
end
for i = 1:T
    j = T + 2 -i;

    %Adjoint
    %k1
    k1L1 = fL1(S_T(j)        ,S_H(j)        ,E_H(j)        ,I_H(j)
,S_V(j)        ,I_V(j)        ,u1(j)        ,u2(j)        ,u3(j)        ,L1(j)
,L2(j)        ,L3(j)        ,L4(j)        ,L5(j)        ,L6(j));
    k1L2 = fL2(S_T(j)        ,S_H(j)        ,E_H(j)        ,I_H(j)
,S_V(j)        ,I_V(j)        ,u1(j)        ,u2(j)        ,u3(j)        ,L1(j)
,L2(j)        ,L3(j)        ,L4(j)        ,L5(j)        ,L6(j));
    k1L3 = fL3(S_T(j)        ,S_H(j)        ,E_H(j)        ,I_H(j)
,S_V(j)        ,I_V(j)        ,u1(j)        ,u2(j)        ,u3(j)        ,L1(j)
,L2(j)        ,L3(j)        ,L4(j)        ,L5(j)        ,L6(j));
    k1L4 = fL4(S_T(j)        ,S_H(j)        ,E_H(j)        ,I_H(j)
,S_V(j)        ,I_V(j)        ,u1(j)        ,u2(j)        ,u3(j)        ,L1(j)
,L2(j)        ,L3(j)        ,L4(j)        ,L5(j)        ,L6(j));
    k1L5 = fL5(S_T(j)        ,S_H(j)        ,E_H(j)        ,I_H(j)
,S_V(j)        ,I_V(j)        ,u1(j)        ,u2(j)        ,u3(j)        ,L1(j)
,L2(j)        ,L3(j)        ,L4(j)        ,L5(j)        ,L6(j));
    k1L6 = fL6(S_T(j)        ,S_H(j)        ,E_H(j)        ,I_H(j)
,S_V(j)        ,I_V(j)        ,u1(j)        ,u2(j)        ,u3(j)        ,L1(j)
,L2(j)        ,L3(j)        ,L4(j)        ,L5(j)        ,L6(j));
    %k2
    k2L1 = fL1(S_T(j)+a2        ,S_H(j)+a2        ,E_H(j)+a2        ,I_H(j)+a2
,S_V(j)+a2        ,I_V(j)+a2        ,u1(j)+a2        ,u2(j)+a2        ,u3(j)+a2
,L1(j)+a2*k1L1        ,L2(j)+a2*k1L2        ,L3(j)+a2*k1L3        ,L4(j)+a2*k1L4
,L5(j)+a2*k1L5        ,L6(j)+a2*k1L6);
    k2L2 = fL2(S_T(j)+a2        ,S_H(j)+a2        ,E_H(j)+a2        ,I_H(j)+a2
,S_V(j)+a2        ,I_V(j)+a2        ,u1(j)+a2        ,u2(j)+a2        ,u3(j)+a2
,L1(j)+a2*k1L1        ,L2(j)+a2*k1L2        ,L3(j)+a2*k1L3        ,L4(j)+a2*k1L4
,L5(j)+a2*k1L5        ,L6(j)+a2*k1L6);
    k2L3 = fL3(S_T(j)+a2        ,S_H(j)+a2        ,E_H(j)+a2        ,I_H(j)+a2
,S_V(j)+a2        ,I_V(j)+a2        ,u1(j)+a2        ,u2(j)+a2        ,u3(j)+a2
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     ,L1(j)+a2*k1L1   ,L2(j)+a2*k1L2   ,L3(j)+a2*k1L3   ,L4(j)+a2*k1L4
,L5(j)+a2*k1L5   ,L6(j)+a2*k1L6);
     k2L4 = fL4(S_T(j)+a2     ,S_H(j)+a2     ,E_H(j)+a2     ,I_H(j)+a2
,S_V(j)+a2      ,I_V(j)+a2     ,u1(j)+a2     ,u2(j)+a2     ,u3(j)+a2
,L1(j)+a2*k1L1   ,L2(j)+a2*k1L2   ,L3(j)+a2*k1L3   ,L4(j)+a2*k1L4
,L5(j)+a2*k1L5   ,L6(j)+a2*k1L6);
     k2L5 = fL5(S_T(j)+a2     ,S_H(j)+a2     ,E_H(j)+a2     ,I_H(j)+a2
,S_V(j)+a2      ,I_V(j)+a2     ,u1(j)+a2     ,u2(j)+a2     ,u3(j)+a2
,L1(j)+a2*k1L1   ,L2(j)+a2*k1L2   ,L3(j)+a2*k1L3   ,L4(j)+a2*k1L4
,L5(j)+a2*k1L5   ,L6(j)+a2*k1L6);
     k2L6 = fL6(S_T(j)+a2     ,S_H(j)+a2     ,E_H(j)+a2     ,I_H(j)+a2
,S_V(j)+a2      ,I_V(j)+a2     ,u1(j)+a2     ,u2(j)+a2     ,u3(j)+a2
,L1(j)+a2*k1L1   ,L2(j)+a2*k1L2   ,L3(j)+a2*k1L3   ,L4(j)+a2*k1L4
,L5(j)+a2*k1L5   ,L6(j)+a2*k1L6);
     %k3
     k3L1 = fL1(S_T(j)+a2     ,S_H(j)+a2     ,E_H(j)+a2     ,I_H(j)+a2
,S_V(j)+a2      ,I_V(j)+a2     ,u1(j)+a2     ,u2(j)+a2     ,u3(j)+a2
,L1(j)+a2*k2L1   ,L2(j)+a2*k2L2   ,L3(j)+a2*k2L3   ,L4(j)+a2*k2L4
,L5(j)+a2*k2L5   ,L6(j)+a2*k2L6);
     k3L2 = fL2(S_T(j)+a2     ,S_H(j)+a2     ,E_H(j)+a2     ,I_H(j)+a2
,S_V(j)+a2      ,I_V(j)+a2     ,u1(j)+a2     ,u2(j)+a2     ,u3(j)+a2
,L1(j)+a2*k2L1   ,L2(j)+a2*k2L2   ,L3(j)+a2*k2L3   ,L4(j)+a2*k2L4
,L5(j)+a2*k2L5   ,L6(j)+a2*k2L6);
     k3L3 = fL3(S_T(j)+a2     ,S_H(j)+a2     ,E_H(j)+a2     ,I_H(j)+a2
,S_V(j)+a2      ,I_V(j)+a2     ,u1(j)+a2     ,u2(j)+a2     ,u3(j)+a2
,L1(j)+a2*k2L1   ,L2(j)+a2*k2L2   ,L3(j)+a2*k2L3   ,L4(j)+a2*k2L4
,L5(j)+a2*k2L5   ,L6(j)+a2*k2L6);
     k3L4 = fL4(S_T(j)+a2     ,S_H(j)+a2     ,E_H(j)+a2     ,I_H(j)+a2
,S_V(j)+a2      ,I_V(j)+a2     ,u1(j)+a2     ,u2(j)+a2     ,u3(j)+a2
,L1(j)+a2*k2L1   ,L2(j)+a2*k2L2   ,L3(j)+a2*k2L3   ,L4(j)+a2*k2L4
,L5(j)+a2*k2L5   ,L6(j)+a2*k2L6);
     k3L5 = fL5(S_T(j)+a2     ,S_H(j)+a2     ,E_H(j)+a2     ,I_H(j)+a2
,S_V(j)+a2      ,I_V(j)+a2     ,u1(j)+a2     ,u2(j)+a2     ,u3(j)+a2
,L1(j)+a2*k2L1   ,L2(j)+a2*k2L2   ,L3(j)+a2*k2L3   ,L4(j)+a2*k2L4
,L5(j)+a2*k2L5   ,L6(j)+a2*k2L6);
     k3L6 = fL6(S_T(j)+a2     ,S_H(j)+a2     ,E_H(j)+a2     ,I_H(j)+a2
,S_V(j)+a2      ,I_V(j)+a2     ,u1(j)+a2     ,u2(j)+a2     ,u3(j)+a2
,L1(j)+a2*k2L1   ,L2(j)+a2*k2L2   ,L3(j)+a2*k2L3   ,L4(j)+a2*k2L4
,L5(j)+a2*k2L5   ,L6(j)+a2*k2L6);
     %k4
     k4L1 = fL1(S_T(j)+a     ,S_H(j)+a     ,E_H(j)+a     ,I_H(j)+a
,S_V(j)+a      ,I_V(j)+a     ,u1(j)+a     ,u2(j)+a     ,u3(j)+a
,L1(j)+a*k3L1   ,L2(j)+a*k3L2   ,L3(j)+a*k3L3   ,L4(j)+a*k3L4
,L5(j)+a*k3L5   ,L6(j)+a*k3L6);
     k4L2 = fL2(S_T(j)+a     ,S_H(j)+a     ,E_H(j)+a     ,I_H(j)+a
,S_V(j)+a      ,I_V(j)+a     ,u1(j)+a     ,u2(j)+a     ,u3(j)+a
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```
,L1(j)+a*k3L1    ,L2(j)+a*k3L2    ,L3(j)+a*k3L3    ,L4(j)+a*k3L4
,L5(j)+a*k3L5    ,L6(j)+a*k3L6);
     k4L3 = fL3(S_T(j)+a      ,S_H(j)+a      ,E_H(j)+a      ,I_H(j)+a
,S_V(j)+a      ,I_V(j)+a      ,u1(j)+a      ,u2(j)+a      ,u3(j)+a
,L1(j)+a*k3L1    ,L2(j)+a*k3L2    ,L3(j)+a*k3L3    ,L4(j)+a*k3L4
,L5(j)+a*k3L5    ,L6(j)+a*k3L6);
     k4L4 = fL4(S_T(j)+a      ,S_H(j)+a      ,E_H(j)+a      ,I_H(j)+a
,S_V(j)+a      ,I_V(j)+a      ,u1(j)+a      ,u2(j)+a      ,u3(j)+a
,L1(j)+a*k3L1    ,L2(j)+a*k3L2    ,L3(j)+a*k3L3    ,L4(j)+a*k3L4
,L5(j)+a*k3L5    ,L6(j)+a*k3L6);
     k4L5 = fL5(S_T(j)+a      ,S_H(j)+a      ,E_H(j)+a      ,I_H(j)+a
,S_V(j)+a      ,I_V(j)+a      ,u1(j)+a      ,u2(j)+a      ,u3(j)+a
,L1(j)+a*k3L1    ,L2(j)+a*k3L2    ,L3(j)+a*k3L3    ,L4(j)+a*k3L4
,L5(j)+a*k3L5    ,L6(j)+a*k3L6);
     k4L6 = fL6(S_T(j)+a      ,S_H(j)+a      ,E_H(j)+a      ,I_H(j)+a
,S_V(j)+a      ,I_V(j)+a      ,u1(j)+a      ,u2(j)+a      ,u3(j)+a
,L1(j)+a*k3L1    ,L2(j)+a*k3L2    ,L3(j)+a*k3L3    ,L4(j)+a*k3L4
,L5(j)+a*k3L5    ,L6(j)+a*k3L6);

    %Update adjoint
    L1(j-1) = L1(j) - (a/6)*(k1L1 + 2*k2L1 + 2*k3L1 + k4L1);
    L2(j-1) = L2(j) - (a/6)*(k1L2 + 2*k2L2 + 2*k3L2 + k4L2);
    L3(j-1) = L3(j) - (a/6)*(k1L3 + 2*k2L3 + 2*k3L3 + k4L3);
    L4(j-1) = L4(j) - (a/6)*(k1L4 + 2*k2L4 + 2*k3L4 + k4L4);
    L5(j-1) = L5(j) - (a/6)*(k1L5 + 2*k2L5 + 2*k3L5 + k4L5);
    L6(j-1) = L6(j) - (a/6)*(k1L6 + 2*k2L6 + 2*k3L6 + k4L6);
end

%Update u1 u2 u3
    u1 = max(0,min(1,(L5.*S_V + L6.*I_V).*(epsilon/(2.*A1))));
    u2 = max(0,min(1,(L4.*gamma.*I_H)/(2.*A2)));
    u3 = max(0,min(1,(1-((S_H+E_H+I_H)/k_1)).*(L3.*r_H.*p3.*E_H/(2.*A3))));

%Objective Function
H = A0.*I_H + A1.*u1.^2 + A2.*u2.^2 + A3.*u3.^2;
test = min(H);
total = A1.*u1.^2 + A2.*u2.^2 + A3.*u3.^2;
end
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BIOGRAPHY

Mr. Natdanai Chanlawong was born on the 23 of October, 1990 at Nakorn Ratchasima Province. He started his primary and secondary education at Assumption College Nakorn Ratchasima School. He received a Bachelor's degree in Industrial Engineering Institute of Engineering at Suranaree University of Technology in 2013. He received a Master's degree in Industrial Engineering Institute of Engineering at Suranaree University of Technology in 2016. From 2016 to 2021 he was a Ph.D student in the school of Industrial Engineering at Suranaree University of Technology.

His expertise includes the field of the logistics and supply chain management, optimizations, epidemic model, and systems engineering. During his Master's degree study, he presented one oral presentation entitled *"EMS Location Analysis to Minimize Service Risk"* at 10th SEATUC Symposium in Shibaura Institute of Technology at Tokyo, Japan. During his Doctoral degree study, he published one paper entitled of *"Reproduction number and sensitivity analysis of cassava mosaic disease spread for policy design"* Mathematical Biosciences and Engineering (MBE), Vol 18, Issue 5. (ISSN 1551-0018, Impact factor = 1.285, and Citescore = 2.1).