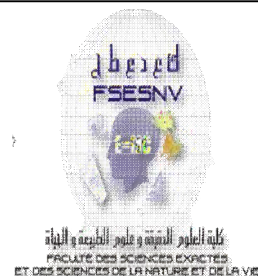




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Theme:

# **Mathematical Modeling and Analysis of Malaria Propagation**

Presented by:  
Boughrara Assia

Examination Committee:

|                          |      |                          |            |
|--------------------------|------|--------------------------|------------|
| Mr, Salem AbdelMalek     | Prof | Larbi Tébessi University | President  |
| Mr, Bahi Mohammed Cherif | MCA  | Larbi Tébessi University | Examiner   |
| Mr, Bouaziz khelifa      | MCA  | Larbi Tébessi University | Supervisor |

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# إهداء

الحمد لله الذي وفقنا لهذا وما كنا لنبلغ لولاه، الحمد لله حمدا كثيرا طيبا مباركا فيه كما ينبغي لجلال وجهه و عظيم سلطانه أما بعد أرفع هذا العمل هدية متواضعة

إلى من حباه الله بالنبل وصدق الاخلاق إلى من علمني أن العلم نور يضيء طريق الانسان وينير صيرته إلى الداعم الأكبر أيي أدامك الله لنا ظلا لا يغيب.

إلى الروح الطيبة والأمان الدائم إلى من زرعت فينا أسمى المبادئ وغرست أنبل القيم أيي.

إلى مؤنساتي الأربع مريم، خديجة، عائشة، إكرام.

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إلى من كانت لي عوناً و سنداً لا يغيب نورة.

إلى رفيقات الروح إكرام و ملاك.

إلى كل الذين رأوا النور في طريقي حين كنت أراه باهتا.

نُ لَيْسَ إِلَّا ۚ نُسَٰنَ إِلَّا مَا سَهَوْنَا (39) عَنِهٖ فُسَّوْا يُرَىٰ (40) سورة النجم.

# شكر و عرفان

الحمد لله أولاً ولاحقاً، وباطناً، إلى أن يبلغ الحمد منتهاه، الذي أنعم عليّ بنعمة السعي في طريق العلم ويسرّ لي إتمام هذا العمل.   
بَنَ قَالَ شَتَعْلَكُ: «تَمُّ لَا زَيْدَتُّكُمْ» [إبراهيم: 7] بالشكر تدوم النعم ولا يفوتني أن تحضر قدوتنا ومعلمنا الأول، محمدًا صلى الله عليه وسلم، الذي علمّ البشرية معنى الشكر والعرفان، فجزاه الله عنا خير ما جازى نبيًا عن أمته.   
أثقتكم بجزيل الشكر والامتنان إلى عائلتي العزيزة، التي كانت دومًا الداعم الأول والملمهم الأكبر، إلى صديقتي الوفية حسيبة التي شاركتني جميع مراحل المشوار وكانت لي سندًا لا يميل.   
كما أخصّ بالشكر والتقدير أساتذتي الكرام أعضاء اللجنة الدكتور سالم عبد المالك، رئيسا للجنة، والدكتور باهي محمد الشريف مناقشا لهذا العمل، راجية من الله أن يجزيكم عني خير الجزاء، وأن يبارك في علمكم وعطاءكم وكذلك إلى من شرفني بإشرافه على هذا العمل الدكتور خليفة بوعزيز لمّا قدّمه من توجيهات قيّمة، وصبره وحرصه على متابعة هذا العمل وعلى رقي تعامله و نبل أخلاقه، إلى كل أساتذه قسم الرياضيات والاعلام الالي وكل الأساتذة الذين كان لهم دور في مسيرتي التعليمية.   
يَضَلَمْنَا عَلَى كَثِيرٍ مِّنْ عِبَادِهِ الْمُؤْمِنِينَ» [المل: 15]

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## Abstract

The aim of this thesis is to study the dynamics model of the malaria parasite. The mathematical model was developed based on the SEIR model for humans and the SI model for mosquitoes. The basic reproduction number was calculated, and then the stability of the disease-free equilibrium point was studied. If  $R_0 > 1$ , it is unstable, but if  $R_0 < 1$ , it is locally asymptotically stable. This was proven using the Poincaré-Lyapunov theorem and globally asymptotically stable. This was proven using the Lyapunov function. The existence and uniqueness of the endemic equilibrium point were studied, and it was proven to be globally asymptotically stable if  $R_0 > 1$ , also using the Lyapunov function, and otherwise unstable.

### Key words

Basic Reproduction Number, Global and Local Asymptotic Stability, and Disease-Free Equilibrium, Endemic Equilibrium, Lyapunov Function, SEIR and SI Model.

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## Résumé

L'objectif de ce mémoire est d'étudier le modèle dynamique du parasite du paludisme. Le modèle mathématique a été développé à partir du modèle SEIR pour les humains et du modèle SI pour les moustiques. Le taux de reproduction de base a été calculé, puis la stabilité du point d'équilibre sans maladie a été étudiée. Si  $R_0 > 1$ , il est instable, mais si  $R_0 < 1$ , il est localement asymptotiquement stable. Ceci a été prouvé par le théorème de Poincaré-Lyapunov et globalement asymptotiquement stable. Ceci a été prouvé par la fonction de Lyapunov. L'existence et l'unicité du point d'équilibre endémique ont été étudiées, et il a été prouvé qu'il est globalement asymptotiquement stable si  $R_0 > 1$ , également en utilisant la fonction de Lyapunov, et instable sinon.

### **mots clés**

Nombre de Reproduction de Base, Stabilité Asymptotique Locale et Globale, Équilibre sans Maladie, Équilibre Endémique, Fonction de Lyapunov, Modèles SEIR et SI.

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## الملخص

الهدف من هذه المذكرة هو دراسة نموذج ديناميكيات انتقال طفيلي الملاريا بين البعوض و البشر حيث تم تطوير النموذج الرياضي بناء على نموذج SEIR بالنسبة للبشر و نموذج SI بالنسبة للبعوض , تم حساب العدد الاساسي للتكاثر و من ثم دراسة استقرار نقطة التوازن الخالي من المرض حيث إذا كان  $R_0 > 1$  فإنها تكون غير مستقرة أما إذا كان  $R_0 < 1$  فإنها تكون مستقرة بشكل غير متماثل محليا و تم اثبات ذلك باستخدام نظرية بوانكاري\_ليابونوف و تكون مستقرة بشكل غير متماثل عالميا و تم اثبات ذلك باستخدام دلالة ليابونوف ، تم دراسة وجود و وحدانية نقطة التوازن المتوطن و إثبات انه مستقر بشكل غير متماثل عالميا إذا كان  $R_0 > 1$  باستخدام دالة ليابونوف غير مسقرة غير ذلك .

## الكلمات المفتاحية:

العدد الأساسي للتكاثر، الاستقرار غير متماثل المحلي والعالمي، توازن خالٍ من المرض، التوازن المتوطن، دالة ليابونوف، نموذج SEIR و SI.

## LIST OF NOTATION

| Symbol/ Notation                                              | Descreption                                                                                 |
|---------------------------------------------------------------|---------------------------------------------------------------------------------------------|
|                                                               | The set of real numbers                                                                     |
|                                                               | The set of all nonnegative real numbers                                                     |
|                                                               | The set of all positive real numbers                                                        |
|                                                               | The set of all<br>N-tuples $x = (x_1, x_2, \dots, x_N)$                                     |
|                                                               | The set of complex numbers                                                                  |
|                                                               | An open bounded subset of $\mathbb{R}^N$                                                    |
| $D(A)$                                                        | The domain of an operator A                                                                 |
|                                                               | The inverse of a matrix M                                                                   |
| $\text{Tr}(M)$                                                | The trace of a matrix M                                                                     |
| $\det(M)$                                                     | The determinant of matrix M                                                                 |
|                                                               | The transpose of matrix M                                                                   |
| $\text{Re}(z)$                                                | The real part of a complex number z                                                         |
|                                                               | The partial derivative of $g: \mathbb{R}^N \rightarrow \mathbb{R}$<br>With respect to $x_k$ |
|                                                               | The nabla operator of a function $g: \mathbb{R}^N \rightarrow \mathbb{R}$                   |
| $\Delta g = \sum_{k=1}^N \frac{\partial^2}{\partial x_k^2} g$ | The Laplacian of a function $g: \mathbb{R}^N \rightarrow \mathbb{R}$                        |
| $C(\Omega)$                                                   | The space of continuous functions on $\Omega$                                               |
|                                                               | The space of continuously k-differentiable functions on $\Omega$                            |

|  |          |                                                          |
|--|----------|----------------------------------------------------------|
|  |          | The multiplication m-times of Banach space $\mathcal{X}$ |
|  |          | Norm in $L^2$                                            |
|  |          | Basic reproduction number                                |
|  | $J(u,v)$ | Jacobian matrix                                          |
|  | ODEs     | Ordinary differential equations                          |
|  | SIS      | Susceptible-infection-susceptible                        |
|  | SIR      | Susceptible-infection-recovered                          |
|  | SIRS     | Susceptible-infection-recovered -susceptible             |

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## General Introduction

Malaria is one of the world's most devastating infectious diseases, causing millions of infections and tens of thousands of deaths annually, particularly in tropical regions and low-income countries. This widespread prevalence of the disease is due to its unique and complex transmission mechanism. The *Anopheles* mosquito is the primary vector for the *Plasmodium* parasite, which causes malaria. Humans are infected when bitten by an infected mosquito, making it crucial to understand the parasite's life cycle and the mechanism of its spread between humans and mosquitoes.

Accordingly, mathematical modeling has emerged as an effective and essential tool for studying and understanding the dynamics of infectious diseases, including malaria. A mathematical model not only describes the progression of the disease over time, but also enables analysis of the impact of biological, environmental, and demographic factors, such as mosquito populations, bite rates, transmission rates, and acquired immunity. These models also allow us to predict how the disease will develop in the future and propose preventive or therapeutic strategies based on accurate scientific foundations.

Most models rely on differential equations that describe the continuous changes in the number of individuals infected or exposed to the disease. These equations are characterized by their ability to simulate reality with a high degree of accuracy, helping researchers understand the complex relationship between the various variables affecting the spread of infection. They also allow us to identify the conditions that lead to the extinction of the disease or its establishment as an endemic within a community.

This thesis is divided into three main chapters, in order to study the dynamics of malaria transmission through mathematical modeling. The first chapter contains the necessary concepts to understand the models studied. The second chapter is the scientific basis for mathematical modeling of malaria. It contains the biological and epidemiological foundations to understand the dynamics of the epidemic spread. It also deals with a historical overview of the development of mathematical models of malaria, with a presentation of the most important models such as the Ronald model and the MacDonald model. The third chapter focuses on analyzing a mathematical model that describes the transmission of malaria between humans and mosquitoes, based on the SEIR model for humans and the SI model for mosquitoes. It presents the formulation of the model and a study of the stability of equilibrium points to understand the basic strategies for combating the epidemic.

# Chapter 1

## Mathematical Prerequisites

### 1.1 General information on EDOs

In this entire section,  $J$  is an open interval of the real line  $\mathbb{R}$ ,  $U$  is an open subset of  $\mathbb{R}^n$  with  $n \geq 1$ . If  $f$  is a real-valued function taking values in  $\mathbb{R}^n$ , we denote by  $x'$  its derivative.

**Definition 1.1** (Differential equation)

Let  $f : J \times U \rightarrow \mathbb{R}^n$  be a function. A first-order differential equation associated with the function is defined as:

$$x'(t) = f(t, x(t)), \quad (1.1)$$

If the function does not explicitly depend on the variable (i.e., it is defined on  $U$  only), then the differential equation is called autonomous. Otherwise, it is called non-autonomous. If moreover  $f$  is affine, i.e., if  $f(t, x) = A(t)x + B(t)$  with  $A(t) \in M_n(\mathbb{R})$  and  $B(t) \in \mathbb{R}^n$ , for all  $t \in J$  then it is called a linear differential equation.

**Definition 1.2** (Local Solution)

A local solution of equation (1.1) is a pair  $(I, x)$ , where  $I \subset J$  is a non-empty open interval of  $\mathbb{R}$ , and  $x$  is a differentiable function from  $I$  to  $\mathbb{R}^n$ , satisfying:

- (i)  $(t, x(t)) \in J \times U$ , for all  $t \in I$ ,
- (ii)  $x'(t) = f(t, x(t))$ , for all  $t \in I$ .

The pair  $(I, x)$  is also called a **local solution** of (1.1).

**Definition 1.3** (Global solution)

A global solution of (1.1) is a solution defined over the entire interval  $J$ , i.e.,  $(J, x)$  is a solution of  $x' = f(t, x)$  where  $f : J \times U \rightarrow \mathbb{R}^n$ .

**Definition 1.4** (Cauchy problem)

Given a point  $(t_0, x_0) \in J \times U$ , the Cauchy problem consists in finding a solution  $(I, x)$  of (1.1) such that and .This problem is generally written as:

$$\begin{cases} x'(t) = f(t, x(t)), \\ x(t_0) = x_0, \end{cases}$$

**Theorem 1.1** (Positively Invariant Set)

A set  $\Omega$  is said to be **Positively invariant** if every solution  $x(t)$  such that  $x(0) \in \Omega$  remains in  $\Omega$  for all  $t \geq 0$ .

**Definition 1.5** (Globally Attractive Set)

A set  $A \subseteq \mathbb{R}^n$  is called a **globally attractive set** if, for every initial condition  $x(0) \in \mathbb{R}^n$ , the solution  $x(t)$  of dynamical system satisfies:

$$\lim_{t \rightarrow \infty} \text{dist}(x(t), A) = 0$$

That is, all trajectories starting anywhere in the phase space converge to the set  $A$  as time goes to infinity.

## 1.2 Existence and Uniqueness of Solutions

**Theorem 1.2** (Chauchy-Peano-Arzela)

Let  $(t_0, x_0) \in J \times U$  and suppose  $f : J \times U \rightarrow \mathbb{R}^n$  is continuous on  $(t_0, x_0)$ . Then there exists a solution to the **Cauchy Problem** associated with the differential equation (1.1) with the initial condition  $(t_0, x_0)$ . A function  $x$  is a solution to the **Cauchy problem** [6] if and only if

- (i) For all  $t \in I$ ,  $(t, x(t)) \in J \times U$ .
- (ii)  $x$  est continuous on  $I$ .

**Corollary 1.1** Assume  $f : J \times U \rightarrow \mathbb{R}^n$  is continuous then for every point  $(t_0, x_0) \in J \times U$ , there exists at least one **maximal solution**  $(I, x)$  to equation (1.1).

Furthermore, the domain of the maximal solution is an open interval of  $J$ . [10]

**Remark 1.1** Under the sole assumption of continuity we cannot guarantee the uniqueness of the solution. For this, we refer to the **Cauchy-Lipschitz Theorem**, which impose additional conditions to ensure uniqueness [10]

Next, we will state theorems that ensure not only **existence** but also the **uniqueness of the solution** to the **Cauchy problem** associated with the differential equation (1.1) with initial condition  $(t_0, x_0)$ . For this, we present a different notion of uniqueness as well as the **Lipschitz** character of the vector field  $f(t, x(t))$ , especially with respect to the second variable. [2].

**Definition 1.6** (Local Lipschitz continuity at a point)

Let  $(t_0, x_0) \in J \times U$ . We say that  $f : J \times U \rightarrow \mathbb{R}^n$  is **locally Lipschitz** with respect to its second variable at  $(t_0, x_0)$  if there exist  $T_0 > 0$  and  $k > 0$  such that:

$$\forall (t, x, y) \in ]t_0 - T_0; t_0 + T_0[ \times B(x_0, r_0)^2, \|f(t, x) - f(t, y)\| \leq k \|x - y\|.$$

**Definition 1.7** (Locally Lipschitzian in the second variable)

We say that  $f : J \times U \rightarrow \mathbb{R}^n$  is **locally Lipschitzian** with respect to its second variable on  $J \times U$  if for every point  $(t_0, x_0) \in J \times U$ ,  $f$  is locally Lipschitz with respect to the second variable at  $(t_0, x_0)$ .

**Definition 1.8** (Globally Lipschitzian)

A function  $f : J \times U \rightarrow \mathbb{R}^n$  is called **Lipschitz (or globally Lipschitzian)** with respect to its second variable if there exists a continuous function  $k : J \rightarrow \mathbb{R}^+$  such that :

$$\forall t \in J, \forall (y_1, y_2) \in U \times U, \|f(t, y_1) - f(t, y_2)\| \leq k(t) \|y_1 - y_2\|.$$

If, moreover, the function  $k$  is constant on  $J$ , then  $f$  is said to be **globally Lipschitzian** with respect to its second variable on  $J \times U$ , uniformly with respect to its first variable.

**Remark 1.2** if  $f$  is **globally Lipschitzian** with respect to its second variable on  $J \times U$ , then it is also **Locally Lipschitzian** with respect to its second variable on  $J \times U$ .

In practice, instead of checking if the function is locally Lipschitzian with respect to the second variable, we can check if the function is of class  $C^1$ . Hence, the following theorem is useful:

**Theorem 1.3** if  $f$  is of class  $C^1$  on  $J \times U$ , then  $f$  is **locally Lipschitz** with respect to its second variable on  $J \times U$ .

**Definition 1.9** (Local uniqueness)

We say that the **Cauchy problem** associated with equation (1.1) and initial condition  $(t_0, x_0) \in J \times U$  admits a **locally unique solution** if there exists a neighborhood  $J_0 \times U_0$  of  $(t_0, x_0)$  in  $J \times U$  such that the following **Cauchy problem**:

$$\begin{cases} x'(t) = \tilde{f}(t, x(t)), \\ x(t_0) = x_0, \end{cases}$$

admits a **unique solution**, where  $\tilde{f}$  is the restriction of  $f$  to  $J_0 \times U_0$ .

**Definition 1.10** (Global uniqueness)

We say that the **Cauchy problem** associated with equation (1.1) and initial condition  $(t_0, x_0) \in J \times U$  admits a **unique solution** if there exists a maximal solution  $(I, x)$  of this problem that is the extension of every other solution to the problem.

## 1.3 Equilibrium Points and Notion of Stability

We consider that the differential equation (1.2) is autonomous and written as:

$$x'(t) = f(x(t)), \quad (1.2)$$

with  $f : U \subset \mathbb{R}^n \rightarrow \mathbb{R}^n$  locally lipschitz on  $U$ . The objective is to ensure the existence and uniqueness of solution for Cauchy problems

### 1.3.1 Equilibrium Point

**Definition 1.11** An equilibrium point is any constant solution of (1.2)

When equation (1.2) models the dynamics of a population, an equilibrium corresponds well to the usual notion of a state of equilibrium, which means that when the system is in the state, then it remains there. In practice, it is known that only equilibrium states with certain properties are significant.

A point  $x^* \in X$  is called an **equilibrium point** [22] (also known as a critical point or stationary point) of system (1.2) if :

$$\forall x^* \in X, \quad f(x^*) = 0,$$

equilibrium points are trajectories of system (1.2) ; they correspond to constant solutions.

### 1.3.2 Local Stability

To understand the basic theories related to the stability of system ODEs, we must first find the Jacobian matrix, a matrix of partial derivatives of the first order. The localized behavior of system of equations near equilibrium is characterized by the Jacobian matrix when it involves many variables.

If we have this system of equations:

$$\begin{cases} f_1(x_1, x_2, \dots, x_n) = 0 \\ f_2(x_1, x_2, \dots, x_n) = 0 \\ \dots \\ f_n(x_1, x_2, \dots, x_n) = 0. \end{cases}$$

The Jacobian matrix denoted by  $J$  is given by

$$J = \begin{pmatrix} \frac{\partial f_1}{\partial x_1} & \frac{\partial f_1}{\partial x_2} & \dots & \frac{\partial f_1}{\partial x_n} \\ \frac{\partial f_2}{\partial x_1} & \frac{\partial f_2}{\partial x_2} & \dots & \frac{\partial f_2}{\partial x_n} \\ \dots & \dots & \dots & \dots \\ \frac{\partial f_n}{\partial x_1} & \frac{\partial f_n}{\partial x_2} & \dots & \frac{\partial f_n}{\partial x_n} \end{pmatrix}.$$

by evaluating the Jacobian matrix at an equilibrium point, we can obtain valuable information about the stability properties of the system by examining the eigenvalues of the matrix

**Definition 1.12** (Linearized System)[7]

A system is said to be the **linearized system** at  $\bar{x}$  if the system is  $\dot{x} = Df(\bar{x})x$ .

Where  $Df(\bar{x})$  is the **Jacobian matrix** (derivative of  $f$ ) evaluated at  $\bar{x}$

**Theorem 1.4** local stability (Poincare-Lyapunov Theorem)[7]

1\_If all eigenvalues of  $Df(\bar{x})$  have strictly negative real parts, then  $\bar{x}$  is **asymptotically stable**.

2\_If  $Df(\bar{x})$  has at least one eigenvalues with strictly positive real part, then  $\bar{x}$  is **unstable**.

### 1.3.3 Global Stability

Proving global stability in epidemiology means proving that the equilibrium point is stable not only locally but also for all possible initial conditions and disturbances. This ensures that the spread of the disease converges to the equilibrium state. We usually use Lyapunov functions to prove this.

#### Lyapunov Stability Theory

The stability of an equilibrium point  $x^*$  of equation (1.2) can be studied using the eigenvalues of the linearized part of  $f$  at  $x^*$ ,  $Df(x^*)$ . However, while this linearization method is attractive due to its ease of implementation, it does not allow us to conclude the stability or instability of the equilibrium point in all cases.

In 1892, the Russian mathematician **A. M. Lyapunov** introduced, in a General Problem of the Stability of Motion, a new criterion to study stability. He generalized the idea that, for a "well", there exists a norm  $\|\cdot\|$  on  $\mathbb{R}^n$  such that  $\|x(t) - x^*\|$  decreases for any solution  $x(t)$  close to  $x^*$ .

**Lyapunov** showed that certain functions, called **Lyapunov functions**, can be used to characterize stability. This method has become a widely used and effective tool to study the stability of equilibrium points, as well as the properties of attraction basins.

Let  $U$  be an open subset of  $\mathbb{R}^n$ . We are interested in the equilibrium points of a first-order autonomous differential equation defined on  $J \times U$ , as follows (1.2)

where  $f : J \times U \subset \mathbb{R} \times \mathbb{R}^n$  is a  $C^1$  class function, hence locally Lipschitz continuous on  $J \times U$ . This ensures the existence and uniqueness of solutions to Cauchy problems.

**Theorem 1.5** (Lyapunov function) [2]

Let  $x^*$  be an equilibrium solution of equation (1.2). Let  $\Omega$  be a neighborhood of  $x^*$  included in  $U$ , and  $V : \Omega \rightarrow \mathbb{R}$  a  $C^1$  function such that:

1.  $V(x^*) = 0$ .
2.  $\forall x \in \Omega \setminus \{x^*\}, V(x) > 0$ .
3.  $\forall x \in \Omega, \dot{V}(x) < 0$ .

Then  $x^*$  is **stable**.

**Theorem 1.6** (Lyapunov Stability Theorem) [2]

Suppose there exists a function  $V$  such that:

1.  $V$  is positive definite.
2.  $\dot{V}$  is negative definite.
3.  $V$  is radially unbounded.

Then the equilibrium point  $x^*$  is globally asymptotically stable for system (1.2).

The LaSalle theorem (1960) allows us to conclude global asymptotic stability of a system in the more general case, i.e., when  $\dot{V}(x) \leq 0$ .

**Theorem 1.7** (LaSalle's Invariant Principle)

Let  $V$  be a function from  $X \subset \mathbb{R}^n \rightarrow \mathbb{R}$ , and suppose that  $X$  is a compact positively invariant set for system (1.2) at  $x^*$ , such that:

1.  $V$  is a positive definite function of class  $C^1$ .

2.  $\dot{V}$  is negative semi-definite on  $X$  (i.e.,  $\dot{V}(x) \leq 0$  for all  $x \in X$ ).
3. The only solution of  $\dot{w} = f(w)$ ,  $V(w) = 0$  is  $w(t) = 0$  for all  $t \in T$ .

Then the equilibrium point  $x^*$  is globally asymptotically stable for system (1.2).

**Theorem 1.8** (Lasalle-Lyapunov Theorem) [7]

Let  $V : D \rightarrow \mathbb{R}^n$  be a Lyapunov function such that  $V(x) \leq 0$  for all  $x \in D$ . Let  $L = \{x \in D : \dot{V}(x) = 0\}$  and  $M$  the largest positively invariant set in  $L$ . then all solutions tend toward  $M$  as  $t \rightarrow \infty$ . In particular, if  $M$  reduces to a single point  $\{\bar{x}\}$ , alors  $\bar{x}$  globally asymptotically stable.

### 1.3.4 Descartes 'Rule

Let  $P$  be a polynomial of degree  $n$  defined by [9] [18]:

$$P(x) = a_0 + a_1x + a_2x^2 + \dots + a_nx^n, a_n \neq 0.$$

**Proposition 1.1** If all the coefficients of  $P$  are positive then  $P$  has no positive roots.

**Corollary 1.2** If all the coefficients of  $P$  are no-zero and alternate in sign, then  $P$  has no negative roots.

**Proposition 1.2** If there is exactly one sign change in the coefficients of  $P$ , then there is exactly one positive root.

**Theorem 1.9** (Descartes' Rule of Signs)

The number of positive real roots of a polynomial  $P$  with real coefficients does not exceed the number of sign changes in its ordered coefficients (ordered by descending powers). A zero coefficient is not counted as a sign change.

## 1.4 Some Useful Notions About Matrices

**Definition 1.13** ([6])

1. A matrix  $A \in M_{n,m}(\mathbb{R})$  is said to be positive [ resp. strictly positive ] and denoted  $A \geq 0$  [resp.  $A > 0$ ] if all its elements are non-negative or positive.
2. A matrix  $A \in M_{n,m}(\mathbb{R})$  is said to be negative [ resp. strictly negative ] and denoted  $A \leq 0$  [resp.  $A < 0$ ] if all its elements are non-positive or negative.

**Definition 1.14** Let  $A$  be a square matrix with real eigenvalues  $\lambda_1, \dots, \lambda_n \in \mathbb{C}$  of  $A$ , the rayon spectral of  $A$ , denoted  $\rho(A)$ , is defined by:

$$\rho(A) = \max_{1 \leq i \leq n} |\lambda_i|$$

The abscisse spectral of  $A$ , denoted  $s(A)$ , is defined by:

$$s(A) = \max_{1 \leq i \leq n} \operatorname{Re} |\lambda_i|$$

**Definition 1.15** we say that the matrix  $A$  is Hurwitz if all its eigenvalues have strictly negative real parts[2].

**Remark 1.3** every Hurwitz matrix is stable

## 1.5 Basic Reproduction Number

The basic reproduction number  $R_0$  (or reproduction rate) is a fundamental concept in epidemiology. This quantity is called  $R_0$  and represents the number of secondary infections resulting from a primary infection in a susceptible population. With the development of mathematical modeling methods in epidemiology,  $R_0$  has become a key concept in preventing epidemics[12]. It also considered an essential tool for understanding how and why the disease spreads in order to know how to control it.

### 1.5.1 Importance of the Basic Reproduction Number

The basic reproduction number  $R_0$  is a key indicator for assessing the dynamics and spread of infectious diseases, for to determine whether the disease will spread or not

•If  $R_0 < 1$  :

Each infected individual transmits the disease to less than one person on average, then the disease gradually dies out over time.

•If  $R_0 > 1$  :

Each infected individual transmits the disease to more than one person then the disease spreads and may lead to an epidemic.

And to determine the behavior of the system, this is done by studying the stability the stability of epidemiological balances, which are:

**1-DFE (Disease-freeEquilibrium):** A state in which there is no disease, and the entire population is either susceptible or recovered

**2-EE (Endemic Equilibrium):** A state in which a disease is stable in a population, remaining present at a certain rate without disappearing.

### 1.5.2 The Next Generation Matrix Method

The application of the next generation matrix method is done through the following steps [21]:

▷ **Model formulation:** Write the system of differential equations and identify the infected compartments.

▷ **Define the infection state vector**  $\psi(t)$  which contains the number of individuals in each infected compartment at time  $t$ .

▷ **Linearize the system at the DFE** to obtain the following equation:  $\dot{\psi}(t) = (F - V) \psi(t)$

•  $F$  : the matrix of new infection rates.

•  $V$  : the matrix of transfers and removals from infected compartments (recovery, death, transition).

Here,  $F$  is non-singular,  $V$ -matrix is assumed to be a non-singular  $M$ -matrix, capturing the internal flow within infected states.

▷ **Interpreting the system dynamically**

Solving the equation gives:  $\psi(t) = \exp(F - V)t \psi(0)$  If all eigenvalues of have negative real parts, the solution decays to zero and the disease dies out. However, instead of solving the system over time, we are interested in the total number of secondary infections caused by a single typical infected individual.

This is captured by the next generation matrix:  $K = FV^{-1}$  and the basic reproduction number is defined as the spectral radius of this matrix:  $R_0 = \rho(FV^{-1})$  and  $\rho(FV^{-1}) = \max\{|\lambda|, \lambda \in \sigma(FV^{-1})\}$ .

## 1.6 Reaction-Diffusion

Reaction-diffusion systems of partial differential equations have long piqued the curiosity of scientists, because they may be used to simulate practical situations, reaction-diffusion systems show how two processes result in the change of certain physical attributes in space and time. Reaction is the first process in which a quantity changes into another; diffusion is the second process in which the quantities spread out over space.

### 1.6.1 Model For Reaction diffusion

We study the population dynamic by merging both mechanisms after investigating different approaches to simulating dispersion and reproduction. Our goal is to track the population size's temporal and spatial behavior while taking various growth models, such logistic and exponential growth, into account. We concentrate in diffusion-reaction systems, where populations can

spread and expand at the same time. An example of a reaction-diffusion system in its most generic form is provided by

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

where

$$U(t, x) = (u_1(t, x), u_2(t, x), \dots, u_n(t, x))^T,$$

is the unknown vector function representing the interaction.

$$f(u) = (f_1(u), f_2(u), \dots, f_n(u))^T,$$

is a functional representing the interaction.

# Chapter 2

## Scientific Basis for Mathematical Modeling of Malaria

This chapter aims to provide the biological foundations necessary to understand the dynamics of malaria transmission. We begin by presenting the life cycle of *Anopheles* and details of its behavior and nutrition. Then we move on to clarifying the mechanisms of disease transmission from humans and mosquitoes and explaining the life cycle of the parasite. We also covered a historical overview of the development of previous mathematical models, presenting the most important of them.

### 2.1 *Anopheles* Mosquito Biology and Behavior

To understand how malaria spreads, one must first understand the life cycle and biological characteristics of some *Anopheles* parasites.

#### 2.1.1 Life Cycle of *Anopheles*

**Life Stages:** Like all mosquitoes, anophelines go through two phases. The first is aquatic and lasts 5-14 days depending on the species and the ambient temperature, and comprises the egg, larval and pupa stages. The second is aerial and involves the adult. The adult females can live up to a month (or more in a laboratory setting) but the majority live 2 weeks or less in nature. The adult stage is when the female *Anopheles* mosquito acts as a malaria vector [19] .

**Eggs:** One to two days after feeding, adult females can lay 50 to 300 eggs per spawning, and can lay 800 to 1000 eggs in their lifetime. The eggs are laid directly on the water surface, and

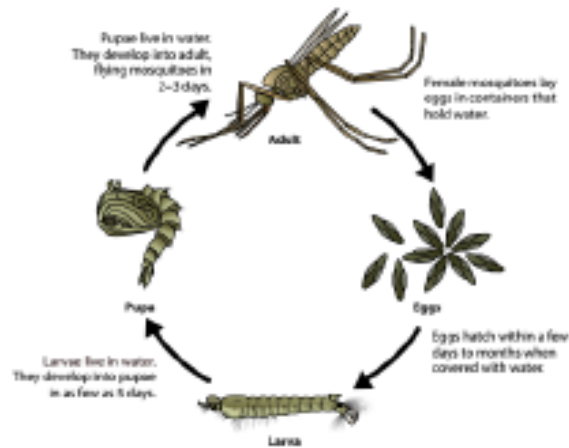


Figure 2.1: Life Cycle of the Anopheles Mosquito.

have one characteristic: they float on both sides of the body. The eggs are not resistant to drying out and hatch within 2-3 days.

**Larvae:** Each egg hatches into a larva that floats parallel to the water surface to breathe. It feeds on particles present in the water. The larvae are only 1 mm in size and undergo 3 molts until they reach a size of 5 mm by the fourth instar. Larvae occur in a wide variety of habitats, but most species prefer clean, unpolluted water. Larvae of *Anopheles gambiae* have been found in freshwater and brackish marshes, mangrove swamps, rice fields, grass ponds, tree gullies, canals, ditches, banks of streams and rivers, and small temporary rain pools. After the fourth instar, the larvae transform into an intermediate stage between larvae and adults, the pupa.

**Pupa:** When viewed from the side, the pupa is comma-shaped. Like the larvae, the pupae must frequently surface to breathe, which they do through a breathing tube in their cephalothorax. After a few days, the adult mosquito emerges from the pupa. The complete cycle from egg to adult takes *An. gambiae* usually 9 to 20 days.

### 2.1.2 Morphology and Feeding Habits

Mosquitoes are slender, long-legged insects that are easily identified by their long proboscis (sharp, piercing mouth parts) and scales on most of their bodies. Mosquitoes belong to the class Insecta, and therefore have the characteristic of having three pairs of legs. They belong to the order Diptera and, like other flies, have only one pair of wings.

The adult *Anopheles* mosquito has an elongated body with three parts: the head, thorax, and abdomen [19]:

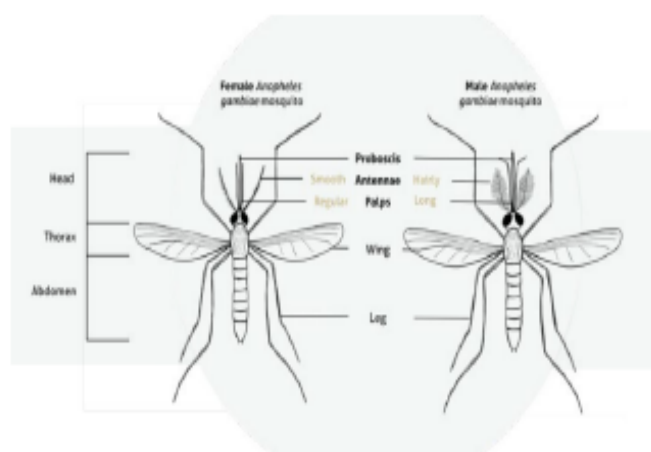


Figure 2.2: Morphological Comparison of Male and Female *Anopheles gambiae* Mosquitoes.

- **The head** is specialized for receiving sensory information and feeding. It contains the eyes and a pair of long, multi-jointed antennae. The antennae are important for detecting the scent of the host as well as the scent of the breeding grounds where the female lays her eggs. The head also has an elongated, forward-projecting trunk used for feeding and two sensory sensors (organs near the mouthparts).
- **The thorax** is specialized for locomotion. Three pairs of legs and a pair of wings are attached to it.
- **The abdomen** is specialized for food digestion and egg development. This segmented body part expands significantly as the female consumes blood. Over time, the blood is digested and becomes a source of protein for the production of eggs, which gradually fill the abdomen.

*Anopheles* mosquitoes are distinguished from other mosquitoes by their tactile organs (sensory organs near the mouthparts) that are as long as their proboscis, and by individual black and white scales on their wings. Adult *Anopheles* mosquitoes can also be identified by their typical resting posture: the abdomen of males and females is stretched upwards, rather than parallel to the surface on which they are lying.

The difference between male and female mosquitoes is Male mosquitoes have more flagella, or tiny hairs, on their antennae, so many that they appear noticeably dense to the naked eye. These flagella are important for male mosquitoes' hearing, which helps them find female mosquitoes. Female mosquitoes have antennae that are less dense and contain a variety of olfactory receptors that help them find food and blood sources for reproduction. Only female mosquitoes bite and transmit malaria.

The female feeds on sugars for energy but needs blood for the development of her eggs. They

usually bite between sunset and sunrise (6:00 PM to 6:00 AM). After feeding on blood, the female rests for two to three days in order to digest the blood and develop her eggs. Once the eggs are fully developed, the female lays them. This cycle repeats until the female dies.

### 2.1.3 Adult Behavior and Ecology

Adult mosquitoes usually mate within a few days of the pupal stage. Male birds form flocks at dusk, usually near village huts, and females fly into the flock to mate. To. Gambia females usually mate only once in their lifetime. Both males and females feed on nectar and other plant secretions. Only females feed on blood - males do not have the appropriate mouthparts.

Preferred sources for blood meals: The degree to which an *Anopheles* species favors feeding on humans or animals, including cattle, is a crucial behavioral component in the transmission of malaria. The malaria parasites are more likely to spread from person to person when *Anopheles* species prefer human blood. The majority of *Anopheles* mosquitoes do not only prefer to feed on humans or animals. Nonetheless, the main malaria vectors in Africa have a strong preference for human blood and are hence the most effective malaria vectors. *Anopheles gambiae* feeds at night, either exophagically (outdoors) or endophagically (indoors). Although some can rest outdoors in appropriate resting spots such burrows, animal sheds, and dense foliage, it prefers to rest indoors after blood eating.

In a lab setting, females can live for up to a month. Temperature and humidity affect their odds of surviving, but so does their capacity to successfully seek a blood meal while dodging host defenses. *Anopheles* typically lives for two weeks in ideal tropical circumstances, depending on natural climatic conditions. Although exceptional insects can fly up to 3–4 kilometers, adult *Anopheles* mosquitoes are believed to normally disseminate within communities across a few hundred meters [19] .

### 2.1.4 Mosquito Theory

The mosquito theory[14] illustrate the relationship between mosquito density and certain biological constants, and how these factors influence the long term stability or eradication of the disease.

This theory is divided into three key points:

- 1- The final prportion of endemic malaria cases is not related to the initial number of malaria cases among the infected individuals, but rather depends on constant conditions such as the number of mosquitoes and other factors. If these factors remain stable, the proportion of infected individuals will reach a steady state.

2- • If the number of anophes mosquito is very high, the disease will remain widespread in the community, with infection rates ranging between 0% and 100% , depending on the intensity of transmission.

• If the number of anopheles mosquito is low (for example, fewer than 40 mosquitoes per 100 people), the disease will gradually decline until it disappears.

• A negative infection rate is unrealistic in practice and is therefore considered zero.

3- Any slight change in factors such as the number of mosquitoes, the biting rate, or other constants leads to significant variations in malaria infection rates. This is known as the system's sensitivity, meaning that malaria control requires careful monitoring of these variables.

## 2.2 Modes of Transmission

Comprehending the malaria cycle facilitates an understanding of the disease's ways of transmission. Malaria is spread at night by the bite of a female *Anopheles* mosquito. Congenital transmission, transfusion, organ transplantation, and unintentional transmission among medical personnel handling tainted blood are among the additional forms of contamination made possible by the blood phase of the cycle. In reality, these transfers are extremely rare and have no bearing on the epidemiology [9].

## 2.3 The Malaria Cycle

The cycle occurs sequentially in the *Anopheles* mosquito (sexual phase in the definitive host) and humans (asexual phase in the intermediate host). The human cycle is divided into two parts[9]: The incubation period is clinically asymptomatic and is referred to as the hepatic or pre-erythrocytic phase (= exo-erythrocytic). The clinical phase of the disease is represented by the blood or erythrocytic phase.

In the water , the female mosquito lays her eggs, which grow into larvae , then pupae, and then into adult mosquitoes, under suitable climatic condition. The female looks for a blood meal to aid in the development of her eggs after mating. Humans, whether healthy or diseased, are bitten by her. The healthy individual then contracts malaria parasites from the female.

We illustrate the two disease cycle in this image:

### 2.3.1 In humans

The hepatic (= exo erythrocytic) schizogony:

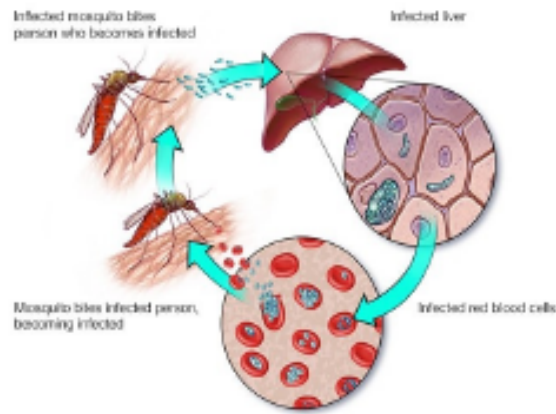


Figure 2.3: Malaria Transmission Cycle by an Infected Mosquito.

The female *Anopheles* injects sporozoites using its proboscis into the human's skin, lymph, and blood. The parasite is represented by these sporozoites. Some of them make it to the liver cells, but the majority are eliminated by phagocytic cells. They grow there into multinucleated pre-erythrocytic schizonts, which mature in one to two weeks. When it reaches the maturation stage, it bursts and releases thousands of merozoites into the blood.

The delayed relapses seen with *Plasmodium vivax* and *Plasmodium ovale* infections can be explained by the fact that some sporozoites may occasionally remain dormant in the liver.

#### **The erythrocytic schizogony :**

Merozoites enter red blood cells and mature into schizonts over the course of two to three days. This process causes the red blood cells to burst, releasing between 8 and 32 new merozoites. These newly released parasites then invade other red blood cells, starting the cycle all over again. As the number of parasites in the blood rises, the symptoms of the disease begin to appear — the patient develops a fever. This marks the clinical phase of the infection. Without treatment, the number of mature schizonts continues to grow, leading to the destruction of many red blood cells.

Following multiple cycles within red blood cells, some merozoites go through a ten-day sexual maturity period where they differentiate into either male or female gametes known as gametocytes. These gametocytes, which the mosquito absorbs following a bite and which enable the cycle to continue, stay in the circulation for ten to fifteen days.

### 2.3.2 In the Anopheles Female Mosquito

When a female Anopheles mosquito bites an infected person, it picks up the male and female gametes. Fertilization occurs between them to form a free-moving egg. This egg migrates, penetrates the mosquito's stomach wall, and attaches to its external surface. The egg matures, and the parasite cells multiply inside it, producing hundreds of sporozoites. These sporozoites migrate to the mosquito's salivary glands, where they are considered the infectious forms, and thus become ready to be injected into the human body during the next blood meal.[9] . The average lifespan of an Anopheles mosquito is 45 days, and the larval cycle stops when the temperature is below 16°C or above 32°C.[14]

## 2.4 History of Mathematical Models of Malaria Transmission

The use of mathematical modeling to understand malaria transmission goes back to the early 20th century. The pioneering work started with Ronald Ross in 1911 and was continued by researchers like Martini (1921), Lotka (1923), Moshkovskii (1950), and finally George MacDonald (1957), who made significant refinements to Ross's original models. Although Ross had been thinking about how malaria spreads and how to control it as early as 1902, it wasn't until 1908 that he published his first mathematical model on malaria. What we now refer to as the Ross-MacDonald model gained recognition around the same time as the launch of the Global Malaria Eradication Program (1955–1969). This model became foundational in developing prevention strategies for mosquito-borne diseases. MacDonald formalized much of the theory in 1950, with later contributions from Garret-Jones. Even before Ross's mathematical model, important discoveries had been made. In 1880, Charles Alphonse Laveran, a military doctor, identified malaria parasites in human blood. In 1897, Ronald Ross confirmed that Anopheles mosquitoes were responsible for transmitting the disease. Then in 1898–1899, Giovanni Batista Grassi described the full life cycle of these mosquitoes. Much later, Hawas et al. (2010) used DNA analysis to explore whether malaria, possibly in combination with a genetic disorder, was responsible for the death of Pharaoh Tutankhamun around 1324.

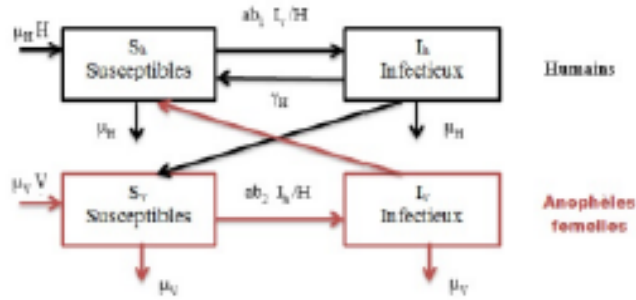


Figure 2.4: Graphic representation of the Ross Model.

## 2.5 Some Mathematical Models of Malaria

### 2.5.1 Ronald -Ross Model

Ronald Ross was among the first to publish a series of papers using mathematical functions to study malaria transmission in the early 1900s. He developed a simple model, now known as the classic "Ross model", which explained the relationship between mosquito populations and the incidence of malaria in humans. His model showed that reducing mosquito populations below a certain threshold—the transmission threshold—was sufficient to control malaria, a concept far ahead of its time[?] . In his work, he divided the human population into two compartments: Susceptible ( $S_h$ ) and Infected ( $I_h$ ). With the return of humans to the susceptible class, this is the therefore S-I-S type for human. He also divided the mosquito population into two compartments: ( $S_v$ ) and Infected ( $I_v$ ), which is an S-I type model for mosquitoes  $S_h(t)$  and  $S_v(t)$  represent the density of susceptible humans and susceptible mosquitoes, respectively.

The density of infected humans is denoted by  $I_h(t)$ , and that of infected mosquitoes by  $I_v(t)$ .

The mathematical model is given as :

$$\begin{cases} \frac{dS_H}{dt} = \mu_H H - \mu_H S_H - ab_1 \frac{I_V}{H} S_H + \gamma_H I_H. \\ \frac{dI_H}{dt} = ab_1 \frac{I_V}{H} S_H - (\mu_H + \gamma_H) I_H. \\ \frac{dS_V}{dt} = \mu_V V - \mu_V S_V - ab_2 \frac{I_H}{H} S_V. \\ \frac{dI_V}{dt} = ab_2 \frac{I_H}{H} S_V - \mu_V I_V. \end{cases}$$

The parametre are given in the following table :

|            |                                                                           |
|------------|---------------------------------------------------------------------------|
| $a$        | Biting rate on humans par unit of time.                                   |
| $b_1$      | Proportion of bites resulting in infection in humans.                     |
| $b_2$      | Proportion of bites through wich a susceptible mosquito becomes infected. |
| $\gamma_h$ | Recovery rate for humans.                                                 |
| $\mu_h$    | Mortality rate of humans.                                                 |
| $\mu_v$    | Mortality rate of mosquitoes.                                             |
| $H$        | Total human population.                                                   |
| $V$        | Total mosquitoes population.                                              |

The evolution of the fractionof individuals in the infected classes  $(I_H, I_V)$  was studied by Ronald Ross using two ordinary differential equations[22] :

$$\begin{cases} \frac{dx}{dt} = rab_1y(1-x) - mx, \\ \frac{dy}{dt} = ab_2x(1-y) - \mu_Vy, \end{cases}$$

$x$  : proportion of infected humans  $x = \frac{I_h}{H}$ .  
 $y$  : proportion of infected mosquitoes  $y = \frac{I_v}{V}$ .  
 $r$  : ratio of the number of female mosquitoes / humans  $r = \frac{V}{H}$  .  
 $m$  : average recovery rate for humans  $\mu_h + \gamma_h$ .

$x$  and  $y$  are proportions such that  $x, y \in [0, 1]$ .

### 2.5.2 Macdonald-Ross Model

The Macdonald model is based on the Ross model , he modified Ross's model by intregrating biological information of latency in the mosquito due to malaria parasite developement[?] , given that the parasite responsible for the disease spends approximately 10 days inside mosquitoes during its life cycle

Macdonald kept the same division of the human population as before and assumed that the vector population is divided as follows [22]:

- $S_v$  susceptible mosquitoes.
- $E_v$  exposed mosquitoes.
- $I_v$  infected mosquitoes.

Therefore, in this model the mosquito population is divided into three compartments  $(SEI)$  [?] . Its is noted that naturel birth and death rates in the human population cannot be neglected, because the time scale over which it evolves is much longer than that of the mosquito population. It is assumed that both the human and mosquito populations remain constant.

$$H = S_h + I_h \quad \text{and} \quad V = S_v + E_v + I_v$$

The mathematical model is given as:

$$\begin{cases} \frac{dx}{dt} = mbaz(t)(1 - x(t)) - \gamma x(t). \\ \frac{dy}{dt} = ac(t)(1 - y(t) - z(t)) - \mu y(t) - acx(t - \tau)(1 - y(t - \tau) - z(t - \tau)) \exp^{-\mu\tau}. \\ \frac{dz}{dt} = acx(t - \tau)(1 - y(t - \tau) - z(t - \tau)) \exp^{-\mu\tau} - \mu z(t). \end{cases}$$

where

$x$  : proportion of infected humans  $x(t) = \frac{I_H(t)}{H}$ .

$y$  : proportion of exposed mosquito  $y(t) = \frac{E_V(t)}{V}$ .

$z$  : proportion of infected mosquitoes  $z(t) = \frac{I_V(t)}{V}$ .

The parametre are given in the following table :

|          |                                                                                         |
|----------|-----------------------------------------------------------------------------------------|
| $m$      | number of mosquitoes per human.                                                         |
| $a$      | number of bites per mosquito per unit of time (time <sup>-1</sup> ).                    |
| $b$      | probability of transmission of infection from an infectious to a human per bite.        |
| $c$      | probability of transmission of infection from an infected human to a mosquito per bite. |
| $\gamma$ | recovery rate for humans.                                                               |
| $\mu$    | mosquito mortality rate (time <sup>-1</sup> ).                                          |
| $\tau$   | the latency period of mosquitoes (estimated between 5 and 15 days).                     |

### 2.5.3 Anderson and May Model

Anderson and May [?] introduced the incubation period of human infection into the Macdonald model, thus creating an additional category of “exposed” in humans, they also considered that the incubation period of the parasite inside the human host lasts 21 days, and introduced the exposed ( $E_h$ ) class in human population in their model. This divided the host population into

three compartments ( $S_h, E_h, I_h$ ), along with that in the mosquito population ( $S_v, E_v, I_v$ ). This, therefore, is a *SEIS* model for the human population, and the model consists of four differential equations describing the time evolution of both the exposed and infected classes for humans and mosquitoes ( $E_v, I_v, E_v, I_v$ ). A comparative study was conducted between the models of Ross (RR), Macdonald (MC), and Anderson-May (AM) regarding the spread of infections in humans and mosquitoes ( $I_h, I_v$ ). The results of this comparison showed that introducing incubation periods

for the parasites in both humans and mosquitoes not only reduces the long-term prevalence of both  $I_h$  and  $I_v$ , but also slows the rates of progression toward these final states of infection.

$$\left\{ \begin{array}{l} \frac{dE_h}{dt} = abmI_v(t)(1 - E_h(t) - I_h(t)) - \gamma E_h(t) - \mu E_h(t) \\ \quad - abmI_v(t - \tau_h)[1 - E_h(t - \tau_h) - I_h(t - \tau_h)] \exp^{-(\gamma + \mu_h)\tau_h} . \\ \frac{dI_h}{dt} = abmI_v(t - \tau_h)[1 - E_h(t - \tau_h) - I_h(t - \tau_h)] \exp^{-(\gamma + \mu_h)\tau_h} - \gamma I_h(t) - \mu_h I_h(t) . \\ \frac{dE_v}{dt} = acI_h(t)[1 - E_v(t) - I_v(t)] . \\ \quad - acI_h(t - \tau_v)[1 - E_v(t - \tau_v) - I_v(t - \tau_v)] \exp^{-\mu_v\tau_v} - \mu_v E_v(t) . \\ \frac{dI_v}{dt} = acI_h(t - \tau_v)[1 - E_v(t - \tau_v) - I_v(t - \tau_v)] \exp^{-\mu_v\tau_v} - \mu_v I_v(t) . \end{array} \right.$$

The parametre are given in the following table[22] :

|          |                                                                                         |
|----------|-----------------------------------------------------------------------------------------|
| $a$      | number of bites per mosquito per unit of time(time <sup>-1</sup> ).                     |
| $b$      | probability of transmission of infection from an infectious to a human per bite.        |
| $c$      | probability of transmission of infection from an infected human to a mosquito per bite. |
| $\gamma$ | average recovery rate for humans.                                                       |
| $m$      | number of mosquitoes per human(time <sup>-1</sup> ).                                    |
| $\mu_H$  | naturel mortality rate of humans (time <sup>-1</sup> ).                                 |
| $\mu_V$  | naturel mortality rate of mosquitoes (time <sup>-1</sup> ).                             |
| $\tau_V$ | the latency period for mosquitoes (estimated between 5 and 15 days).                    |
| $\tau_H$ | the latency period for mosquitoes (estimated between 10 and 100 days).                  |

### 2.5.4 Tumwiine and Mugisha Model

The model of Tumwiine and Mugisha is based is based on the *SIR* (Susceptible-Infected-Immune) model for the human population and the *SI* model for the mosquitoes population. Individuals in all classes have the same mortality rate. They exclude mosquitoes from the model once they no longer participate in the infection cycle. Their model takes the following form [17] [22] :

$$\left\{ \begin{array}{l} \frac{dS_h}{dt} = \lambda_h N_h - \frac{abS_h I_v}{N_h} + \nu I_H + \gamma R_h - \mu_h S_h . \\ \frac{dI_H}{dt} = \frac{abS_H I_v}{N_H} - \nu I_H - r I_h - \delta I_h - \mu_h I_h . \\ \frac{dR_H}{dt} = r I_h - \gamma R_h - \mu_h R_h . \\ \frac{dS_v}{dt} = \lambda_v N_v - \frac{acS_v I_h}{N_h} - \mu_v S_v . \\ \frac{dI_v}{dt} = \frac{acS_v I_h}{N_h} - \mu_v I_v . \end{array} \right.$$

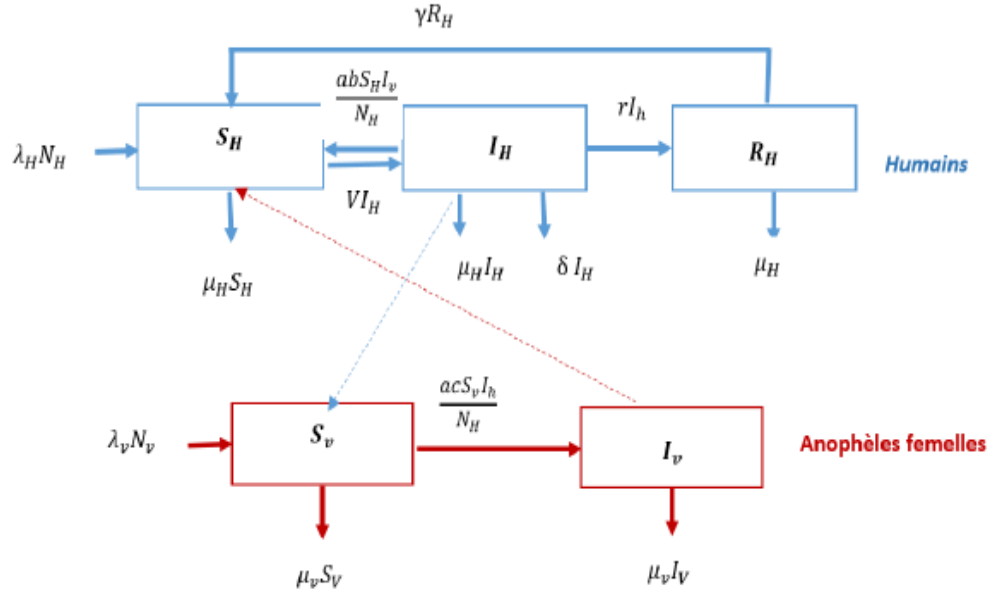


Figure 2.5: Graphical Representation of the Tumwiine Mugisha Model.

The total population sizes  $N_H$  and  $N_V$  can be determined by  $S_H + I_H + R_H = N_H$  and  $S_V + I_V = N_V$  or from the differential equations

$$\begin{cases} \frac{dN_H}{dt} = (\lambda_H - \mu_H)N_H - \delta I_H. \\ \frac{dN_v}{dt} = (\lambda_v - \mu_v)N_v. \end{cases}$$

Our model has the following variables and parameters :

|             |                                                                             |
|-------------|-----------------------------------------------------------------------------|
| $a$         | the average daily biting rate on man by a single mosquito (infection rate). |
| $b$         | the proportion of bites on man that produce an infection.                   |
| $c$         | the probability that a mosquito becomes infectious.                         |
| $m$         | number of female mosquitoes per human host.                                 |
| $\gamma$    | the per capita rate of loss of immunity in human hosts.                     |
| $r$         | the rate at which human hosts acquire immunity.                             |
| $\delta$    | the per capita death rate of infected human hosts due to the disease.       |
| $\nu$       | the rate of recovery of human hosts from the disease.                       |
| $\lambda_h$ | the per capita natural birth rate of humans.                                |
| $\lambda_v$ | the per capita natural birth rate of the mosquitoes.                        |
| $\mu_h$     | the per capita natural death rate of the humans.                            |
| $\mu_v$     | the per capita natural death rate of the mosquitoes.                        |

$S_h, I_h, R_h$  represent the density of susceptible, infected, and partially immune hosts.  $S_v, I_v$  represent the density of susceptible, infected mosquitoes. Tumwiine and Mugisha's model takes into account the possibility of transitions from the infected class to the immune class by adding a new term  $\gamma R_h$  to the immune class and subtracting the same term from the infected class. Their model shows that the total population is not constant because it takes into account disease-related mortality, which was not accounted for in previous models.

## Chapter 3

# Mathematical Modeling and Analysis of Malaria Transmission Dynamics

### 3.1 Model Formulation

We present a mathematical model that describes the dynamics of malaria transmission between humans and mosquitoes, based on a compartmental approach that divides the population into categories according to their disease status. These categories are represented by differential equations. A **SEIR**-type model was used for the human population and a simplified **SI**-type model for the mosquito population, our model is shown in

#### 3.1.1 Human Population Model

The human model is the **SEIR** model, which divides the population into four categories shown in **Figure6**, which are:

- $S_h$  : Susceptible individuals who are at risk of infection.
- $L_h$  : Latent (Exposed) individuals who are infected but not yet infectious.
- $I_h$  : Infectious individuals who can transmit the disease.
- $R_h$  : Recovered individuals who have acquired temporary immunity.

Since continued exposure is necessary to ensure the maintenance of immunity [7] , if a person stops being exposed to malaria for a long period, it is possible that they will gradually lose immunity, and become susceptible to infection again. We assume that immunity is acquired, but temporary. People who recover acquire immunity against the disease, but only for a limited period of time. The size of the susceptible group changes over time, as a result of several factors:

- **The human birth rate  $\alpha_h$**  : as new individuals added to the susceptible class at birth.

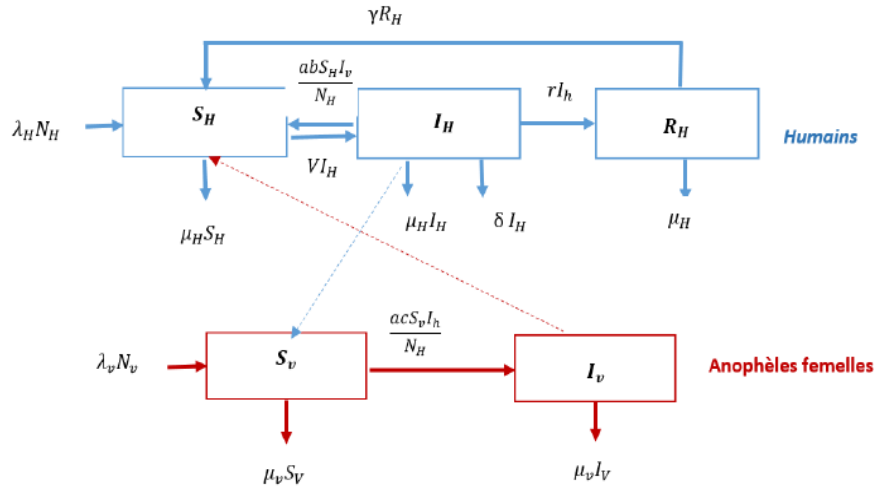


Figure 3.1: Flow Diagram for the Tnasmision Dynamics of Malaria.

- **The rate of immunity loss  $\gamma$**  : which some recoveries to revert to a susceptible state.
- **The natural death rate  $\mu_h$**  : which reduces the total number of individuals in the population.
- **Infection resulting from bites by infectious mosquitoes:** as individuals move from the susceptible population to the latent population when bitten by an infected mosquito with a probability denoted by  $b$ .

### 3.1.2 Mosquito Population Model

The mosquito model is represent by an **SI** model, which divides the population into two categories shown in **figure3**, which are:

- **$S_v$**  : Mosquito susceptible to infection.
- **$I_v$**  : Mosquito infected with the diseaseand able to transmit it .

There is no latent or recoved class in mosquitoes[4] [10], sinse mosquitoes do not recover from the infection and do not require a long inclubation period within their bodies. Mosquitoes become infected when they suck blood from an infectious human. The size of the susceptible group changes over time, as a result of several factors:

- **The birth rate for mosquitoes  $\alpha_v$**  : as new individuals added to the susceptible class at birth.
- **The natural death rate  $\mu_h$**  : which reduces the total number of individuals in the population.
- **Infection caused by a human being bitten by a mosquito** : where the mosquito moves from the susceptible category to the infected category when it bites an infected human with a probability referred to as  $c$ .

### 3.1.3 Model Assumptions

- 1) All newborns are considered susceptible to infection in both communities, so that every new individual born, whether human or mosquito, automatically joins the susceptible group, meaning that no individual is born with prior immunity or latent infection.
- 2) All individuals of all classes, whether in mosquitoes (susceptible, infected) or humans (susceptible, latent, infected, recovered) are exposed to death at a natural mortality rate  $\mu_h$  (human),  $\mu_v$  (mosquitoes).
- 3) The category of infected humans has an additional mortality rate  $\eta$  associated with the disease, meaning that malaria may lead to death above the normal rate, so this factor was added to the model. Unlike mosquitoes, no special mortality rate is added in the case of infection in them, as it does not affect their lifespan.
- 4) The mortality rate of mosquitoes is equal in both categories (susceptible, infected), with the same natural mortality rate  $\mu_v$ .
- 5) Population numbers do not remain constant over time, whether in mosquitoes or humans.
- 6) Recovered individuals can transmit the disease, but at a low rate, so its effect is negligible in the model.
- 7) Recovered individuals return to a susceptible state, so they do not acquire permanent immunity, and the person may become ill again after a period of time.

### 3.1.4 Mathematical Formulation of the Model Equations

We present the differential equations that describe the dynamics of disease transmission based on the previous model [13], which is represented by the following equations:

$$\left\{ \begin{array}{l} \frac{dS_h}{dt} = \alpha_h N_h - \frac{\sigma b S_h I_v}{N_h} + \gamma R_h - \mu_h S_h, \\ \frac{dL_h}{dt} = \frac{\sigma b S_h I_v}{N_h} - (\mu_h + \delta) L_h, \\ \frac{dI_h}{dt} = \delta L_h - (\eta + \mu_h + \lambda) I_h, \\ \frac{dR_h}{dt} = \lambda I_h - (\mu_h + \gamma) R_h, \\ \frac{dS_v}{dt} = \alpha_v N_v - \frac{\sigma c S_v I_h}{N_h} - \mu_v S_v, \\ \frac{dI_v}{dt} = \frac{\sigma c S_v I_h}{N_h} - \mu_v I_v, \end{array} \right. \quad (3.1)$$

these equations were derived based on the Balance Law, which takes into account the rates of transmission between groups, birth and death rates, and the probability of transmission of infection. These equations aim to monitor the development of the epidemiological situation over time within an unbalanced population environment.

### 3.1.5 Definition of Model Constants and Variables

1)The following table shows the variable in the model's equations:

|       |                                           |
|-------|-------------------------------------------|
| $S_h$ | class (number) of susceptible humans.     |
| $L_h$ | class (number) of latent humans.          |
| $I_h$ | class (number) of infectious humans.      |
| $R_h$ | class (number) of recovered humans.       |
| $N_h$ | total population for humans (host).       |
| $S_v$ | class (number) of susceptible mosquitoes. |
| $I_v$ | class (number) of infectious mosquitoes.  |
| $N_v$ | total population for mosquitoes (vector). |

2)The following table shows the parametre in the model's equations:

|            |                                                                                                  |
|------------|--------------------------------------------------------------------------------------------------|
| $\alpha_h$ | birth rate for humans.                                                                           |
| $\alpha_v$ | birth rate for mosquitoes.                                                                       |
| $\mu_h$    | human natural mortality rate.                                                                    |
| $\mu_v$    | mosquito mortality rate.                                                                         |
| $\eta$     | human malaria-induced death rate.                                                                |
| $\sigma$   | number of bites of a mosquito to a human per unit of time.                                       |
| $\delta$   | rate of progression from latent to infectious state for humans.                                  |
| $\lambda$  | rate of proression from infectious to recovred state for humans.                                 |
| $\gamma$   | rate of progression from recovred to susceptible state for humans.                               |
| $b$        | the probability of being infected for a human bitten by an infectious mosquito per unit of time. |
| $c$        | the probability of being infected for a mosquito biting an infectious human per unit of time.    |

All variables are assumed to be non-negative, greater than or equal to 0.

## 3.2 Existence and Positivity of Solutions

We will study whether the proposed system is well-posed ( i.e., whether it admits unique and stable solutions ) both mathematically and epidemiologically. This includes determining the existence of solutions and proving that their path remains constant within the system over time.

We define the feasible region (biological group) as follows

$$\Omega = \{(S_h, L_h, I_h, R_h, S_v, I_v) \in \mathbb{R}_+^6 : 0 \leq \mu_h \leq \alpha_h, 0 \leq \mu_v \leq \alpha_v\}.$$

**Definition 3.1 Theorem 3.1** *The system (3.1) always admits positive solutions for all positive initial conditions and the biological region  $\Omega \in \mathbb{R}_+^6$  is positively invariant and globally attractive for the same system .*

**Proof.** We write system(3.1) in the form  $\dot{x}(t) = f(x(t))$  where

$$x = (x_1, x_2, x_3, x_4, x_5, x_6) = (S_h, L_h, I_h, R_h, S_v, I_v).$$

and

$$\dot{x} = \left( \dot{x}_1, \dot{x}_2, \dot{x}_3, \dot{x}_4, \dot{x}_5, \dot{x}_6 \right) = \left( \frac{dS_h}{dt}, \frac{dL_h}{dt}, \frac{dI_h}{dt}, \frac{dR_h}{dt}, \frac{dS_v}{dt}, \frac{dI_v}{dt} \right).$$

and

$$f(x) = (f_1(x), f_2(x), f_3(x), f_4(x), f_5(x), f_6(x))$$

then, the system becomes

$$\begin{cases} \dot{x}_1 = \frac{dx_1}{dt} = \alpha_h (x_1 + x_2 + x_3 + x_4) - \frac{\sigma b x_1 x_6}{x_1 + x_2 + x_3 + x_4} + \gamma x_4 - \mu_h x_1, \\ \dot{x}_2 = \frac{dx_2}{dt} = \frac{\sigma b x_1 x_6}{x_1 + x_2 + x_3 + x_4} - A x_2, \\ \dot{x}_3 = \frac{dx_3}{dt} = \delta x_2 - B x_3, \\ \dot{x}_4 = \frac{dx_4}{dt} = \lambda x_3 - C x_4, \\ \dot{x}_5 = \frac{dx_5}{dt} = \alpha_v (x_5 + x_6) - \frac{\sigma c x_3 x_5}{x_1 + x_2 + x_3 + x_4} - \mu_v x_5, \\ \dot{x}_6 = \frac{dx_6}{dt} = \frac{\sigma c x_3 x_5}{x_1 + x_2 + x_3 + x_4} - \mu_v x_6, \end{cases}$$

With parametrs  $A = (\mu_h + \delta)$  and  $B = (\eta + \mu_h + \lambda)$  and  $C = (\mu_h + \gamma)$

Therefore, since the second member in the system(3.1) is locally Lipschitzian, then it asmits a unique solution . Moreover, it is clear that

$$\forall j = 1, \dots, 6, f_j(x) \geq 0 \text{ if } x \in [0, +\infty]^6$$

Ensuring that solutions always remain positive .

When we add the firs four equiations for humans and add the last 2 equiations for mosquitoes , we get the two equations:

$$\begin{cases} \dot{N}_h = \frac{dN_h}{dt} = \alpha_h N_h - \mu_h N_h - \eta I_h, \\ \dot{N}_v = \frac{dN_v}{dt} = \alpha_h N_v - \mu_h N_v, \end{cases} \quad (3.2)$$

which represent the change in the total popultion of the two societies over time, so that the change in the total human population is ralated to the number of births , natural deaths, and

deaths resulting from the epidemic, while for mosquitoes it is related to the number of deaths and natural births. And from the equation (3.2) we have  $\dot{N}_h \leq \alpha_h N_h - \mu_h N_h$  if  $\alpha_h \leq \mu_h$  and  $\dot{N}_v \leq \alpha_v N_v - \mu_v N_v$  if  $\alpha_v \leq \mu_v$  so

$$\begin{cases} N_h(t) \leq N(0) \exp[(\alpha_h - \mu_h)t] , \\ N_v(t) \leq N(0) \exp[(\alpha_v - \mu_v)t] , \end{cases}$$

this means that the human and mosquito populations remain limited, decreasing, or stable, and there cannot be a population explosion. That is, population changes remain logical and compatible with reality, and thus the solutions are within a realistic biological range so we conclude that the region  $\Omega$  is positively invariant.

Moreover, if  $\alpha_h < \mu_h$  and  $\alpha_v < \mu_v$  we see the solution of the system (3.1) enter  $\Omega$  in finite time, i.e.  $N_h(t)$  asymptotically approaches  $\alpha_h$  and  $N_v(t)$  asymptotically approaches  $\alpha_v$ .

Therefore, any solution of the system that begins in the positive orthant  $\mathbb{R}_+^6$  eventually enter  $\Omega$ , that is, even if we start with positive initial conditions but outside  $\Omega$ , the solution path will inevitably enter  $\Omega$  over time. that is,  $\Omega$  attracts all possible solutions in positive space  $\mathbb{R}_+^6$ , and therefore it is globally attractive for the same system, and every solution of the model with initial conditions in  $\Omega$  remains in  $\Omega$  for all  $t > 0$ . So the problem is then mathematically and epidemiologically well posed. ■

### 3.3 the Basic Reproduction Number $R_0$

To calculate the stability of epidemic equilibria, we need to know the basic reproduction number  $R_0$ . The next generation matrix method for calculating  $R_0$  as established by Watmough and Van Den Driessche [12].

The system is divided into infected and non-infected categories, as follows:

For humans:  $\begin{cases} L_h, I_h : \text{infected states,} \\ S_h, R_h : \text{uninfected states,} \end{cases}$

we know  $N_h = S_h + L_h + I_h + R_h$  in the infection free state  $L_h = I_h = R_h = 0 \implies N_h = S_h$ .

For mosquitoes:  $\begin{cases} I_v : \text{infected states,} \\ S_v : \text{uninfected states,} \end{cases}$

we know  $N_v = S_v + I_v$  in the infection free state  $I_v = 0 \implies N_v = S_v$ .

In the next-generation matrix method, we focus only the groups that contribute to transmission. Meaning we track the evolution of only these three infected groups shown in the following linear system :

$$\begin{cases} \frac{dL_h}{dt} = \sigma b I_v - (\mu_h + \delta) L_h, \\ \frac{dI_h}{dt} = \delta L_h - (\eta + \mu_h + \lambda) I_h, \\ \frac{dI_v}{dt} = \frac{\sigma c N_v I_h}{N_h} - \mu_v I_v, \end{cases} \quad (3.3)$$

so the model defines a matrix  $X = (L_h, I_h, I_v)^T$  where the prime denote the transpose. The infection subsystem linearized is then in the form:

$$\dot{X} = (T + \Sigma) X$$

$T$  : Represents new infections (through contact with infected people).

$\Sigma$  : Represents transitions between or out of infected groups (recovery, progression, death).

It means

$$\dot{X} = \begin{pmatrix} -(\mu_h + \delta) & 0 & \sigma b \\ \delta & -(\eta + \mu_h + \lambda) & 0 \\ 0 & \frac{\sigma c N_v I_h}{N_h} & -\mu_v \end{pmatrix} X$$

With

$$T = \begin{pmatrix} 0 & 0 & \sigma b \\ 0 & 0 & 0 \\ 0 & \frac{\sigma c N_v}{N_h} & 0 \end{pmatrix} \quad \text{and} \quad M = \begin{pmatrix} -(\mu_h + \delta) & 0 & 0 \\ \delta & -(\eta + \mu_h + \lambda) & 0 \\ 0 & 0 & -\mu_v \end{pmatrix}$$

So, the next generation matrix  $K = -T\Sigma^{-1}$  where  $\Sigma^{-1} = \frac{1}{|\Sigma|} \cdot \Sigma^{Adj}$ .

$\Sigma^{Adj} = [com(\Sigma)]^T$  and  $com(\Sigma)$  is the matrix of cofactors of  $\Sigma$

we have

$$|\Sigma| = -(\mu_h + \delta)(\eta + \mu_h + \lambda)(\mu_v)$$

And

$$\Sigma^{Adj} = \begin{pmatrix} (\eta + \mu_h + \lambda)(\mu_v) & 0 & 0 \\ \delta\mu_v & (\mu_h + \delta) & 0 \\ 0 & 0 & (\mu_h + \delta)(\eta + \mu_h + \lambda) \end{pmatrix}$$

Then

$$\Sigma^{-1} = \begin{pmatrix} -\frac{1}{\delta\mu_v} & 0 & 0 \\ \frac{\delta}{(\mu_h + \delta)(\eta + \mu_h + \lambda)} & -\frac{1}{(\eta + \mu_h + \lambda)} & 0 \\ 0 & 0 & \frac{1}{-\mu_v} \end{pmatrix}$$

Accordingly

$$K = \begin{pmatrix} 0 & 0 & -\sigma b \\ 0 & 0 & 0 \\ 0 & -\frac{\sigma c N_v}{N_h} & 0 \end{pmatrix} \times \begin{pmatrix} -\frac{1}{\delta \mu_v} & 0 & 0 \\ \frac{\delta}{(\mu_h + \delta)(\eta + \mu_h + \lambda)} & -\frac{1}{-(\eta + \mu_h + \lambda)} & 0 \\ 0 & 0 & \frac{1}{-\mu_v} \end{pmatrix}$$

As a result

$$K = \begin{pmatrix} 0 & 0 & \frac{\sigma b}{\mu_v} \\ 0 & 0 & 0 \\ \frac{\delta \sigma c N_v}{N_h(\mu_h + \delta)(\eta + \mu_h + \lambda)} & \frac{\sigma c N_v}{N_h(\eta + \mu_h + \lambda)} & 0 \end{pmatrix} \quad (3.4)$$

now we calculate the dominant eigenvalue of  $K$  which is the reproduction number basic

$$R_0 = \rho(K)$$

$$\det(K - \lambda I) = \begin{vmatrix} -\lambda & 0 & \frac{\sigma b}{\mu_v} \\ 0 & -\lambda & 0 \\ \frac{\delta \sigma c N_v}{N_h(\mu_h + \delta)(\eta + \mu_h + \lambda)} & \frac{\sigma c N_v}{N_h(\eta + \mu_h + \lambda)} & -\lambda \end{vmatrix} = 0$$

$$\lambda^2 \left( \frac{b \delta \sigma^2 c N_v}{\mu_v N_h (\mu_h + \delta) (\eta + \mu_h + \lambda)} - \lambda^2 \right) = 0$$

$$\lambda_1 = 0 \quad \text{and} \quad \lambda_2 = \pm \sigma \sqrt{\frac{b \delta c N_v}{\mu_v N_h (\mu_h + \delta) (\eta + \mu_h + \lambda)}}$$

Then

$$R_0 = \rho(K) = \sigma \sqrt{\frac{b \delta c N_v}{\mu_v N_h (\mu_h + \delta) (\eta + \mu_h + \lambda)}} \quad (3.5)$$

Since one of the determinants of the matrix is equal to zero, this indicates that  $K$  is singular and non-invertible, meaning that not all compartments represented by  $K$  contribute independently to the disease transmission dynamics. As a result the rang of  $K$  is strictly less than its dimension, To simplify the analysis without losing the essential dynamics, we reduce  $K$  a smaller matrix  $K^*$ . This reduce matrix contains only the compartments that directly contribute to the generation of new infections.

This reduction preserves the dominant eigenvalue, i.e.,  $\rho(K) = \rho(K^*)$

Thus,  $K^*$  can be used to compute the basic reproduction number  $R_0$  more easily and efficiently:

We have

$$K^* = E^T K E = -E^T T \Sigma^{-1} E, \quad \text{with } E = \begin{pmatrix} 1 & 0 \\ 0 & 0 \\ 0 & 1 \end{pmatrix},$$

$$K^* = \begin{pmatrix} 1 & 0 & 0 \\ 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} 0 & 0 & \frac{\sigma b}{\mu_v} \\ 0 & 0 & 0 \\ \frac{\delta \sigma c N_v}{N_h(\mu_h + \delta)(\eta + \mu_h + \lambda)} & \frac{\sigma c N_v}{N_h(\eta + \mu_h + \lambda)} & 0 \end{pmatrix} \begin{pmatrix} 1 & 0 \\ 0 & 0 \\ 0 & 1 \end{pmatrix},$$

$$K^* = \begin{pmatrix} 0 & \frac{\sigma b}{\mu_v} \\ \frac{\delta \sigma c N_v}{N_h(\mu_h + \delta)(\eta + \mu_h + \lambda)} & 0 \end{pmatrix},$$

since  $K^*$  is a  $2 \times 2$  matrix, we have

$$R_0 = \rho(K^*) = \frac{1}{2} \left[ \text{tr}(K^*) + \sqrt{\text{tr}(K^*)^2 - 4 \det(K^*)} \right],$$

we have  $\text{tr}(K^*) = 0$  so

$$R_0 = \rho(K^*) = \sqrt{-\det(K^*)},$$

$$R_0 = \sigma \sqrt{\frac{b \delta c N_v}{\mu_v N_h (\mu_h + \delta) (\eta + \mu_h + \lambda)}}.$$

## 3.4 The Equilibrium Points

Equilibrium points represent the states in which the system remains unchanged over time, and they are fundamental to understanding the behavior of dynamical systems.

### 3.4.1 Disease Free Equilibrium (DFE)

The disease -free equilibrium point in an epidemic model, which is the state where the number of infected, exposed, and recovered individuals equal to zero meaning that the disease is not present in the community.

We use this point to analyze whether or not a disease can invade the population, based on the value of the basic reproduction number:

• If  $R_0 < 1$  then the DFE is stable and the disease is extinct.

• If  $R_0 > 1$  then the DFE is unstable and the disease is spreading.

$E_0$  which is obtained by adding the condition  $L_h = I_h = R_h = I_v = 0$  in the system (3.1) for  $\dot{S}_h = \dot{L}_h = \dot{I}_h = \dot{R}_h = \dot{S}_v = \dot{I}_v = 0$

$$\left\{ \begin{array}{l} \alpha_h N_h - \mu_h S_h = 0, \\ -(\mu_h + \delta) L_h = 0, \\ -(\eta + \mu_h + \lambda) I_h = 0, \\ -(\mu_h + \gamma) R_h = 0, \\ \alpha_v N_v - \mu_v S_v = 0, \\ -\mu_v I_v = 0, \end{array} \right. \quad (3.6)$$

We obtain:

$$\left\{ \begin{array}{l} S_h^0 = \frac{\alpha_h N_h}{\mu_h} \\ L_h^0 = 0 \\ I_h^0 = 0 \\ R_h^0 = 0 \\ S_v^0 = \frac{\alpha_v N_v}{\mu_v} \\ I_v^0 = 0 \end{array} \right.$$

Which gives the disease- free equilibruim as:

$$E_0 = (S_h^0, L_h^0, I_h^0, R_h^0, S_v^0, I_v^0) = \left( \frac{\alpha_h N_h}{\mu_h}, 0, 0, 0, \frac{\alpha_v N_v}{\mu_v}, 0 \right) \quad (3.7)$$

### 3.4.2 Endemic Equilibrium Point (EE)

The Endemic Equilibrium point is an equilibrium state in an epidemiological model, where a disease remains permantly present in a community, but at a constant level of infection. This means that the disease does not disapper, but rather stabilizes at a certain level within the population. The model requires that the values of  $S_h, L_h, I_h, R_h, S_v, I_v$  are not to be equal to zero at equilibrium state in the system (3.1) for  $\dot{S}_h = \dot{L}_h = \dot{I}_h = \dot{R}_h = \dot{S}_v = \dot{I}_v = 0$ .

#### calculate of EE

This type of equilibrium usually appears when the reproduction basic number  $R_0 > 0$ ,

$$E_1 = (S_h^*, L_h^*, I_h^*, R_h^*, S_v^*, I_v^*) \quad (3.8)$$

using this notion the system ( 3.1)becomes:

$$\left\{ \begin{array}{l} \alpha_h N_h - \frac{\sigma b S_h^* I_v^*}{N_h} + \gamma R_h^* - \mu_h S_h^* = 0, \\ \frac{\sigma b S_h^* I_v^*}{N_h} - (\mu_h + \delta) L_h^* = 0, \\ \delta L_h^* - (\eta + \mu_h + \lambda) I_h^* = 0, \\ \lambda I_h^* - (\mu_h + \gamma) R_h^* = 0, \\ \alpha_v N_v - \frac{\sigma c S_v^* I_h^*}{N_h} - \mu_v S_v^* = 0, \\ \frac{\sigma c S_v^* I_h^*}{N_h} - \mu_v I_v^* = 0, \end{array} \right.$$

from this system we deduce that

$$\left\{ \begin{array}{l} S_h^* = \frac{N_h (\alpha_h N_h + \gamma R_h^*)}{\sigma b I_v^* + \mu_h N_h}, \\ L_h^* = \frac{\sigma b S_h^* I_v^*}{N_h (\mu_h + \delta)}, \\ I_h^* = \frac{\delta}{(\eta + \mu_h + \lambda)} L_h^*, \\ R_h^* = \frac{\lambda}{(\mu_h + \gamma)} I_h^*, \\ S_v^* = \frac{\alpha_v N_v N_h}{\sigma c I_h^* + N_h \mu_v}, \\ I_v^* = \frac{\sigma c S_v^* I_h^*}{N_h \mu_v}, \end{array} \right.$$

and from it

$$E_1 = \left( \frac{N_h (\alpha_h N_h + \gamma R_h^*)}{\sigma b I_v^* + \mu_h N_h}, \frac{\sigma b S_h^* I_v^*}{N_h (\mu_h + \delta)}, \frac{\delta}{(\eta + \mu_h + \lambda)} L_h^*, \frac{\lambda}{(\mu_h + \gamma)} I_h^*, \frac{\alpha_v N_v N_h}{\sigma c I_h^* + N_h \mu_v}, \frac{\sigma c S_v^* I_h^*}{N_h \mu_v} \right).$$

### Existence and uniqueness of EE

**Proposition 3.1** The Endemic Equilibrium point “EE” exists if and only if  $R_0 > 1$ .

**Proof.** Recall that the endemic equilibrium point,  $E_1$ , found previously was determined implicitly due to the complexity of this system. With the notions of the equilibrium point, the system ( 3.1)becomes:

$$\left\{ \begin{array}{l} S_h^* = \frac{N_h (\alpha_h N_h + \gamma R_h^*)}{\sigma b I_v^* + \mu_h N_h}, \\ L_h^* = \frac{\sigma b S_h^* I_v^*}{N_h (\mu_h + \delta)}, \\ I_h^* = \frac{\delta}{(\eta + \mu_h + \lambda)} L_h^*, \\ R_h^* = \frac{\lambda}{(\mu_h + \gamma)} I_h^*, \\ S_v^* = \frac{\alpha_v N_v N_h}{\sigma c I_h^* + N_h \mu_v}, \\ I_v^* = \frac{\sigma c S_v^* I_h^*}{N_h \mu_v}, \end{array} \right.$$

we choose  $I_h^*$  as the main variable for the equilibrium analysis because it is the main driver of conta-

gion and all other variables can be easily expressed in terms of it , so we can write

$$\begin{cases} S_h^* = N_h - I_h^* \left(1 + \frac{(\eta + \mu_h + \lambda)}{\delta} + \frac{\lambda}{(\mu_h + \gamma)}\right), \\ L_h^* = \frac{(\eta + \mu_h + \lambda)}{\delta} I_h^*, \\ R_h^* = \frac{\lambda}{(\mu_h + \gamma)} I_h^*, \\ S_v^* = \frac{\alpha_v N_v N_h}{\sigma c I_h^* + N_h \mu_v}, \\ I_v^* = \frac{\sigma c \alpha_v N_v I_h^*}{(\sigma c I_h^* + \mu_v) \mu_v}, \end{cases}$$

by making substitutions in  $0 = \alpha_h N_h - \frac{\sigma b S_h^* I_v^*}{N_h} + \gamma R_h^* - \mu_h S_h^*$  we notice that the EE satisfies the following polynomial function:

$$\begin{aligned} P(I_h^*) &= \sigma^2 b c \delta \gamma \lambda \alpha_v N_v I_h^{*2} - (\mu_h + \delta) (\eta + \mu_h + \lambda) (\mu_h + \gamma) (\sigma^2 b c \alpha_v N_v + \sigma c \mu_h \mu_v N_h) I_h^{*2} \\ &\quad + N_h (\mu_h + \gamma) (\sigma^2 b c \delta \alpha_v \alpha_h N_v - (\mu_h + \delta) (\eta + \mu_h + \lambda) \mu_h \mu_v N_h) I_h^{*2} = 0, \end{aligned}$$

it can be written in the form

$$P(I_h^*) = I_h^* = (\Psi_1 I_h^* + \Psi_2) = 0, \quad (3.9)$$

where

$$\Psi_1 = \sigma^2 b c \delta \gamma \lambda \alpha_v N_v - A B C (\sigma^2 b c \alpha_v N_v + \sigma c \mu_h \mu_v N_h),$$

$$\Psi_2 = N_h C (\sigma^2 b c \delta \alpha_v \alpha_h N_v - A B \mu_h \mu_v N_h),$$

$P(I_h^*)$  have two solution:  $I_h^* = 0$  which is the solution of DFE , or  $I_h^* = \frac{-\Psi_2}{\Psi_1}$ ,  $I_h^* = \frac{-\Psi_2}{\Psi_1} > 0$  if  $R_0 > 1$  , hence the uniqueness of endemic equilibrium point , otherwise no endemic equilibrium point . ■

## 3.5 Stability of Disease Free Equilibrium(DFE)

### 3.5.1 Locally asymptotically stable

**Definition 3.2 Theorem 3.2** The disease-free equilibrium(DFE) noted  $E_0$  , of Equation (3.1), given by Equation (3.2) , is locally asymptotically stable if  $R_0 < 1$  , and unstable if  $R_0 > 1$ .

**Proof.** We analyze the local stability of DFE point , The Jacobian matrix  $J(M)$  of Equation (3.1)

at point  $M = (S_h, L_h, I_h, R_h, S_v, I_v)$  is calculated as:

we have

$$\begin{bmatrix} \frac{dS_h}{dt} \\ \frac{dL_h}{dt} \\ \frac{dI_h}{dt} \\ \frac{dR_h}{dt} \\ \frac{dS_v}{dt} \\ \frac{dI_v}{dt} \end{bmatrix} = \begin{bmatrix} \alpha_h N_h - \frac{\sigma b S_h I_v}{N_h} + \gamma R_h - \mu_h S_h \\ \frac{\sigma b S_h I_v}{N_h} - (\mu_h + \delta) L_h \\ \delta L_h - (\eta + \mu_h + \lambda) I_h \\ \lambda I_h - (\mu_h + \gamma) R_h \\ \alpha_v N_v - \frac{\sigma c S_v I_h}{N_h} - \mu_v S_v \\ \frac{\sigma c S_v I_h}{N_h} - \mu_v I_v \end{bmatrix},$$

and

$$J(M) = \begin{bmatrix} \frac{\partial \dot{S}_h}{\partial S_h} & \frac{\partial \dot{S}_h}{\partial L_h} & \frac{\partial \dot{S}_h}{\partial I_h} & \frac{\partial \dot{S}_h}{\partial R_h} & \frac{\partial \dot{S}_h}{\partial S_v} & \frac{\partial \dot{S}_h}{\partial I_v} \\ \frac{\partial \dot{L}_h}{\partial S_h} & \frac{\partial \dot{L}_h}{\partial L_h} & \frac{\partial \dot{L}_h}{\partial I_h} & \frac{\partial \dot{L}_h}{\partial R_h} & \frac{\partial \dot{L}_h}{\partial S_v} & \frac{\partial \dot{L}_h}{\partial I_v} \\ \frac{\partial \dot{I}_h}{\partial S_h} & \frac{\partial \dot{I}_h}{\partial L_h} & \frac{\partial \dot{I}_h}{\partial I_h} & \frac{\partial \dot{I}_h}{\partial R_h} & \frac{\partial \dot{I}_h}{\partial S_v} & \frac{\partial \dot{I}_h}{\partial I_v} \\ \frac{\partial \dot{R}_h}{\partial S_h} & \frac{\partial \dot{R}_h}{\partial L_h} & \frac{\partial \dot{R}_h}{\partial I_h} & \frac{\partial \dot{R}_h}{\partial R_h} & \frac{\partial \dot{R}_h}{\partial S_v} & \frac{\partial \dot{R}_h}{\partial I_v} \\ \frac{\partial \dot{S}_v}{\partial S_h} & \frac{\partial \dot{S}_v}{\partial L_h} & \frac{\partial \dot{S}_v}{\partial I_h} & \frac{\partial \dot{S}_v}{\partial R_h} & \frac{\partial \dot{S}_v}{\partial S_v} & \frac{\partial \dot{S}_v}{\partial I_v} \\ \frac{\partial \dot{I}_v}{\partial S_h} & \frac{\partial \dot{I}_v}{\partial L_h} & \frac{\partial \dot{I}_v}{\partial I_h} & \frac{\partial \dot{I}_v}{\partial R_h} & \frac{\partial \dot{I}_v}{\partial S_v} & \frac{\partial \dot{I}_v}{\partial I_v} \end{bmatrix},$$

so

$$J(M) = \begin{bmatrix} -\frac{\sigma b I_v}{N_h} - \mu_h & 0 & 0 & \gamma & 0 & -\frac{\sigma b S_h}{N_h} \\ \frac{\sigma b I_v}{N_h} & -(\mu_h + \delta) & 0 & 0 & 0 & \frac{\sigma b S_h}{N_h} \\ 0 & \delta & -(\eta + \mu_h + \lambda) & 0 & 0 & 0 \\ 0 & 0 & \lambda & -(\mu_h + \gamma) & 0 & 0 \\ 0 & 0 & -\frac{\sigma c S_v}{N_h} & 0 & -\frac{\sigma c I_h}{N_h} - \mu_v & 0 \\ 0 & 0 & \frac{\sigma c S_v}{N_h} & 0 & \frac{\sigma c I_h}{N_h} & -\mu_v \end{bmatrix},$$

the Jacobian matrix in Equation(3.1) at point  $E_0$  becomes:

$$J(E_0) = \begin{bmatrix} -\mu_h & 0 & 0 & \gamma & 0 & -\frac{\sigma b \alpha_h}{\mu_h} \\ 0 & -(\mu_h + \delta) & 0 & 0 & 0 & \frac{\sigma b \alpha_h}{\mu_h} \\ 0 & \delta & -(\eta + \mu_h + \lambda) & 0 & 0 & 0 \\ 0 & 0 & \lambda & -(\mu_h + \gamma) & 0 & 0 \\ 0 & 0 & -\frac{\sigma c \alpha_h N_v}{\mu_v N_h} & 0 & -\mu_v & 0 \\ 0 & 0 & \frac{\sigma c \alpha_h N_v}{\mu_v N_h} & 0 & \frac{\sigma c I_h}{N_h} & -\mu_v \end{bmatrix},$$

consider  $P(\lambda^*)$  the chararacteristic polynomial of  $J(E_0)$ , we then have:

$$|J(E_0) - \lambda^* I_6| = P(\lambda^*),$$

$$P(\lambda^*) = \begin{bmatrix} -\mu_h - \lambda^* & 0 & 0 & \gamma & 0 & -\frac{\sigma b \alpha_h}{\mu_h} \\ 0 & -(\mu_h + \delta) - \lambda^* & 0 & 0 & 0 & \frac{\sigma b \alpha_h}{\mu_h} \\ 0 & \delta & -(\eta + \mu_h + \lambda) - \lambda^* & 0 & 0 & 0 \\ 0 & 0 & \lambda & -(\mu_h + \gamma) - \lambda^* & 0 & 0 \\ 0 & 0 & -\frac{\sigma c \alpha_h N_v}{\mu_v N_h} & 0 & -\mu_v - \lambda^* & 0 \\ 0 & 0 & \frac{\sigma c \alpha_h N_v}{\mu_v N_h} & 0 & \frac{\sigma c I_h}{N_h} & -\mu_v - \lambda^* \end{bmatrix},$$

by expending, we have:

$$\begin{aligned} P(\lambda^*) &= \lambda^{*6} + (A + B + C + \mu_h + 2\mu_v) \lambda^{*5} \\ &+ [\mu_v (2\mu_h + \mu_v) + (\mu_h + 2\mu_v) (A + B + C) + AB + AC + BC] \lambda^{*4} \\ &+ [\mu_h \mu_v^2 + \mu_v (2\mu_h + \mu_v) (A + B + C) \\ &+ (\mu_h + 2\mu_v) (AB + AC + BC) - D] \lambda^{*3} \\ &+ [\mu_h \mu_v^2 (A + B + C) + \mu_v (2\mu_h + \mu_v) (AB + AC + BC) \\ &+ (\mu_h + 2\mu_v) ABC - (C + \mu_h + \mu_v) D] \lambda^{*2} \\ &+ [\mu_h \mu_v^2 (AB + AC + BC) + \mu_v (2\mu_h + \mu_v) ABC - (\mu_h \mu_v + C \mu_h + C \mu_v) D] \lambda^* \\ &+ ABC \mu_h \mu_v^2 - CD \mu_h \mu_v. \end{aligned} \quad (3.10)$$

Where  $A = (\mu_h + \delta)$  and  $B = (\eta + \mu_h + \lambda)$  and  $C = (\mu_h + \gamma)$  and  $D = \left( \frac{bc\sigma^2 \delta \alpha_h \alpha_v N_v}{\mu_v \mu_v N_h} \right)$ .

If  $R_0 < 0$  and with Descartes rule of signs [13] all the coefficients of  $P(\lambda^*)$  are strictly positive then  $P(\lambda^*)$  does not have a positive root because there is no change in the sign of the transactions, i.e. they are of the same sign. So,  $J(E_0)$  it does not have positive eigenvalue has all its eigenvalue with strictly negative real part, hence by the Poincarre-lyaponv theorem  $E_0$  is **locally asymptotically stable**. otherwise, if  $R_0 > 0$  and with Descartes rule of signs there is a change in the sign of the coefficients and therefore a polynomial characteristic that has a positive root. So,  $J(E_0)$  has at least one eigenvalue with a strictly positive real part, hence by the Poincarre-lyaponv theorem  $E_0$  is **unstable**. ■

### 3.5.2 Globally asymptotically stable

**Theorem 3.3** The disease-free equilibrium point (DFE) of the model, denoted  $E_0$ , is globally asymptotically stable if  $R_0 < 1$  and unstable if  $R_0 > 1$ .

**Proof.** First, we define the Lyapunov condidate function for  $E_0$  as follows:

$$V = \frac{1}{2} \left( S_h - \frac{\alpha_h N_h}{\mu_h} \right)^2 + \frac{1}{2} L_h^2 + \frac{1}{2} I_h^2 + \frac{1}{2} R_h^2 + \frac{1}{2} \left( S_v - \frac{\alpha_v N_v}{\mu_v} \right)^2 + \frac{1}{2} I_v^2$$

$V$  is the sum of the squares of the deviations of each variable from its value at DFE. this means that the further the system is from the DFE point, the greater the value of  $V$ . When the system is at the DFE point  $V = 0$ .

Now we calculate the first derivative of  $\dot{V}$ .

We know  $\frac{d}{dt} \left( \frac{1}{2} x^2 \right) = x \frac{dx}{dt}$  so

$$\begin{aligned} \dot{V} &= \left( S_h - \frac{\alpha_h N_h}{\mu_h} \right) \dot{S}_h + \dot{L}_h + \dot{I}_h + \dot{R}_h + \left( S_v - \frac{\alpha_v N_v}{\mu_v} \right) \dot{S}_v + \dot{I}_v \\ \dot{V} &= 2\alpha_h N_h S_h + \gamma R_h S_h + \frac{\sigma \alpha_h b S_h I_v}{\mu_h} + \frac{\sigma b S_h I_v}{\mu_h} + \delta L_h I_h + \lambda I_h R_h \\ &\quad + 2\alpha_v N_v S_v + \frac{\sigma c \alpha_v N_v S_v I_h}{\mu_v N_v} + \frac{\sigma c S_v I_v I_h}{N_h} - \left( \frac{\sigma \alpha_h b S_h I_v}{\mu_h} + \mu_h S_h^2 + \frac{\alpha_h^2 N_h^2}{\mu_h} \right. \\ &\quad \left. + \frac{\gamma \alpha_h N_h R_h}{\mu_h} \right) - \left[ (\mu_h + \delta) L_h^2 + (\eta + \mu_h + \lambda) I_h^2 + (\gamma + \mu_h) R_h^2 + \frac{\sigma c S_v^2 I_h}{N_h} \right. \\ &\quad \left. \mu_v S_v^2 + \frac{\alpha_v^2 N_v^2}{\mu_v} + \mu_v I_v^2 \right]. \end{aligned} \quad (3.11)$$

It can be written in the form  $\dot{V} = P(B_1) - P(B_2)$  So that  $P(B_1) = R_0 \times \Phi(x) + A_0$  we subtract and add  $\Phi(x)$  we find  $P(B_1) = (R_0 - 1) \times \Phi(x) + \Phi(x) + A_0$  So  $\dot{V} = (R_0 - 1) \times \Phi(x) + \Phi(x) + A_0 - P(B_2)$  it means  $\dot{V} = (R_0 - 1) \times \Phi(x) - \Psi(x)$

we know  $\Psi(x)$  and  $\Phi(x)$  are strictly positive. Hence, the sign of  $\dot{V}$  is related to  $(R_0 - 1)$ , the Lyapunov candidate function  $V$  thus defined is in the strict sense in the whole domain of  $\Omega$ . Hence, the largest compact invariant set in  $\left\{ (S_h, L_h, I_h, R_h, S_v, I_v) \in \Omega : \dot{V} < 0 \right\}$  is the DFE,  $E_0$ . Therefore, by Lyapunov-Lasalle's Invariance Principle, the disease free equilibrium is globally asymptotically stable in  $\Omega$  if  $R_0 < 1$  and unstable if  $R_0 > 1$ . ■

### 3.6 Stability of Endemic Equilibrium(EE)

**Theorem 3.4** *The endemic equilibrium point (EE) noted  $E_1$ , is globally asymptotically stable if  $R_0 > 1$ .*

**Proof.** First, we define the Lyapunov candidate function for  $E_1$  as follows:

$$V = \frac{1}{2} (S_h - S_h^*)^2 + \frac{1}{2} (L_h - L_h^*)^2 + \frac{1}{2} (I_h - I_h^*)^2 + \frac{1}{2} (R_h - R_h^*)^2 + \frac{1}{2} (S_v - S_v^*)^2 + \frac{1}{2} (I_v - I_v^*)^2,$$

is the sum of the squares of the deviations of each variable from its value at EE. this means that the further the system is from the EE point ,the greater the value of  $V$ . When the system is at the EE point  $V = 0$ .

Now we calculatate the first derivate of  $\dot{V}$ .

We know  $\frac{d}{dt} \left( \frac{1}{2}x^2 \right) = x \frac{dx}{dt}$  so

$$\begin{aligned} \dot{V} &= (S_h - S_h^*) \dot{S}_h + (L_h - L_h^*) \dot{L}_h + (I_h - I_h^*) \dot{I}_h \\ &\quad + (R_h - R_h^*) \dot{R}_h + (S_v - S_v^*) \dot{S}_v + (I_v - I_v^*) \dot{I}_v. \end{aligned}$$

$$\begin{aligned} \dot{V} &= \left[ S_h (\alpha_h N_h + \gamma R_h) + S_h^* \left( \frac{\sigma b S_h I_v}{N_h} + \mu_h S_h \right) + \frac{\sigma b S_h I_v L_h}{N_h} + (\mu_h + \delta) L_h L_h^* \right. \\ &\quad + \delta L_h I_h + (\eta + \mu_h + \lambda) I_h I_h^* + \lambda I_h R_h + (\mu_h + \gamma) R_h R_h^* + \alpha_v N_v S_v + \frac{\sigma c I_h S_v}{N_h} S_v^* \\ &\quad + \mu_v S_v S_v^* + \frac{\sigma c S_v I_h I_v}{N_h} + \mu_v I_v I_v^* \left. \right] - \left[ S_h \left( \frac{\sigma b S_h I_v}{N_h} + \mu_h S_h \right) + S_h^* (\alpha_h N_h + \gamma R_h) \right. \\ &\quad + (\mu_h + \delta) L_h^2 + \frac{\sigma b S_h I_v L_h^*}{N_h} + (\eta + \mu_h + \lambda) I_h^2 + \delta L_h I_h^* + (\mu_h + \gamma) R_h^2 + \lambda I_h R_h^* \\ &\quad \left. + \frac{\sigma c I_h S_v^2}{N_h} + \mu_v (S_v^2 + I_v^2) + \alpha_v N_v S_v + \frac{\sigma c S_v I_h I_v^*}{N_h} \right]. \end{aligned} \quad (3.12)$$

It can be written in the form  $\dot{V} = (1 - R_0^2) \times \Phi(x) - \Psi(x)$  we know  $\Psi(x)$  and  $\Phi(x)$  are strictly positive. Hence, the sign of  $\dot{V}$  is raleted to  $(1 - R_0^2)$  ,the Lyapunov candidate function  $V$  thus defined is in the strict sense in the whole domain of  $\Omega$ . Hence, the largest compact invariant set in  $\left\{ (S_h, L_h, I_h, R_h, S_v, I_v) \in \Omega : \dot{V} < 0 \right\}$  is the EE,  $E_1$ . Therefore, by Lyapunov-La-salle's Invariance Principle, it follows that every solution in  $\Omega$  approaches  $E_1$  for  $R_0 > 1$  ast  $t \rightarrow \infty$  . So the EE,  $E_1$  , is globally asymptotically stable. The epidemiological implication of this result is that malaria will persist and invade population whenever  $R_0 > 1$  . ■

### 3.7 Numerical Simulation of Malaria Model in Burandi

In this section, we focus on a numerical model analysis of the system of differential equations built in the previous sections, which describes the dynamics of malaria transmission between humans and mosquitoes in Burundi, a country in East Africa. The goal of this simulation is to understand the behavior of the system when different and specific validation parameters are applied to the model space and to determine the effect of important parameters such as the bite rate on the spread of the disease.To do this, we collect a reasonable set of data for the parameters

of the model. Most of these are obtained from models developed in the literature and other parameters will be assumed.

In what follows, we will use the below parameters [13]:

$\alpha_h$  : The human birth rate is 38.377 per year per 1000 in habitants [20] .

$\alpha_v$  : The vector birth rate is 130 adult mosquitoes per year per 1000 female mosquitoes [23] .

$\mu_h$  : Human (natural) mortality rate is 7.766 per year per 1000 in habitants.

$\mu_v$  : Mosquito mortality rate is 0.003 [23].

$\eta$  : Human malaria-induced death rate is 3 [15].

$\sigma$  : 20.425 bites per man per night (average bites per man per day inside and outside the home) [Assumed].

$b$  : The probability of being infected for a human bitten by an infectious mosquito per unit of time is 0.0181 [1].

$c$  : The probability of being infected for a mosquito biting an infectious human per unit of time is 0.11 per day [16] .

$\delta$  : Rate of progression from latent to infectious state for humans is 0.1 [Assumed].

$\lambda$  : Rate of progression from infectious to recovered state for humans is 0.0022 per day [3].

$\gamma$  : Rate of progression from recovered to susceptible state for humans  $5.5 \times 10^{-4}$  [3].

The data of confirmed are obtained from the Ministry of Public Health and the Fight against HIV/AIDS for the period 2012 to 2018 . As given in the literature, we initialize parameters and use minimize function with noise in python for obtaining parameter values corresponding to the data in study. Initial conditions of states are  $S_h = 498901$ ;  $L_h = 374176$ ;  $I_h = 823$ ;  $R_h = 560$ ;  $S_v = 3582$ ;  $I_v = 66$ , we represent the development of the number of infected  $I_h$  in the following graph:

Using the parameters derived from the fitted model above and we simulate in two cases:

• First case:

$N_v = 1000$  [Assumed] and  $N_h = 11890781$  [20], the basic reproduction number as mentioned in section (4) is  $R_0 = 0.8092009797722537$  it is less than 1. So that each person transmits the disease to less than one person, this means that the disease will gradually decline until it disappears, meaning that the system of equations is heading towards the DFE, and it is locally asymptotically stable and globally stable , and this is consistent with the theoretical part.

• Second case:

$N_v = 10000$  [Assumed] and  $N_h = 11890781$  [20] , the basic reproduction number as mentioned in section (4) is  $R_0 = 2.55891809201627$  it is greater than 1. So that every infected person transmits the disease to more than one person, meaning that malaria will spread and become an endemic disease in the community. The system is heading towards an EE.

We conclude from this simulation that any increase in the number of mosquitoes leads to the

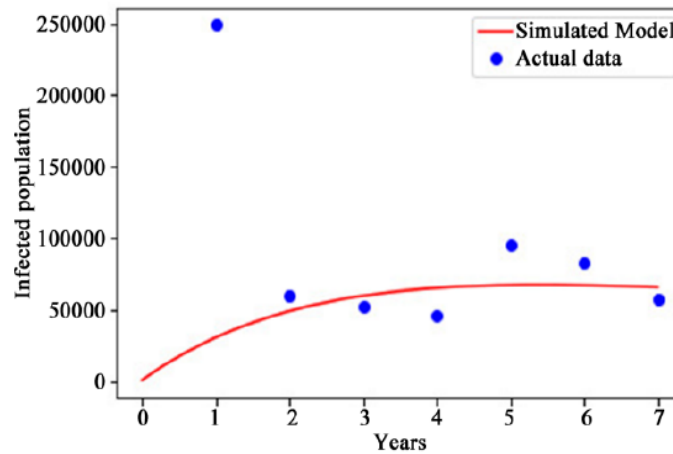


Figure 3.2: Infected human Population.

system shifting from a DF state to an EE state, such that an increase in the number of daily bites  $\sigma$ , increases the probability of a person being infected  $b$ . The probability of mosquito being infected  $c$ .

### 3.8 Conclusion

In this thesis, we have studied the transmission of malaria using mathematical modeling, where we have presented the mathematical and biological basics in terms of its transmission cycle and its behaviors associated with infection. The mathematical model was analyzed in terms of the existence of solutions. The basic reproduction number  $R_0$  was calculated in order to study the stability of both the disease-free equilibrium state, which is locally and globally asymptotically stable when  $R_0 < 1$ , and the endemic equilibrium state, which is stable when  $R_0 > 1$ . A numerical simulation was conducted in Burundi, and it was proven that the increase in the mosquito population  $N_v$  causes an increase in both the number of mosquito bites to humans ( $\sigma$ ), the probability of being infected for a human bitten by an infectious mosquito by unit of time ( $b$ ), and the probability of being infected for a mosquito biting a human infectious per unit of time ( $c$ ), which causes a greater spread of the disease. Therefore, these parameters must be reduced by using bed nets and other effective strategies.

# Bibliography

- [1] Burundi .Ministère de la Santé Publique et de la Lutte contre le VIH/SIDA. ( 2018 ). Ac-célérer la réduction de l'incidence du paludisme auBurundi, Plan stratégique national de lutte contre le paludisme 2018–2023. Ministère de la Santé Publique et de la Lutte contre le VIH/SIDA,
- [2] Chitnis , N. , Cushing , J. M., & Hyman , J. M. ( 2006 ). Analyse de bifurcation d'un modèle mathématique pour la transmission du paludisme .Sje suisJournal sur lesMathématiques UNappliquées, 67 , 24–45. Anglais. est-ce que je:10.1137/050638941.
- [3] Chitnis , N. , Hyman , J. M., & Cushing , J. M. ( 2008 ). Détermination des paramètres importants dans la propagation du paludisme grâce à l'analyse de sensibilité d'un mod-èle mathématique .Bulletin deBiologie Mathématique, 70 ,UNarticle n ou. 1272 .est-ce que je:10.1007/s11538-008-9299-0.
- [4] Chiyaka , C. , Garira , W., & Dubé , S. (2007) . Modèle de transmission du paludisme humain endémique dans une population partiellement immunisée .ModélisationMathématique etje-informatique, 46 , 806–822 .est-ce que je:10.1016/j.mcm. 2006. 12 . 01 0.
- [5] <cliniquevoyageur.ca>. <<https://cliniquevoyageur.ca>>.
- [6] Demailly, P (1996). Analyse numérique et équations différentielles .Collection GrenobleSs-ciences.
- [7] Diouf , M. L. ( 2016 ). Analyse de modèles épidémiologiques à plusieurs classes d'infectés: stabilité et observabilité. Mathématiques [mathématiques] .Sénégal: Université Gaston BERGER de Saint-Louis .
- [8] Houzé, S., Delhaes, L. et al. (2022). Parasitologie et mycologie médicales .Sciences de laSa-vant Elsevier.

- [9] Lévine, S. (2002). La règle des signes de Descartes – est-ce que ça peut être dur?
- [10] Mandal, S. (2011). Modèles mathématiques du paludisme – une revue. *Journal du paludisme*, 10, 202. est-ce que je: 10.1186/1475-2875-10-202 [http : . <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3162588/pdf/1475-2875-10-202.pdf> .](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3162588/pdf/1475-2875-10-202.pdf)
- [11] Moulay, D. (2011). Modélisation et analyse mathématique de systèmes dynamiques en épidémiologie. Application au cas où rando. Thèses de doctorat .Université du Havre.
- [12] Muhammad DAUHO. UNctes, E. T. Equestions. (septembre 2018 ), 62 , p. 123–138 , Laurent DUMAS , Pierre G Abrielet Pauline L afitte.
- [13] Ndamuzi, E., & Gahungu , P (2021) . Modélisation mathématique de la dynamique de transmission du paludisme: cas du Burundi. *Journal de Mathématiques UN appliquées et de Physique*, 9, 2447 - 2460, Article 2021.910156. est-ce que je: 10.4236/jamp.
- [14] Niyukuri , F ( 2015 ). Modélisation mathématique de la propagation du paludisme.
- [15] <<https://reliefweb.int>>. (2017)- bip. D' ACCORD outou, 26. <ird.fr>.
- [16] Olaniyi , S. , Okosun , K.O., Adesanya , S.O., & Lebelo , R.S. ( 2020 ). Modélisation de la dynamique du paludisme avec immunité partielle et voyageurs protégés: contrôle optimal et analyse coût-efficacité *Journal de dynamique biologique* , 14( 1 ), 90–115. est-ce que je: 10.1080/17513758.2020.1722265.
- [17] Tumwiine, J. (1953–1965). JYT Mugisha et LS Luboob. Un modèle mathématique pour la dynamique du paludisme chez l'hôte humain et le moustique vecteur avec une immunité temporaire ( 2007 ), *Mathématiques appliquées et calcul*, 189.
- [18] Tumwiine , J. , Mugisha , J. Oui. T., & Luboobi , L. S. ( 2008 ). Résultats de seuil et de stabilité pour un modèle de paludisme dans une population avec intervention protectrice parmi les groupes à haut risque . *Modélisation Mathématique et UN analyser*, 13 , 443–460 . est-ce que je: 10.3846/1392-6292.2008.13.443-460.
- [19] Paludisme, T . ( 2020 ). *Anopheles gambiae* sl : morphologie, cycle biologique, écologie. Ciblez le. Disponible en ligne sur [https : .](https://targetmalaria.org/wp-content/uploads/2020/11/Écologie_FS_FR_Anopheles-gambiae-sl-morphologie.pdf) 20 août . pdf, vérifié Le , 4(26), 2022. <[http://targetmalaria.org / wpcontent / uploads / 2020 / 11 / Écologie \\_FS\\_FR\\_ Anopheles-gambiae-sl-morphologie](http://targetmalaria.org/wp-content/uploads/2020/11/Écologie_FS_FR_Anopheles-gambiae-sl-morphologie.pdf)> .
- [20] <<https://perspective.usherbrooke.ca>> .

- [21] Van Den Driessche , P., & Watmough , J. (2002) . Nombres de reproduction et équilibres endémiques sous-seuil pour la transmissioncompartimentédes maladies .BiosciencesMathématiques, 180 , 29–48 .est-ce que je:10.1016/S0025-5564(02)00108-6.
- [22] Yacheur, S. Modélisation et étude mathématique de la propagation d’une maladie vectorielle (paludisme) au sein d’une population. Mathématiques [mathématiques] .Université de Lorraine; Université Abou Bekr Belkaid (Tlemcen, Algérie). (2021). Français. ffNNT : 2021LORR0311ff. fftel-03620055ff.
- [23] Zongo , P (2009) . Modélisation mathématique de la dynamique de transmission du paludisme Thèse de doctorat Université de Ouagadougou. Burkina Faso.