STABILITY ANALYSIS AND NUMERICAL SIMULATION OF RABIES SPREAD MODEL WITH DELAY EFFECTS

BACHELOR THESIS

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MATHEMATICS STUDY PROGRAM

DEPARTMENT OF MATHEMATICS

FACULTY OF MATHEMATICS AND NATURAL SCIENCES

HASANUDDIN UNIVERSITY

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Proposed as one of the requirements to obtain Bachelor of Science degree on Mathematics Study Program, Department of Mathematics, Faculty of Mathematics and Natural Sciences, Hasanuddin University

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PREFACE

First of all, praises the author wishes upon Allah SWT, for with His grace and blessings that the author is able to finish this bachelor thesis entitled **"Stability Analysis and Numerical Simulation of Rabies Spread Model with Delay Effects"** as a requirement to achieve the Bachelor of Science degree on Mathematics Study Program, Department of Mathematics, Faculty of Mathematics and Natural Science, Hasanuddin University.

The author recognizes a lot of parties who have contributed in aiding, guiding, and motivating the author in finishing this bachelor thesis. Therefore, in this occasion, allow the author to thank several parties who have helped directly or indirectly in the writing of this bachelor thesis. First off, allow the author to thank the author's parents, **Meyliani, S.Sos.** and **Nurdiansyah, S.Sos.** who have cared, raised, and guided the author until the author reaches this point in life. Also thank you for my brother, **Zacky**, and all the family who have given their support to the author. In this occasion, the author would also love to thank:

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The author realizes that there are still flaws in the writing of this bachelor thesis. Therefore, any constructive criticism and suggestions are very appreciated to make this bachelor thesis better.

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Makassar, August 1, 2023

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ABSTRACT

In this research, a delay differential equations model is constructed to observe the spread of rabies among human and dog population by considering two delay effects on incubation period and vaccine efficacy. Other parameters that affect the spread of rabies are also analyzed. By using the basic reproduction number, it is shown that dog population and the two delays given affect the spread of rabies. Although, using local stability analysis around two equilibria, it is found that both delays given do not affect the stability of disease-free equilibrium and endemic equilibrium. It is discovered using numerical simulation that coupled strategies, such as increasing dog vaccination, reducing contact with infected dogs, and controlling puppies' birth, are required to eradicate the disease. Numerical simulation is also used to give representation to the analysis result.

Keywords: rabies, delay differential equations, stability analysis, basic reproduction number, equilibria

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ABSTRAK

Pada penelitian ini, model persamaan differensial tundaan dibentuk untuk mengamati penyebaran rabies antara populasi manusia dan anjing dengan mempertimbangkan dua efek tundaan pada masa inkubasi dan keefektifan vaksin. Parameter lain yang memengaruhi penyebaran rabies juga dianalisa. Dengan menggunakan bilangan reproduksi dasar, terlihat bahwa populasi anjing and kedua tundaan yang diberikan memengaruhi penyebaran rabies. Meskipun begitu, dengan menggunakan analisa kestabilan lokal di sekitar dua titik kesetimbangan, terlihat bahwa kedua tundaan yang diberikan tidak memengaruhi kestabilan titik kesetimbangan bebas wabah dan titik kesetimbangan endemik. Dapat diamati menggunakan simulasi numerik bahwa strategi ganda, seperti meningkatkan vaksinasi anjing, mengurangi kontak dengan anjing terinfeksi, dan mengendalikan kelahiran anjing, diperlukan untuk menghilangkan penyakit. Simulasi numerik juga diberikan untuk memberikan representasi dari hasil analisa.

***Kata Kunci**: rabies, persamaan differensial tundaan, analisa kestabilan, bilangan reproduksi dasar, titik kesetimbangan*

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CHAPTER I

INTRODUCTION

1.1 Background

The concept of derivative was introduced to represent the rate of changes of the value of a function. This concept has helped researchers to understand some of the phenomena in the daily life. These phenomena usually can be written as a mathematical model. One commonly known type of mathematical model is differential equation model. Differential equation is an equation of a function along with its derivative(s). Often times real-world problems are far more complicated to be represented as a single differential equation. Therefore, the problem is represented as several differential equations, which makes a system of differential equations. One of the problems that can be represented as a system of differential equations is a disease spread problem, because it helps to understand the dynamic of the infected population and the recovery of the infected.

One disease that is still becoming a problem in the medical world until today is rabies. Rabies is a disease caused by virus infection, usually from dog or bat bites, which causes symptoms such as seizures, hallucinations, and paralysis. (Clinic, 2022). Nowadays, rabies is still at large and continuously becoming a threat to some of the parts of the world. Rabies has taken about 59,000 lives every year, occurring in more than 150 countries around the world, with most cases happening in the rural parts of Asia and Africa (Clinic, 2022).

Researches have tried to build a model of rabies spread and analyzed the model to find the best possible control measure to suppress or even eradicate this deadly disease. In 2017, Asamoah et al. examined an optimal control method to eradicate rabies transmission from dogs to humans. Some control methods are including preexposure (vaccination) and postexposure (treatment) prophylaxis. They obtained that deaths are able to be eradicated through mass vaccination of susceptible dogs and continuous use of pre and postexposure prophylaxis on human population. Then in 2020, Huang and Li studied the spread of rabies among humans, domesticated, and wild dogs. The model was analyzed by fitting data obtained from literatures and officials in China, as well as studying the effectivity of different suppression methods. It is observed relative suppression measures are including controlling birth of domesticated and wild dogs along with increasing immunity among domesticated dogs. The research considering the rabies spread as a delay differential equations model has also been done before. In 2021, Abdulmajid and Hassan analyzed a delay differential equations model on the spread of rabies among human and dog populations. The model was constructed by incorporating one delay on incubation, and the stability of the system was then analyzed. They found that increasing dog vaccination and birth control of puppies to be an effective measure in controlling the spread of rabies.

Based on the review of some literatures above, we are interested in researching more about the rabies disease spread model by incorporating delay effects. The model that was developed by Abdulmajid and Hassan (2021) incorporated a discrete time delay on disease incubation. The model can be further developed by incorporating other factor that can generate delay effect, for example vaccination effect. Since vaccines do not react instantaneously at first injection, it can create a delay on vaccine efficacy. Therefore, we are interested in bringing up the topic of research in this bachelor thesis entitled

"**Stability Analysis and Numerical Simulation of Rabies Spread Model with Delay Effects.**"

1.2 Problems Identification

Some problems that have been identified for this research are given as follows:

1. How do we develop a mathematical model for rabies spread by considering two discrete time delay that appeared as incubation period and vaccine efficacy?
2. How do we analyze the stability of the model's solution?
3. How do we analyze the effects of two discrete time delay on the stability of the model's solution?
4. What is the best possible recommendation to reduce or eradicate rabies spread?

1.3 Problems Limitations

Several limitations are made to simplify the problems, which are given as follows:

1. The model that we built only observes the spread of rabies among human and dog populations.
2. No migrations happen within the system, such that the population size depends only on birth and death.
3. The transmission of rabies only comes from rabid dogs. No transmission of rabies between susceptible and infected humans, nor there is any transmission between susceptible dogs and infected humans.
4. All vaccinated population are assumed to have permanent immunity.

1.4 Research Objectives

The objectives for the research are stated as follows:

1. To formulate a mathematical model for rabies spread on human and dog population by considering two discrete time delays.
2. To analyze the stability of the model's solution.
3. To analyze the effects of two discrete time delays on the stability of the model's solution.
4. To find the best possible recommendation to reduce or eradicate rabies spread.

1.5 Expected Benefits

Benefits that are expected from this research is to contribute as a reference for future researches for the development in the field of applied mathematics, especially in the topic of mathematical biology and epidemiology.

1.6 Structures of Writing

The structure of the bachelor thesis written are divided into five parts with the details of each part are explained as follows:

CHAPTER I INTRODUCTION

In this chapter, it will be explained about the introduction, the problems identification, the limitations of the problems, the research objectives, the expected benefits, and the structure of writing, which gives a short description on the contents of this bachelor thesis.

CHAPTER II THEORITICAL FUNDAMENTALS

In this chapter, it will be explained about several theories that will help on discussing about the problems, which consisted of rabies, system of differential equations, system of delay differential equations, linearization, equilibrium stability, Hopf bifurcation, Lambert W function, and basic reproduction number.

CHAPTER III RESEARCH METHODOLOGY

In this chapter, it will be explained about the procedure of the research and a flowchart to show how this research went.

CHAPTER IV RESULTS AND DISCUSSION

In this chapter, it will be explained about the model that is developed from Abdulmajid and Hassan (2021), by incorporating two discrete delays of incubation and vaccination. After that, it will be explained about the two types of equilibrium of the model, as well as the basic reproduction number. On the next part is where both equilibria are analyzed to determine the stability conditions of each equilibrium. Finally, numerical simulations are performed to back up the result of the stability analysis of both equilibria, as well as to determine the best possible solution to reduce/eradicate the disease.

CHAPTER V CONCLUSIONS

In this chapter, it will be given several conclusions based on the results obtained in the previous chapter to answer the problems that has been identified for this research, as well as giving several recommendations for development for future researches.

CHAPTER II

THEORITICAL FUNDAMENTALS

2.1 Rabies

Rabies is a viral disease spreading from animals that attack the nervous system. Rabies is said to be 100% fatal once symptoms appear. Rabies usually spreads through bites, scratches, or direct contacts through eyes, mouth, or wounds (WHO, 2023).

Rabies can be found in wild animals, like bats, skunks, racoons, and foxes, and domestic animals, like pet dogs and cats (Clinic, 2022). Rabies only affects mammals, including humans. It cannot be easily determined if whether an animal has rabies or not, but requires a laboratory testing. However, one can observe that rabid animals may act strangely compared to other animals. Some behavior that may be noticed are aggressive and tends to bite people or other animals, or excessive drooling (CDC, 2022).

Rabies has taken approximately 59,000 lives worldwide each year, occurring in more than 150 countries. Rabies is most commonly found in rural areas in Asia and Africa, though rabies can be found in most continents, except Antarctica. Rabies more commonly attacks children than adults (Clinic, 2022; WHO, 2023).

In Indonesia itself, according to Indonesia's Ministry of Health (2020), the death toll of rabies is still around 100-156 deaths a year with 100% fatality rate. According to the statistics, 98% of infections are caused by dogs, and the rest is caused by cats and monkeys. It is reported, per 2020, that only 8 provinces in Indonesia are free of rabies, meanwhile the rest of the provinces are still in endemic status.

Rabies does not show right after someone has been bitten or scratched. The incubation period can take up to 2-3 months, although it may vary from weeks to years, depending on certain factors (WHO, 2023). The only problem is, there is no approved methods of treatment for rabies once symptoms appear. If someone has been exposed to rabies, either by bites or scratches, contact a healthcare professional as soon as possible (Clinic, 2022).

Rabies can be prevented with vaccines. Vaccination in dogs is very effective to prevent rabies from its source. Education on dog behavior and bite prevention is also effective to decrease possible transmission on human. Vaccinations can also be done to people after or before rabies exposure. Prevention is recommended for people with occupations with high risk of being in contact with rabies, like laboratory workers and animal control staff. Prevention is also recommended for people travelling or people living in areas with high rabies cases (WHO, 2023).

2.2 System of Differential Equations

A system of differential equations is a collection of coupling differential equations. The general form of a first order system of differential equations is given as follows

$$\begin{aligned}\frac{dx_1(t)}{dt} &= g_1(t, x_1, x_2, \dots, x_n),\\ \frac{dx_2(t)}{dt} &= g_2(t, x_1, x_2, \dots, x_n),\\ &\vdots\\ \frac{dx_n(t)}{dt} &= g_n(t, x_1, x_2, \dots, x_n).\end{aligned} \tag{2.1}$$

The system (2.1) is said to be linear if $g_1, g_2, \dots, g_n$ are linear on dependent variables $x_1, x_2, \dots, x_n$. Therefore, the general form of a first order system of linear differential equations is given as follows

$$\begin{aligned}\frac{dx_1(t)}{dt} &= a_{11}(t)x_1 + a_{12}(t)x_2 + \cdots + a_{1n}(t)x_n + f_1(t),\\ \frac{dx_2(t)}{dt} &= a_{21}(t)x_1 + a_{22}(t)x_2 + \cdots + a_{2n}(t)x_n + f_2(t),\\ &\vdots\\ \frac{dx_n(t)}{dt} &= a_{n1}(t)x_1 + a_{n2}(t)x_2 + \cdots + a_{nn}(t)x_n + f_n(t),\end{aligned} \tag{2.2}$$

where the coefficients $a_{ij}(t)$ and the functions $f_i(t)$ are continuous functions within the same interval I. The system (2.2) is called a homogenous system if

$f_i(t) = 0$ for $i = 1, 2, \dots, n$, otherwise it is called non-homogenous system (Zill and Cullen, 2009).

Now, suppose we denote the following matrices

$$\boldsymbol{x} = \begin{pmatrix} x_1(t) \\ x_2(t) \\ \vdots \\ x_n(t) \end{pmatrix}, \qquad A = \begin{pmatrix} a_{11}(t) & a_{12}(t) & \cdots & a_{1n}(t) \\ a_{21}(t) & a_{22}(t) & \cdots & a_{2n}(t) \\ \vdots & \vdots & \ddots & \vdots \\ a_{n1}(t) & a_{n2}(t) & \cdots & a_{nn}(t) \end{pmatrix}, \qquad \boldsymbol{F} = \begin{pmatrix} f_1(t) \\ f_2(t) \\ \vdots \\ f_n(t) \end{pmatrix},$$

then the system of differential equations (2.2) can be written as

$$\dot{\boldsymbol{x}} = A\boldsymbol{x} + \boldsymbol{F}. \tag{2.3}$$

If the system is homogenous, then from (2.3), we obtain (Zill and Cullen, 2009)

$$\dot{\boldsymbol{x}} = A\boldsymbol{x}. \tag{2.4}$$

A system which does not depend on the independent variable explicitly is called an autonomous system. An autonomous system of differential equations is written as following (Zill and Cullen, 2009)

$$\begin{aligned} \frac{dx_1(t)}{dt} &= g_1(x_1, x_2, \dots, x_n), \\ \frac{dx_2(t)}{dt} &= g_2(x_1, x_2, \dots, x_n), \\ &\vdots \\ \frac{dx_n(t)}{dt} &= g_n(x_1, x_2, \dots, x_n). \end{aligned} \tag{2.5}$$

Suppose that $g_1, g_2, \dots, g_n$ in (2.5) are linear on dependent variables $x_1, x_2, \dots, x_n$, we obtain the autonomous system of linear differential equations as following

$$\begin{aligned} \frac{dx_1(t)}{dt} &= a_{11}x_1 + a_{12}x_2 + \cdots + a_{1n}x_n, \\ \frac{dx_2(t)}{dt} &= a_{21}x_1 + a_{22}x_2 + \cdots + a_{2n}x_n, \\ &\vdots \\ \frac{dx_n(t)}{dt} &= a_{n1}x_1 + a_{n2}x_2 + \cdots + a_{nn}x_n. \end{aligned} \tag{2.6}$$

Observe that in system (2.6) a_{ij}, for $i = 1, 2, \dots, n$ and $j = 1, 2, \dots, n$ are constants, contrary to the system (2.2) where a_{ij} are given as functions of t. Suppose, if we denote the following matrices

$$\boldsymbol{x} = \begin{pmatrix} x_1(t) \\ x_2(t) \\ \vdots \\ x_n(t) \end{pmatrix} \quad \text{and} \quad A = \begin{pmatrix} a_{11} & a_{12} & \cdots & a_{1n} \\ a_{21} & a_{22} & \cdots & a_{2n} \\ & \vdots & \ddots & \vdots \\ a_{n1} & a_{n2} & \cdots & a_{nn} \end{pmatrix},$$

then the system of differential equations (2.6) can be written as

$$\dot{\boldsymbol{x}} = A\boldsymbol{x}. \tag{2.7}$$

2.3 System of Delay Differential Equations

Often times, certain events in life do not happen instantaneously. Therefore, quite a lot of systems can be constructed by incorporating delays. Time delay is a natural property of a system where the response of an action has a delayed effect. Some systems that may have time delay effect are like biological, ecological, economic, social, and engineering systems. One example in biological field is cancer may be caused by over-exposure to radiation, but the cancer usually only starts to develop years after the exposure to radiation (Zhong, 2006).

Suppose that $N(t)$ is the number of populations at time t. We will build a mathematical model by considering a delay. The basic idea to build this model is considering that the population gives a delayed response to the environment. Therefore, the rate of changes of the population is affected by the number of past populations $N(t-\tau)$, where τ is the delay time. The model that we have here is given by:

$$\frac{dN(t)}{dt} = f\big(N(t-\tau)\big),$$

where this equation is called the delay differential equation (Haberman, 1998).

Now, we are going to construct a system of delay differential equations. Let us consider the following

$$\boldsymbol{x} = \begin{pmatrix} x_1(t) \\ x_2(t) \\ \vdots \\ x_n(t) \end{pmatrix} \quad \text{and} \quad \boldsymbol{x}_\tau = \begin{pmatrix} x_1(t-\tau) \\ x_2(t-\tau) \\ \vdots \\ x_n(t-\tau) \end{pmatrix},$$

where $\tau > 0$ is a delay parameter. From (2.5), we can develop the autonomous system by incorporating delay as following

$$\begin{aligned}\frac{dx_1(t)}{dt} &= g_1(\boldsymbol{x}, \boldsymbol{x}_\tau),\\ \frac{dx_2(t)}{dt} &= g_2(\boldsymbol{x}, \boldsymbol{x}_\tau),\\ &\vdots\\ \frac{dx_n(t)}{dt} &= g_n(\boldsymbol{x}, \boldsymbol{x}_\tau).\end{aligned} \tag{2.8}$$

Suppose that for the system (2.8), g_i for $i = 1, 2, \dots, n$ are linear on dependent variables x_i and $x_i(t-\tau)$, for $i = 1, 2, \dots, n$, the system (2.8) can be written as

$$\begin{aligned}\frac{dx_1(t)}{dt} &= p_{11}x_1(t) + \dots + p_{1n}x_n(t) + q_{11}x_1(t-\tau) + \dots + q_{1n}x_n(t-\tau),\\ \frac{dx_2(t)}{dt} &= p_{21}x_1(t) + \dots + p_{2n}x_n(t) + q_{21}x_1(t-\tau) + \dots + q_{2n}x_n(t-\tau),\\ &\vdots\\ \frac{dx_n(t)}{dt} &= p_{n1}x_1(t) + \dots + p_{nn}x_n(t) + q_{n1}x_1(t-\tau) + \dots + q_{nn}x_n(t-\tau).\end{aligned} \tag{2.9}$$

Suppose that

$$P = \begin{pmatrix} p_{11} & p_{12} & \cdots & p_{1n} \\ p_{21} & p_{22} & \cdots & p_{2n} \\ & \vdots & \ddots & \vdots \\ p_{n1} & p_{n2} & \cdots & p_{nn} \end{pmatrix} \quad \text{and} \quad Q = \begin{pmatrix} q_{11} & q_{12} & \cdots & q_{1n} \\ q_{21} & q_{22} & \cdots & q_{2n} \\ & \vdots & \ddots & \vdots \\ q_{n1} & q_{n2} & \cdots & q_{nn} \end{pmatrix}.$$

We can write the system of (2.9) in matrix form as

$$\dot{\boldsymbol{x}} = P\boldsymbol{x} + Q\boldsymbol{x}_\tau. \tag{2.10}$$

The system (2.8) can be generalized for multiple delay parameters. Suppose we have a total of m delays, namely $\tau_1, \tau_2, \dots, \tau_m$, where $\tau_1, \tau_2, \dots, \tau_m > 0$. From (2.8), we develop a system with a total of m delays, given as follows

$$\begin{aligned}\frac{dx_1(t)}{dt} &= g_1\left(\boldsymbol{x}, \boldsymbol{x}_{\tau_1}, \boldsymbol{x}_{\tau_2}, \dots, \boldsymbol{x}_{\tau_m}\right),\\ \frac{dx_2(t)}{dt} &= g_2\left(\boldsymbol{x}, \boldsymbol{x}_{\tau_1}, \boldsymbol{x}_{\tau_2}, \dots, \boldsymbol{x}_{\tau_m}\right),\\ &\vdots\\ \frac{dx_n(t)}{dt} &= g_n\left(\boldsymbol{x}, \boldsymbol{x}_{\tau_1}, \boldsymbol{x}_{\tau_2}, \dots, \boldsymbol{x}_{\tau_m}\right),\end{aligned} \tag{2.11}$$

where $\boldsymbol{x}_{\tau_i} = \left(x_1(t-\tau_i), x_2(t-\tau_i), \dots, x_n(t-\tau_i)\right)$, for $i = 1, 2, \dots, m$.

Now suppose that the system (2.11), g_i for $i = 1, 2, \dots, n$ are linear on all dependent variables $\boldsymbol{x}$ and $\boldsymbol{x}_{\tau_i}$. Then, suppose that P_0 is the coefficient matrix corresponding to $\boldsymbol{x}$, and P_i, for $i = 1, 2, \dots, m$, is the coefficient matrix corresponding to $\boldsymbol{x}_{\tau_i}$, defined as

$$P_0 = \begin{pmatrix} p_{11} & p_{12} & \cdots & p_{1n} \\ p_{21} & p_{22} & \cdots & p_{2n} \\ & \vdots & \ddots & \vdots \\ p_{n1} & p_{n2} & \cdots & p_{nn} \end{pmatrix} \quad \text{and} \quad P_i = \begin{pmatrix} p_{11_i} & p_{12_i} & \cdots & p_{1n_i} \\ p_{21_i} & p_{22_i} & \cdots & p_{2n_i} \\ & \vdots & \ddots & \vdots \\ p_{n1_i} & p_{n2_i} & \cdots & p_{nn_i} \end{pmatrix}.$$

Therefore, the matrix form of the linear system (2.11) can be written as

$$\dot{\boldsymbol{x}} = P_0\boldsymbol{x} + P_1\boldsymbol{x}_{\tau_1} + P_2\boldsymbol{x}_{\tau_2} + \cdots + P_m\boldsymbol{x}_{\tau_m}. \qquad (2.12)$$

2.4 Linearization

Non-linear systems are harder to solve than linear systems. One way to approach a non-linear system is by doing a linearization around an equilibrium point, then observing the local behavior of the system nearby the equilibrium. The definition of equilibrium is given on Definition 2.4.1.

Definition 2.4.1 (Equilibria) *Consider an autonomous system given as follows*

$$\dot{\boldsymbol{x}} = \boldsymbol{f}(\boldsymbol{x}), \quad \boldsymbol{x} \in \mathbb{R}^n. \qquad (2.13)$$

The equilibrium of the system (2.13) is given as a point $\boldsymbol{x}^* \in \mathbb{R}^n$ *such that (Wiggins, 2003)*

$$\boldsymbol{f}(\boldsymbol{x}^*) = \boldsymbol{0}.$$

Consider the system (2.13), with an equilibrium point $\boldsymbol{x}^* \in \mathbb{R}^n$, where $\boldsymbol{x}^* = (x_1^*, x_2^*, \dots, x_n^*)$. Now, we may write the solutions near the equilibrium $\boldsymbol{x}^*$ as

$$\boldsymbol{x} = \boldsymbol{x}^* + \boldsymbol{y}. \qquad (2.14)$$

By substituting (2.14) to the system (2.13), we obtain the Taylor series expansion around $\boldsymbol{x}^*$ as

$$\dot{\boldsymbol{x}} = \dot{\boldsymbol{x}}^* + \dot{\boldsymbol{y}} = f(\boldsymbol{x}^*) + Df(\boldsymbol{x}^*)\boldsymbol{y} + \mathcal{O}(|\boldsymbol{y}|^2), \qquad (2.15)$$

where Df is the derivative of f, and $|\dots|$ denotes a norm on $\mathbb{R}^n$. Since $\dot{\boldsymbol{x}}^* = f(\boldsymbol{x}^*)$, then we can write (2.15) as

$$\dot{\boldsymbol{y}} = Df(\boldsymbol{x}^*)\boldsymbol{y} + \mathcal{O}(|\boldsymbol{y}|^2). \qquad (2.16)$$

The stability of $\boldsymbol{x}^*$ can be determined by observing the solutions arbitrarily close to $\boldsymbol{x}^*$, which can be determined by studying the associated linear equation of (2.16), given by (Wiggins, 2003)

$$\dot{\boldsymbol{y}} = Df(\boldsymbol{x}^*)\boldsymbol{y}. \tag{2.17}$$

Now since (2.17) is a linearized system of n variables, therefore we will have a total number of n differentials Df, which if we arrange in the form of a matrix, gives us the Jacobian matrix of coefficients of $\boldsymbol{y}$. The example below might help to give understanding how linearization works on a system of n functions/dependent variables.

Suppose that the autonomous system (2.5) is a non-linear system with an equilibrium at $\boldsymbol{x}^*$. Now we will linearize the system (2.5) around the equilibrium point $\boldsymbol{x}^*$. By applying (2.15) to (2.5), we obtain the linearization around $\boldsymbol{x}^*$ as

$$\begin{aligned}
g_1(\boldsymbol{x}) &= g_1(\boldsymbol{x}^*) + \frac{\partial g_1}{\partial x_1}(x_1 - x_1^*) + \cdots + \frac{\partial g_1}{\partial x_n}(x_n - x_n^*) + \mathcal{O}_1(\boldsymbol{x}^2),\\
g_2(\boldsymbol{x}) &= g_2(\boldsymbol{x}^*) + \frac{\partial g_2}{\partial x_1}(x_1 - x_1^*) + \cdots + \frac{\partial g_2}{\partial x_n}(x_n - x_n^*) + \mathcal{O}_2(\boldsymbol{x}^2),\\
&\vdots\\
g_n(\boldsymbol{x}) &= g_n(\boldsymbol{x}^*) + \frac{\partial g_n}{\partial x_1}(x_1 - x_1^*) + \cdots + \frac{\partial g_n}{\partial x_n}(x_n - x_n^*) + \mathcal{O}_n(\boldsymbol{x}^2),
\end{aligned} \tag{2.18}$$

where $\boldsymbol{x} = \big(x_1(t), x_2(t), \dots, x_n(t)\big)$ and $\mathcal{O}_i(\boldsymbol{x}^2)$ is defined as

$$\begin{aligned}
\mathcal{O}_i(\boldsymbol{x}^2) = \frac{1}{2!}\bigg[&\frac{\partial^2 g_i}{\partial {x_1}^2}(x_1 - x_1^*)^2 + \cdots + \frac{\partial^2 g_i}{\partial {x_n}^2}(x_n - x_n^*)^2 + 2\frac{\partial^2 g_i}{\partial x_1 \partial x_2}(x_1 - x_1^*)(x_2 - x_2^*)\\
&+ \cdots + 2\frac{\partial^2 g_i}{\partial x_{n-1}\partial x_n}(x_{n-1} - x_{n-1}^*)(x_n - x_n^*)\bigg] + \cdots
\end{aligned}$$

for $i = 1, 2, \dots, n$.

Since $\boldsymbol{x}^*$ is an equilibrium, then it applies that $g_i(\boldsymbol{x}^*) = 0$ for $i = 1, 2, \dots, n$. Next, since $x_1, x_2, \dots, x_n$ observed are very close to the equilibrium, then $x_i - {x_i}^*$ must tends to 0. Since $x_i - {x_i}^*$ is a small number, then $(x_i - {x_i}^*)^2$ must be an even smaller number, therefore we can omit the higher order terms $\mathcal{O}_i(\boldsymbol{x}^2)$ (assuming that it must be very close to 0). Considering these conditions, (2.18) can be simplified as

$$
\begin{aligned}
g_1(\boldsymbol{x}) &= \frac{\partial g_1}{\partial x_1}(x_1 - x_1^*) + \frac{\partial g_1}{\partial x_2}(x_2 - x_2^*) + \cdots + \frac{\partial g_1}{\partial x_n}(x_n - x_n^*),\\
g_2(\boldsymbol{x}) &= \frac{\partial g_2}{\partial x_1}(x_1 - x_1^*) + \frac{\partial g_2}{\partial x_2}(x_2 - x_2^*) + \cdots + \frac{\partial g_2}{\partial x_n}(x_n - x_n^*),\\
&\vdots\\
g_n(\boldsymbol{x}) &= \frac{\partial g_n}{\partial x_1}(x_1 - x_1^*) + \frac{\partial g_n}{\partial x_2}(x_2 - x_2^*) + \cdots + \frac{\partial g_n}{\partial x_n}(x_n - x_n^*).
\end{aligned}
\tag{2.19}
$$

Suppose we let

$$
\boldsymbol{y} = \begin{pmatrix} x_1 - x_1^* \\ x_2 - x_2^* \\ \vdots \\ x_n - x_n^* \end{pmatrix} \quad \text{and} \quad J = \begin{pmatrix} \frac{\partial g_1}{\partial x_1} & \frac{\partial g_1}{\partial x_2} & \cdots & \frac{\partial g_1}{\partial x_n} \\ \frac{\partial g_2}{\partial x_1} & \frac{\partial g_2}{\partial x_2} & \cdots & \frac{\partial g_2}{\partial x_n} \\ & \vdots & \ddots & \vdots \\ \frac{\partial g_n}{\partial x_1} & \frac{\partial g_n}{\partial x_2} & \cdots & \frac{\partial g_n}{\partial x_n} \end{pmatrix}_{\boldsymbol{x}=\boldsymbol{x}^*},
$$

where J is called the Jacobian matrix. Since we have that $\boldsymbol{y} = \boldsymbol{x} - \boldsymbol{x}^*$, then we have that $\dot{\boldsymbol{y}} = \dot{\boldsymbol{x}}$. The system (2.19) now can be written as

$$
\dot{\boldsymbol{y}} = J\boldsymbol{y}. \tag{2.20}
$$

Now, consider back the delay system (2.8). Suppose that g_i for $i = 1, 2, \dots, n$ contains one or more non-linear terms, and $\boldsymbol{x}^*$ is the equilibrium point of the system (2.8). The result of the linearization of (2.8) is given as

$$
\begin{aligned}
\dot{\boldsymbol{x}} = &\begin{pmatrix} \frac{\partial g_1}{\partial x_1} & \frac{\partial g_1}{\partial x_2} & \cdots & \frac{\partial g_1}{\partial x_n} \\ \frac{\partial g_2}{\partial x_1} & \frac{\partial g_2}{\partial x_2} & \cdots & \frac{\partial g_2}{\partial x_n} \\ & \vdots & \ddots & \vdots \\ \frac{\partial g_n}{\partial x_1} & \frac{\partial g_n}{\partial x_2} & \cdots & \frac{\partial g_n}{\partial x_n} \end{pmatrix}_{\boldsymbol{x}=\boldsymbol{x}^*} \begin{pmatrix} x_1(t) \\ x_2(t) \\ \vdots \\ x_n(t) \end{pmatrix} \\
&+ \begin{pmatrix} \frac{\partial g_1}{\partial x_1(t-\tau)} & \frac{\partial g_1}{\partial x_2(t-\tau)} & \cdots & \frac{\partial g_1}{\partial x_n(t-\tau)} \\ \frac{\partial g_2}{\partial x_1(t-\tau)} & \frac{\partial g_2}{\partial x_2(t-\tau)} & \cdots & \frac{\partial g_2}{\partial x_n(t-\tau)} \\ & \vdots & \ddots & \vdots \\ \frac{\partial g_n}{\partial x_1(t-\tau)} & \frac{\partial g_n}{\partial x_2(t-\tau)} & \cdots & \frac{\partial g_n}{\partial x_n(t-\tau)} \end{pmatrix}_{\boldsymbol{x}=\boldsymbol{x}^*} \begin{pmatrix} x_1(t-\tau) \\ x_2(t-\tau) \\ \vdots \\ x_n(t-\tau) \end{pmatrix}.
\end{aligned}
\tag{2.21}
$$

Now let

$$J_0 = \begin{pmatrix} \frac{\partial g_1}{\partial x_1} & \frac{\partial g_1}{\partial x_2} & \cdots & \frac{\partial g_1}{\partial x_n} \\ \frac{\partial g_2}{\partial x_1} & \frac{\partial g_2}{\partial x_2} & \cdots & \frac{\partial g_2}{\partial x_n} \\ & \vdots & \ddots & \vdots \\ \frac{\partial g_n}{\partial x_1} & \frac{\partial g_n}{\partial x_2} & \cdots & \frac{\partial g_n}{\partial x_n} \end{pmatrix}_{\boldsymbol{x}=\boldsymbol{x}^*}, \quad J_\tau = \begin{pmatrix} \frac{\partial g_1}{\partial x_1(t-\tau)} & \frac{\partial g_1}{\partial x_2(t-\tau)} & \cdots & \frac{\partial g_1}{\partial x_n(t-\tau)} \\ \frac{\partial g_2}{\partial x_1(t-\tau)} & \frac{\partial g_2}{\partial x_2(t-\tau)} & \cdots & \frac{\partial g_2}{\partial x_n(t-\tau)} \\ & \vdots & \ddots & \vdots \\ \frac{\partial g_n}{\partial x_1(t-\tau)} & \frac{\partial g_n}{\partial x_2(t-\tau)} & \cdots & \frac{\partial g_n}{\partial x_n(t-\tau)} \end{pmatrix}_{\boldsymbol{x}=\boldsymbol{x}^*},$$

$$\boldsymbol{x} = \begin{pmatrix} x_1(t) \\ x_2(t) \\ \vdots \\ x_n(t) \end{pmatrix}, \qquad \boldsymbol{x}_\tau = \begin{pmatrix} x_1(t-\tau) \\ x_2(t-\tau) \\ \vdots \\ x_n(t-\tau) \end{pmatrix}.$$

The linearized form of (2.21) is given in the matrix form

$$\dot{\boldsymbol{x}} = J_0\boldsymbol{x} + J_\tau \boldsymbol{x}_\tau. \tag{2.22}$$

Now, suppose that we have the system of differential equations (2.11), with a total of n variables and m delays. Therefore, we have the linearization result of (2.11) given as

$$\begin{aligned} \dot{\boldsymbol{x}} = &\begin{pmatrix} \frac{\partial g_1}{\partial x_1} & \frac{\partial g_1}{\partial x_2} & \cdots & \frac{\partial g_1}{\partial x_n} \\ \frac{\partial g_2}{\partial x_1} & \frac{\partial g_2}{\partial x_2} & \cdots & \frac{\partial g_2}{\partial x_n} \\ & \vdots & \ddots & \vdots \\ \frac{\partial g_n}{\partial x_1} & \frac{\partial g_n}{\partial x_2} & \cdots & \frac{\partial g_n}{\partial x_n} \end{pmatrix}_{\boldsymbol{x}=\boldsymbol{x}^*} \begin{pmatrix} x_1(t) \\ x_2(t) \\ \vdots \\ x_n(t) \end{pmatrix} \\ &+ \begin{pmatrix} \frac{\partial g_1}{\partial x_1(t-\tau_1)} & \frac{\partial g_1}{\partial x_2(t-\tau_1)} & \cdots & \frac{\partial g_1}{\partial x_n(t-\tau_1)} \\ \frac{\partial g_2}{\partial x_1(t-\tau_1)} & \frac{\partial g_2}{\partial x_2(t-\tau_1)} & \cdots & \frac{\partial g_2}{\partial x_n(t-\tau_1)} \\ & \vdots & \ddots & \vdots \\ \frac{\partial g_n}{\partial x_1(t-\tau_1)} & \frac{\partial g_n}{\partial x_2(t-\tau_1)} & \cdots & \frac{\partial g_n}{\partial x_n(t-\tau_1)} \end{pmatrix}_{\boldsymbol{x}=\boldsymbol{x}^*} \begin{pmatrix} x_1(t-\tau_1) \\ x_2(t-\tau_1) \\ \vdots \\ x_n(t-\tau_1) \end{pmatrix} \\ &+ \cdots \\ &+ \begin{pmatrix} \frac{\partial g_1}{\partial x_1(t-\tau_m)} & \frac{\partial g_1}{\partial x_2(t-\tau_m)} & \cdots & \frac{\partial g_1}{\partial x_n(t-\tau_m)} \\ \frac{\partial g_2}{\partial x_1(t-\tau_m)} & \frac{\partial g_2}{\partial x_2(t-\tau_m)} & \cdots & \frac{\partial g_2}{\partial x_n(t-\tau_m)} \\ & \vdots & \ddots & \vdots \\ \frac{\partial g_n}{\partial x_1(t-\tau_m)} & \frac{\partial g_n}{\partial x_2(t-\tau_m)} & \cdots & \frac{\partial g_n}{\partial x_n(t-\tau_m)} \end{pmatrix}_{\boldsymbol{x}=\boldsymbol{x}^*} \begin{pmatrix} x_1(t-\tau_m) \\ x_2(t-\tau_m) \\ \vdots \\ x_n(t-\tau_m) \end{pmatrix}. \end{aligned} \tag{2.23}$$

Now let

$$J_0 = \begin{pmatrix} \frac{\partial g_1}{\partial x_1} & \frac{\partial g_1}{\partial x_2} & \cdots & \frac{\partial g_1}{\partial x_n} \\ \frac{\partial g_2}{\partial x_1} & \frac{\partial g_2}{\partial x_2} & \cdots & \frac{\partial g_2}{\partial x_n} \\ & \vdots & \ddots & \vdots \\ \frac{\partial g_n}{\partial x_1} & \frac{\partial g_n}{\partial x_2} & \cdots & \frac{\partial g_n}{\partial x_n} \end{pmatrix}_{x=x^*}, \quad J_i = \begin{pmatrix} \frac{\partial g_1}{\partial x_1(t-\tau_i)} & \frac{\partial g_1}{\partial x_2(t-\tau_i)} & \cdots & \frac{\partial g_1}{\partial x_n(t-\tau_i)} \\ \frac{\partial g_2}{\partial x_1(t-\tau_i)} & \frac{\partial g_2}{\partial x_2(t-\tau_i)} & \cdots & \frac{\partial g_2}{\partial x_n(t-\tau_i)} \\ & \vdots & \ddots & \vdots \\ \frac{\partial g_n}{\partial x_1(t-\tau_i)} & \frac{\partial g_n}{\partial x_2(t-\tau_i)} & \cdots & \frac{\partial g_n}{\partial x_n(t-\tau_i)} \end{pmatrix}_{x=x^*},$$

$$\boldsymbol{x} = \begin{pmatrix} x_1(t) \\ x_2(t) \\ \vdots \\ x_n(t) \end{pmatrix}, \qquad \boldsymbol{x}_{\tau_i} = \begin{pmatrix} x_1(t-\tau_i) \\ x_2(t-\tau_i) \\ \vdots \\ x_n(t-\tau_i) \end{pmatrix},$$

with $i = 1, 2, \dots, m$. From here, we obtained the linearized form of (2.23) given in the matrix form as the following equation (Jao, 2019)

$$\dot{\boldsymbol{x}} = J_0\boldsymbol{x} + J_1\boldsymbol{x}_{\tau_1} + \cdots + J_m\boldsymbol{x}_{\tau_m}. \tag{2.24}$$

2.5 Equilibrium Stability

The local stability of an equilibrium of a linear system or a linearized system can be determined by characteristic of the eigenvalues.

Theorem 2.7.1 *(Olsder, 1998) Suppose we have a system of differential equations* $\dot{\boldsymbol{x}} = A\boldsymbol{x}$, *where* A *is an* $n \times n$ *matrix with eigenvalues* $\lambda_1, \lambda_2, \dots, \lambda_n$. *The equilibrium* $\boldsymbol{x}^*$ *is asymptotically stable if and only if* $Re(\lambda_i) < 0$, *for* $i = 1, 2, \dots, n$. *Meanwhile, the equilibrium is stable if* $Re(\lambda_i) \leq 0$, *for* $i = 1, 2, \dots, n$.

From Theorem 2.7.1 we can conclude that the equilibrium of a linear system or a linearized system with eigenvalues $\lambda_1, \lambda_2, \dots, \lambda_n$ is:

1. Stable, if for any real eigenvalues, it applies that $\lambda_i \leq 0$, and for any complex eigenvalues, it applies that $Re(\lambda_i) \leq 0$, with $i = 1, 2, \dots, n$. Here, $Re(\lambda_i)$ means the real part of the complex eigenvalue λ_i. Additionally, if it also applies that $\lambda_i \neq 0$ and $Re(\lambda_i) \neq 0$, for $i = 1, 2, \dots, n$, then the equilibrium is asymptotically stable.
2. Unstable, if there exists a real eigenvalue where $\lambda_i > 0$ or a complex eigenvalue with $Re(\lambda_i) > 0$.

2.6 Lambert W Function

The Lambert W function is defined as the multivalued inverse of the function ze^z. The function, denoted by $W(z)$, satisfies

$$W(z)e^{W(z)} = z,$$

for some complex z (Corless et al., 1996).

Now, suppose that $z \in \mathbb{R}$, then for $-\frac{1}{e} \leq z \leq 0$, there are two possible real values of $W(z)$. The branch that satisfies $W(z) \geq -1$ is denoted by $W_0(z)$. The branch $W_0(z)$ is called the principal branch. Meanwhile, the branch that satisfies $W(z) \leq -1$ is denoted by $W_{-1}(z)$ (Corless et al., 1996). The two real branches of $W(z)$ can be seen on Figure 2.2.

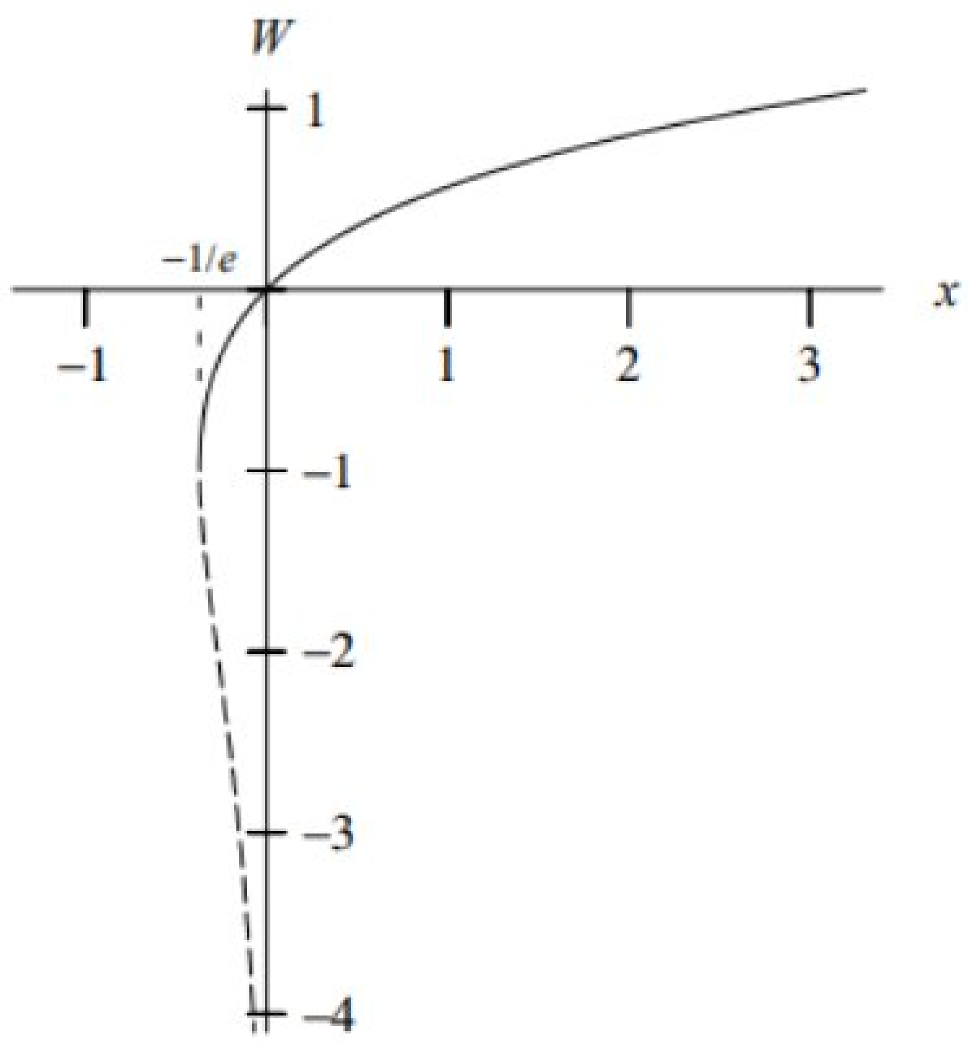

Figure 2.1 The two real branches of $W(z)$

(*Source: Corless et al., 1996*)

2.7 Basic Reproduction Number

Basic reproduction number, denoted by R_0, is defined as the number of secondary infections caused by a primary infection when it is introduced to a susceptible population within the infectious period of this primary infection. R_0 determines whether an epidemic happens or not, where $R_0 < 1$ means no epidemic, and $R_0 > 1$ means an epidemic happens (Brauer & Chaves, 2012).

For a complex system, we require a few extra steps to determine the R_0. Diekmann et al. (2009), wrote that it can be done by defining a matrix which relates the numbers of new infections in the various categories in consecutive generations. The matrix is called **next generation matrix** (NGM), denoted by K. The basic reproduction number R_0 is defined as the dominant eigenvalue of K. R_0 is computed by computing the dominant eigenvalue, or the spectral radius, of the matrix $-T\Sigma^{-1}$, where T is called the transmission matrix, describing the production of new infections, and Σ is the transition matrix, describing the changes of state from the infectious part (either by death or gaining immunity). The matrix $-T\Sigma^{-1}$ here will be referred to as K_L, where K_L is called next generation matrix with large domain. It can be shown that $\rho(K_L) = \rho(K)$ (Diekmann et al., 2009). In short, we compute R_0 by using the formula

$$R_0 = \rho(K) = \rho(K_L) = \rho(-T\Sigma^{-1}).$$

Example:

Determine R_0 of the following epidemic model

$$\begin{aligned} \dot{S} &= kN - mS - \beta\frac{SI}{N}, \\ \dot{E} &= \beta\frac{SI}{N} - (m+\alpha)E, \\ \dot{I} &= \alpha E - (m+r)I, \\ \dot{R} &= rI - mR, \end{aligned} \tag{2.29}$$

where $N = S + E + I + R$. Now we observe that at the disease-free equilibrium $E = I = R = 0$, therefore $S = \frac{kN}{m}$. Therefore, the linearized infectious subsystem of (2.29) is given by

$$\begin{aligned} \dot{E} &= \frac{k\beta}{m}I - (m+\alpha)E, \\ \dot{I} &= \alpha E - (m+r)I. \end{aligned} \tag{2.30}$$

From (2.30), we can arrange the matrix T and Σ as following

$$T = \begin{pmatrix} 0 & \frac{k\beta}{m} \\ 0 & 0 \end{pmatrix}, \qquad \Sigma = \begin{pmatrix} -(m+\alpha) & 0 \\ \alpha & -(m+r) \end{pmatrix}.$$

We obtain the matrix Σ^{-1} as following

$$\Sigma^{-1} = \begin{pmatrix} -\frac{1}{(m+\alpha)} & 0 \\ \frac{-\alpha}{(m+\alpha)(m+r)} & -\frac{1}{(m+r)} \end{pmatrix}.$$

The matrix K_L is given as

$$K_L = -T\Sigma^{-1}$$

$$= -\begin{pmatrix} 0 & \frac{k\beta}{m} \\ 0 & 0 \end{pmatrix} \begin{pmatrix} -\frac{1}{(m+\alpha)} & 0 \\ \frac{-\alpha}{(m+\alpha)(m+r)} & -\frac{1}{(m+r)} \end{pmatrix},$$

$$= \begin{pmatrix} \frac{k\beta\alpha}{m(m+\alpha)(m+r)} & \frac{k\beta}{m(m+r)} \\ 0 & 0 \end{pmatrix}.$$

Therefore, we obtain the spectral radius of K_L, which is equal to R_0, given as

$$R_0 = \rho(K_L) = \frac{k\beta\alpha}{m(m+\alpha)(m+r)}.$$

2.8 State of The Art

Rabies is a fatal disease that have taken thousands of lives every year. Rabies is still becoming a constant threat in some parts of the world, mostly being endemic in some areas in Asia and Africa. Researches have tried to build a model of rabies spread and analyzed it to find the best possible control measure to suppress or even eradicate this deadly disease.

Zhang et al. (2011) has developed a model to help analyzing the rabies spread in China. The model observes the spread of rabies among dog and human populations. They also compare the effects of culling and vaccination on dogs to the spread of rabies. The results found is that the most effective methods to control the spread of rabies is by controlling birth of dogs and increasing vaccination coverage for dogs. Their analysis also stated that the method of culling may be substituted with vaccination to control the spread of rabies. In 2015, Chen et al., investigates on how migration of dogs affects inter-provincial spread of rabies in China, by proposing a multi-patch model to describe the transmissions between humans and dogs. They found out that the immigration of dogs may create a disease endemic even if the disease dies out when there is no immigration in the isolated patch. They stated that the migration of dogs should be better monitored and always under surveillance.

Meanwhile, Tohma et al., in 2015, observed inter-island transmission of rabies in Philippines. They stated that to control the spread of rabies, it is important to acknowledge that inter-island transmission can occur because rabies can become endemic when the virus is introduced to an island which was previously rabies-free. Continuous rabies control program in Philippines, such as controlling transportation of dogs should be implemented to prevent rabies spread.

Asamoah et al. (2017) examined an optimal control method using a mathematical model of rabies spread among dogs and humans. The goal is to eradicate rabies transmission from dogs to humans. Some control methods are including preexposure (vaccination) and postexposure (treatment) prophylaxis. They obtained that the deaths are able to be eradicated through mass vaccination of susceptible dogs and continuous use of pre and postexposure prophylaxis on human population.

Ndii et al. (2018) formulated a deterministic model to investigate rabies transmission among dog populations. Their result shows that limiting the growth of dog population and reducing potential contacts between susceptible and infected dogs can help suppressing a rabies epidemic.

Bornaa et al. (2020) developed a mathematical model to analyze the transmission of rabies in dogs and humans. They found that the efforts to control the spread of disease should focus more on the dogs rather than humans, which they stated that the disease can be controlled through reducing contact with infectious dogs, increasing vaccination, screening of recruited dogs, and culling of infectious dogs. Similarly, Renald et al. (2020), in their research about the spread of rabies among domestic, stray, and Maasai dogs, found that the efforts of controlling the spread of rabies should focus more on stray dogs.

Also studying the case of rabies spread in China, Huang and Li (2020) studied the spread of rabies among humans, domesticated, and wild dogs. The model was analyzed by fitting data obtained from literatures and officials in China, as well as studying the effectivity of different suppression methods. It is observed relative suppression measures are including controlling birth of domesticated and wild dogs along with increasing immunity among domesticated dogs.

Meanwhile, Pantha et al. (2021) developed a mathematical model to study the transmission of rabies in Nepal. The transmission was observed among the populations of human, dog, and jackal. The results showed that jackals and dogs both played important roles in the spread of rabies in Nepal, although dogs played a greater role in the spread. They also observed that rabies might still occur even with controlled spread between jackals and dogs because of interspecies transmission.

The model that was built and analyzed before can still be developed further. One way we can develop the model is by considering a time delay effect. One aspect that can be viewed as delay is the disease incubation. Abdulmajid and Hassan (2021) formulated a delay differential equations model to assess the effects of controls and time delay of incubation period on transmission dynamics of rabies in human and dog populations. Increasing dog vaccination rate and decreasing annual birth of puppies are more effective in human population. Meanwhile in dog population, vaccination and birth control have equal effective measures in controlling the spread of rabies.