# CHAPTER 2 LITERATURE REVIEWS AND BASIC MATHEMATICS

## 2.1 Literature Reviews

Population dispersal, as common phenomenon in human society, living styles, sexual practices and rising international travel, which can be easily transmitted from one region to other regions. In order to predict the spreading of infectious disease among regions, epidemic model with transport–related infection have been proposed and analyzed in recent years. Cui *et al.* [17] introduced a model based on $SIS$ model to describe the transmission of infectious diseases related by transports. The model was given by

$$\begin{aligned}
\frac{dS_1}{dt} &= a - \frac{\beta\, S_1 I_1}{S_1 + I_1} - bS_1 + dI_1 + \alpha S_2 - \alpha S_1 - \frac{\gamma\alpha\, S_2 I_2}{S_2 + I_2}, \\
\frac{dI_1}{dt} &= \frac{\beta\, S_1 I_1}{S_1 + I_1} - (c + d + \alpha) I_1 + \alpha I_2 + \frac{\gamma\alpha\, S_2 I_2}{S_2 + I_2}, \\
\frac{dS_2}{dt} &= a - \frac{\beta\, S_2 I_2}{S_2 + I_2} - bS_2 + dI_2 + \alpha S_1 - \alpha S_2 - \frac{\gamma\alpha\, S_1 I_1}{S_1 + I_1}, \\
\frac{dI_2}{dt} &= \frac{\beta\, S_2 I_2}{S_2 + I_2} - (c + d + \alpha) I_2 + \alpha I_1 + \frac{\gamma\alpha\, S_1 I_1}{S_1 + I_1}.
\end{aligned} \tag{2.1}$$

Here $S_i$ and $I_i$ represent the number of susceptible and infected individuals in region $i$ $(i = 1, 2)$, respectively. They assumed that both regions are identical, i.e. the demographic parameters are the same for each region. They adopted the fixed number of offspring, denoted by $a$, joins into the susceptible class per unit time. Natural death rate for susceptible individuals is a constant per capita rate $b$. Infected individuals recover at a constant per capita rate $d$, and the per capita mortality rate for infected individual is $c$. Since $c$ includes both natural and disease induced mortality, one may assume that $c > b$. In the model (2.1), disease is transmitted with the incidence rate (that is, the number of new cases of infection per unit time) $\frac{\beta\, S_j I_j}{S_j + I_j}$ within region $j (j = 1, 2)$. The transmission rate within a region is a constant $\beta$. Susceptible and infected individuals of region $i$ leave to region $j (j \neq i, i, j = 1, 2)$ at a per capita rate $\alpha$. When the individuals in region $j$ travel to region $i$, disease is transmitted with the incidence rate $\frac{\gamma\alpha\, S_j I_j}{S_j + I_j}$ where $\gamma$ is the transport–related transmission rate.

Cui *et al.* [17] defined the following reproduction numbers:

$$\mathcal{R}_0 = \frac{\beta}{c + d}, \quad \mathcal{R}_{0\gamma} = \mathcal{R}_0 + \frac{\gamma\alpha}{c + d} = \frac{\beta + \gamma\alpha}{c + d}, \tag{2.2}$$

where $\mathcal{R}_{0\gamma}$ is basic reproduction number for (2.1) and $\mathcal{R}_0$ is the basic reproduction number for each city when there are no individual move between regions (that is

$\gamma = 0$). They had shown that when $\mathcal{R}_0 < 1$, each region is disease free, but there may be $\mathcal{R}_{0\gamma} > 1$. This implied that transport–related infection on disease can make the disease be endemic even if all the isolated regions are disease free. But when only susceptible individuals travel between two regions, it is clear that $\mathcal{R}_0 = \mathcal{R}_{0\gamma}$ when $\gamma = 0$. That is, the travel of susceptible individual would not change the endemic condition of the regions. Thus, they suggested that restricting travel of infected individual is important for controlling disease expansion.

In 2003, when SARS was spreading, entry and exist screening included visual inspection to detect symptom, temperature screening via thermal scanning, signs, public address announcements, distributing health alert notice and administering questionnaires to assess symptoms and possible exposure were done at the station or airport to identify infected individual [20, 21]. Then, Lui *et al.* [18] considered entry screening and exit screening to detect infected individuals (with probability of successfully detecting an infected individual $\theta_e$, $\theta_d$, $0 \le \theta_e$, $\theta_d < 1$, respectively). They proposed an $SIQS$ model and mathematically studied the following special case of $\theta_e = \theta$, $\theta_d = 0$:

$$
\begin{aligned}
\frac{dS_1}{dt} &= a - \frac{\beta\, S_1 I_1}{S_1 + I_1} - bS_1 + dI_1 + \alpha S_2 - \alpha S_1 - \frac{\gamma\alpha\, S_2 I_2}{S_2 + I_2} + fQ_1,\\
\frac{dI_1}{dt} &= \frac{\beta\, S_1 I_1}{S_1 + I_1} - (c + d + \alpha) I_1 + (1 - \theta)\alpha I_2 + \frac{(1-\theta)\gamma\alpha\, S_2 I_2}{S_2 + I_2},\\
\frac{dQ_1}{dt} &= \theta\alpha I_2 + \frac{\theta\gamma\alpha\, S_2 I_2}{S_2 + I_2} - (e + f) Q_1,\\
\frac{dS_2}{dt} &= a - \frac{\beta\, S_2 I_2}{S_2 + I_2} - bS_2 + dI_2 + \alpha S_1 - \alpha S_2 - \frac{\gamma\alpha\, S_1 I_1}{S_1 + I_1} + fQ_2,\\
\frac{dI_2}{dt} &= \frac{\beta\, S_2 I_2}{S_2 + I_2} - (c + d + \alpha) I_2 + (1 - \theta)\alpha I_1 + \frac{(1-\theta)\gamma\alpha\, S_1 I_1}{S_1 + I_1},\\
\frac{dQ_2}{dt} &= \theta\alpha I_1 + \frac{\theta\gamma\alpha\, S_1 I_1}{S_1 + I_1} - (e + f) Q_2.
\end{aligned}
\tag{2.3}
$$

The variable $Q_i$, $i = 1, 2$ denotes the number of isolated infected individuals in region $i$, $e$ is the capita mortality rate for isolated infected individuals and $f$ is per capita recovery rate of isolated infected individuals while treating. This research studied the local asymptotic stability and permanence of model (2.3) and proved that the endemic equilibrium was locally asymptotically stable if it existed and that the disease was endemic in the sense of permanence. The result of this research suggested that the entry screening is to be helpful for disease eradication since it could always have the possibility to eradicate the disease led by transport–related infection and had the possibility to eradicate disease even when the disease was endemic in both isolated cities.

For many disease (e.g. influenza, measles chickenpox, etc), after recovery, the individual have immunity to the disease. Thus an $SIR$ or $SIRS$ model is more suitable for this kind of disease. To study the effect of transport–related infection, Lui and Zhou [22] considered the following $SIRS$ model:

$$\begin{aligned}
\frac{dS_1}{dt} &= a - \frac{\beta S_1 I_1}{S_1+I_1+R_1} - bS_1 + \alpha_2 R_1 + \alpha_1 S_2 - \alpha_1 S_1 - \frac{\gamma\alpha_1 S_2 I_2}{S_2+I_2+R_2},\\
\frac{dI_1}{dt} &= \frac{\beta S_1 I_1}{S_1+I_1+R_1} - (b+d+\alpha_1)I_1 + \alpha_1 I_2 + \frac{\gamma\alpha_1 S_2 I_2}{S_2+I_2+R_2},\\
\frac{dR_1}{dt} &= dI_1 - (b+\alpha_1+\alpha_2)R_1 + \alpha_1 R_2,\\
\frac{dS_2}{dt} &= a - \frac{\beta S_2 I_2}{S_2+I_2+R_2} - bS_2 + \alpha_2 R_2 + \alpha_1 S_1 - \alpha_1 S_2 - \frac{\gamma\alpha_1 S_1 I_1}{S_1+I_1+R_1},\\
\frac{dI_2}{dt} &= \frac{\beta S_2 I_2}{S_2+I_2+R_2} - (b+d+\alpha_1)I_2 + \alpha_1 I_1 + \frac{\gamma\alpha_1 S_1 I_1}{S_1+I_1+R_1},\\
\frac{dR_2}{dt} &= dI_2 - (b+\alpha_1+\alpha_2)R_2 + \alpha_1 R_1.
\end{aligned} \tag{2.4}$$

Here, the variable $R_i$, $i = 1, 2$ represents the number of recovered individual in each region. This research described an explicit formula for the reproduction number $\mathcal{R}_{0\gamma}$:

$$\mathcal{R}_{0\gamma} = \frac{\beta + \gamma\alpha_1}{b+d}.$$

Their analysis showed that the disease–free equilibrium is globally asymptotically stable if $\mathcal{R}_{0\gamma} < 1$. They gave some sufficient condition for global stability of endemic equilibrium when $\mathcal{R}_0 > 1$. They also found that the disease is endemic in the sense of permanence if and only if the endemic equilibrium exists. This implied that transport–related infection on disease could make the disease endemic even if all the isolate regions were disease free.

Obviously, model (2.1), (2.3) and (2.4) assume that a susceptible individual become infectious immediately after infected. However, for many disease, a host stay in a latent period before becoming infectious after infected. To understand the effect of some travelling exposed individuals on the spread and control of infectious disease, Wan and Cui [10] formulated the following $SEIS$ model:

$$
\begin{aligned}
\frac{dS_1}{dt} &= a - bS_1 - \frac{\beta\, S_1 I_1}{S_1 + E_1 + I_1} + dI_1 - \alpha S_1 + \alpha S_2 - \frac{\gamma\, \alpha S_2 I_2}{S_2 + E_2 + I_2}, \\
\frac{dE_1}{dt} &= \frac{\beta\, S_1 I_1}{S_1 + E_1 + I_1} - (b + c + \alpha)\, E_1 + \alpha E_2 + \frac{\gamma\, \alpha S_2 I_2}{S_2 + E_2 + I_2}, \\
\frac{dI_1}{dt} &= cE_1 - (e + d + \alpha)\, I_1 + \alpha I_2, \\
\frac{dS_2}{dt} &= a - bS_2 - \frac{\beta\, S_2 I_2}{S_2 + E_2 + I_2} + dI_2 - \alpha S_2 + \alpha S_1 - \frac{\gamma\, \alpha S_1 I_1}{S_1 + E_1 + I_1}, \\
\frac{dE_2}{dt} &= \frac{\beta\, S_2 I_2}{S_2 + E_2 + I_2} - (b + c + \alpha)\, E_2 + \alpha E_1 + \frac{\gamma\, \alpha S_1 I_1}{S_1 + E_1 + I_1}, \\
\frac{dI_2}{dt} &= cE_2 - (e + d + \alpha)\, I_2 + \alpha I_1,
\end{aligned}
\tag{2.5}
$$

where $E_i$, $i = 1, 2$ represents the number of exposed (latent) individual in each region and the parameter $c$ denotes the transfer rate from exposed individuals to infectious individuals. This research mainly studied locally asymptotically stable of model (2.5) and the endemic equilibrium was proved to be asymptotically stable with an addition condition besides the condition for its existence. This research showed that the travelling of the exposed(means exposed but not yet infectious) individual could bring disease from one region to other regions even if the infectious individuals were inhibited from travelling among regions.

In this thesis, the model (2.5) is modified into the $SEIRS$ model to describe the transmission of infectious disease related by transports and will discuss in Chapter 3.

## 2.2 Basic Mathematics

In this section, some theories and basic mathematics are reviewed, and will use in Chapter 3.

### 2.2.1 Linear Stability Analysis

Linear stability of the system of ordinary differential equations such as interacting population models and reaction kinetics systems is determined by the roots of a polynomial. The stability analysis are concerned with involving linear systems in the vector form

$$
\frac{d\mathbf{x}}{dt} = A\mathbf{x}, \tag{2.6}
$$

where $A$ is the Jacobian matrix about the equilibrium point of (2.6) and $\mathbf{x} = (x_1, x_2, ..., x_n)^T$, $T$ denotes transpose. Solutions of (2.6) are obtained by setting

$$
\mathbf{x} = \mathbf{v}e^{\lambda t}, \tag{2.7}
$$

in (2.6) where $\mathbf{v}$ is a constant vector (eigenvector corresponding to eigenvalue $\lambda$) and the eigenvalues $\lambda$ are the roots of the *characteristic polynomial*

$$|A - \lambda I| = 0, \tag{2.8}$$

where $I$ is an identity matrix. The solution of (2.6) is said to be **stable** if all roots $\lambda$ of the characteristic polynomial lie on the left-hand complex plane, that is the real part of $\lambda$, $(\text{Re}(\lambda))$, is less than zero for all roots $\lambda$ [23].

The stability of linear system (2.6) is given in the following definition and theorem. (see more detail in [24])

**Definition 2.1 Stable Critical Point** [24]
Let $\mathbf{x}^*$ be an equilibrium (critical) point of (2.6), and let $\mathbf{x} = \mathbf{x}(t)$ denote the solution which satisfies the initial condition $\mathbf{x}(0) = \mathbf{x}_0$ where $\mathbf{x}_0 \neq \mathbf{x}^*$. The equilibrium $\mathbf{x}^*$ is a **stable critical point** if given any radius $\rho > 0$, there is a corresponding radius $r > 0$, such that if initial position $\mathbf{x}_0$ satisfies $| \mathbf{x}_0 - \mathbf{x}^* | < r$, then the corresponding solution $\mathbf{x}(t)$ satisfies $| \mathbf{x}(t) - \mathbf{x}^* | < \rho$ for all $t > 0$. In addition, if $\lim_{t \longrightarrow \infty} \mathbf{x}(t) = \mathbf{x}^*$ wherever $| \mathbf{x}_0 - \mathbf{x}^* | < r$, then $\mathbf{x}^*$ is an **asymptotically stable critical point.**

**Definition 2.2 Unstable Critical Point** [24]
Let $\mathbf{x}^*$ be an equilibrium (critical) point of (2.6), and let $\mathbf{x} = \mathbf{x}(t)$ denote the solution which satisfies the initial condition $\mathbf{x}(0) = \mathbf{x}_0$ where $\mathbf{x}_0 \neq \mathbf{x}^*$. The equilibrium $\mathbf{x}^*$ is a **unstable critical point** in this case: There is a disk of radius $\rho > 0$ with the property that, for any $r > 0$, there is an initial position $\mathbf{x}_0$ satisfies $| \mathbf{x}_0 - \mathbf{x}^* | < r$, yet the corresponding solution $\mathbf{x}(t)$ satisfies $| \mathbf{x}(t) - \mathbf{x}^* | \geq \rho$ for at least one $t > 0$.

**Theorem 2.1** [24] Let $\mathbf{x}^*$ be a critical point of (2.6) and $A$ is the Jacobian matrix at $\mathbf{x}^*$. Then:

(*i*) If all eigenvalues of $A$ have negative real part, then $\mathbf{x}^*$ is an locally asymptotically stable ($LAS$) critical point.

(*ii*) If some eigenvalues of $A$ have positive real part, then $\mathbf{x}^*$ is an unstable critical point.

### 2.2.2 Linearization of Nonlinear System

In this section, the linearization of system described by nonlinear differential equation is performed. The procedure is based on the Taylor series expansion and on knowledge of the behavior solution of linear system. The main idea is to approximate a nonlinear system by a linearized system (around the equilibrium point), which is known that the behavior of the solutions of the linear system will be the same as the nonlinear one.

Consider the general nonlinear system given by

$$\frac{d\mathbf{x}}{dt} = \mathbf{F}(\mathbf{x}), \tag{2.9}$$

where

$$\mathbf{x} = \begin{pmatrix} x_1 \\ x_2 \\ \cdot \\ \cdot \\ \cdot \\ x_n \end{pmatrix} \text{ and } \mathbf{F}(\mathbf{x}) = \begin{pmatrix} F_1(x_1, ..., x_n) \\ F_2(x_1, ..., x_n) \\ \cdot \\ \cdot \\ \cdot \\ F_n(x_1, ..., x_n) \end{pmatrix}.$$

Supposed that $\mathbf{x}^* = (x_1^*, x_2^*, ..., x_n^*)^T$ is a equilibrium point which is obtained by setting $\frac{d\mathbf{x}}{dt} = \mathbf{0}$, where $\mathbf{0}$ is an $n \times 1$ zero matrix. Linearize (2.9) about $\mathbf{x}^*$ by setting $\mathbf{z} = \mathbf{x} - \mathbf{x}^*$, where $\mathbf{z} = (z_1, z_2, ..., z_n)^T$ represents a small quantity. Using Taylor's expansion on the right–hand side of (2.9), it yields that

$$\begin{aligned} \frac{dz_1}{dt} &= F_1(x_1^*, x_2^*, ..., x_n^*) + z_1\frac{\partial F_1}{\partial x_1} + z_2\frac{\partial F_1}{\partial x_2} + ... + z_n\frac{\partial F_1}{\partial x_n} + \text{higher order term}, \\ \frac{dz_2}{dt} &= F_2(x_1^*, x_2^*, ..., x_n^*) + z_1\frac{\partial F_2}{\partial x_1} + z_2\frac{\partial F_2}{\partial x_2} + ... + z_n\frac{\partial F_2}{\partial x_n} + \text{higher order term}, \\ &\cdot \\ &\cdot \\ &\cdot \\ \frac{dz_n}{dt} &= F_n(x_1^*, x_2^*, ..., x_n^*) + z_1\frac{\partial F_n}{\partial x_1} + z_2\frac{\partial F_n}{\partial x_2} + ... + z_n\frac{\partial F_n}{\partial x_n} + \text{higher order term}, \end{aligned} \tag{2.10}$$

where all partial derivatives are evaluated at $\mathbf{x}^*$. Cancelling higher order terms (which contain very small quantities), the matrix form of (2.10) is given by

$$\frac{d}{dt}\begin{pmatrix} z_1 \\ z_2 \\ \cdot \\ \cdot \\ \cdot \\ z_n \end{pmatrix} \approx \begin{pmatrix} F_1(x_1^*, x_2^*, ..., x_n^*) \\ F_2(x_1^*, x_2^*, ..., x_n^*) \\ \cdot \\ \cdot \\ \cdot \\ F_n(x_1^*, x_2^*, ..., x_n^*) \end{pmatrix} + \begin{pmatrix} \frac{\partial F_1}{\partial x_1} & \frac{\partial F_1}{\partial x_2} & \cdots & \frac{\partial F_n}{\partial x_n} \\ \frac{\partial F_2}{\partial x_1} & \frac{\partial F_2}{\partial x_2} & & \frac{\partial F_n}{\partial x_n} \\ \cdot & & \cdot & \cdot \\ \cdot & & \cdot & \cdot \\ \cdot & & \cdot & \cdot \\ \frac{\partial F_n}{\partial x_1} & \frac{\partial F_n}{\partial x_2} & \cdots & \frac{\partial F_n}{\partial x_n} \end{pmatrix} \begin{pmatrix} z_1 \\ z_2 \\ \cdot \\ \cdot \\ \cdot \\ z_n \end{pmatrix},$$

or

$$\frac{d\mathbf{z}}{dt} \approx \mathbf{F}(\mathbf{x}^*) + J(\mathbf{x}^*)\mathbf{z},$$

where $J(\mathbf{x}^*)$ is called the Jacobian matrix. Since $\mathbf{F}(\mathbf{x}^*)$=$\mathbf{0}$, the linearized system can be represented as

$$\frac{d\mathbf{z}}{dt} \approx J(\mathbf{x}^*)\mathbf{z}. \tag{2.11}$$

The stability of nonlinear system (2.9) may be analyzed in a neighborhood of the equilibrium point $\mathbf{x}^*$ by studying the linearized system (2.11).

### 2.2.3 Routh–Hurwitz Criteria

Important criteria that give necessary and sufficient conditions for all of the roots of characteristic polynomial (with real coefficients) to lie in the left half of the complex plane are known as the *Routh–Hurwitz criteria.* According to theorem 2.1, if the roots of the characteristic polynomial lie in the left half of the complex plane, then any solution to the linear, homogeneous differential equation converges to zero. Hence, the Routh–Hurwitz criteria are used in Chapter 3 to determine local asymptotic stability of an equilibrium for nonlinear system of differential equations. The Routh–Hurwitz criteria are stated in next theorem.

**Theorem 2.2** [23] Given a polynomial equation in $\lambda$,

$$P(\lambda) = \lambda^n + a_1\lambda^{n-1} + ... + a_n = 0, \tag{2.12}$$

where the coefficients $a_i$ are real constants, $i = 1, ..., n$. The $n$ Hurwitz matrices are defined by using the coefficients $a_i$ of the characteristic polynomial and given by

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

and

$$H_j = \begin{pmatrix} a_1 & a_3 & . & . & . & . \\ 1 & a_2 & a_4 & . & . & . \\ 0 & a_1 & a_3 & . & . & . \\ 0 & 1 & a_2 & . & . & . \\ . & . & . & . & . & . \\ 0 & 0 & . & . & . & a_j \end{pmatrix}, \quad j = 1, 2, ..., n.$$

All of the roots of polynomial $P(\lambda)$ are negative or have negative real part, $Re(\lambda) < 0$, if the determinants of all Hurwitz matrices are positive:

$$\det(H_j) > 0, \quad j = 1, 2, ..., n. \tag{2.13}$$

As an example, for $n = 2$ gives a quadratic equation $\lambda^2 + a_1\lambda + a_2 = 0$. The Routh–Hurwitz criteria for $Re(\lambda) < 0$ are $det(H_1) = a_1 > 0$ and

$$\det(H_2) = \begin{vmatrix} a_1 & 0 \\ 1 & a_2 \end{vmatrix} = a_1a_2 > 0$$

which implies that $a_1 > 0$ and $a_2 > 0$.

For $n = 4$ gives a polynomial equation $\lambda^4 + a_1\lambda^3 + a_2\lambda^2 + a_3\lambda + a_4 = 0$. The Routh–Hurwitz criteria are

$$H_1 = a_1 > 0, \quad H_2 = \begin{vmatrix} a_1 & a_3 \\ 1 & a_2 \end{vmatrix} = a_1a_2 - a_3 > 0,$$

$$H_3 = \begin{vmatrix} a_1 & a_3 & 0 \\ 1 & a_2 & a_4 \\ 0 & a_1 & a_3 \end{vmatrix} = a_1a_2a_3 - a_3^2 - a_1^2a_4 > 0, \quad H_4 = \begin{vmatrix} a_1 & a_3 & 0 & 0 \\ 1 & a_2 & a_4 & 0 \\ 0 & a_1 & a_3 & 0 \\ 0 & 1 & a_2 & a_4 \end{vmatrix} > 0.$$

The conditions in equation (2.13) is necessary but not sufficient for confirming the roots of the polynomial $P(\lambda)$ to lie in the left half of the complex plane. Then, the sufficient conditions are the coefficients of $P(\lambda)$ being strictly positive. This result is stated in the next corollary.

**Corollary 2.1** Suppose the coefficients of the characteristic polynomial are real. If all of the roots of the characteristic polynomial

$$P(\lambda) = \lambda^n + a_1\lambda^{n-1} + a_2\lambda^{n-2} + ... + a_n$$

are negative or have negative real part, then the coefficients $a_i > 0$ for $i = 1, 2, ..., n$.

Therefore, the Routh–Hurwitz criteria for polynomials equation of degree 2,4 ($n = 2, 4$) will be used in Chapter 3, and are summarized

$$\begin{aligned} n = 2 \ &: \ a_1 > 0 \quad \text{and} \quad a_2 > 0 \\ n = 4 \ &: \ a_i, i = 1, 2, 3, 4, \quad a_1a_2 - a_3 > 0, \quad a_1a_2a_3 > a_3^2 + a_1^2a_4. \end{aligned}$$

Next, the Routh-Hurwitz criteria (Theorem 2.2) is stated for the special kind of the following matrix $J$:

$$J = \begin{pmatrix} a_{11} & a_{12} & a_{13} & a_{14} \\ a_{21} & a_{22} & a_{23} & a_{24} \\ 0 & a_{32} & a_{33} & 0 \\ 0 & 0 & a_{43} & a_{44} \end{pmatrix}. \qquad (2.14)$$

It is found that the characteristic polynomial of matrix $J$ is given by

$$\lambda^4 + A_1\lambda^3 + A_2\lambda^2 + A_3\lambda + A_4 = 0$$

where

$$A_1 = -trace(J), \quad A_2 = J_1 + J_2 + J_3, \quad A_3 = Q_1 + Q_2 + Q_3, \quad A_4 = det(J)$$

and

$$\begin{aligned} J_1 &= a_{44}a_{33} + a_{44}a_{22} + a_{44}a_{11} + a_{33}a_{11}, \\ J_2 &= a_{33}a_{22} - a_{32}a_{23}, \quad J_3 = a_{22}a_{11} - a_{21}a_{12}, \\ Q_1 &= -a_{44}(J_2 + J_3), \quad Q_2 = -a_{33}(J_3), \\ Q_3 &= -(a_{32}(a_{21}a_{13} + a_{43}a_{24}) + a_{11}(a_{44}a_{33} - a_{32}a_{23})). \end{aligned}$$

Here, $trace(J)$ denotes the sum of the elements on the main diagonal of $J$. Hence, by Theorem 2.2 (Routh-Hurwitz theorem), the following result is established.

**Lemma 2.1** The matrix $J$ (2.14) is stable (i.e. each eigenvalue of $J$ has negative real part) if and only if the following conditions hold:

*(i)* $A_i > 0$

*(ii)* $A_1A_2 - A_3 > 0$

*(iii)* $A_1A_2A_3 - A_3^2 - A_1^2A_4 > 0$.

### 2.2.4 Next Generation Method

The next generation method is used to establish the local asymptotic stability of disease–free equilibrium (*DFE*). The method was first introduced by Diekmann and Hesterbeek [25], and refined for epidemiological models by van den Driessche and Watmough [26]. The formulation in [26], which is based on disease transmission model, is reproduced below. Suppose that the given disease transmission model, with nonnegative initial conditions, can be written in terms of the following system:

$$\frac{dx_i}{dt} = f_i(\mathbf{x}) = \mathcal{F}_i(\mathbf{x}) - \mathcal{V}_i(\mathbf{x}), \quad i = 1, ..., n \tag{2.15}$$

where $\mathcal{V}_i(\mathbf{x}) = \mathcal{V}_i^-(\mathbf{x}) - \mathcal{V}_i^+(\mathbf{x})$, and $\mathbf{x} = (x_1, ..., x_n)^t$, $x_i \geq 0$ represents the number of individuals in each compartment of the model. First of all,

$$\mathbf{X}_s = \{\mathbf{x} \geq 0 \mid x_i = 0, \quad i = 1, ..., m\} \tag{2.16}$$

with $m < n$ is defined as the disease–free state (non–infected state variable of the model) of the model. It is assumed that functions $\mathcal{F}_i(\mathbf{x})$, $\mathcal{V}_i^+(\mathbf{x})$, $\mathcal{V}_i^-(\mathbf{x})$ are at least twice continuously differentiable in each variable, and they satisfy the five axioms below.

(A1) If $\mathbf{x} \geq \mathbf{0}$, then $\mathcal{F}_i(\mathbf{x})$, $\mathcal{V}_i^+(\mathbf{x})$, $\mathcal{V}_i^-(\mathbf{x}) \geq 0$ for $i = 1, 2, ..., m$.

(A2) If $x_i = 0$, then $\mathcal{V}_i^-(\mathbf{x}) = 0$. In particular, if $\mathbf{x} \in \mathbf{X}_s$ then $\mathcal{V}_i^-(\mathbf{x}) = 0$ for $i = 1,...,m$.

(A3) $\mathcal{F}_i(\mathbf{x}) = 0$ if $i > m$.

(A4) If $\mathbf{x} \in \mathbf{X}_s$ then $\mathcal{F}_i(\mathbf{x}) = 0$ and $\mathcal{V}_i^+(\mathbf{x}) = 0$ for $i$=1,...,$m$.

(A5) If $\mathcal{F}(\mathbf{x})$ is set to zero, then all eigenvalues of $Df\,(\tilde{\mathbf{x}}_0)$ have negative real parts.

Here,

$\mathcal{F}_i(\mathbf{x})$ represents vector consisting the rate of appearance of new infections in compartment $i$,

$\mathcal{V}_i^-(\mathbf{x})$ represents vector consisting the rate of transfer of individuals out of compartment $i$,

$\mathcal{V}_i^+(\mathbf{x})$ represents vector consisting the rate of transfer of individuals into compartment $i$,

$\tilde{\mathbf{x}}_0$ denotes the disease–free equilibrium,

$Df(\tilde{\mathbf{x}}_0)$ is partial derivative $(\partial f_i/\partial x_j)$ evaluated at $\tilde{\mathbf{x}}_0$.

**Lemma 2.2** If $\tilde{\mathbf{x}}_0$ is a disease–free equilibrium of (2.15) and $f_i(\mathbf{x})$ satisfies (A1)–(A5), then the derivatives $D\mathcal{F}(\tilde{\mathbf{x}}_0)$ and $D\mathcal{V}(\tilde{\mathbf{x}}_0)$ are partitioned as

$$D\mathcal{F}(\tilde{\mathbf{x}}_0) = \begin{pmatrix} F & 0 \\ 0 & 0 \end{pmatrix} \quad \text{and} \quad D\mathcal{V}(\tilde{\mathbf{x}}_0) = \begin{pmatrix} V & 0 \\ K_3 & K_4 \end{pmatrix}$$

where $F$ and $V$ are the $m \times m$ matrices defined by

$$F = \left( \frac{\partial \mathcal{F}_i}{\partial x_j}(\tilde{\mathbf{x}}_0) \right) \quad \text{and} \quad V = \left( \frac{\partial \mathcal{V}_i}{\partial x_j}(\tilde{\mathbf{x}}_0) \right) \quad \text{with} \quad 1 \leq i, \quad j \leq m.$$

Further, $F$ is non-negative, $V$ is a non-singular $M$-matrix, $K_3$, $K_4$ are matrices associated with the transition term of the model and all eigenvalues of $K_4$ have positive real part.

Finally, the following stability result follows.

**Theorem 2.3** [26] Consider an arbitary disease transmission model given by (2.15) with $f_i(\mathbf{x})$ satisfying the axioms (A1)–(A5). If $\mathbf{x}_0$ is a *DFE* of the model, then $\mathbf{x}_0$ is locally asymptotically stable (*LAS*) if $\mathcal{R}_0 = \rho(FV^{-1}) < 1$, but unstable if $\mathcal{R}_0 > 1$, where $\rho$ is the spectral radius.

**Definition 2.3** Let $\lambda_1$, $\lambda_2$,...,$\lambda_n$ be the eigenvalues of square matrix $A$. Then its spectral radius denoted by $\rho(A)$, that is defined as

$$\rho(A) = \max_{1 \leq j \leq n} (\mid \lambda_j \mid).$$