

# Stability analysis of mathematical model of Caprine arthritis encephalitis

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**Abstract:** A mathematical model of Caprine arthritis encephalitis (CAE) that has a great economic impact in goat farming was investigated. Infection route of CAE virus is mainly by vertical transmission through breast milk. Droplet infection and sexual infection is known as other transmission path. From these facts, mathematical model of CAE was created based on the model of spread of sexually transmitted disease (STD) in the human case. The model is analyzed to determine the stability.

**Keywords:** Caprine Arthritis Encephalitis (CAE), Mathematical Model, Stability Analysis, Goat

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## 1. Introduction

Caprine arthritis encephalitis (CAE) is viral disease caused by CAE virus (CAEV), a lentivirus of the family Retroviridae. The disease occurs all over the world including Southeast Asia. The CAEV transmission is mainly due to mother-to-child transmission through breast milk. And it has been reported that the case of infection by contact over a long period of time in same cage or pen [1]. Thus, CAEV has been found in semen [2], there is a possibility that there is an infection by mating.

The symptoms of CAE are varied, and it can be divided two groups, arthritis symptoms type and neurological symptoms type. Mature goats can develop persistent arthritis. Finally they will not able to stand. Young goats can develop encephalomyelitis and pneumonia. Goats don't develop can be hold the virus and be source of infection. There is no cure and the case of developed, the prognosis is poor.

CAEV infection can reduce the milk yield and effect on the quality of milk production in goats [1].

In order to implement appropriate quarantine treatments, it is necessary to understand the characteristics of the spread of CAE.

We propose new mathematical model in transmission of

CAE improved on the basis of sexually transmitted disease (STD) model. In addition, it was discussed that stability and generality of this new model. The proof the stability of the proposed CAE model is given by the following procedure. At first, the bounded is clarified by the comparison theorem. Then, locally asymptotically stability is confirmed by the Routh-Hurwitz criterion.

## 2. Mathematical Model

### 2.1. Mathematical Model of Infection Spread

It is known that spread of the infection can be modeled by a simple differential equation. There are various kinds of mathematical model of infectious diseases, but the simplest model is known as the SIR model. SIR model was proposed by W. O. Kermack and A. G. McKendrick in 1927 [3].

Under this SIR model, the goat population is divided into three categories, susceptible animal (S), infected animal (I), removed animal (R), then, the increase and decrease of the each category are indicated by the differential equations as follows;

$$\begin{cases} \frac{dS}{dt} = -\beta SI \\ \frac{dI}{dt} = \beta SI - \gamma I \\ \frac{dR}{dt} = \gamma I \end{cases}$$

Here  $\beta$  is the infectivity, and  $\gamma$  is the recovery rate or the isolation rate.

In recent years, mathematical model of infection spread have been proposed based on the SIR model.

These models are represented by differential equations, and include the pathological characteristic of infection including infection route, immunization rate and recovery rate.

## 2.2. Mathematical Model of CAE

Infection route of CAEV is mainly vertical transmission through breast milk and a horizontal transmission by sexual intercourse. This feature is very similar to the case of sexually transmitted disease (STD) in humans. Therefore, by referring to the mathematical model of STD, CAE model might be proposed.

Hashigo [4] has proposed a mathematical model for the infection of sexually transmitted disease (STD) in human case. In this model, the population is divided into 4 categories, men of infected and non-infected, women of infected and non-infected.

$$\begin{cases} M'_S = \lambda_M - \mu_M M_S - \beta_M c_M \frac{F_I}{F_S + F_I} M_S + f_M M_I \\ M'_I = -(\mu_M + \delta) M_I + \beta_M c_M \frac{F_I}{F_S + F_I} M_S - f_M M_I \\ F'_S = \lambda_F - \mu_F F_S - \beta_F c_F \frac{M_I}{M_S + M_I} F_S + f_F F_I \\ F'_I = -(\mu_F + \delta) F_I + \beta_F c_F \frac{M_I}{M_S + M_I} F_S - f_F F_I \end{cases}$$

Here,  $M_S$  is not-infected men,  $M_I$  is infected men,  $F_S$  is not-infected women,  $F_I$  is infected women,  $\lambda_M$  is number of births of male goat,  $\lambda_F$  is number of births of female goat,  $\mu_M$  is mortality rate of male,  $\mu_F$  is mortality rate of female,  $\delta$  is direct mortality of infectious disease,  $\beta_M$  is infection speed (female to male) and  $\beta_F$  is infection speed (male to female),  $c_M$  is frequency of sexual contact of men,  $c_F$  is frequency of sexual contact of women,  $f_M$  is cure rate (male),  $f_F$  is cure rate (female).

We constructed the mathematical model of CAE based on STD model. We used difference equations, because it is necessary to observe the change of goat per day in the rearing of goats. In case of CAEV, Vertical transmission to kid goat has been pointed out unlike STD in human case, the population is divided into 6 categories including kid. To consider kid goat, we introduce growth rate and vertical transmission rate. CAE is incapable cured, it is not necessary to consider cure rate. And to simplify CAE

model,  $c$  is total number of births,  $\beta c$  is omitted in  $\beta$ .

$$\mathcal{S} := \begin{cases} J'_S = (1-e)c - \mu_J J_S - g J_S \\ J'_I = ec - (\mu_J + \delta) J_I - g J_I \\ M'_S = \frac{1}{2} g J_S - \mu_M M_S - \beta_M \frac{M_S F_I}{F_S + F_I} \\ M'_I = \frac{1}{2} g J_I - (\mu + \delta) M_I + \beta_M \frac{M_S F_I}{F_S + F_I} \\ F'_S = \frac{1}{2} g J_S - \mu_F F_S - \beta_F \frac{M_I F_S}{M_S + M_I} \\ F'_I = \frac{1}{2} g J_I - (\mu + \delta) F_I + \beta_F \frac{M_I F_S}{M_S + M_I} \end{cases} \quad (2.1)$$

Where  $J_S$  is not-infected kid goat,  $J_I$  is infected kid goat,  $M_S$  is not-infected mature male goat,  $M_I$  is infected mature male goat,  $F_S$  is not-infected mature female goat,  $F_I$  is infected mature female goat,  $\mu_J$  is natural mortality of kid goat,  $\mu_M$  is natural mortality of male goat,  $\mu_F$  is natural mortality of female goat,  $\delta$  is direct mortality by CAE,  $\beta_M$  is infection speed (female to male goat) and  $\beta_F$  is infection speed (male to female goat),  $e$  is vertical transition rate,  $c$  is total number of births of per time unit,  $g$  is growth rate of per time unit.

This model describes the interaction among the goats. The population is divided into three classes. First is non-infected kid goat and infected-kid goat that caused by maternal infection. The second is non-infected male goat and infected male one that caused by contact infection. The third is non-infected female goat and infected one, similarly.

Remark that all constants are positive. Moreover,  $c$  is sufficiently large than constants  $e$ ,  $\delta$ ,  $\beta_M$ ,  $\beta_F$ . Furthermore, mortality rate  $\mu_J$ ,  $\mu_M$ ,  $\mu_F$ , are less than  $e$ ,  $\delta$ ,  $\beta_M$ ,  $\beta_F$ .

## 3. Stability Analysis

In this section, we refer the bounded and stability of the system of Eqs. (2-1) of  $\mathcal{S}$ . Consider the solutions in the Region  $Int \mathfrak{R}_+^6$ . In this region, the local existence, uniqueness and continuation result are guaranteed by standard theorem [6]. Namely, there exist the unique and bounded solution  $(J_S(t), J_I(t), M_S(t), M_I(t), F_S(t), F_I(t))$  of the system  $\mathcal{S}$  with  $J_S(0) > 0, J_I(0) > 0, M_S(0) > 0, M_I(0) > 0, F_S(0) > 0, F_I(0) > 0$  that exists on its maximum interval. Here,  $J_S(0), J_I(0), M_S(0), M_I(0), F_S(0), F_I(0)$  denote initial values of Eq. (2-1) in  $Int \mathfrak{R}_+^6$ . If the solution remains bounded, then the maximum interval is  $\forall t \in [0, \infty)$ . Furthermore the solution with  $(J_S(0), J_I(0), M_S(0), M_I(0), F_S(0), F_I(0))x \in Int \mathfrak{R}_+^6$  is always positive whenever the solution exists [7].

At first, to progress the analysis of the bounded and stability of the solution of the system  $S$  based on above presupposing. In advance, we consider two cases, one is infection-free environment and the other is infection existence one.

[Infection Free Environment]

We consider the infection-free environment in goat group. In this case, we only consider the non-infected terms in Eqs. (3-1),(3-3),(3-5).

$$\begin{cases} J'_S = c - (\mu_J + g)J_S \\ M'_S = \frac{1}{2}gJ_S - \mu_M M_S \\ F'_S = \frac{1}{2}gJ_S - \mu_F F_S \end{cases} \quad (3.1)$$

The above simultaneous differential equation is linear and ordinary type, hence, the equation can be solved easily, and result is as follow,

$$\begin{cases} J_S = \left( J_S(0) - \frac{1}{(\mu_J + g)} \right) \exp\{-(\mu_J + g)t\} + \frac{c}{(\mu_J + g)} \\ M_S = M_S(0) \exp(-\mu_M t) + \frac{c}{2\mu_M(\mu_J + g)} (1 - \exp(-\mu_M t)) \\ \quad + \frac{1}{2(\mu_M - \mu_J - g)} \left( J_S(0) - \frac{c}{(\mu_J + g)} \right) (\exp\{-(\mu_J + g)t\} - \exp\{-\mu_M t\}) \\ F_S = F_S(0) \exp(-\mu_F t) + \frac{c}{2\mu_F(\mu_J + g)} (1 - \exp(-\mu_F t)) \\ \quad + \frac{1}{2(\mu_F - \mu_J - g)} \left( J_S(0) - \frac{c}{(\mu_J + g)} \right) (\exp\{-(\mu_J + g)t\} - \exp\{-\mu_F t\}) \end{cases} \quad (3.2)$$

From the above solutions, the equilibrium  $e_0^*$  of infection free system can be given by  $J_S = M_S = F_S = 0$ , then we have

$$e_0^* = \left( \frac{c}{(\mu_J + g)}, \frac{c}{2\mu_M(\mu_J + g)}, \frac{c}{2\mu_F(\mu_J + g)} \right) \quad (3.3)$$

In this case, the equilibrium is asymptotically stable.

[Infection Existence Environment]

Secondary, we consider infection existence environment in goat, in this case, we divide the system  $S$  of Eqs. (2-1)-(2-6) into three subsystems, that is

$S'_J = \{J'_S, J'_I\}, S'_M = \{M'_S, M'_I\}, S'_F = \{F'_S, F'_I\}$  for  $\forall t \in [0, \infty)$ . Then, define  $J \triangleq J_S + J_I, M \triangleq M_S + M_I, F \triangleq F_S + F_I$ . At first, the subsystem  $S_{sub,J}$  is given by

$$S_{sub,J} := \begin{cases} J'_S = c(1-e) - (\mu_J + g)J_S \\ J'_I = ce - (\mu_J + g + \delta_J)J_I \end{cases} \quad (3.4)$$

Above subsystem is linearly independent, so the solution pair is given by

$$S_{sub,J} = \begin{cases} J_S(t) = \left( J_S(0) - \frac{c(1-e)}{(\mu_J + g)} \right) \exp\{-(\mu_J + g)t\} + \frac{c(1-e)}{(\mu_J + g)} \\ J_I(t) = \left( J_I(0) - \frac{ce}{(\mu_J + g + \delta_J)} \right) \exp\{-(\mu_J + g + \delta_J)t\} \\ \quad + \frac{ce}{(\mu_J + g + \delta_J)} \end{cases} \quad (3.5)$$

To find the equilibrium  $e_{0,J}^*$  of the system  $S_{sub,J}$ , we take  $J'_S = J'_I = 0$ , then,

$$e_{0,J}^* = (J_S^*, J_I^*) = \left( \frac{c(1-e)}{(\mu_J + g)}, \frac{ce}{(\mu_J + g + \delta_J)} \right) \quad (3.6)$$

From the solution of (5-5), we conclude that the equilibrium of system  $S_{sub,J}$  is asymptotically stable. Now, we define the newly infected number  $R_{J,0}$  of kindling, as

$$R_{J,0} = \frac{ce}{(\mu_J + g + \delta_J)} \quad (3.7)$$

The number  $R_{J,0}$  means the rate at which one infected adult female goat breeds a infected kindling. From the definition of  $R_{J,0}$ , if  $R_{J,0} > 1$  the infection ratio is increasing, and if  $R_{J,0} < 1$ , the ratio is constant or decreasing. In other words, if  $R_{J,0} > 1$ , the number of infected kid goat by maternal infection are increased and CAE is spread widely.

Now, we could see the asymptotically stability of the subsystem  $S_{sub,J}$ , the left behind problem is to show the bounded and stability of the subsystem  $S_{sub,M}$  and  $S_{sub,F}$ . In advance to prove this, we evaluate the maximum and minimum solutions  $\bar{J}$  and  $\underline{J}$  of  $J \triangleq J_S + J_I$ . By applying the comparison theorem and Eq.(5-4) with  $J$ , we have following inequalities,

$$\begin{cases} J' \leq \bar{J}' = c - (\mu_J + g)\bar{J} \\ J' \geq \underline{J}' = c - (\mu_J + g + \delta_J)\underline{J} \end{cases} \quad (3.8)$$

To solve the above equation, there exist positive constants  $J_{max}$  and  $J_{min}$ , then

$$\begin{cases} J(t) \leq \bar{J}(t) = \left( \bar{J}(0) - \frac{c(1-e)}{(\mu_J + g)} \right) \exp\{-(\mu_J + g)t\} \\ \quad + \frac{c(1-e)}{(\mu_J + g)} < J_{max} \\ J(t) \geq \underline{J}(t) = \left( \underline{J}(0) - \frac{ce}{(\mu_J + g + \delta_J)} \right) \exp\{-(\mu_J + g + \delta_J)t\} \\ \quad + \frac{ce}{(\mu_J + g + \delta_J)} > J_{min} \end{cases} \quad (3.9)$$

where  $J_{max}$  and  $J_{min}$  represent  $J_{max} > \max \bar{J}(t)$ ,  $J_{min} < \min \underline{J}(t)$ , for  $\forall t \in [0, \infty)$ , respectively. Then, above preparation, let us discuss the bounded of the system  $S$ .

Now, we consider the bounded solution of the subsystems  $S_{sub,M}, S_{sub,F}$ . By using definition of  $M$  and  $F$ , we have conjunction equations as follows,

$$\begin{cases} S_{sub,M} : M' = \frac{1}{2}gJ - \mu_M M - \delta_M M_I \\ S_{sub,F} : F' = \frac{1}{2}gJ - \mu_F F - \delta_F F_I \end{cases} \quad (3.10-11)$$

The following theorem implies that the solution starting in  $\mathfrak{R}_+^6$ , and it remain bounded in  $\mathfrak{R}_+^6$  for  $\forall t \in [0, \infty)$ .

**Theorem 1**

If  $(J_S(0), J_I(0), M_S(0), M_I(0), F_S(0), F_I(0)) \in \text{Int}\mathfrak{R}_+^6$  holds, and always exist in  $\mathfrak{R}_+^6$ , then  $(J_S(t), J_I(t), M_S(t), M_I(t), F_S(t), F_I(t))$  is ultimately bounded in  $\mathfrak{R}_+^6$  for  $\forall t \in [0, \infty)$ .

**Proof.**

From the conjunction equation in Eq.(3.10), then,

$$M' = \frac{1}{2}gJ - \mu_M M - \delta_M M_I < \frac{1}{2}gJ_{\max} - \mu_M M. \quad (3.12)$$

From the comparison theorem, we have following inequality,

$$M(t) < (M(0) - \frac{1}{2\mu_M}gJ_{\max})\exp\{-(\mu_M)t\} + \frac{1}{2\mu_M}gJ_{\max} \quad (3.13)$$

It implies that  $M$  is bounded above, ultimately. Moreover, from Eq. (5-10), we obtain

$$M' = \frac{1}{2}gJ - \mu_M M - \delta_M M_I > \frac{1}{2}gJ_{\min} - (\mu_M + \delta_M)M \quad (3.14)$$

From the comparison theorem again, we have

$$\begin{aligned} M(t) &> (M(0) - \frac{1}{2(\mu_M + \delta_M)}gJ_{\min})\exp\{-(\mu_M + \delta_M)t\} \\ &+ \frac{1}{2(\mu_M + \delta_M)}gJ_{\min} \end{aligned} \quad (3.15)$$

It implies that  $M$  is bounded below, ultimately. Thus, we can conclude that there exist positive constants  $M_{\max}$  and  $M_{\min}$  such that  $M_{\min} < M < M_{\max}$  for sufficiently large time. In the similar manner, we can also conclude that there exist some positive constants  $F_{\min}$  and  $F_{\max}$  such that  $F_{\min} < F < F_{\max}$  for sufficiently large time. Consequently, if  $(J_S(0), J_I(0), M_S(0), M_I(0), F_S(0), F_I(0)) \in \text{Int}\mathfrak{R}_+^6$  holds, then  $(J_S(t), J_I(t), M_S(t), M_I(t), F_S(t), F_I(t))$  is always ultimately bounded in  $\mathfrak{R}_+^6$ . This shows that the solution with  $(J_S(0), J_I(0), M_S(0), M_I(0), F_S(0), F_I(0)) \in \text{Int}\mathfrak{R}_+^6$  exists and bounded in  $\mathfrak{R}_+^6$  for  $\forall t \in [0, \infty)$  □

Next, we will consider the stability of the equilibrium of Eq. (2-1)-(2-6). To advance analyse, we introduce the convenient form of the system  $\hat{S}$ , as

$$S := \begin{cases} J_S' = (1-e)c - \mu_J J_S - gJ_S \\ J_I' = ec - (\mu_J + \delta)J_I - gJ_I \\ M_S' = \frac{1}{2}gJ_S - \mu M_S - \beta_M \frac{M_S F_I}{F} \\ M_I' = \frac{1}{2}gJ_I - (\mu + \delta)M_I + \beta_M \frac{M_S F_I}{F} \\ F_S' = \frac{1}{2}gJ_S - \mu F_S - \beta_F \frac{M_I F_S}{M} \\ F_I' = \frac{1}{2}gJ_I - (\mu + \delta)F_I + \beta_F \frac{M_I F_S}{M} \end{cases} \quad (3.16-21)$$

In above system, we take the positive constants  $\widetilde{M}$  and  $\widetilde{F}$  as  $\widetilde{M} = \min(M_S(t) + M_I(t))$  and  $\widetilde{F} = \min(F_S(t) + F_I(t))$  for  $\forall t \in [0, \infty)$ , respectively. The reason of introducing the system  $\hat{S}$  instead of the system  $S$  is as follows. In the analysis of the stability of the  $S$ , first of all, we focus on the local stability of the equilibrium described by Eqs.(2.1)-(2.6). Therefore, it is reasonable to replace the variables  $M, F$  with  $\widetilde{M}, \widetilde{F}$  without loss of generality. In advance to give the proof of locally asymptotically stability of the system  $\hat{S}$ , we take on the assumption that the ratio of infected male and female goat are greater than non-infected ones in the existence of infection environment. It means that for the equilibrium points  $M_I^*, F_I^*$  are greater than  $M_S^*, F_S^*$ , that is,  $M_S^*, F_S^*$  and  $M_I^* > M_S^*$ . The framework of the proof of the Theorem 2 is as follows. First step is to obtain the  $e^* = \{M_S^*, M_I^*, F_S^*, F_I^*\}$  of the system  $\hat{S}$  (see Appendix1). Next is to calculate the characteristic equation correspond to the Jacobian matrix with Eqs.(5.16)-(5.21). Finally, to evaluate the stability of the system  $\hat{S}$  based on Routh-Hurwitz criterion.

**Theorem 2.**

If the equilibrium satisfied following inequality, that is  $F_I^* > F_S^*$ , and  $M_I^* > M_S^*$ , then  $e^* = \{F_S^*, F_I^*, M_S^*, M_I^*\}$  is asymptotically stable on  $\text{Int}\mathfrak{R}_+^6$ .

**Proof.**

At first, the equilibrium  $e^* = \{F_S^*, F_I^*, M_S^*, M_I^*\}$  of the system  $\hat{S}$  is given by(see Appendix1),

$$\begin{cases} M_S^* = \frac{g\mu_M \beta_F \delta F J_S^*}{2\mu_M \delta^2 F + \beta_M g(\mu_M + \delta)J^*} \\ M_I^* = \frac{2g\mu_M \beta_F \delta M J_I^* + \beta_M \beta_F g^2 J_I^{*2}}{4\mu_M \delta^2 M + 2\beta_M g(\mu_M + \delta)J^*} \\ F_S^* = \frac{g\mu_F \beta_M \delta M J_S^*}{2\mu_F \delta^2 M + \beta_F g(\mu_F + \delta)J^*} \\ F_I^* = \frac{2g\mu_F \beta_M \delta M J_I^* + \beta_F \beta_M g^2 J_I^{*2}}{4\mu_F \delta^2 M + 2\beta_F g(\mu_F + \delta)J^*} \end{cases} \quad (3.21)$$

The Jacobian matrix of the vector fields corresponding the equilibrium of the system  $\hat{S}$  is given by

$$J^* = \begin{pmatrix} -\mu_M - \alpha_M F_I^* & 0 & 0 & -\alpha_F M_S^* \\ -\alpha_M F_I^* & -(\mu_M + \delta) & 0 & \alpha_F M_S^* \\ 0 & -\alpha_M F_S^* & -\mu_F - \alpha_F M_I^* & 0 \\ 0 & \alpha_M F_S^* & \alpha_F M_I^* & -(\mu_F + \delta) \end{pmatrix} \quad (3.22)$$

where  $\alpha_M = \beta_M / \tilde{F}$  and  $\alpha_F = \beta_F / \tilde{M}$ . Then, the characteristic equation of the system  $\hat{S}$  is as follows

$$|\lambda I - J^*| = \lambda^4 + a_1 \lambda^3 + a_2 \lambda^2 + a_3 \lambda + a_4 = 0. \quad (3.23)$$

The coefficients  $(a_1, a_2, a_3, a_4)$  of the characteristic equation are given by Appendix2. By using these coefficients, and to evaluate all the eigenvalues of the characteristic equation, we construct the Hurwitz matrix as

$$H = \begin{bmatrix} a_1 & a_3 & 0 & 0 \\ 1 & a_2 & a_4 & 0 \\ 0 & a_1 & a_3 & 0 \\ 0 & 1 & a_2 & a_4 \end{bmatrix}. \quad (3.24)$$

We could confirm the leading principal minors by calculation, all of these are positive (see Appendix2). Then, from the Routh-Hurwitz stability criterion, all the eigenvalues have negative real parts. Consequently, we conclude that the equilibrium of system  $\hat{S}$  is locally asymptotically stable in  $Int \mathfrak{R}_+^6$  for  $\forall t \in [0, \infty)$ .

According to above Theorem 1 and 2, we can conclude that the proposed CAE model is assured bounded and locally asymptotically stability.

### 4. Discussion and Conclusion

To verify the effectiveness of the proposed CAE model, numerical simulations are carried out both infection free and existence environments. The parameters were shown in Table 1, and initial values of the goats are given in the same Table. Since the report on mathematical epidemiology related to CAE is poor, the parameters of infection force are dummy. But parameters for mortality and growth of goats were taken as the value inferred from field works in Tarama Island in Okinawa, JAPAN. Fig. 1 is shown the behaviors of infection free case. From this figure, the number of kids, male and female goat is reached the equilibrium points, respectively. On the other hand, Fig. 2 is shown the infection existence case. From this figure, the number of infected kid, male and female goats are increasing according to time, after that, they converge to neighborhood of its equilibrium. That is, it can be clear that the solution of the proposed CAE model is stable. Therefore, the model proposed here is valid as one of the CAE model.

Table 1. Initial values and parameters.

		Infection free	Infection existence
<i>Initial values</i>			
$J_S$	Susceptible kid goat	200	200
$J_I$	Infected kid goat	20	20
$M_S$	Susceptible male goat	400	400
$M_I$	Infected male goat	40	40
$F_S$	Susceptible female goat	400	400
$F_I$	Infected male goat	40	40
<i>Parameters</i>			
$\eta$	Birth rate per unit time (day)	0.0023	0.0023
$e$	Infection rate of vertical	0	0.5
$\mu_k$	Mortality of kid goats	0.0065	0.0065
$\mu_M$	Mortality of male goats	0.0003	0.0003
$\mu_F$	Mortality of female goats	0.0004	0.0004
$\delta$	Direct mortality of disease	0	0
$\beta_1$	Infection speed (female to male)	0	0.3
$\beta_2$	Infection speed (male to female)	0	0.2
$g$	Growth rate of per time unit	0.0027	0.0027

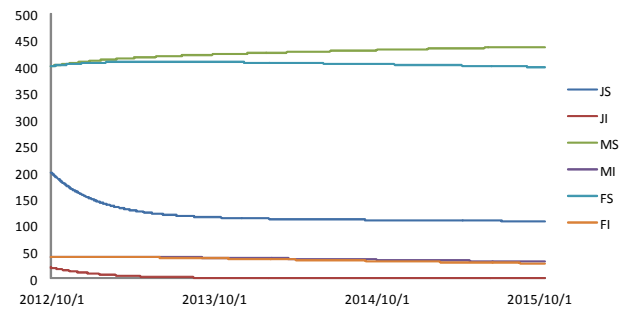


Fig 1. Result of simulation in case of infection free

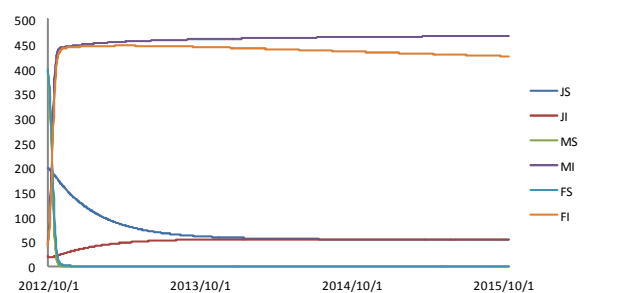


Fig 2. Result of simulation in case of infection existence

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## Appendix

### Appendix1

Equilibrium of the system  $S$ . To obtain the equilibrium  $e_S^* = \{M_S^*, M_F^*, F_S^*, F_I^*\}$  for the system  $\hat{S}$ , we consider the following four-dimensional simultaneous nonlinear equation.

$$\begin{cases} \frac{1}{2}gJ_S^* - \mu M_S^* - \alpha_M \frac{M_S^* F_I^*}{M} = 0 & (A1-1) \end{cases}$$

$$\begin{cases} \frac{1}{2}gJ_I^* - (\mu + \delta)M_I^* + \alpha_M \frac{M_S^* F_I^*}{M} = 0 & (A1-2) \end{cases}$$

$$\begin{cases} \frac{1}{2}gJ_S^* - \mu F_S^* - \alpha_F \frac{F_S^* M_S^*}{F} = 0 & (A1-3) \end{cases}$$

$$\begin{cases} \frac{1}{2}gJ_I^* - (\mu + \delta)F_I^* + \alpha_F \frac{F_S^* M_S^*}{F} = 0 & (A1-4) \end{cases}$$

At first, we find a solution of  $F_I^*$  for the system  $S$ . From the definition of  $J$ , we have  $(J_S^* + J_I^*)/2 = J^*/2$ . Then, from eq. (A1-1) and (A1-2),

$$\frac{1}{2}J^* - \mu_M(M_S^* + M_I^*) - \delta M_I^* = 0 \quad (A1-5)$$

Then, we have

$$M_I^* = \frac{1}{\mu_M + \delta} \left( \frac{1}{2}gJ^* - \mu_M M_S^* \right) \quad (A1-6)$$

From, eqs. (A1-3), and (A1-4),

$$F_S^* = \frac{1}{\mu_F} \left( \frac{1}{2}gJ^* - (\mu_F + \delta)F_I^* \right) \quad (A1-7)$$

Furthermore, form (1)

$$M_S^* = \frac{gJ^* F}{2(\mu_F F + \beta_M F_I^*)} \quad (A1-8)$$

From above equation, and substituting  $M_S^*$  into eq. (A1-6), we have

$$M_I^* = \frac{g\beta_M J^* F_I^*}{2(\mu_M + \delta)(\mu_F F + \beta_M F_I^*)} \quad (A1-9)$$

Furthermore, from (A1-7) to (A1-9),  $F_S^* \cdot M_I^*$  is given by

$$F_S^* \cdot M_I^* = \frac{g\beta_M J^* F_I^* \left( gJ^* - 2(\mu_M + \delta)F_I^* \right)}{4\mu_F (\mu_M + \delta)(\mu_F F + \beta_M F_I^*)} \quad (A1-10)$$

Finally, to derive the second order algebraic equation for  $F_I^*$ , and multiplying  $M$  to (A1-4), then, we have

$$\Omega_1 F_I^{*2} + \Omega_2 F_I^* + \Omega_3 = 0 \quad (A1-11)$$

Where, the coefficients  $\Omega_1, \Omega_2, \Omega_3$  are given by as follows.

$$\begin{cases} \Omega_1 = -4(\mu_F + \delta)(\mu_M + \delta)\mu_M \beta_M M - 2\beta_F \beta_M g(\mu_F + \delta)J^* \\ \approx -4\mu_F \delta^2 \beta_M M - 2\beta_F \beta_M g(\mu_F + \delta)J^* \\ \Omega_2 = -4(\mu_F + \delta)(\mu_M + \delta)\mu_M \beta_M M - 2\beta_F \beta_M g(\mu_F + \delta)J^* \\ \approx -4\mu_F \delta^2 \beta_M M - 2\beta_F \beta_M g(\mu_F + \delta)J^* \\ \Omega_3 = 2g\mu_F \mu_M (\mu_M + \delta)MF = 0 \end{cases} \quad (A1-12)$$

where,  $\mu_F, \mu_M$  is smaller enough to other parameters  $\beta_F, \beta_M, g, \delta$ , hence  $\mu_F \mu_M, \mu_F \mu_M^2$  can be negligible. Consequently, the second order algebraic equation for  $F_I^*$  is reduced to

$$\begin{aligned} & (4\mu_F \delta^2 \beta_M M + 2\beta_F \beta_M g(\mu_F + \delta)J^*) F_I^{*2} \\ & - (2g\mu_F \beta_M \delta M J_I^* + \beta_F \beta_M g^2 J_I^{*2}) F_I^* = 0 \end{aligned} \quad (A1-13)$$

Furthermore  $F_S^*$  is calculated by relation of  $F_S^*$  and  $F_I^*$  in eq.(A1-8).

Then, we have the meaningful solution of  $F_S^*$  and  $F_I^*$  as follow,

$$\begin{cases} F_S^* = \frac{g\mu_F \beta_M \delta M J_S^*}{2\mu_F \delta^2 M + \beta_F g(\mu_F + \delta)J^*} \\ F_I^* = \frac{2g\mu_F \beta_M \delta M J_I^* + \beta_F \beta_M g^2 J_I^{*2}}{4\mu_F \delta^2 M + 2\beta_F g(\mu_F + \delta)J^*} \end{cases} \quad (A1-14)$$

Similarity,  $M_S^*$  and  $M_I^*$  are given by as follows.

$$\begin{cases} M_S^* = \frac{g\mu_M \beta_F \delta F J_S^*}{2\mu_M \delta^2 F + \beta_M g(\mu_M + \delta)J^*} \\ M_I^* = \frac{2g\mu_M \beta_F \delta M J_I^* + \beta_M \beta_F g^2 J_I^{*2}}{4\mu_M \delta^2 M + 2\beta_M g(\mu_M + \delta)J^*} \end{cases} \quad (A1-15)$$

From above consideration, we obtain Eq.(5-21).

### Appendix2

In this appendix, we give the detail explanation for Theorem 2.

At first, we give the coefficients of the characteristic equation of Jacobian matrix.

$$|\lambda I - J_*| = \lambda^4 + a_1 \lambda^3 + a_2 \lambda^2 + a_3 \lambda + a_4 = 0 \quad (A2-1)$$

where,

$$\begin{cases} a_1 = 4\mu + 2\delta + \alpha_F M_I^* + \alpha_M F_I^* \\ a_2 = -\alpha_F M_S^* \alpha_M F_S^* + 3\delta \alpha_F M_I^* + 6\mu\delta \\ \quad + 3\mu \alpha_M F_I^* + 2\delta \alpha_F M_I^* + \alpha_F M_F^* \alpha_M F_F^* \\ a_3 = -2\mu \alpha_M F_S^* \alpha_F M_S^* + 2\mu \alpha_F M_I^* \alpha_M F_I^* \\ \quad + 2\delta \alpha_M F_I^* + 4\mu \delta \alpha_F M_I^* + 2\mu \delta^2 + \delta^2 \alpha_M F_I^* \\ a_4 = 2\mu \delta \alpha_F M_I^* \alpha_M F_I^* + \delta^2 \alpha_M F_I^* \alpha_F M_I^* \\ \quad + \mu \delta^2 \alpha_M F_I^* + \mu \delta^2 \alpha_F M_I^* \end{cases} \quad (A2-2)$$

For conveniently, we put the coefficients  $\mu_M = \mu_F = \mu$ . Furthermore, in above equations, we take the higher order of  $\mu$  equals to zero, that is,  $\mu^n \approx 0, (n \geq 2)$ , under the assumption that  $\mu_F, \mu_M$  are sufficiently small comparing with the other coefficients  $\alpha_F, \alpha_M, g, \delta$  (given by Section 2), hence,  $\mu_F \mu_M, \mu_F \mu_M^2$  (etc.) can be negligible.

From the Routh-Hurwitz Criterion, necessary and sufficiently condition for the stability of the system given by Eq. (A2-1) is that all of the roots have negative real part. In the other words, to prove the stability of the Eq. (A2-1), it is necessary to check the following conditions, 1) all of the coefficient  $a_1, a_2, a_3, a_4$  of the Eq.(A2-1) exist and positive, and , 2) all of the leading principal minor of Hurwitz matrix are positive.

First of all, it is self-evidence that all the coefficients are exist. Secondary, it is clear that  $a_1$  and  $a_4$  are positive. Furthermore,  $a_2$  and  $a_3$  are also positive from the assumption of  $M_I^* > M_S^*, F_I^* > F_S^*$ . In the above description, in can be shown that all of the coefficient  $a_1, a_2, a_3, a_4$  of the Eq.(A2-1) exist and positive.

Next, to show that all of the leading principal minor of Hurwitz matrix are positive, we give the Hurwitz matrix, again.

$$H = \begin{bmatrix} a_1 & a_3 & 0 & 0 \\ 1 & a_2 & a_4 & 0 \\ 0 & a_1 & a_3 & 0 \\ 0 & 1 & a_2 & a_4 \end{bmatrix}. \quad (A2-3)$$

Where, we take the leading principal minors  $H_1, H_2, H_3,$  and  $H_4$  as follows.

$$\begin{aligned} H_1 &= a_1, & H_2 &= \begin{vmatrix} a_1 & a_3 \\ 1 & a_2 \end{vmatrix} \\ H_3 &= \begin{vmatrix} a_1 & a_3 & 0 \\ 1 & a_2 & a_4 \\ 0 & a_1 & a_3 \end{vmatrix}, & H_4 &= \begin{vmatrix} a_1 & a_3 & 0 & 0 \\ 1 & a_2 & a_4 & 0 \\ 0 & a_1 & a_3 & 0 \\ 0 & 1 & a_2 & a_4 \end{vmatrix} \end{aligned} \quad (A2-4)$$

Substituting the coefficients given in (A2-2) into (A2-4),

the elements of leading principal minors can be calculated. At first, we have

$$H_1 = a_1 = 4\mu + 2\delta + \alpha_F M_I^* + \alpha_M F_I^* > 0. \quad (A2-5)$$

In order to clear the expression, we focus the negative-part of elements for  $H_2, H_3$  and  $H_4$ , respectively, then comparing with the corresponding positive elements based on the assumption of  $M_I^* > M_S^*, F_I^* > F_S^*$ . For instance, calculating procedure of  $H_2$  is as follows.

$$\begin{aligned} H_2 &= \begin{vmatrix} a_1 & a_3 \\ 1 & a_2 \end{vmatrix} = a_1 a_2 - a_3 \\ &= -(\alpha_M F_I^* \alpha_M F_S^* \alpha_F M_S^* + \alpha_M F_S^* \alpha_F M_S^* \alpha_M F_I^* \\ &\quad + 2\delta \alpha_F M_S^* \alpha_M F_S^* + 2\mu \alpha_F M_S^* \alpha_M F_S^*) \\ &\quad + \{\alpha_F M_I^* (\alpha_M F_I^*)^2 + (\alpha_F M_I^*)^2 \alpha_M F_I^* + 2(\alpha_M F_I^*)^2 \\ &\quad + 3\mu (\alpha_M F_I^*)^2\} + \{4\delta \alpha_F M_I^* \alpha_M F_I^* + 8\mu \alpha_F M_I^* \alpha_M F_I^* \\ &\quad + 2\delta (\alpha_F M_I^*)^2 + 3\mu (\alpha_F M_I^*)^2 + 4\delta^2 \alpha_M F_I^* \\ &\quad + 16\delta \mu \alpha_F M_S^* + 4\delta^2 \alpha_F M_I^* + 16\delta \mu + 14\delta^2 \mu\} \\ &= (\alpha_F M_I^* \alpha_M F_I^* - \alpha_F M_S^* \alpha_M F_S^*) \alpha_M F_I^* \\ &\quad + (\alpha_F M_I^* \alpha_M F_I^* - \alpha_F M_S^* \alpha_M F_S^*) \alpha_F M_I^* \\ &\quad + 2\delta (2\alpha_F M_I^* \alpha_M F_I^* - \alpha_F M_S^* \alpha_M F_S^*) \\ &\quad + 2\mu (4\alpha_F M_I^* \alpha_M F_I^* - \alpha_F M_S^* \alpha_M F_S^*) \\ &\quad + \{4\delta \alpha_F M_I^* \alpha_M F_I^* + 8\mu \alpha_F M_I^* \alpha_M F_I^* \\ &\quad + 2\delta (\alpha_F M_I^*)^2 + 3\mu (\alpha_F M_I^*)^2 + 4\delta^2 \alpha_M F_I^* \\ &\quad + 16\delta \mu \alpha_F M_S^* + 4\delta^2 \alpha_F M_I^* + 16\delta \mu + 14\delta^2 \mu\} \end{aligned} \quad (A2-6)$$

Hence, the first to fourth terms of the right-hand side are positive by the assumption. Therefore, it can be shown that  $H_2 > 0$ . Similarity, it can be indicated that  $H_3, H_4$  are positive by using above procedure.

As a result, we have shown that the system  $\hat{S}$  satisfied the Routh-Hurwitz stability condition. We have thus the proved that all the roots of the characteristic polynomial(A2-1) have negative real part.

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