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Kermack and McKendrick Revisited: The Variable Susceptibility Model for Infectious Diseases*

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In this paper, we reformulate Kermack's and McKendrick's variable susceptibility model for infectious diseases as a nonlinear age-dependent population dynamics model, then we prove an existence and uniqueness result for the endemic steady state. Subsequently we discuss the local stability of the endemic steady state. Finally we show that Pease's evolutionary epidemic model can be seen as a special case of the variable susceptibility model and discuss possible extensions.

Key words: Kermack and McKendrick, epidemic model, endemic threshold, age-dependent population dynamics, variable susceptibility

1. Introduction: Kermack's and McKendrick's Epidemic Models

It is well known that Kermack and McKendrick were most important pioneers in the field of mathematical epidemiology. Between World War I and II, they published a series of papers about deterministic structured population models for the spread of infectious diseases, which have been so far referred by many authors again and again as an important origin of idea. Nevertheless, in my opinion, possibilities and implications of their epidemic models have been not necessarily fully examined.

The first paper published in 1927 [10] was especially famous among researchers, in which they developed, what we call, SIR (susceptible-infected-removed) epidemic model with duration dependent (variable) infectivity, that is, the infection rate depends on the duration in the infected and infectious status and the infection happens only one time in the life of host individual. So let us call this early Kermack's and McKendrick's model as the *variable infectivity model*. If the infectivity is assumed to be constant, this structured SIR model is reduced to the well known ordinary differential equation model. Even now, unfortunately most people keep referring to the simplest ODE case of this Kermack's and McKendrick's SIR epidemic model as if it were the only Kermack and McKendrick model. But this leads a historical misunderstanding, and should stop (Diekmann, Heesterbeek and Metz [4]). Re-examination of the variable infectivity model has been started by Metz [14] and Diekmann [3] (see also Metz and Diekmann [13], Iannelli [6]), and up to now its mathematical features are well understood. The importance of this kind of structured SIR model is now widely recognized, since it can be used to formulate models

*This paper is dedicated to the memory of Professor YAMAGUTI Masaya (1925–1998).

for epidemic with long incubation period and variable infectivity such as HIV/AIDS epidemic (Thieme and Castillo-Chavez [19]). During the past two decades SIR-type epidemic models have been well studied and extended to various kind of epidemic-demographic situations (Anderson [1], Anderson and May [2]).

On the other hand, as far as I know, Kermack's and McKendrick's more general complex models developed in two papers written in 1932 [11] and 1933 [12] have been still neglected. In those papers they have proposed a kind of duration-dependent epidemic model, where the transmission rate depends on both duration of infected host (*disease-age/infection age*) and duration of susceptible host. The total population is decomposed into three compartments, the never infected (completely susceptible), infected and recovered (partially susceptible) populations. The host population is structured by duration variable in each status, but the chronological age is neglected. The demography of host population is introduced through birth rate, death rate and migration. We call this model as the *variable susceptibility model*, since the infection rate from infecteds to recovered population depends on not only the disease-age but also the duration variable of recovered host. That is, in this model, recovered individuals can be reinfected repeatedly, and their reinfection probability depends on how long it takes since the last infection. Kermack and McKendrick concentrated to the problem of endemicity of this model, that is, they examined conditions under which existence and uniqueness of the endemic steady state could be established. Though from modern mathematical point of view their treatments for the problem were not necessarily rigorous, it is possible to complete their proofs.

Why so far has their variable susceptibility model been paid less attention and neglected? Though one reason would be that their model was too complex to be analyzed analytically, another important reason would be that they did not give an answer to the question what kind of real epidemic could be well described by this type of model and whether it is worth while studying this complex model. However, today we can recognize that their idea of variable susceptibility is very much important, since their formulation is so flexible that we can take into account the genetic change of virus or the variation of host immunity structure. In fact their exists at least two main reasons that the host immunity will decay as time passes, one possibility is that there is a natural decay of host immunity, another reason is the antigenic change in virus. The second reason is now becoming more and more important, because we are confronting with difficulty to control epidemic in which by the genetic changes in virus the vaccination and the host immunity becomes less effective. The evolutionary mechanism would be one of most important factors which reemerge infectious diseases at the present day.

In this paper, we reformulate Kermack's and McKendrick's variable susceptibility model as a nonlinear age-dependent population dynamics model, by which its well-posedness will naturally become clear to the reader, since the reduced nonlinear age-dependent model can be studied by the well known technique developed by Gurtin and MacCamy [5]. Next we prove an existence and uniqueness result for the endemic steady state. Thought this result was the main theme of Kermack's

and McKendrick' papers, their proof is loosely stated. Hence we will complete their original proof with mathematical rigor. Subsequently we study the stability of the endemic steady state. Finally we show its applications to the evolutionary epidemic model and discuss possible extensions.

2. The Variable Susceptibility Model

Here we formulate the variable susceptibility model as an initial-boundary value problem of McKendrick partial differential equation system. Then we discuss the existence and uniqueness of the nonnegative solutions. For simplicity, we do not present the variable susceptibility model in its most general formula. That is, we neglect the (chronological) age structure of host populations and migration effect.

Let $s(t,\tau)$ be the density of susceptible population without experience of infection (which is also called as *virgin* population in the terminology of Kermack and McKendrick) at time t and duration (the time elapsed from entry into the s-state) τ. Let $i(t,\tau)$ be the density of infected and infectious population at time t and duration (the time elapsed from infection) τ, which is often called as *disease age* or *infection age*, and let $r(t,\tau)$ be the density of recovered population (partially susceptible population) at time t and duration τ (the time elapsed from the last recovery). The duration τ in each state is also called as *class age*.

Let m and μ denote the crude birth rate and death rate, $\gamma(\tau)$ the recovery rate at class age τ, $\beta_1(\tau)\beta_2(\sigma)$ the infection rate from infected individual at class age σ to recovered host at class age τ. For the transmission rate, we adopt the following intuitively reasonable assumption:

ASSUMPTION 2.1. *We assume that* $\gamma, \beta_j \in L^\infty_+(\mathbf{R}_+)$, $(j = 1,2)$ *and* $\beta_1(\tau)$ *is a monotone non-decreasing function, and the infection rate from infecteds at class age* σ *to never infected individuals is given by* $\beta_1(\infty)\beta_2(\sigma)$, *where* $\beta_1(\infty) := \sup_{\tau\geq 0}\beta_1(\tau)$.

Biologically speaking, $\beta_2(\tau)$ reflects the variable infectivity of infected individuals and $\beta_1(\tau)$ denotes the variable susceptibility of recovered individuals, and its monotonicity reflects the relative decay of immunity level of recovered population. Since here we assume that there is no correlation between those two forces, the transmission rate is assumed to be given by the proportionate mixing assumption. Then the variable susceptibility model is formulated as follows:

$$\frac{\partial s(t,\tau)}{\partial t} + \frac{\partial s(t,\tau)}{\partial \tau} = -\mu s(t,\tau) - s(t,\tau)\beta_1(\infty)\int_0^\infty \beta_2(\sigma) i(t,\sigma)d\sigma, \tag{2.1}$$

$$\frac{\partial i(t,\tau)}{\partial t} + \frac{\partial i(t,\tau)}{\partial \tau} = -(\mu + \gamma(\tau))i(t,\tau), \tag{2.2}$$

$$\frac{\partial r(t,\tau)}{\partial t} + \frac{\partial r(t,\tau)}{\partial \tau} = -\mu r(t,\tau) - r(t,\tau)\beta_1(\tau)\int_0^\infty \beta_2(\sigma) i(t,\sigma)d\sigma, \tag{2.3}$$

$$s(t,0) = m\int_0^\infty (s(t,\tau)+i(t,\tau)+r(t,\tau))d\tau, \tag{2.4}$$

$$i(t,0) = \int_0^\infty \{\beta_1(\infty)s(t,\tau)+\beta_1(\tau)r(t,\tau)\}d\tau \int_0^\infty \beta_2(\tau)i(t,\tau)d\tau, \tag{2.5}$$

$$r(t,0) = \int_0^\infty \gamma(\tau)i(t,\tau)d\tau, \tag{2.6}$$

$$s(0,a) = s_0(a), \quad i(0,a) = i_0(a), \quad r(0,a) = r_0(a), \tag{2.7}$$

where (s_0, i_0, r_0) denotes an initial data. Let $N(t)$ be the total size of host population given by

$$N(t) := \int_0^\infty (s(t,\tau)+i(t,\tau)+r(t,\tau))d\tau. \tag{2.8}$$

If we are concerned with the classical solution, it is reasonable to seek the solution in the positive cone of the Sobolev space $W^{1,1}$, hence we can assume that $s(t,\infty) = i(t,\infty) = r(t,\infty) = 0$. Therefore it follows from (2.1)–(2.6) that

$$\frac{dN(t)}{dt} = (m-\mu)N(t),$$

so if $m = \mu$, the total size of the host population is constant given by

$$N(t) = N := \int_0^\infty (s_0(\tau)+i_0(\tau)+r_0(\tau))d\tau. \tag{2.9}$$

Let us define a population vector $p(t,\tau) := (s(t,\tau), i(t,\tau), r(t,\tau))^{\mathrm{T}}$ (T denotes the transpose of a vector) and the state space E_+ as the positive cone of a Banach space $E := L^1(\mathbf{R}_+)\times L^1(\mathbf{R}_+)\times L^1(\mathbf{R}_+)$. For $q = (q_1,q_2,q_3)^{\mathrm{T}} \in E_+$, define the aging function $Q(\tau;q)$ and the birth function $M(\tau;q)$ as

$$Q(\tau;q) := \begin{pmatrix} \mu+\beta_1(\infty)\langle\beta_2,q_2\rangle & 0 & 0 \\ 0 & \mu+\gamma(\tau) & 0 \\ 0 & 0 & \mu+\beta_1(\tau)\langle\beta_2,q_2\rangle \end{pmatrix},$$

$$M(\tau;q) := \begin{pmatrix} m & m & m \\ \beta_1(\infty)\langle\beta_2,q_2\rangle & 0 & \beta_1(\tau)\langle\beta_2,q_2\rangle \\ 0 & \gamma(\tau) & 0 \end{pmatrix},$$

where $\langle\beta_2,q_2\rangle$ is defined by

$$\langle\beta_2,q_2\rangle := \int_0^\infty \beta_2(\tau)q_2(\tau)d\tau.$$

Then the system (2.1)–(2.7) can be written as the following well known formula of non-linear age-dependent population dynamics:

$$\left(\frac{\partial}{\partial t}+\frac{\partial}{\partial \tau}\right)p(t,\tau)+Q(\tau;p(t,*))p(t,\tau)=0, \tag{2.10}$$

$$p(t,0) = \int_0^\infty M(\tau;p(t,*))p(t,\tau)d\tau, \tag{2.11}$$

$$p(0,\tau) = p_0(\tau), \tag{2.12}$$

where $p_0(\tau) := (s_0(\tau), i_0(\tau), r_0(\tau))^{\mathrm{T}} \in E_+$ is an initial data.

For this type of non-linear age-dependent population dynamics model, there are several kind of well known methods to establish its well posedness (Gurtin and MacCamy [5], Iannelli [6], Thieme [18], Webb [20]). Hence instead of repeating general approach to existence and uniqueness of system (2.1)–(2.7), here we give a brief sketch of elementary classical treatment for this problem with a condition $m = \mu$. In this case, the boundary condition (2.4) can be replaced as $s(t,0) = \mu N$.

First we consider the control variable

$$C(t) := \int_0^\infty \beta_2(\tau)i(t,\tau)d\tau, \tag{2.13}$$

as a given function of t so that the system (2.1)–(2.7) can be viewed as an non autonomous linear problem. Integrating along the characteristics, we obtain

$$s(t,\tau) = \begin{cases} \mu N L_s(\tau, t-\tau; C), & t-\tau > 0 \\ s_0(\tau-t)L_s(t,0;C), & \tau - t > 0 \end{cases} \tag{2.14}$$

$$i(t,\tau) = \begin{cases} B_i(t-\tau)\Gamma_0(\tau), & t-\tau > 0 \\ i_0(\tau-t)\dfrac{\Gamma_0(\tau)}{\Gamma_0(\tau-t)}, & \tau - t > 0 \end{cases} \tag{2.15}$$

$$r(t,\tau) = \begin{cases} B_r(t-\tau)L_r(\tau, t-\tau, 0; C), & t-\tau > 0 \\ r_0(\tau-t)L_r(t,0,\tau-t;C), & \tau - t > 0 \end{cases} \tag{2.16}$$

where L_s and L_r and Γ_0 are survival rates for individuals in each state defined by

$$L_s(h,t;C) := e^{-\mu h - \beta_1(\infty)\int_0^h C(t+\sigma)d\sigma}, \tag{2.17}$$

$$\Gamma_0(\tau) := e^{-\mu\tau - \int_0^\tau \gamma(\sigma)d\sigma}, \tag{2.18}$$

$$L_r(h,t,\tau;C) := e^{-\mu h - \int_0^h \beta_1(\tau+\sigma)C(t+\sigma)d\sigma}, \tag{2.19}$$

and $B_i(t) := i(t,0)$ and $B_r(t) := r(t,0)$ are unknown boundary values satisfying the following integral equations:

$$B_i(t) = G(t;C) + \int_0^t \Psi(t,\tau;C)B_r(t-\tau)d\tau, \tag{2.20}$$

$$B_r(t) = H(t) + \int_0^t \gamma(\tau)\Gamma_0(\tau)B_i(t-\tau)d\tau, \tag{2.21}$$

where G, Ψ and H are given by

$$G(t;C) := C(t)\left[\beta_1(\infty)\int_0^\infty s(t,\tau)d\tau + \int_t^\infty \beta_1(\tau)L_r(t,0,\tau-t;C)r_0(\tau-t)d\tau\right], \tag{2.22}$$

$$\Psi(t,\tau;C) := C(t)\beta_1(\tau)L_r(\tau,t-\tau,0;C), \tag{2.23}$$

$$H(t) := \int_t^\infty \gamma(\tau)\frac{\Gamma_0(\tau)}{\Gamma_0(\tau-t)}i_0(\tau-t)d\tau. \tag{2.24}$$

Note that $s(t,r)$ can be seen as a known function determined by (2.14) if $C(t)$ is a given function. From (2.20) and (2.21), we obtain a single integral equation for $B_i(t)$:

$$B_i(t) = F(t;C) + \int_0^t \Phi(t,\tau;C)B_i(t-\tau)d\tau, \tag{2.25}$$

where F and Φ are given by

$$F(t;C) := G(t;C) + \int_0^t \Psi(t,\tau;C)H(t-\tau)d\tau, \tag{2.26}$$

$$\Phi(t,\tau;C) := \int_0^\tau \Psi(t,\sigma;C)\gamma(\tau-\sigma)\Gamma_0(\tau-\sigma)d\sigma. \tag{2.27}$$

That is, if once $C(t)$ is given, $i(t,\tau)$ is determined by (2.15) and (2.25), subsequently $r(t,\tau)$ is given by (2.16) and (2.21).

From the above argument, we can conclude that our problem (2.1)–(2.7) can be reduced to the following pair of coupled integral equations for C and B_i:

$$B_i(t) = F(t;C) + \int_0^t \Phi(t,\tau;C)B_i(t-\tau)d\tau, \tag{2.28}$$

$$C(t) = J(t) + \int_0^t \beta_2(\tau)\Gamma_0(\tau)B_i(t-\tau)d\tau, \tag{2.29}$$

where $J(t)$ is a given function as

$$J(t) := \int_t^\infty \beta_2(\tau)\frac{\Gamma_0(\tau)}{\Gamma_0(\tau-t)}i_0(\tau-t)d\sigma.$$

Existence and uniqueness of continuous solutions for this type of coupled integral equations system is already well studied by Gurtin and MacCamy [5]. Though

we omit the proof, under the Assumption 2.1, using the fixed point technique as given by Gurtin and MacCamy it can be shown that the integral equation system (2.28)–(2.29) has a unique nonnegative continuous solution for all time $t \geq 0$. If once B_i, B_r and C are determined, (2.14)–(2.16) will give a classical solution for (2.1)–(2.7) under appropriate consistency conditions and differentiability of initial data.

3. Endemic Threshold

For many epidemic models for infectious diseases, it is known that the basic reproduction number R_0 plays a role as threshold value. That is, if R_0 is less than one, the disease-free steady state is a unique steady state which is stable in some sense, otherwise it will be unstable and endemic steady state appears.

In the following we show that this threshold phenomena holds for the variable susceptibility model under simple condition that $m = \mu$, that is, the total size of host population is constant.

Let $(s^*(\tau), i^*(\tau), r^*(\tau))$ be the steady state for system (2.1)–(2.6). Then we have

$$s^*(\tau) = \mu N e^{-\mu\tau - i^*(0)\langle \beta_2, \Gamma_0 \rangle \beta_1(\infty)\tau}, \tag{3.1}$$

$$i^*(\tau) = i^*(0)\Gamma_0(\tau), \tag{3.2}$$

$$r^*(\tau) = i^*(0)\langle \gamma, \Gamma_0 \rangle e^{-\mu\tau - i^*(0)\langle \beta_2, \Gamma_0 \rangle \int_0^\tau \beta_1(\sigma)d\sigma}, \tag{3.3}$$

where $\langle\, , \rangle$ is defined by

$$\langle u, v \rangle := \int_0^\infty u(x)v(x)dx.$$

Then corresponding to $i^*(0) = 0$, there exists a disease-free steady state as

$$(s^*(\tau), i^*(\tau), r^*(\tau)) = (\mu N e^{-\mu\tau}, 0, 0). \tag{3.4}$$

In the initial invasion phase at the disease-free steady state, it follows from (2.5) that the linearized equation is given as follows:

$$B(t) = \beta_1(\infty) N \int_0^\infty \beta_2(\tau) i(t, \tau) d\tau, \tag{3.5}$$

where $B(t) =: i(t, 0)$ is the number of newly infected individuals per unit time. Then we obtain the following renewal integral equation for $B(t)$:

$$B(t) = N\beta_1(\infty) \int_0^t \beta_2(\zeta)\Gamma_0(\zeta)B(t - \zeta)d\zeta + N\beta_1(\infty)J(t). \tag{3.6}$$

Then we know that the basic reproduction number for this epidemic system is defined by

$$R_0 = N\beta_1(\infty) \int_0^\infty \beta_2(\zeta)\Gamma_0(\zeta)d\zeta. \tag{3.7}$$

Then it is easily seen that the following global stability result holds:

PROPOSITION 3.1. *If $R_0 < 1$, then the disease-free steady state is globally asymptotically stable.*

Proof. Observe that

$$B_i(t) = C(t)\int_0^\infty \{\beta_1(\infty)s(t,\tau) + \beta_1(\tau)r(t,\tau)\}d\tau \le \beta_1(\infty)NC(t).$$

Therefore we know that the birth rate satisfies the integral inequality as

$$B_i(t) \le N\beta_1(\infty)\int_0^t \beta_2(\zeta)\Gamma_0(\zeta)B_i(t-\zeta)d\zeta + N\beta_1(\infty)J(t). \tag{3.8}$$

Then we can conclude that $B_i(t) \le B(t)$, and if $R_0 < 1$, it follows that $\lim_{t\to\infty} B_i(t) = 0$, which implies the global stability of the disease-free steady state. □

Next in order to investigate existence and uniqueness of endemic steady state, we prepare the following technical lemma due to Kermack and McKendrick:

LEMMA 3.2. *If $i^*(0) \neq 0$, it follows that*

$$\int_0^\infty s^*(\tau)d\tau = \frac{1 - \langle \gamma, \Gamma_0 \rangle(1 - \mu\Phi(i^*(0)))}{\beta_1(\infty)\langle \beta_2, \Gamma_0 \rangle}, \tag{3.9}$$

where

$$\Phi(x) := \int_0^\infty e^{-\mu\tau - x\langle \beta_2, \Gamma_0 \rangle \int_0^\tau \beta_1(\sigma)d\sigma}d\tau. \tag{3.10}$$

Proof. From (3.1)–(3.3), we can observe that

$$\begin{aligned} N &= \int_0^\infty s^*(\tau)d\tau + \int_0^\infty i^*(\tau)d\tau + \int_0^\infty r^*(\tau)d\tau \\ &= \frac{\mu N}{\mu + \langle \beta_2, \Gamma_0 \rangle \beta_1(\infty)i^*(0)} + i^*(0)\|\Gamma_0\|_{L^1} + i^*(0)\langle \gamma, \Gamma_0 \rangle \Phi(i^*(0)). \end{aligned} \tag{3.11}$$

If $i^*(0) \neq 0$, we can solve the above equation for μN, hence we obtain that

$$\mu N = \frac{\mu + \langle \beta_2, \Gamma_0 \rangle \beta_1(\infty)i^*(0)}{\langle \beta_2, \Gamma_0 \rangle \beta_1(\infty)} \mu\{\|\Gamma_0\|_{L^1} + \langle \gamma, \Gamma_0 \rangle \Phi(i^*(0))\}. \tag{3.12}$$

If we note that

$$\mu\|\Gamma_0\|_{L^1} = 1 - \langle \gamma, \Gamma_0 \rangle, \quad \int_0^\infty s^*(\tau)d\tau = \frac{\mu N}{\mu + \langle \beta_2, \Gamma_0 \rangle \beta_1(\infty)i^*(0)},$$

then we arrive at the expression (3.9). □

It follows from (3.9) and (3.11) that

$$N = \frac{1 - \langle \gamma, \Gamma_0 \rangle}{\langle \beta_2, \Gamma_0 \rangle \beta_1(\infty)} + \frac{\langle \gamma, \Gamma_0 \rangle}{\langle \beta_2, \Gamma_0 \rangle \beta_1(\infty)} \Phi(i^*(0))\{\mu + i^*(0)\langle \beta_2, \Gamma_0 \rangle \beta_1(\infty)\} + i^*(0)\|\Gamma_0\|_{L^1}. \tag{3.13}$$

Now we define a function $F(x)$ by

$$F(x) := \frac{1 - \langle \gamma, \Gamma_0 \rangle}{\langle \beta_2, \Gamma_0 \rangle \beta_1(\infty)} + \frac{\langle \gamma, \Gamma_0 \rangle}{\langle \beta_2, \Gamma_0 \rangle \beta_1(\infty)} G(x) + x\|\Gamma_0\|_{L^1}, \tag{3.14}$$

where $G(x)$ is defined by

$$G(x) := \Phi(x)\{\mu + x\langle \beta_2, \Gamma_0 \rangle \beta_1(\infty)\}. \tag{3.15}$$

Then we know that if the equation $F(x) = N$ has a positive solution $x^* \in (0, N/\|\Gamma_0\|]$, the endemic steady state is given by (3.1)–(3.3) with $i^*(0) = x^*$. Since $F(x)$ is a continuous function and it is easy to see that $F(0) = N/R_0$ and $F(N/\|\Gamma_0\|_{L^1}) > N$. Therefore we can conclude that

PROPOSITION 3.3. *If $R_0 > 1$, there exists at least one endemic steady state.*

Note that we so far do not use the monotonicity of $\beta_1(\tau)$ to show the above existence theorem of endemic steady state. If we adopt the Assumption 1.1 and improve the original proof by Kermack and McKendrick, we can show the uniqueness result as follows:

PROPOSITION 3.4. *Under the Assumption* 1.1, *if $R_0 > 1$, there exists a unique endemic steady state.*

Proof. It is sufficient to show that under the Assumption 1.1, $F(x)$ is monotone increasing for $x \in (0, N/\|\Gamma_0\|_{L^1}]$. Integrating by parts, we can observe that

$$\mu\Phi(x) = 1 - x\langle \beta_2, \Gamma_0 \rangle \int_0^\infty \beta_1(\tau) e^{-\mu\tau - x\langle \beta_2, \Gamma_0 \rangle \int_0^\tau \beta_1(\sigma)d\sigma} d\tau.$$

Then we have

$$G(x) = 1 + x\langle \beta_2, \Gamma_0 \rangle \int_0^\infty (\beta_1(\infty) - \beta_1(\tau)) e^{-\mu\tau - x\langle \beta_2, \Gamma_0 \rangle \int_0^\tau \beta_1(\sigma)d\sigma} d\tau. \tag{3.16}$$

Here we can assume without loss of generality that there exists a number $\tau_0 \geq 0$ such that $\beta_1(\tau) = 0$ for $\tau \in [0, \tau_0]$ and $\beta_1(\tau) > 0$ for $\tau > \tau_0$. That is, the recovered individuals can keep a complete immunity for the time interval $[0, \tau_0]$. Let $h > 0$ be an arbitrary small number. Then we have

$$\int_0^\infty (\beta_1(\infty) - \beta_1(\tau)) e^{-\mu\tau - x\langle \beta_2, \Gamma_0 \rangle \int_0^\tau \beta_1(\sigma)d\sigma} d\tau$$

$$= \left\{ \int_0^{a_0} + \int_{a_0}^{a_0+h} + \int_{a_0+h}^{\infty} \right\} (\beta_1(\infty) - \beta_1(\tau)) e^{-\mu\tau - x\langle \beta_2, \Gamma_0 \rangle \int_0^\tau \beta_1(\sigma)d\sigma} d\tau$$
$$= J_1(x) + J_2(x) + J_3(x),$$

where each integrals are calculated as follows:

$$J_1(x) := x\langle \beta_2, \Gamma_0 \rangle \int_0^{a_0} \beta_1(\infty) e^{-\mu\tau} d\tau = \beta_1(\infty) x\langle \beta_2, \Gamma_0 \rangle \frac{1 - e^{-\mu a_0}}{\mu},$$

$$J_2(x) := x\langle \beta_2, \Gamma_0 \rangle \int_{a_0}^{a_0+h} (\beta_1(\infty) - \beta_1(\tau)) e^{-\mu\tau - x\langle \beta_2, \Gamma_0 \rangle \int_{a_0}^\tau \beta_1(\sigma)d\sigma} d\tau,$$

$$J_3(x) := x\langle \beta_2, \Gamma_0 \rangle \int_{a_0+h}^{\infty} (\beta_1(\infty) - \beta_1(\tau)) e^{-\mu\tau - x\langle \beta_2, \Gamma_0 \rangle \int_{a_0}^\tau \beta_1(\sigma)d\sigma} d\tau$$
$$= -\int_{a_0+h}^{\infty} \frac{\beta_1(\infty) - \beta_1(\tau)}{\beta_1(\tau)} e^{-\mu\tau} \frac{\partial}{\partial\tau} e^{-x\langle \beta_2, \Gamma_0 \rangle \int_{a_0}^\tau \beta_1(\sigma)d\sigma} d\tau$$
$$= \frac{\beta_1(\infty) - \beta_1(a_0+h)}{\beta_1(a_0+h)} e^{-\mu(a_0+h) - x\langle \beta_2, \Gamma_0 \rangle \int_{a_0}^{a_0+h} \beta_1(\sigma)d\sigma} + H(x),$$

where $H(x)$ is defined as

$$H(x) := \int_{a_0+h}^{\infty} \frac{\partial}{\partial\tau} \left\{ \frac{\beta_1(\infty) - \beta_1(\tau)}{\beta_1(\tau)} e^{-\mu\tau} \right\} e^{-x\langle \beta_2, \Gamma \rangle \int_{a_0}^\tau \beta_1(\sigma)d\sigma} d\tau.$$

It follows from the monotonicity of $\beta_1(\tau)$ that

$$\frac{\partial}{\partial\tau} \left\{ \frac{\beta_1(\infty) - \beta_1(\tau)}{\beta_1(\tau)} e^{-\mu\tau} \right\} \leq 0.$$

Then we have $H'(x) \geq 0$. Observe that

$$F'(x) = \frac{\langle \gamma, \Gamma_0 \rangle}{\langle \beta_2, \Gamma_0 \rangle \beta_1(\infty)} (J_1'(x) + J_2'(x) + J_3'(x)) + \|\Gamma_0\|_{L^1}$$
$$= \|\Gamma_0\|_{L^1} + \langle \gamma, \Gamma_0 \rangle \frac{1 - e^{-\mu a_0}}{\mu}$$
$$+ \frac{\langle \gamma, \Gamma_0 \rangle}{\beta_1(\infty)} \int_{a_0}^{a_0+h} (\beta_1(\infty) - \beta_1(\tau)) e^{-\mu\tau - x\langle \beta_2, \Gamma_0 \rangle \int_{a_0}^\tau \gamma_1(\sigma)d\sigma} d\tau$$
$$- \frac{x\langle \gamma, \Gamma_0 \rangle \langle \beta_2, \Gamma_0 \rangle}{\beta_1(\infty)} \int_{a_0}^{a_0+h} (\beta_1(\infty) - \beta_1(\tau))$$
$$\times \left\{ \int_{a_0}^\tau \beta_1(\sigma)d\sigma \right\} e^{-\mu\tau - x\langle \beta_2, \Gamma_0 \rangle \int_{a_0}^\tau \beta_1(\sigma)d\sigma} d\tau + \frac{\langle \gamma, \Gamma_0 \rangle}{\beta_1(\infty)\langle \beta_2, \Gamma_0 \rangle}$$
$$\times \left\{ -\frac{\beta_1(\infty) - \beta_1(a_0+h)}{\beta_1(a_0+h)} \langle \beta_2, \Gamma_0 \rangle \right.$$
$$\left. \times \left[\int_{a_0}^{a_0+h} \beta_1(\sigma)d\sigma \right] e^{-\mu(a_0+h) - x\langle \beta_2, \Gamma_0 \rangle \int_{a_0}^{a_0+h} \beta_1(\sigma)d\sigma} + H'(x) \right\}.$$

For $x \in (0, N/\|\Gamma_0\|_{L^1}]$, the minus parts of the above expression can be estimated as follows:

$$\left| \frac{x\langle \gamma, \Gamma_0 \rangle \langle \beta_2, \Gamma_0 \rangle}{\beta_1(\infty)} \int_{a_0}^{a_0+h} (\beta_1(\infty) - \beta_1(\tau)) \right.$$
$$\left. \times \left\{ \int_{a_0}^{\tau} \beta_1(\sigma) d\sigma \right\} e^{-\mu\tau - x\langle \beta_2, \Gamma_0 \rangle \int_{a_0}^{\tau} \beta_1(\sigma) d\sigma} d\tau \right|$$
$$\leq \frac{N\langle \gamma, \Gamma_0 \rangle \langle \beta_2, \Gamma_0 \rangle}{\|\Gamma_0\|_{L^1} \beta_1(\infty)} \beta_1(\infty)^2 \frac{h^2}{2},$$

$$\left| -\frac{\beta_1(\infty) - \beta_1(a_0+h)}{\beta_1(a_0+h)} \langle \beta_2, \Gamma_0 \rangle \left[\int_{a_0}^{a_0+h} \beta_1(\sigma) d\sigma \right] e^{-\mu(a_0+h) - x\langle \beta_2, \Gamma_0 \rangle \int_{a_0}^{a_0+h} \beta_1(\sigma) d\sigma} \right|$$
$$\leq \beta_1(\infty) \langle \beta_2, \Gamma_0 \rangle h.$$

Therefore if we choose a $h > 0$ small enough in advance, we can conclude that $F'(x) \geq 0$, hence that $F(x)$ is a monotone non-decreasing function. Thus the endemic steady state exists uniquely. □

4. Local Stability of the Endemic Steady State

In this section, we consider the stability of the endemic steady state. Again we assume that the total size of host population is constant ($m = \mu$) and $R_0 > 1$, so there exists a unique endemic steady state (s^*, i^*, r^*).

Let us introduce new variables x, y and z as

$$\begin{cases} s(t,\tau) = s^*(\tau) + x(t,\tau), \\ i(t,\tau) = i^*(\tau) + y(t,\tau), \\ r(t,\tau) = r^*(\tau) + z(t,\tau). \end{cases} \tag{4.1}$$

Then the basic system (2.1)–(2.7) can be rewritten as follows:

$$x_t(t,\tau) + x_\tau(t,\tau) = -(\mu + \beta_1(\infty)\langle \beta_2, i^* \rangle) x(t,\tau)$$
$$- (s^*(\tau) + x(t,\tau)) \beta_1(\infty) \langle \beta_2, y(t,*) \rangle, \tag{4.2}$$

$$y_t(t,\tau) + y_\tau(t,\tau) = -(\mu + \gamma(\tau)) y(t,\tau), \tag{4.3}$$

$$z_t(t,\tau) + z_\tau(t,\tau) = -(\mu + \beta_1(\tau)\langle \beta_2, i^* \rangle) z(t,\tau)$$
$$- (r^*(\tau) + z(t,\tau)) \beta_1(\tau) \langle \beta_2, y(t,*) \rangle, \tag{4.4}$$

$$x(t,0) = 0, \tag{4.5}$$

$$y(t,0) = [\beta_1(\infty)\langle 1, x(t,*) \rangle + \langle \beta_1, z(t,*) \rangle] \langle \beta_2, i^* + y(t,*) \rangle$$
$$+ [\beta_1(\infty)\langle 1, s^* \rangle + \langle \beta_1, r^* \rangle] \langle \beta_2, y(t,*) \rangle, \tag{4.6}$$

$$z(t,0) = \langle \gamma, y(t,*) \rangle. \tag{4.7}$$

Since the total population size is constant, it must follow that

$$\langle 1, x(t,*)\rangle + \langle 1, y(t,*)\rangle + \langle 1, z(t,*)\rangle = 0. \tag{4.8}$$

Then the system (4.2)–(4.7) can be reduced to (y,z) system as

$$y_t(t,\tau) + y_\tau(t,\tau) = -(\mu + \gamma(\tau))y(t,\tau), \tag{4.9}$$

$$\begin{aligned} z_t(t,\tau) + z_\tau(t,\tau) = {} & -(\mu + \beta_1(\tau)\langle \beta_2, i^*\rangle)z(t,\tau) \\ & - (r^*(\tau) + z(t,\tau))\beta_1(\tau)\langle \beta_2, y(t,*)\rangle, \end{aligned} \tag{4.10}$$

$$\begin{aligned} y(t,0) = {} & -[\beta_1(\infty)\langle 1, y(t,*)\rangle + \langle \beta_1(\infty) - \beta_1, z(t,*)\rangle]\langle \beta_2, i^* + y(t,*)\rangle \\ & + [\beta_1(\infty)\langle 1, s^*\rangle + \langle \beta_1, r^*\rangle]\langle \beta_2, i^* + y(t,*)\rangle, \end{aligned} \tag{4.11}$$

$$z(t,0) = \langle \gamma, y(t,*)\rangle. \tag{4.12}$$

If we find the solution for (y,z) system, $x(t,\tau)$ is determined by (4.2) with (4.5) and it satisfies the condition (4.8) as long as the initial condition satisfies (4.8). That is, instead of (x,y,z) system with condition (4.8), it is sufficient to consider (y,z) system without condition.

The state space of the epidemic system (4.9)–(4.12) is given by $X := L^1(\mathbf{R}_+) \times L^1(\mathbf{R}_+)$. Hence the above initial boundary value problem can be written as a semilinear Cauchy problem on X as

$$\frac{d}{dt}u(t) = Au(t) + F(u(t)), \quad u(0) = u_0, \tag{4.13}$$

where $u(t,\tau) = (y(t,\tau), z(t,\tau))^{\mathrm{T}}$, $u_0 := (i_0 - i^*, r_0 - r^*)^{\mathrm{T}}$ and the first order differential operator A and the nonlinear perturbation F are defined as follows:

$$(Au)(\tau) = \begin{pmatrix} -\partial_\tau u_1(\tau) - (\mu + \gamma(\tau))u_1(\tau) \\ -\partial_\tau u_2(\tau) - (\mu + \beta_1(\tau)\langle \beta_2, i^*\rangle)u_2(\tau) \end{pmatrix}, \tag{4.14}$$

$$\begin{aligned} D(A) := \{ & u = (u_1,u_2)^{\mathrm{T}} \in X : u_1(0) = -[\beta_1(\infty)\langle 1, u_1\rangle \\ & + \langle \beta(\infty) - \beta_1, u_2\rangle]\langle \beta_2, i^* + u_1\rangle \\ & + [\beta_1(\infty)\langle 1, s^*\rangle + \langle \beta_1, r^*\rangle]\langle \beta_2, i^* + u_1\rangle,\ u_2(0) = \langle \gamma, u_2\rangle\}, \end{aligned}$$

where $D(A)$ denotes the domain of the operator A, and the bounded operator F is given by

$$F(u)(\tau) := \begin{pmatrix} 0 \\ -(r^*(\tau) + u_2(\tau))\beta_1(\tau)\langle \beta_2, u_1\rangle \end{pmatrix}, \tag{4.15}$$

for $u = (u_1,u_2)^{\mathrm{T}} \in X$.

Since the principle of linearized stability for this type of Cauchy problem has been proved by the semigroup method (Webb [20], Thieme [18]), let us consider the resolvent equation for the linearized operator $\mathcal{A}+\mathcal{F}$:

$$(\lambda-(\mathcal{A}+\mathcal{F}))u=f,\quad u\in D(\mathcal{A}),\quad f\in X,\quad \lambda\in\mathbf{C}, \tag{4.16}$$

where $\mathcal{A}$ and $\mathcal{F}$ denote respectively linearization of operators A and F defined by

$$(\mathcal{A}u)(\tau)=\begin{pmatrix}-\partial_\tau u_1(\tau)-(\mu+\gamma(\tau))u_1(\tau)\\ -\partial_\tau u_2(\tau)-(\mu+\beta_1(\tau)\langle\beta_2,i^*\rangle)u_2(\tau)\end{pmatrix}, \tag{4.17}$$

$$\begin{aligned}D(\mathcal{A}):=\{&(u_1,u_2)\in X: u_1(0)=-[\beta_1(\infty)\langle 1,u_1\rangle+\langle\beta(\infty)-\beta_1,u_2\rangle]\langle\beta_2,i^*\rangle\\ &+[\beta_1(\infty)\langle 1,s^*\rangle+\langle\beta_1,r^*\rangle]\langle\beta_2,u_1\rangle,\ u_2(0)=\langle\gamma,u_2\rangle\},\end{aligned}$$

$$\mathcal{F}(u)(\tau):=\begin{pmatrix}0\\ -r^*(\tau)\beta_1(\tau)\langle\beta_2,u_1\rangle\end{pmatrix}. \tag{4.18}$$

By formal integration, we can solve the resolvent equation (4.16) as follows:

$$u_1(\tau)=u_1(0)\Gamma_\lambda(\tau)+\int_0^\tau\frac{\Gamma_\lambda(\tau)}{\Gamma_\lambda(\sigma)}f_1(\sigma)d\sigma, \tag{4.19}$$

$$\begin{aligned}u_2(\tau)=&\left[u_1(0)\langle\gamma,\Gamma_\lambda\rangle+\int_0^\infty\gamma(\tau)\int_0^\tau\frac{\Gamma_\lambda(\tau)}{\Gamma_\lambda(\sigma)}f_1(\sigma)d\sigma d\tau\right]\\ &\times e^{-(\lambda+\mu)\tau-\langle\beta_2,i^*\rangle\int_0^\tau\beta_1(\sigma)d\sigma}\\ &+\int_0^\tau e^{-(\lambda+\mu)(\tau-\sigma)-\langle\beta_2,i^*\rangle\int_\sigma^\tau\beta_1(\sigma)d\sigma}f_2(\sigma)d\sigma\\ &-\left[u_1(0)\langle\beta_2,\Gamma_\lambda\rangle+\int_0^\infty\beta_2(\tau)\int_0^\tau\frac{\Gamma_\lambda(\tau)}{\Gamma_\lambda(\sigma)}f_1(\sigma)d\sigma d\tau\right]\\ &\times\int_0^\tau e^{-(\lambda+\mu)(\tau-\sigma)-\langle\beta_2,i^*\rangle\int_\sigma^\tau\beta_1(\sigma)d\sigma}r^*(\sigma)\beta_1(\sigma)d\sigma,\end{aligned} \tag{4.20}$$

where

$$\Gamma_\lambda(\tau):=e^{-(\mu+\lambda)\tau-\int_0^\tau\gamma(\sigma)d\sigma},$$

and $u_1(0)$ is determined by inserting (4.20) into the boundary condition for $u_1(0)$, then we have

$$\begin{aligned}&(1-\Delta(\lambda))u_1(0)\\ &=[\beta_1(\infty)\langle 1,s^*\rangle+\langle\beta_1,r^*\rangle]\int_0^\infty\beta_2(\tau)\int_0^\tau\frac{\Gamma_\lambda(\tau)}{\Gamma_\lambda(\sigma)}f_1(\sigma)d\sigma d\tau\\ &\quad-\langle\beta_2,i^*\rangle\left[\beta_1(\infty)\int_0^\infty\int_0^\tau\frac{\Gamma_\lambda(\tau)}{\Gamma_\lambda(\sigma)}f_1(\sigma)d\sigma d\tau+\int_0^\infty\gamma(\tau)\int_0^\tau\frac{\Gamma_\lambda(\tau)}{\Gamma_\lambda(\sigma)}f_1(\sigma)d\sigma d\tau\right.\end{aligned}$$

$$\times \int_0^\infty (\beta_1(\infty)-\beta_1(\tau))e^{-(\lambda+\mu)\tau-\langle \beta_2,i^*\rangle \int_0^\tau \beta_1(\sigma)d\sigma}d\tau$$
$$+\int_0^\infty (\beta_1(\infty)-\beta_1(\tau))\int_0^\tau e^{-(\lambda+\mu)(\tau-\sigma)-\langle \beta_2,i^*\rangle \int_\sigma^\tau \beta_1(\sigma)d\sigma} f_2(\sigma)d\sigma d\tau$$
$$-\int_0^\infty (\beta_1(\infty)-\beta_1(\tau))\int_0^\tau e^{-(\lambda+\mu)(\tau-\sigma)-\langle \beta_2,i^*\rangle \int_\sigma^\tau \beta_1(\sigma)d\sigma} r^*(\sigma)\beta_1(\sigma)d\sigma d\tau$$
$$\times \int_0^\infty \beta_2(\tau)\int_0^\tau \frac{\Gamma_\lambda(\tau)}{\Gamma_\lambda(\sigma)}f_1(\sigma)d\sigma d\tau\Bigg]. \tag{4.21}$$

In the above expression, complex function $\Delta(\lambda)$ is defined as follows:

$$\Delta(\lambda)=f(i^*(0),\lambda)+g(i^*(0),\lambda), \tag{4.22}$$

where $f(x,\lambda)$ is given by

$$f(x,\lambda):=R(x)\hat{K}(\lambda), \tag{4.23}$$

where

$$\hat{K}(\lambda)=\int_0^\infty e^{-\lambda\tau}K(\tau)d\tau, \tag{4.24}$$

$$K(\tau):=\frac{\beta_2(\tau)\Gamma_0(\tau)}{\int_0^\infty \beta_2(\tau)\Gamma_0(\tau)d\tau}, \tag{4.25}$$

$$R(x):=\langle \beta_2,\Gamma_0\rangle\Bigg[\mu N\beta_1(\infty)\int_0^\infty e^{-(\mu+x\langle \beta_2,\Gamma_0\rangle\beta_1(\infty))\tau}d\tau$$
$$+x\langle \gamma,\Gamma_0\rangle\int_0^\infty e^{-\mu\tau-x\langle \beta_2,\Gamma_0\rangle\int_0^\tau \beta_1(\sigma)\sigma}d\tau\Bigg], \tag{4.26}$$

and $g(x,\lambda)$ is given by

$$g(x,\lambda):=-x\langle \beta_2,\Gamma_0\rangle\beta_1(\infty)\langle 1,\Gamma_\lambda\rangle - x\langle \beta_2,\Gamma_0\rangle\langle \gamma,\Gamma_\lambda\rangle$$
$$\times\int_0^\infty(\beta_1(\infty)-\beta_1(\tau))e^{-(\lambda+\mu)\tau-x\langle \beta_2,\Gamma_0\rangle\int_0^\tau\beta_1(\sigma)d\sigma}d\tau$$
$$+x^2\langle \beta_2,\Gamma_0\rangle\langle \beta_2,\Gamma_\lambda\rangle\langle \gamma,\Gamma_0\rangle$$
$$\times\int_0^\infty(\beta_1(\infty)-\beta_1(\tau))e^{-\mu\tau-x\langle \beta_2,\Gamma_0\rangle\int_0^\tau\beta_1(\zeta)d\zeta}\int_0^\tau e^{-\lambda(\tau-\sigma)}\beta_1(\sigma)d\sigma d\tau. \tag{4.27}$$

PROPOSITION 4.1. *In the half plane $\Re\lambda>-\mu$, all of the spectrum of $\mathcal{A}+\mathcal{F}$ are the point spectrum, and they are given as roots of characteristic equation $\Delta(\lambda)=1$.*

Proof. Since $\mathcal{F}$ is a one-dimensional operator, it is a compact perturbation. Hence it follows that $\omega_1(\mathcal{A}+\mathcal{F})=\omega_1(\mathcal{A})$, where $\omega_1(\mathcal{A})$ denotes the α-growth bound

of $e^{t\mathcal{A}}$. It is well known that operator $\mathcal{A}$ generates a strongly continuous semigroup $T(t)$ such that $T(t) = U(t) + V(t)$, where $V(t)$ is a compact operator for all $t > 0$ and $\|U(t)\| \leq e^{-\mu t}$ (Prüss [16] [17], Webb [20]). Therefore we obtain that

$$\begin{aligned}\omega_1(\mathcal{A}) &= \lim_{t\to\infty} \frac{\log \alpha(e^{t\mathcal{A}})}{t} \\ &\leq \lim_{t\to\infty} \frac{\log \alpha(U(t))}{t} \leq \lim_{t\to\infty} \frac{\log \|U(t)\|}{t} \leq -\mu. \end{aligned} \tag{4.28}$$

Then it follows that $\omega_1(\mathcal{A}+\mathcal{F}) \leq -\mu$ and all of the spectrum of $\mathcal{A}+\mathcal{F}$ in the half plane $\Re\lambda > -\mu$ are the point spectrum and they are poles of the resolvent $(\lambda - (\mathcal{A}+\mathcal{F}))^{-1}$ (Webb [20, p. 166]). Poles of the resolvent $(\lambda - (\mathcal{A}+\mathcal{F}))^{-1}$ are no other than isolated zeros of finite order of a holomorphic function $\Delta(\lambda)$ in $\Re\lambda > -\mu$. This completes our proof. □

From the above observation, we know that it is sufficient to see the location of zeros of the characteristic equation $\Delta(\lambda) = 1$ in order to judge the local stability of the endemic steady state. So let us consider the following characteristic equation:

$$f(i^*(0), \lambda) + g(i^*(0), \lambda) = 1, \tag{4.29}$$

where $i^*(0)$ is the boundary value of the infected population at the steady state. Note that $R(x)$ denotes the effective reproductive rate, it follows that

$$R(i^*(0)) = 1 \quad \text{for} \quad i^*(0) \neq 0 \quad \text{and} \quad R(0) = R_0. \tag{4.30}$$

That is, for $x = 0$, we obtain the characteristic equation for eigenvalue λ at the disease-free steady state as

$$R_0 \hat{K}(\lambda) = 1. \tag{4.31}$$

Then if $R_0 > 1$, the characteristic equation has a positive root, so we obtain

PROPOSITION 4.2. *If $R_0 > 1$, the disease-free steady state is unstable.*

Next for $x = i^*(0) > 0$, we have the characteristic equation for eigenvalue λ at the endemic steady state as

$$\hat{K}(\lambda) + g(x, \lambda) = 1. \tag{4.32}$$

Mathematical technique to study this type of characteristic equation has been shown in Iannelli [6]. According to Iannelli's argument, we can prove the following:

PROPOSITION 4.3. *There exists $\delta > 0$ such that if $x \in (0, \delta)$, all the roots of equation (4.32) in the half plane $\Re\lambda > -\mu$ have negative real part. Therefore the endemic steady state is locally asymptotically stable if the size of infected population at the endemic steady state is sufficiently small.*

Proof. From the expression (4.27) it is easy to see that for some number $\alpha \in (-\mu, 0)$ there exist numbers $A > 0$ and $B > 0$ such that for $\Re\lambda \geq \alpha$ and $x \geq 0$

$$|g(x,\lambda)| < (A + Bx)x. \tag{4.33}$$

For example, A and B can be chosen as

$$A = \beta_1(\infty)\langle \beta_2, \Gamma_0 \rangle \left\{ \frac{1}{\alpha+\mu} + \frac{2\bar{\gamma}}{(\alpha+\mu)^2} \right\},$$

$$B = \langle \beta_2, \Gamma_0 \rangle \langle \gamma, \Gamma_0 \rangle \frac{2\beta_1^2(\infty)\bar{\beta}_2}{\mu(\alpha+\mu)^2},$$

where $\bar{\gamma} = \sup_{\tau\geq 0}\gamma(\tau)$ and $\bar{\beta}_2 = \sup_{\tau\geq 0}\beta_2(\tau)$. We can choose $\alpha \in (-\mu, 0)$ in advance such that Lotka type characteristic equation

$$\hat{K}(\lambda) = 1, \tag{4.34}$$

has the unique root $\lambda = 0$ in the half plane $\Re\lambda \geq \alpha$. Let us choose a positive number M as

$$M := \inf_{y\in(-\infty,\infty)} |1 - \hat{K}(\alpha + iy)| > 0. \tag{4.35}$$

Moreover it follows from Riemann-Lebesgue lemma that we can take a large number $L > 0$ such that for $|\lambda| > L$, $\Re\lambda \geq \alpha$,

$$\frac{1}{2} < |1 - \hat{K}(\lambda)|.$$

Then if $x > 0$ is sufficiently small such that

$$0 < (A + Bx)x < \min\left(M, \frac{1}{2}\right),$$

then we obtain

$$|g(x,\lambda)| < |1 - \hat{K}(\lambda)|,$$

on the domain $\{\lambda \in \mathbf{C} : |\lambda| > L, \Re\lambda > \alpha\}$ and on the vertical line $\{\lambda \in \mathbf{C} : \Re\lambda = \alpha\}$. Therefore it follows from the Rouché theorem, equation (4.32) has one and only one root in the half plane $\Re\lambda \geq \alpha$, since equation $1 - \hat{K}(\lambda) = 0$ has only one zero in this half plane. Let $\lambda(x)$ be the unique root of equation (4.32) in the half plane $\Re\lambda \geq \alpha$. Note that $\lambda(0) = 0$ and

$$\frac{d\lambda}{dx}\bigg|_{x=0} = \left(\int_0^\infty \tau K(\tau)d\tau\right)^{-1} \frac{\partial g}{\partial x}(0,0).$$

It is easy to see that

$$\frac{\partial g}{\partial x}(0,0) = -\langle \beta_2, \Gamma_0 \rangle \left[\beta_1(\infty) \langle 1, \Gamma_0 \rangle + \langle \gamma, \Gamma_0 \rangle \int_0^\infty (\beta_1(\infty) - \beta_1(\tau)) e^{-\mu\tau} d\tau \right].$$

Therefore we have $\partial g/\partial x < 0$ at $(x, \lambda) = (0, 0)$. Thus the path starting from $\lambda(0) = 0$ goes to the left of the imaginary axis as x increases from zero, so we can conclude that in the half plane $\Re\lambda > -\mu$ all the roots of characteristic equation (4.32) have negative real parts for sufficiently small positive x. This completes our proof. □

5. Discussion

Finally in order to show that the variable susceptibility model could be a useful tool to take into account the effect of changes in the host immunity structure or the antigenic change of virus, we show that Pease's influenza model [15] can be seen as a special case of the variable susceptibility model.

In the type A influenza epidemic, genetic changes in the virus are thought to play an important role in causing recurrent epidemic. The virus changes genetically, and hence immunologically from one epidemic to the next. Therefore a descendant virus strain can infect hosts who are immune to the progenitor strain diseases, and hence reinvade communities that recently suffered an epidemic of the progenitor strain. It is also observed that the more a virus has changed genetically from its progenitor, the more easily it will be able to reinfect a host that is immune to its progenitor.

In order to formulate the influenza model, Pease makes three major biological assumptions: First the probability of reinfection is a monotone increasing function of the number of amino acid substitutions between the immunizing and challenge virus strains. Though Pease's original assumption is that the probability is proportional to the number of amino acid substitutions, but we could assume that the infection rate is upper bounded, since the arbitrarily large susceptibilities seem unrealistic as Pease pointed out. Second, only one virus strain circulates in a human community at any one time. Third, random drift, and not frequency-dependent selection by the host, causes amino acid substitutions to occur in the influenza virus. Random drift occurs continually and causes gradual changes in the virus antigens, thereby genetic changes in the pathogen from epidemic to epidemic cause previously immune hosts to become susceptible.

Under the above assumptions, the Pease model is formulated as follows: Let $I(t)$ be the number of infected hosts at time t and let $S(t, a)$ be the density of uninfected hosts, so that $\int_{a_0}^{a_1} S(t, a)da$ is the number of uninfected hosts that were last infected by a virus which differed by more than a_0 and less than a_1 amino acid substitution from the virus strain prevailing at time t. We assume that the number of amino acid substitution is a continuous variable, and it is causing the antigenic drift in the virus strain. Then the Pease's evolutionary epidemic model

is formulated by the following integrodifferential equations:

$$\frac{\partial S(t,a)}{\partial t} + k\frac{\partial S(t,a)}{\partial a} = -\beta(a)S(t,a)I(t), \tag{5.1}$$

$$\frac{dI(t)}{dt} = -\gamma I(t) + I(t)\int_0^\infty \beta(a)S(t,a)da, \tag{5.2}$$

$$kS(t,0) = \gamma I(t), \tag{5.3}$$

where γ is the (constant) rate at which infected hosts recover, k is the (constant) rate at which amino acid substitutions occur in the virus population and $\beta(a)$ specifies how amino acid substitutions affect the probability of reinfection.

On the other hand, in the basic model (2.1)–(2.7) if we assume that $m = \mu = 0$, β_2, γ are constant respectively and neglect the virgin population, we obtain a simpler system as

$$\frac{dI(t)}{dt} = -\gamma I(t) + \beta_2 I(t)\int_0^\infty \beta_1(\tau)r(t,\tau)d\tau, \tag{5.4}$$

$$\frac{\partial r(t,\tau)}{\partial t} + \frac{\partial r(t,\tau)}{\partial \tau} = -r(t,\tau)\beta_1(\tau)\beta_2 I(t), \tag{5.5}$$

$$r(t,0) = \gamma I(t), \tag{5.6}$$

where $I(t) := \int_0^\infty i(t,\tau)d\tau$. Therefore it is easy to see that Pease's influenza model is a special case of the variable susceptibility model by Kermack and McKendrick. Conversely speaking, if we introduce a class of completely susceptible (never infected) population into Pease's model, it can be extended to take into account the demography of host population.

As is seen above, the Pease model is a kind of the variable susceptibility model, but of course it is an important model in its own right and its mathematical properties are not automatically obtained from our analysis in this paper. From the analysis of Pease model (Inaba [7] [8]), we know that there exists a correlation between the prevalence at the endemic steady state and its stability, and the recurrent outbreak (periodic solution) could be produced by the evolutionary mechanism, that is, the decay of host immunity by the antigenic drift of the type A virus. Though in the rigorous sense, the question whether the sustained oscillation can be realized for realistic value of the prevalence is still open, those observations suggest potential abilities of the variable susceptibility model.

For the general variable susceptibility model, under appropriate conditions we have proved the endemic threshold criteria, that is, the basic reproduction number R_0 is less than one, the infected population will be eradicated as time passes, otherwise R_0 is grater than the unity, there exists unique endemic steady state. Moreover as long as the prevalence of the endemic steady state is small enough, it is locally asymptotically stable. But up to now there are no results for global

stability of the endemic steady state. Moreover, even in the full model (2.1)–(2.7), there are many neglected factors, for example, the chronological age, the disease induced death rate, vaccination term, etc.

Among those factors, to consider the effect of vaccination is particularly interesting, because one of most important reasons to develop mathematical models for infectious diseases is to clear conditions for control of diseases. Let v be the rate of vaccination applied to all susceptible populations. If we assume that vaccinated individuals have the same immunity level just as recovered individuals, then the basic system is rewritten as follows:

$$\begin{cases} s_t(t,\tau) + s_\tau(t,\tau) = -(\mu+v)s(t,a) - s(t,\tau)\beta_1(\infty)\displaystyle\int_0^\infty \beta_2(\sigma)i(t,\sigma)d\sigma, \\ i_t(t,\tau) + i_\tau(t,\tau) = -(\mu+\gamma(\tau))i(t,\tau), \\ r_t(t,\tau) + r_\tau(t,\tau) = -(\mu+v)r(t,\tau) - r(t,\tau)\beta_1(\tau)\displaystyle\int_0^\infty \beta_2(\sigma)i(t,\sigma)d\sigma, \\ s(t,0) = \mu N, \\ i(t,0) = \displaystyle\int_0^\infty \{\beta_1(\infty)s(t,\tau) + \beta_1(\tau)r(t,\tau)\}d\tau \int_0^\infty \beta_2(\tau)i(t,\tau)d\tau, \\ r(t,0) = v\left[\displaystyle\int_0^\infty s(t,\tau)d\tau + \int_0^\infty r(t,\tau)d\tau\right] + \int_0^\infty \gamma(\tau)i(t,\tau)d\tau. \end{cases} \tag{5.7}$$

In this model, the disease-free steady state is given as follows:

$$(s^*(\tau), 0, r^*(\tau)) = (\mu N e^{-(\mu+v)\tau}, 0, vNe^{-(\mu+v)\tau}). \tag{5.8}$$

Hence the effective reproductive rate is calculated as

$$R := \left(\frac{\mu N\beta_1(\infty)}{\mu+v} + vN\int_0^\infty \beta_1(\tau)e^{-(\mu+v)\tau}d\tau\right)\int_0^\infty \beta_2(\tau)\Gamma_0(\tau)d\tau. \tag{5.9}$$

Then it is easy to see that if v is large enough, the effective reproduction rate becomes less than one, hence the disease-free steady state is locally stable. But note that in case that $R < 1 < R_0$, the disease could invade into the host population if the ratio of completely susceptible population is high enough. To analyze the effect of vaccination will be interesting future problem.

In summary, we can say that the possibilities of Kermack's and McKendrick's models have not yet been exhausted, which is the reason why we still have to continue to revisit Kermack and McKendrick again and again, though even more than 60 years have passed since their work.

References

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