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出版情報：MI lecture note series. 60, pp.50-58, 2014-11-28. 九州大学マス・フォア・インダストリ研究所
バージョン：
権利関係：

Rivisiting the Late Kermack–McKendrick Epidemic Model

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概　要　In a series of papers published at 1930s, Kermack and McKendrick have proposed infection-age structured endemic models, which take into account the demography of host population, the waning immunity (variable susceptibility) and reinfection of recovered individuals. The aim of this short note is to show the wide applicability of the late Kermack–McKenderick model and its variations, and to discuss the reinfection threshold phenomena.

1 Introduction

In a series of papers published during 1930s, although they have been paid less attention in contrast with the famous outbreak model in 1927 ([8]), Kermack and McKendrick have proposed infection-age structured *endemic* models, which take into account the demography of host population, the waning immunity (variable susceptibility) and reinfection of recovered individuals ([9], [10]). The total population is decomposed into three compartments, the never infected (full susceptible), infectious and recovered (partially susceptible) populations. The host population is structured by duration variable in each status, while the chronological age is neglected. The susceptibility of recovered individuals depends on the duration since the last recovery.

The idea of reinfection becomes more and more important to understand emerging and reemerging infectious diseases, since it makes the control of infectious diseases difficult, and the waning immunity is widely observed if there is no (natural or artificial) boosting. In fact, their exist at least two main reasons that the host immunity will decay and the recovered individuals will become susceptibles again as time passes, one possibility is that there is a natural decay of host immunity, another reason is the genetic change in virus.

As was pointed out by Gomes, et al. ([2]), we can introduce the *reinfection threshold* of R_0 at which qualitative change in the epidemiological implication occurs for the prevalence and controllability in the reinfection model. The aim of this short note is to show the possible applicability of the late Kermack–McKenderick model and its variations, and to discuss its reinfection threshold phenomena.

2 The Late Kermack–McKendrick Model

First we formulate the late Kermack–Mckendrick model from the modern point of view. Let $s(t,\tau)$ be the density of susceptible population who have never been infected (*virgin* population in the terminology of Kermack and McKendrick) at time t and duration (the time elapsed from entry into the s-state) τ, which can be interpreted as the chronological age when the entry into s-state is birth. Let $i(t,\tau)$ be the density of infected and infectious population at time t and infection-age (the time elapsed from infection) τ 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). Let m and μ denote the birth (or immigration) rate and the death rate, $\gamma(\tau)$ the recovery rate at infection-age τ.

We assume that the force of infection applied to the full susceptible population (virgin population) is given by

$$\lambda(t) = \int_0^\infty \beta(\sigma) i(t,\sigma) d\sigma, \tag{2.1}$$

where $\beta(\tau)$ denotes the infectivity to the virgin population at infection-age τ. The force of (re)infection applied to the recovered population at duration τ is assumed to be given by $\theta(\tau)\lambda(t)$, where $\theta(\tau)$ is the relative susceptibility schedule of recovered individuals at time since recovery τ. It is assumed that $\theta \leq 1$ if there is no enhancement of susceptibility due to infection, and θ is a monotone non-decresing function if it reflects the natural decay of immunity level of recovered individuals.

Then the late Kermack–McKendrick model is formulated as follows:

$$\begin{aligned}
&\frac{\partial s(t,\tau)}{\partial t} + \frac{\partial s(t,\tau)}{\partial \tau} = -\mu s(t,\tau) - \lambda(t)s(t,\tau),\\
&\frac{\partial i(t,\tau)}{\partial t} + \frac{\partial i(t,\tau)}{\partial \tau} = -(\mu+\gamma(\tau))i(t,\tau),\\
&\frac{\partial r(t,\tau)}{\partial t} + \frac{\partial r(t,\tau)}{\partial \tau} = -\mu r(t,\tau) - \theta(\tau)\lambda(t)r(t,\tau),\\
&s(t,0) = m\int_0^\infty (s(t,\tau)+i(t,\tau)+r(t,\tau))d\tau,\\
&i(t,0) = \lambda(t)\int_0^\infty (s(t,\tau)+\theta(\tau)r(t,\tau))\,d\tau,\\
&r(t,0) = \int_0^\infty \gamma(\tau)i(t,\tau)d\tau,
\end{aligned} \tag{2.2}$$

with an initial data

$$s(0,\tau) = s_0(\tau), \quad i(0,\tau) = i_0(\tau), \quad r(0,\tau) = r_0(\tau).$$

The model (2.2) can be rewritten as the Gurtin–MacCamy model for age-dependent population, its mathematical well-posedness has been established ([5]). If $\theta \equiv 0$, (2.2) becomes the SIR model with permanent immunity, and if $\theta \equiv 1$, the recovered population can be identified with the virgin population, so (2.2) is reduced to the duration-dependent SIS epidemic model.

Let $N(t)$ be the total size of host population given by

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

Then it is easy to see that if $m = \mu$, the total size of the host population is constant. In the following we consider the case of constant total population size, denoted by N, so the boundary condition of $s(t,a)$ is replaced by $s(t,0) = \mu N$. Then the linearized equation at the diseas-free steady state is given by

$$\begin{aligned}
&\frac{\partial i(t,\tau)}{\partial t} + \frac{\partial i(t,\tau)}{\partial \tau} = -(\mu+\gamma(\tau))i(t,\tau),\\
&i(t,0) = \lambda(t)N,
\end{aligned} \tag{2.3}$$

so it is easy to see that the basic reproduction number for the basic model (2.2) is given by

$$R_0 = N\int_0^\infty e^{-\mu\tau}\beta(\tau)\Gamma(\tau)d\tau, \tag{2.4}$$

where $\Gamma(\tau) := \exp(-\int_0^\tau \gamma(x)dx)$. Then it holds that

Proposition 2.1 ([5]) *If $R_0 < 1$, the disease-free steady state is globally asymptotically stable. If $R_0 > 1$, the disease-free steady state is unstable and there exists a unique endemic steady state, which is locally asymptotically stable as long as the prevalence is small enough.*

Here we sketch an alternative integral equation formulation. For simplicity, instead of the initial value problem, we assume that the epidemic starts at $t = -\infty$. Then the partial differential equations in (2.2) can be replaced by the following set of equations:

$$\begin{aligned} s(t,\tau) &= \mu N e^{-\mu\tau - \int_0^\tau \lambda(t-\tau+\sigma)d\sigma}, \\ i(t,\tau) &= b_1(t-\tau)e^{-\mu\tau}\Gamma(\tau), \\ r(t,\tau) &= b_2(t-\tau)e^{-\mu\tau - \int_0^\tau \lambda(t-\tau+\sigma)\theta(\sigma)d\sigma}, \end{aligned} \tag{2.5}$$

where $b_1(t) := i(t,0)$ and $b_2(t) := r(t,0)$. Inserting the above equations into the boundary conditions, we obtain a set of integral equations:

$$\begin{aligned} b_1(t) &= \lambda(t)\left[\int_0^\infty \mu N e^{-\mu\tau - \int_0^\tau \lambda(t-\tau+\sigma)d\sigma}d\tau + \int_0^\infty \theta(\tau)b_2(t-\tau)e^{-\mu\tau - \int_0^\tau \lambda(t-\tau+\sigma)\theta(\sigma)d\sigma}d\tau\right], \\ b_2(t) &= \int_0^\infty b_1(t-\tau)e^{-\mu\tau}\gamma(\tau)\Gamma(\tau)d\tau, \end{aligned} \tag{2.6}$$

where

$$\lambda(t) = \int_0^\infty e^{-\mu\tau}\beta(\tau)\Gamma(\tau)b_1(t-\tau)d\tau. \tag{2.7}$$

Inserting the expression of b_2 into the equation for b_1 in (2.6) and changing the order of integrals, we obtain

$$b_1(t) = \lambda(t)\int_0^\infty S(t,\tau)d\tau, \tag{2.8}$$

$$\begin{aligned} S(t,\tau) :&= \mu N e^{-\mu\tau - \int_0^\tau \lambda(t-\tau+\sigma)d\sigma} \\ &\quad + b_1(t-\tau)e^{-\mu\tau}\int_0^\tau \theta(\sigma)e^{-\int_0^\sigma \theta(\zeta)\lambda(t-\sigma+\zeta)d\zeta}\gamma(\tau-\sigma)\Gamma(\tau-\sigma)d\sigma. \end{aligned} \tag{2.9}$$

where $\int_0^\infty S(t,\tau)d\tau$ is the *effective size of susceptibles*. The expression (2.8) implies a simple fact that the new incidence at time t is given by the force of infection times the size of effective susceptibles.

From (2.8) and (2.9), we obtain a linear renewal equation for b_1 if we see the force of infection λ as a given function, so by solving the linear renewal equation formally, we have an expression of b_1 with unknown λ. Inserting this solution into (2.7), we arrive at a nonlinear "scalar" renewal equation for λ. Alternatively, eliminating λ from (2.7), (2.8) and (2.9), we can again get a nonlinear scalar integral equation for b_1.

3 The reinfection threshold

Using the late Kermack–McKendrick model, let us consider the effect of vaccination (host immunization). In fact, it is intuitively clear that the reinfection phenomena would make the disease control more difficult, so we need an index to capture the difficulty. One of important effects of the vaccination policy is to reduce the effective size of susceptible population (*S-control*), so we are naturally led to the idea of the *reinfection threshold*.

Suppose that newborns or immigrants in the virgi n population are mass vaccinated with the coverage $\varepsilon \in [0,1]$ and the immunological status of newly vaccinated individuals can be identical with the newly recovered individuals. Then the boundary condition in (2.2) is replaced as follows:

$$\begin{aligned} s(t,0) &= (1-\varepsilon)\mu N, \\ i(t,0) &= \lambda(t)\int_0^\infty \left(s(t,\tau) + \theta(\tau)r(t,\tau)\right)d\tau, \\ r(t,0) &= \varepsilon\mu N + \int_0^\infty \gamma(\tau)i(t,\tau)d\tau. \end{aligned} \tag{3.1}$$

In particular, if $\varepsilon \to 1$, the virgin population is eradicated, we obtain the limiting IR system as

$$\begin{aligned}
&\frac{\partial i(t,\tau)}{\partial t} + \frac{\partial i(t,\tau)}{\partial \tau} = -(\mu + \gamma(\tau))i(t,\tau),\\
&\frac{\partial r(t,\tau)}{\partial t} + \frac{\partial r(t,\tau)}{\partial \tau} = -\mu r(t,\tau) - \theta(\tau)\lambda(t)r(t,\tau),\\
&i(t,0) = \lambda(t)\int_0^\infty \theta(\tau)r(t,\tau)d\tau,\\
&r(t,0) = \mu N + \int_0^\infty \gamma(\tau)i(t,\tau)d\tau.
\end{aligned} \tag{3.2}$$

This new system (3.2) can be seen as a duration-dependent SIS model again if we see the recovered class as a new susceptible class. Then (3.2) has a disease-free steady state $(i^*, r^*) = (0, \mu N e^{-\mu\tau})$, the linearized system at the disease free steady state is given as follows:

$$\begin{aligned}
&\frac{\partial i(t,\tau)}{\partial t} + \frac{\partial i(t,\tau)}{\partial \tau} = -(\mu + \gamma(\tau))i(t,\tau),\\
&i(t,0) = \int_0^\infty \theta(\tau)r^*(\tau)d\tau \int_0^\infty \beta(\tau)i(t,\tau)d\tau
\end{aligned} \tag{3.3}$$

Therefore we can calculate the effective reproduction number for the limiting system (3.2) as

$$R_e = R_0 \int_0^\infty \theta(\tau)\mu e^{-\mu\tau}d\tau. \tag{3.4}$$

If $\theta(\tau) \le 1$ for all τ, that is, there is no enhancement of susceptibility by infection, we have $R_e \le R_0$. Let

$$\theta^* := \frac{R_e}{R_0} = \int_0^\infty \theta(\tau)\mu e^{-\mu\tau}d\tau. \tag{3.5}$$

Then if $1 < R_e = \theta^* R_0$, the disease is uncontrollable by the vaccination, because the fully vaccinated population can be invaded by the disease. On the other hand, if $\theta^* > 1$, that is, there is enhancement of susceptibility due to infection, the backward bifurcation of the endemic steady state can occur ([13]).

Since the qualitative change in the epidemiological implication occurs for the prevalence and controllability at $R_0 = 1/\theta^*$, Gomes *et al.* ([2], [3]) called $1/\theta^*$ the *reinfection threshold* of R_0. As is seen above, the reinfection threshold value of R_0 corresponds to the fact that $\theta^* R_0$ is the effective reproduction number of the limiting system (3.2), that is, $R_0 = 1/\theta^*$ does not imply a bifurcation point of the basic system (2.2), but it is a threshold of the limiting system (3.2).

If the epidemic time scale is much shorter than the time scale of the host demography, we can neglect the birth and death rates; $\mu = 0$. Moreover, if β and γ are assumed to be constant, the late Kermack–McKendrick model (3.2) can be formulated as follows:

$$\begin{aligned}
&\frac{dU(t)}{dt} = -\beta I(t)U(t),\\
&\frac{dI(t)}{dt} = -\gamma I(t) + \beta I(t)\left(U(t) + \int_0^\infty \theta(\tau)r(t,\tau)d\tau\right),\\
&\frac{\partial r(t,\tau)}{\partial t} + \frac{\partial r(t,\tau)}{\partial \tau} = -\beta\theta(\tau)r(t,\tau)I(t),\\
&r(t,0) = \gamma I(t),
\end{aligned} \tag{3.6}$$

where $U(t) := \int_0^\infty s(t,\tau)d\tau$ and $I(t) := \int_0^\infty i(t,\tau)d\tau$. In this case, it is easy to see that $R_0 = \beta N/\gamma$, and the following endemic threshold property holds:

Proposition 3.1 *Suppose that $\theta(\tau)$ is monotone non-decresing function and there exists a limit $\theta(\infty) = \lim_{\tau\to\infty}\theta(\tau)$. If $R_0\theta(\infty) \le 1$, there is no endemic steady state. If $R_0\theta(\infty) > 1$, there exists a unique endemic steady state.*

Proof. Let $(U^*, I^*, r^*(\tau))$ be an endemic steady state. Then we have $U^* = 0$ and

$$N = I^* + \int_0^\infty r^*(\tau)d\tau = I^* + \gamma I^* \int_0^\infty e^{-\beta I^* \int_0^\tau \theta(x)dx} d\tau. \tag{3.7}$$

By changing the variables, we obtain

$$I^* \int_0^\infty e^{-\beta I^* \int_0^\tau \theta(x)dx} d\tau = \int_0^\infty e^{-\beta \int_0^\tau \theta(\frac{x}{I^*})dx} d\tau.$$

Therefore the right hand side of (3.7) is a monotone increasing function of $I^* \in [0, N]$. If $I^* \to 0$, the right hand side of (3.7) goes to $\gamma/\beta\theta(\infty)$, so it has a unique positive root I^* if and only if $R_0\theta(\infty) > 1$. □

Therefore, if $\theta(\infty) < 1$ and $1 < R_0 < \theta(\infty)^{-1}$, the disease can invade into the completely susceptible host population (that is, outbreak occurs), but the disease will be naturally eradicated and there is no endemic steady state. That is, different from the classical SIR model, the invasion threshold does not equal the endemic threshold. This phenomena have been observed by Thieme and Yang ([14]) and Katriel ([7]).

Note that the subset $\Omega_0 := \{0\} \times \mathbb{R}_+ \times L^1(\mathbb{R}_+)$ of the state space of (3.6) is positively invariant, and the system (3.6) on Ω_0 is described by the following *IR* system on $\mathbb{R}_+ \times L^1(\mathbb{R}_+)$:

$$\begin{aligned} &\frac{dI(t)}{dt} = -\gamma I(t) + \beta I(t) \int_0^\infty \theta(\tau) r(t,\tau) d\tau, \\ &\frac{\partial r(t,\tau)}{\partial t} + \frac{\partial r(t,\tau)}{\partial \tau} = -\beta\theta(\tau) I(t) r(t,\tau), \\ &r(t,0) = \gamma I(t), \end{aligned} \tag{3.8}$$

which is known as the Pease model for type A influenza ([12]).

For the Pease model, as was shown by Inaba ([4], [6]), the prevalence of disease is related to the stability of the endemic steady state, that is, if the prevalence at the endemic steady state is grater than fifty percent, the endemic steady state is locally asymptotically stable. Since the prevalence in the real world may be small, the fifty percent prevalence rule would not cover the domain of realistic parameter values for type A influenza epidemic. For the type A influenza epidemic, between pandemics we can observe recurrent small outbreaks caused by antigenic drift of a dominant virus. Therefore it is a most interesting question whether the Pease model could allow sustained periodic solutions for parameter values escaping from the fifty percent prevalence rule. A possible mechanism to create a periodic solution is a Hopf bifurcation of an equilibrium, which occurs if a pair of complex conjugate characteristic root crosses the imaginary axis transversally from the left half plain to the right half plain. In such a case, the destabilization of the endemic steady state will lead a periodic solution. This aspect is studied by Magal and Ruan ([11]).

4 The two-stage model

Finally note that the late Kermack–McKendrick reinfection model can be also formulated as an age-structured *two-stage* model ([1]). Now we divide the host population into two subpopulations, susceptibles $s(t,\tau)$ and infecteds $i(t,\tau)$, where susceptibles mean never infected individuals, and the infecteds

imply individuals who have been once infected, no matter whether they have recovered or not. Then we can rewrite the basic model (2.2) as follows:

$$\begin{aligned}
&\frac{\partial s(t,\tau)}{\partial t}+\frac{\partial s(t,\tau)}{\partial \tau}=-\mu s(t,\tau)-\lambda(t)s(t,\tau),\\
&\frac{\partial i(t,\tau)}{\partial t}+\frac{\partial i(t,\tau)}{\partial \tau}=-(\mu+\lambda(t)\theta(\tau))i(t,\tau),\\
&s(t,0)=\mu N,\\
&i(t,0)=\lambda(t)\int_0^\infty (s(t,\tau)+\theta(\tau)i(t,\tau))\,d\tau,
\end{aligned} \tag{4.1}$$

where the force of infection is given by

$$\lambda(t)=\int_0^\infty \beta(\tau)i(t,\tau)d\tau. \tag{4.2}$$

The key idea of the two-stage formulation (4.1) is the assumption that the infectivity and the susceptibility of once infected individuals can be expressed by functions $\beta(\tau)$ and $\theta(\tau)$ of the infection-age (the time elapsed from the last infection) τ (the "one clock" model, [1]). In the late Kermack–McKendrick model, we have used two "clocks" for infected and recovered individuals, the reduction of susceptibility is a function of the time (since recovery) shown by the second clock. Since the recovery is expressed by the loss of infectivity and the acquired immunity, the waning immunity is expressed by the growth of susceptibility, it is reasonable to assume that there exist numbers $0<\tau_1\le\tau_2$ such that $\beta(\tau)=0$ for $\tau>\tau_1$ and $\theta(\tau)=0$ for $\tau<\tau_2$, so the interval $[\tau_1,\tau_2]$ is the complete immune period. Then the basic reproduction number is given by

$$R_0=N\int_0^\infty \beta(\tau)e^{-\mu\tau}d\tau. \tag{4.3}$$

If we omit the initial data (by assuming that the initial time is $t=-\infty$), the model (4.1) is reduced to a system of renewal equations:

$$\begin{aligned}
&\lambda(t)=\int_0^\infty \beta(\tau)e^{-\mu\tau-\int_0^\tau \lambda(t-\tau+\zeta)\theta(\zeta)d\zeta}b(t-\tau)d\tau,\\
&b(t)=\lambda(t)\int_0^\infty \left[\mu N e^{-\mu\tau-\int_0^\tau \lambda(t-\tau+\zeta)d\zeta}+\theta(\tau)e^{-\mu\tau-\int_0^\tau \lambda(t-\tau+\zeta)\theta(\zeta)d\zeta}b(t-\tau)\right]d\tau,
\end{aligned} \tag{4.4}$$

where $b(t):=i(t,0)$ is the density of newly infected individuals.

Again we obtain a scalar nonlinear renewal equation for λ if we insert the expression of $b(t)$ in (4.4) into the first equation for $\lambda(t)$. This point is first stressed by Breda, et al. ([1]).

One of problems for the two-stage model is how to introduce a vaccinated population. A simple solution is to introduce a vaccinated class $v(t,\tau)$ with a time τ elapsed from vaccination and a relative susceptibility schedule $\tilde{\theta}(\tau)$, which may be different from θ. Then the limiting system (the fully vaccinated model) is formulated as

$$\begin{aligned}
&\frac{\partial v(t,\tau)}{\partial t}+\frac{\partial v(t,\tau)}{\partial \tau}=-(\mu+\lambda(t)\tilde{\theta}(\tau))v(t,\tau),\\
&\frac{\partial i(t,\tau)}{\partial t}+\frac{\partial i(t,\tau)}{\partial \tau}=-(\mu+\lambda(t)\theta(\tau))i(t,\tau),\\
&v(t,0)=\mu N,\\
&i(t,0)=\lambda(t)\int_0^\infty \left(\tilde{\theta}(\tau)v(t,\tau)+\theta(\tau)i(t,\tau)\right)d\tau.
\end{aligned} \tag{4.5}$$

Note that in the model (4.5), we can interpret $v(t,\tau)$ as a virgin population with variable susceptibility. In fact, even among never infected individuals, their susceptibility is not necessarily constant (for example, due to the maternal antibody).

Then it is easy to see that the effective reproduction number is given by

$$R_e = R_0 \int_0^\infty \tilde{\theta}(\tau)\mu e^{-\mu\tau} d\tau, \tag{4.6}$$

so the reinfection threshold R_0/R_e is given by the reciprocal of the average susceptibility of vaccinated individuals. If $R_e > 1$, the fully vaccinated host can be invaded by the disease:

Proposition 4.1 *If $R_e > 1$, there exists at least one endemic steady state for* (4.5)*.*

Proof. Let λ^* be the force of infection at the steady state. Then the steady state is calculated as

$$v^*(\tau) = \mu N e^{-\mu\tau - \lambda^* \int_0^\tau \tilde{\theta}(\sigma)d\sigma},$$

$$i^*(\tau) = i^*(0) e^{-\mu\tau - \lambda^* \int_0^\tau \theta(\sigma)d\sigma}.$$

Inserting the above expressions into the boundary condition and use the relation,

$$\lambda^* = i^*(0) \int_0^\infty \beta(\tau) e^{-\mu\tau - \lambda^* \int_0^\tau \theta(\sigma)d\sigma} d\tau,$$

we have

$$\begin{aligned} 1 = {} & \lambda^* \int_0^\infty \theta(\tau) e^{-\mu\tau - \lambda^* \int_0^\tau \theta(\sigma)d\sigma} d\tau \\ & + \mu N \int_0^\infty \tilde{\theta}(\tau) e^{-\mu\tau - \lambda^* \int_0^\tau \tilde{\theta}(\sigma)d\sigma} d\tau \int_0^\infty \beta(\tau) e^{-\mu\tau - \lambda^* \int_0^\tau \theta(\sigma)d\sigma} d\tau =: f(\lambda^*). \end{aligned} \tag{4.7}$$

Then $f(0) = R_e$ and $f(\infty) = 0$, so $f(\lambda^*) = 1$ has at least one positive root if $R_e > 1$, which root gives the force of infection at the endemic steady state. □

The equation (4.7) suggests that a backward bifurcation of endemic steady states could occur, at least if $R_e > R_0$, that is, there is the enhancement of susceptibility.

Finally, let us extend the two-stage model (4.1) to an (chronological-)age-structured model, which is an essential extension to consider the real world applications.

$$\begin{aligned} & \frac{\partial s(t,a)}{\partial t} + \frac{\partial s(t,a)}{\partial \tau} = -(\mu(a) + \lambda(t))s(t,a), \\ & \frac{\partial i(t,\tau;a)}{\partial t} + \frac{\partial i(t,\tau;a)}{\partial \tau} = -\mu(a+\tau)i(t,\tau;a) - \lambda(t)\theta(\tau)i(t,\tau;a), \\ & s(t,0) = \int_0^\infty m(a) \left(s(t,a) + \int_0^a i(t,\tau;a-\tau)d\tau \right) da, \\ & i(t,0;a) = \lambda(t) \left(s(t,a) + \int_0^a \theta(\tau) i(t,\tau;a-\tau)d\tau \right), \end{aligned} \tag{4.8}$$

where m is the age-specific birth rate and the force of infection is given by

$$\lambda(t) = \int_0^\infty \int_0^\infty \beta(\tau) i(t,\tau;a) d\tau da, \tag{4.9}$$

the variable a denotes the chronological age, and $i(t,\tau;a)$ denotes the density of infecteds with infection-age τ who are infected at age a.

If we assume that the host population is in the demographic steady state, the boundary condition of $s(t,0)$ is replaced as $s(t,0)=b=1/\int_0^\infty \ell(x)dx$, where b is the crude birth rate and $\ell(a)=\exp(-\int_0^a \mu(\sigma)d\sigma)$ is the demographic survival rate.

By integrating along the characteristic line, we have

$$\begin{aligned} s(t,a) &= b\ell(a)e^{-\int_0^a \lambda(t-a+\sigma)d\sigma}, \\ i(t,\tau;a) &= i(t-\tau,0;a)\frac{\ell(a+\tau)}{\ell(a)}e^{-\int_0^\tau \theta(\sigma)\lambda(t-\tau+\sigma)d\sigma}. \end{aligned} \tag{4.10}$$

Let $B(t,a):=i(t,0;a)$ be the density of newly infecteds. Then we have

$$\begin{aligned} \lambda(t) &= \int_0^\infty \int_0^\infty \beta(\tau)B(t-\tau,a)\frac{\ell(a+\tau)}{\ell(a)}d\tau da, \\ B(t,a) &= \lambda(t)\left(b\ell(a)e^{-\int_0^a \lambda(t-a+\sigma)d\sigma} + \int_0^a \theta(\tau)\frac{\ell(a)}{\ell(a-\tau)}e^{-\int_0^\tau \theta(\sigma)\lambda(t-\tau+\sigma)d\sigma}B(t-\tau,a-\tau)d\tau\right), \end{aligned} \tag{4.11}$$

from which we can induce a nonlinear scalar renewal equation for B or λ.

In the invasion phase, the age density of newly infecteds satisfies the renewal equation:

$$B(t,a)=N(a)\int_0^\infty \int_0^\infty \beta(\tau)\frac{\ell(\tau+\eta)}{\ell(\eta)}B(t-\tau,\eta)d\eta d\tau, \tag{4.12}$$

where $N(a):=b\ell(a)$ is the host steady state population.

Then it is easy to see that the next generation operator K is given by

$$(Kf)(a)=N(a)\int_0^\infty \int_0^\infty \beta(\tau)\frac{\ell(\tau+\eta)}{\ell(\eta)}f(\eta)d\eta d\tau, \quad f\in L^1(\mathbb{R}_+), \tag{4.13}$$

so the basic reproduction number is calculated as follows:

$$R_0=\int_0^\infty \int_0^\infty \beta(\tau)\frac{\ell(\eta+\tau)}{\ell(\eta)}N(\eta)d\eta d\tau. \tag{4.14}$$

Although detailed analysis for the age-dependent reinfection model is an open problem, it suggests that to incorporate individual epidemiological history with host population dynamics is an important point of view to develop more realistic epidemic models. In fact, the functions β and θ could be understood as a result of virus (or parasite) dynamics in vivo, that is, they express the continuous process of the developments of infectivity and immunity. It is an interesting challenge to link within-host and between-host dynamics for infections diseases.

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