

Endemic Threshold Analysis for the Kermack–McKendrick Reinfection Model

稲葉 寿 (Hisashi INABA)

東京大学大学院数理科学研究科

Graduate School of Mathematical Sciences, University of Tokyo

email: inaba@ms.u-tokyo.ac.jp

1 Introduction

In a seminal series of papers published during the 1930s, Kermack and McKendrick proposed an infection–age structured *endemic* model that takes into account the demography of the host population, the waning immunity (variable susceptibility) and *reinfection* of recovered individuals ([13], [14]). Their model has less attention than the well-known outbreak model proposed in 1927 ([12]). In their model, the total population is decomposed into three compartments, the never infected (full susceptible), infectious and recovered populations. The host population is structured by a duration variable for each status, while the chronological age is neglected. The susceptibility of recovered individuals depends on the time that has passed since the last recovery, and the model thus has much flexibility to capture many facets of reinfection phenomena.

The concept of reinfection is becoming increasingly important in understanding emerging and reemerging infectious diseases, since it makes the control of infectious diseases difficult, and a waning immunity is widely observed if there is no (natural or artificial) boosting. In fact, the recovered individuals or vaccinated individuals could be reinfected as time passes owing to the natural decay of host immunity, or a genetic change in the virus. Reinfection often leads to non-clinical infection. It is thus likely that its occurrence is overlooked, and that we will fail in calculating the basic reproduction number and the critical coverage of immunization by neglecting the effect of reinfection.

As was pointed out by Gomes, *et al.* ([7]), we can introduce the *reinfection threshold* of R_0 at which a qualitative change in the epidemiological implication occurs for the prevalence and controllability in the reinfection model. Moreover, owing to enhancement of susceptibility or infectivity by reinfection, we expect that there is a backward bifurcation of endemic steady states. In such a case, we have bistable endemic steady states, and attaining a subcritical level of R_0 is not a complete policy for disease prevention.

In this short article, we introduce the Kermack–McKendrick reinfection model as an age-structured population model and sketch its basic endemic threshold phenomena. For more details, extensions and proofs, readers may refer to [11].

2 Kermack–McKendrick reinfection model

We first formulate the Kermack–McKendrick reinfection model as an age-structured population model. Let $s(t, \tau)$ be the density of the susceptible population who have never been infected (*virgin* population in the terminology of Kermack and McKendrick) at time t and duration τ (the time elapsed since entry into the s -state), which can be interpreted as the chronological age when a person enters the s -state at birth. Let $i(t, \tau)$ be the density of the infected and infectious population at time t and infection-age (the time elapsed since infection) τ and let $r(t, \tau)$ be the density of the recovered population at time t and duration τ (the time elapsed since the last recovery). Let m and μ respectively denote the birth (or immigration) rate and the death rate, and $\gamma(\tau)$ denotes the recovery rate at infection-age τ .

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

$$\lambda(t) = \int_0^{\infty} \beta(\sigma) i(t, \sigma) d\sigma, \quad (1)$$

where $\beta(\tau)$ denotes the infectivity for 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 . The relative susceptibility would be inversely correlated with the waning of immunity.

Assumption 2.1 It is assumed that $\beta, \gamma, \theta \in L_+^{\infty}(\mathbb{R}_+)$, and that the state space of the age distribution functions s, i and r is $L_+^1(\mathbb{R}_+)$.

The Kermack–McKendrick reinfection model is then formulated as

$$\begin{aligned} \frac{\partial s(t, \tau)}{\partial t} + \frac{\partial s(t, \tau)}{\partial \tau} &= -\mu s(t, \tau) - \lambda(t) s(t, \tau), \\ \frac{\partial i(t, \tau)}{\partial t} + \frac{\partial i(t, \tau)}{\partial \tau} &= -(\mu + \gamma(\tau)) i(t, \tau), \\ \frac{\partial r(t, \tau)}{\partial t} + \frac{\partial r(t, \tau)}{\partial \tau} &= -\mu r(t, \tau) - \theta(\tau) \lambda(t) r(t, \tau), \\ s(t, 0) &= m \int_0^{\infty} (s(t, \tau) + i(t, \tau) + r(t, \tau)) d\tau, \\ i(t, 0) &= \lambda(t) \int_0^{\infty} (s(t, \tau) + \theta(\tau) r(t, \tau)) d\tau, \\ r(t, 0) &= \int_0^{\infty} \gamma(\tau) i(t, \tau) d\tau, \end{aligned} \quad (2)$$

with initial data

$$s(0, \tau) = s_0(\tau), \quad i(0, \tau) = i_0(\tau), \quad r(0, \tau) = r_0(\tau). \quad (3)$$

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

$$N(t) := \int_0^\infty (s(t, \tau) + i(t, \tau) + r(t, \tau)) d\tau. \quad (4)$$

It is then easily seen that the total size of the host population is constant if $m = \mu$. In the following we consider the case of a constant total population size, denoted by N , and the boundary condition of $s(t, a)$ is thus replaced by $s(t, 0) = \mu N$.

The basic system (2) has a trivial, disease-free (completely susceptible) steady state $(s^*, i^*, r^*) = (\mu N e^{-\mu\tau}, 0, 0)$. The linearized equation for the infected population in the disease-free steady state is then given by

$$\begin{aligned} \frac{\partial \zeta(t, \tau)}{\partial t} + \frac{\partial \zeta(t, \tau)}{\partial \tau} &= -(\mu + \gamma(\tau))\zeta(t, \tau), \\ \zeta(t, 0) &= N \int_0^\infty \beta(\tau)\zeta(t, \tau) d\tau, \end{aligned} \quad (5)$$

and it is easily seen that the basic reproduction number for the basic model (2) is given by

$$R_0 = N \int_0^\infty e^{-\mu\tau} \beta(\tau) \Gamma(\tau) d\tau, \quad (6)$$

where $\Gamma(\tau) := \exp(-\int_0^\tau \gamma(x) dx)$ is the survival probability. By the principle of linearized stability, the stability of zero solution of (5) determines the local stability of the disease-free steady state of system (2), and the disease-free steady state is thus locally asymptotically stable if $R_0 < 1$, while it is unstable if $R_0 > 1$. Readers may refer to [5], [6] and [10] for the role of the basic reproduction number in population dynamics.

Model (2) can be rewritten as the Gurtin–MacCamy model for an age-dependent population. Its mathematical well-posedness has been established ([9]).

For simplicity, instead of considering the initial value problem, we assume that the epidemic starts at $t = -\infty$. Integrating the partial differential equations in (2) along the characteristic line, we have a set of equations:

$$\begin{aligned} s(t, \tau) &= \mu N e^{-\mu\tau - \int_0^\tau \lambda(t-\tau+\sigma) d\sigma}, \\ i(t, \tau) &= b_1(t - \tau) e^{-\mu\tau} \Gamma(\tau), \\ r(t, \tau) &= b_2(t - \tau) e^{-\mu\tau - \int_0^\tau \lambda(t-\tau+\sigma) \theta(\sigma) d\sigma}, \end{aligned} \quad (7)$$

where $b_1(t) := i(t, 0)$ and $b_2(t) := r(t, 0)$. Inserting equations (7) into the

boundary conditions of (2), we obtain a set of integral equations:

$$b_1(t) = \lambda(t) \left[\int_0^\infty \mu N e^{-\mu\tau - \int_0^\tau \lambda(t-\tau+\sigma) d\sigma} d\tau + \int_0^\infty \theta(\tau) b_2(t-\tau) e^{-\mu\tau - \int_0^\tau \lambda(t-\tau+\sigma) \theta(\sigma) d\sigma} d\tau \right], \quad (8)$$

$$b_2(t) = \int_0^\infty b_1(t-\tau) e^{-\mu\tau} \gamma(\tau) \Gamma(\tau) d\tau,$$

where

$$\lambda(t) = \int_0^\infty e^{-\mu\tau} \beta(\tau) \Gamma(\tau) b_1(t-\tau) d\tau. \quad (9)$$

Inserting the expression for b_2 into the equation for b_1 in (8) and changing the order of integrals, we obtain

$$b_1(t) = \lambda(t) \int_0^\infty S(t, \tau) d\tau, \quad (10)$$

$$\begin{aligned} S(t, \tau) &:= s(t, \tau) + \theta(\tau) r(t, \tau) \\ &= \mu N e^{-\mu\tau - \int_0^\tau \lambda(t-\tau+\sigma) d\sigma} \\ &\quad + b_1(t-\tau) e^{-\mu\tau} \int_0^\tau \theta(\sigma) e^{-\int_0^\sigma \theta(\zeta) \lambda(t-\sigma+\zeta) d\zeta} \gamma(\tau-\sigma) \Gamma(\tau-\sigma) d\sigma, \end{aligned} \quad (11)$$

where $\int_0^\infty S(t, \tau) d\tau$ is the *effective size of susceptibles*. The expression (10) implies a simple fact that the new incidence at time t is given by the force of infection times the size of effective susceptibles ([2]).

From (10) and (11), we obtain a linear renewal equation for b_1 if we see the force of infection λ as a given function, and thus, by solving the linear renewal equation formally, we have an expression of b_1 with unknown λ . Inserting this solution into (9), we arrive at a nonlinear “scalar” renewal equation for λ . Alternatively, eliminating λ from (9), (10) and (11), we again obtain a nonlinear scalar integral equation for b_1 . We can then establish the well-posedness of the Kermack–McKendrick reinfection model (2) based on the well-known method of the nonlinear integral equation.

If $\theta \equiv 0$, (2) becomes the susceptible-infected-recovered (SIR) model with permanent immunity, and it has a unique endemic steady state if and only if $R_0 > 1$ and it is globally stable ([16]). If $\theta \equiv 1$, the recovered population can be identified with the virgin population, and (2) is thus reduced to the infection-age dependent SIS epidemic model, and it is formulated by a nonlinear renewal equation, its endemic steady state is unique but can lose stability and Hopf bifurcations can occur when $R_0 > 1$ ([3], [4], [17]). Under the assumption that θ is monotone increasing and less than unity, it is concluded that if $R_0 > 1$, there exists a unique endemic steady state that is locally asymptotically stable as long as $|R_0 - 1|$ is small enough ([9]).

If $\sup \theta > 1$, we conjecture that the subcritical condition $R_0 < 1$ does not necessarily guarantee the eradication of diseases. In fact, from (10), we formally define a time-dependent (period) reproduction number as

$$\mathcal{R}(t) := \tilde{S}(t) \int_0^\infty \beta(\tau) \Gamma(\tau) e^{-\mu\tau} d\tau, \quad (12)$$

where $\tilde{S}(t) := \int_0^\infty S(t, \tau) d\tau$ is the effective size of susceptibility. Since $\tilde{S}(t)$ can be larger than the total population size N , $\mathcal{R}(t)$ can be larger than R_0 , and $R_0 < 1$ would thus not be a sufficient condition for eradication of the disease.

Let $\alpha := \max\{1, \sup_{\tau \geq 0} \theta(\tau)\}$. Then $\tilde{S} \leq \alpha N$ and it follows from (10) that

$$b_1(t) \leq \alpha N \int_0^\infty \beta(\tau) \Gamma(\tau) e^{-\mu\tau} b_1(t - \tau) d\tau. \quad (13)$$

Using the comparison argument, we know that $\lim_{t \rightarrow \infty} b_1(t) = 0$ if $\alpha R_0 < 1$. We then have a simple criterion for the global stability of the disease-free steady state.

Proposition 2.2 *If $R_0 < 1/\alpha$, the disease-free steady state of (2) is globally asymptotically stable.*

2.1 Bifurcation of endemic steady states

We now check the bifurcation of endemic steady states. Let $s^*(\tau)$, $i^*(\tau)$ and $r^*(\tau)$ be the steady state solution. It then holds that

$$\begin{aligned} s^*(\tau) &= \mu N e^{-(\mu + \lambda^*)\tau}, \\ i^*(\tau) &= i^*(0) e^{-\mu\tau} \Gamma(\tau), \\ r^*(\tau) &= r^*(0) e^{-\mu\tau - \lambda^* \int_0^\tau \theta(\sigma) d\sigma}, \end{aligned} \quad (14)$$

where

$$\begin{aligned} i^*(0) &= \lambda^* \int_0^\infty (s^*(\tau) + \theta(\tau) r^*(\tau)) d\tau, \\ r^*(0) &= \int_0^\infty \gamma(\tau) i^*(\tau) d\tau. \end{aligned} \quad (15)$$

and λ^* is the force of infection in the steady state given by

$$\lambda^* = \int_0^\infty \beta(\tau) i^*(\tau) d\tau = b^* \langle \beta, \Gamma \rangle. \quad (16)$$

In expression (16), $b^* := i^*(0)$ is the density of the newly infecteds in the steady state and we have used the notation as

$$\langle \beta, \Gamma \rangle := \int_0^\infty \beta(\tau) \Gamma(\tau) e^{-\mu\tau} d\tau. \quad (17)$$

Inserting (16) into the first equation of (15), we obtain

$$b^* = b^* \langle \beta, \Gamma \rangle \int_0^\infty (\mu N e^{-(\mu+\lambda^*)\tau} + r^*(0)\theta(\tau)e^{-\mu\tau-\lambda^* \int_0^\tau \theta(\sigma) d\sigma}) d\tau, \quad (18)$$

which shows a renewal relation in a steady state with the force of infection λ^* . Since $\langle \beta, \Gamma \rangle = R_0/N$ and $r^*(0) = b^* \langle \gamma, \Gamma \rangle$, we arrive at an equation for unknown λ^* :

$$\begin{aligned} R(\lambda^*) &:= \frac{\mu R_0}{\mu + \lambda^*} + \langle \gamma, \Gamma \rangle \lambda^* \int_0^\infty \theta(\tau) e^{-\mu\tau - \lambda^* \int_0^\tau \theta(\sigma) d\sigma} d\tau \\ &= \frac{\mu R_0}{\mu + \lambda^*} + \langle \gamma, \Gamma \rangle \left(1 - \int_0^\infty \mu e^{-\mu\tau - \lambda^* \int_0^\tau \theta(\sigma) d\sigma} d\tau \right) = 1, \end{aligned} \quad (19)$$

where we used the notation as

$$\langle \gamma, \Gamma \rangle := \int_0^\infty \gamma(\tau) \Gamma(\tau) e^{-\mu\tau} d\tau. \quad (20)$$

Equation (19) implies that the effective reproduction number, given by $R(\lambda^*)$, must be unity in a steady state.

It follows from (19) that there exists at least one endemic steady state if $R_0 > 1$, because $R(0) = R_0 > 1$ and $\lim_{\lambda \rightarrow \infty} R(\lambda) = \langle \gamma, \Gamma \rangle < 1$. Given that $R(\lambda^*)$ is not monotone decreasing, there is a possibility that multiple endemic steady states exist.

Proposition 2.3 *If the inequality*

$$\langle \gamma, \Gamma \rangle \theta^* > 1, \quad (21)$$

holds, where

$$\theta^* := \int_0^\infty \theta(\tau) \mu e^{-\mu\tau} d\tau, \quad (22)$$

then endemic steady states backwardly bifurcate from the disease-free steady state when R_0 crosses unity, i.e., multiple endemic steady states exist if $R_0 < 1$ and $|R_0 - 1|$ is small enough.

proof: Define a function $f(\lambda, R_0) := R(\lambda) - 1$, where R_0 is seen as a bifurcation parameter and $f(0, 1) = 0$. Observe that

$$\left. \frac{\partial f}{\partial \lambda} \right|_{(\lambda, R_0) = (0, 1)} = \frac{1}{\mu} (\theta^* \langle \gamma, \Gamma \rangle - 1), \quad \left. \frac{\partial f}{\partial R_0} \right|_{(\lambda, R_0) = (0, 1)} = 1.$$

Therefore if condition (21) holds, then $f = 0$ is solved as $\lambda = \lambda(R_0)$ with $\lambda(1) = 0$ at the neighborhood of $(\lambda, R_0) = (0, 1)$. Since $d\lambda(1)/dR_0 < 0$, we have $\lambda(R_0) > 0$ for $R_0 \in (1-\eta, 1)$ for sufficiently small $\eta > 0$. For each $R_0 \in (1-\eta, 1)$, we have $f(0, R_0) < 1$, $f(\lambda(R_0), R_0) = 0$ and $\lim_{\lambda \rightarrow \infty} f(\lambda, R_0) = \langle \gamma, \Gamma \rangle - 1 < 0$, and there are then at least two endemic steady states. \square

Condition (21) was first given in [18] by using the ordinary differential equation version of (2). It is easily seen that condition (21) does not hold if there is no enhancement of susceptibility, i.e., if $\theta(\tau) \leq 1$ for all $\tau \geq 0$.

3 Vaccination model and reinfection threshold

3.1 Reinfection threshold

We now introduce a mass vaccination (host immunization) in the basic model (2). In fact, it is intuitively clear that reinfection phenomena would make disease control more difficult and complex, and we thus need an index to capture the difficulty. An important effect of vaccination policy is the reduction of the effective size of the susceptible population. In the reinfection model, there is a possibility that a disease can invade a fully vaccinated population, and we are naturally led to the idea of the *reinfection threshold*.

Suppose that newborns or immigrants in the virgin population are mass vaccinated with coverage $\epsilon \in [0, 1]$ and, for simplicity, the immunological status of newly vaccinated individuals is identical to that of the newly recovered individuals. This assumption will be relaxed in section 5. The boundary condition in the basic system (2) is then replaced:

$$\begin{aligned} s(t, 0) &= (1 - \epsilon)\mu N, \\ i(t, 0) &= \lambda(t) \int_0^\infty (s(t, \tau) + \theta(\tau)r(t, \tau)) d\tau, \\ r(t, 0) &= \epsilon\mu N + \int_0^\infty \gamma(\tau)i(t, \tau)d\tau. \end{aligned} \tag{23}$$

The disease-free steady state is then given by

$$(s^*, i^*, r^*) = ((1 - \epsilon)\mu N e^{-\mu\tau}, 0, \epsilon\mu N e^{-\mu\tau}),$$

and the linearized renewal equation in the initial invasion phase is thus given by

$$\xi(t) = ((1 - \epsilon)N + \epsilon N\theta^*) \int_0^\infty e^{-\mu\tau} \beta(\tau)\Gamma(\tau)\xi(t - \tau)d\tau, \tag{24}$$

where $\xi(t) := \zeta(t, 0)$ denotes a small perturbation in the infected population density.

Therefore, the effective reproduction number, denoted by $\mathcal{R}(\epsilon)$, in the partially immunized disease-free steady state is given by

$$\mathcal{R}(\epsilon) = (1 - \epsilon)R_0 + \epsilon R_1 = (1 - \epsilon(1 - \theta^*))R_0, \tag{25}$$

where $R_1 := \theta^* R_0$. Then if $\mathcal{R}(\epsilon) < 1$, the disease-free steady state is locally asymptotically stable, while it is unstable if $\mathcal{R}(\epsilon) > 1$. However, it is unclear whether the disease-free steady state becomes globally asymptotically stable when $\mathcal{R}(\epsilon) < 1$.

Here we note that R_1 is the effective reproduction number for the fully vaccinated system. In fact, if $\epsilon = 1$, the virgin population is eradicated, and we obtain the limiting recovered-infected-recovered system as

$$\begin{aligned}
\frac{\partial i(t, \tau)}{\partial t} + \frac{\partial i(t, \tau)}{\partial \tau} &= -(\mu + \gamma(\tau))i(t, \tau), \\
\frac{\partial r(t, \tau)}{\partial t} + \frac{\partial r(t, \tau)}{\partial \tau} &= -\mu r(t, \tau) - \theta(\tau)\lambda(t)r(t, \tau), \\
i(t, 0) &= \lambda(t) \int_0^\infty \theta(\tau)r(t, \tau)d\tau, \\
r(t, 0) &= \mu N + \int_0^\infty \gamma(\tau)i(t, \tau)d\tau.
\end{aligned} \tag{26}$$

This new system (26) can be seen as a duration-dependent SIS model with vaccination if we view the recovered class as a new susceptible class. Then (26) has a disease-free steady state $(i^*, r^*) = (0, \mu N e^{-\mu\tau})$, and the linearized system in the disease free steady state is given as

$$\begin{aligned}
\frac{\partial \zeta(t, \tau)}{\partial t} + \frac{\partial \zeta(t, \tau)}{\partial \tau} &= -(\mu + \gamma(\tau))\zeta(t, \tau), \\
\zeta(t, 0) &= \theta^* N \int_0^\infty \beta(\tau)\zeta(t, \tau)d\tau.
\end{aligned} \tag{27}$$

Therefore the effective reproduction number for the limiting system (26) is given by $R_1 = \theta^* R_0$.

Suppose that $R_0 > 1$. From (25), the critical coverage of immunization ϵ^* such that $\mathcal{R}(\epsilon^*) = 1$ is given by

$$\epsilon^* = \left(1 - \frac{1}{R_0}\right) \frac{1}{1 - \theta^*}, \tag{28}$$

but it is meaningful only when $\theta^* < 1$. The disease is uncontrollable by the vaccination if $\theta^* \geq 1$. Moreover, if $R_1 = \theta^* R_0 > 1$, we have $\mathcal{R}(\epsilon) > 1$ for all $\epsilon \in [0, 1]$, and the disease is thus again uncontrollable by the vaccination, because the fully vaccinated population can be invaded by the disease.

Let $\sigma := R_1/R_0$, i.e., σ is the ratio of the effective reproduction number of the fully vaccinated system to the basic reproduction number. Given that the qualitative change in the epidemiological implication occurs for the prevalence and controllability at $R_0 = 1/\sigma$, Gomes *et al.* ([7], [8]) referred to $1/\sigma$ as the *reinfection threshold* of R_0 . As seen above, the reinfection threshold of R_0 corresponds to the fact that $\sigma R_0 = R_1 = 1$, i.e., $R_0 = 1/\sigma$ does not imply a bifurcation point of the basic system (2), but the threshold condition $R_1 = 1$ of the fully vaccinated system (26). In the above setting, we have $\sigma = \theta^*$, but its value depends on the basic model assumptions.

3.2 Bifurcation of endemic steady states

Let (s^*, i^*, r^*) be the steady state of the basic system (2) with the boundary condition (23). We then have

$$\begin{aligned} s^*(\tau) &= (1 - \epsilon)\mu N e^{-\mu\tau - \lambda^*\tau}, \\ i^*(\tau) &= i^*(0)e^{-\mu\tau}\Gamma(\tau), \\ r^*(\tau) &= r^*(0)e^{-\mu\tau - \lambda^* \int_0^\tau \theta(x)dx}, \end{aligned} \quad (29)$$

where

$$\begin{aligned} \lambda^* &= i^*(0)\langle\beta, \Gamma\rangle, \\ i^*(0) &= \lambda^* \int_0^\infty (s^*(\tau) + \theta(\tau)r^*(\tau))d\tau, \\ r^*(0) &= \epsilon\mu N + i^*(0)\langle\gamma, \Gamma\rangle. \end{aligned} \quad (30)$$

From the above equations, we can calculate $i^*(0)$ as

$$\begin{aligned} i^*(0) &= \lambda^* \int_0^\infty (s^*(\tau) + \theta(\tau)r^*(\tau))d\tau \\ &= \lambda^* \frac{(1 - \epsilon)\mu N}{\mu + \lambda^*} + \lambda^* r^*(0) \int_0^\infty \theta(\tau)e^{-\mu\tau - \lambda^* \int_0^\tau \theta(x)dx} d\tau \\ &= \lambda^* \frac{(1 - \epsilon)\mu N}{\mu + \lambda^*} + \lambda^* (\epsilon\mu N + i^*(0)\langle\gamma, \Gamma\rangle) \int_0^\infty \theta(\tau)e^{-\mu\tau - \lambda^* \int_0^\tau \theta(x)dx} d\tau. \end{aligned} \quad (31)$$

We then have the expression:

$$i^*(0) = \frac{\lambda^* \frac{(1 - \epsilon)\mu N}{\mu + \lambda^*} + \epsilon\mu N \lambda^* \int_0^\infty \theta(\tau)e^{-\mu\tau - \lambda^* \int_0^\tau \theta(x)dx} d\tau}{1 - \lambda^* \langle\gamma, \Gamma\rangle \int_0^\infty \theta(\tau)e^{-\mu\tau - \lambda^* \int_0^\tau \theta(x)dx} d\tau}. \quad (32)$$

From (32) and the relation

$$\lambda^* = \frac{R_0}{N} i^*(0),$$

we know that a positive root $\lambda^* > 0$ must satisfy the equation:

$$1 = R_0 \frac{v(\lambda^*)}{u(\lambda^*)}, \quad (33)$$

where

$$\begin{aligned} v(\lambda) &:= \frac{(1 - \epsilon)\mu}{\mu + \lambda} + \epsilon\mu \int_0^\infty \theta(\tau)e^{-\mu\tau - \lambda \int_0^\tau \theta(x)dx} d\tau, \\ u(\lambda) &:= 1 - \langle\gamma, \Gamma\rangle \phi(\lambda). \end{aligned} \quad (34)$$

Here we have used the notation (20) and

$$\phi(\lambda) := \lambda \int_0^\infty \theta(\tau)e^{-\mu\tau - \lambda \int_0^\tau \theta(x)dx} d\tau. \quad (35)$$

Observe that

$$\lambda \int_0^{\infty} \theta(\tau) e^{-\mu\tau - \lambda \int_0^{\tau} \theta(x) dx} d\tau = 1 - \int_0^{\infty} \mu e^{-\mu\tau - \lambda \int_0^{\tau} \theta(x) dx} d\tau. \quad (36)$$

ϕ is then an increasing function, and $u(\lambda)$ is thus a decreasing function. We can now conclude the following.

Proposition 3.1 *If $\mathcal{R}(\epsilon) > 1$, there exists at least one endemic steady state. Suppose that the condition*

$$\theta^* \langle \gamma, \Gamma \rangle > \frac{1 - \epsilon(1 - \theta^{**})}{1 - \epsilon(1 - \theta^*)}, \quad (37)$$

holds, where

$$\theta^{**} := \mu^2 \int_0^{\infty} e^{-\mu\tau} \theta(\tau) \int_0^{\tau} \theta(x) dx d\tau. \quad (38)$$

Endemic steady states then backwardly bifurcate from the disease-free steady state when $\mathcal{R}(\epsilon)$ crosses unity, i.e., multiple endemic steady states exist if $\mathcal{R}(\epsilon) < 1$ and $|\mathcal{R}(\epsilon) - 1|$ is small enough.

proof: Relation (33) implies that the effective reproduction number in the endemic steady state with the force of infection λ^* is given by

$$R(\lambda^*) = R_0 \frac{v(\lambda^*)}{u(\lambda^*)} = \frac{\mathcal{R}(\epsilon) v(\lambda^*)}{v(0) u(\lambda^*)}.$$

Then $R(0) = \mathcal{R}(\epsilon)$ and $R(\infty) = 0$, and thus $R(\lambda^*) = 1$ has at least one positive root if $\mathcal{R}(\epsilon) > 1$, which implies that there exists one endemic steady state. If $R(0) = \mathcal{R}(\epsilon) = R_0 v(0) = 1$ and condition (37) holds, $R'(0) = v(0)^{-1} v'(0) - u'(0) > 0$. $R(\lambda^*) = 1$ then has at least one positive root. Moreover, it has at least two positive roots if $R(0) = \mathcal{R}(\epsilon) < 1$ and $|\mathcal{R}(\epsilon) - 1|$ is small enough. To see this precisely, let us again define a function $f(\lambda, R_0) := R(\lambda) - 1$. Then $f(0, v(0)^{-1}) = 0$ and

$$\left. \frac{\partial f}{\partial R_0} \right|_{(\lambda, R_0) = (0, v(0)^{-1})} = 1, \quad \left. \frac{\partial f}{\partial \lambda} \right|_{(\lambda, R_0) = (0, v(0)^{-1})} = v(0)^{-1} v'(0) - u'(0),$$

where

$$v'(0) = -\frac{1}{\mu}(1 - \epsilon(1 - \theta^{**})), \quad u'(0) = -\frac{1}{\mu} \langle \gamma, \Gamma \rangle \theta^*.$$

If condition (37) holds, $f = 0$ is solved as $\lambda = \lambda(R_0)$ satisfying $\lambda(v(0)^{-1}) = 0$ and $d\lambda(v(0)^{-1})/dR_0 < 0$ in the neighborhood of $(\lambda, R_0) = (0, v(0)^{-1})$. If $R_0 v(0) < 1$ and $|R_0 v(0) - 1|$ is small enough, for each R_0 , there exist multiple positive roots such that $f(\lambda, R_0) = 0$, because $f(0, R_0) < 1$, $f(\lambda(R_0), R_0) = 0$ and $f(\infty, R_0) = -1 < 0$. \square

Proposition 3.1 tells us that the subcritical condition $\mathcal{R}(\epsilon) < 1$ is not sufficient to eradicate the disease if condition (37) holds. Note that if $\epsilon = 1$ in (37), we know that a backward bifurcation occurs even in the recovered–infected–recovered model if $(\theta^*)^2 > \theta^{**}$, though this condition does not hold when θ is constant.

4 Discussion

As shown above, it is not easy to realize subcritical endemic steady states without enhancement of susceptibility in the reinfection model. However, we can consider more realistic reinfection mechanisms that allow backward bifurcations. Let us consider two examples, malaria and measles.

Although reinfected individuals are not distinguished from the infecteds resulting from completely susceptible individuals in the original Kermack–McKendrick model, it will become a natural extension if we assume that epidemiological parameters for the reinfecteds are different from parameters of the infecteds produced from completely susceptible individuals. In fact, Águas, *et al.* ([1]) developed an age-structured population model for the dynamics of malaria transmission, and observed that stable endemic steady states coexist with stable disease-free steady states. In their model, the infecteds resulting from completely susceptible individuals are clinical malaria cases, and recovery from clinical cases confers protection against the clinical manifestation of diseases, but not against infection *per se*. A recovered individual can then be reinfected and develops a non-clinical form of malaria, which can be called an *asymptomatic infection*. If the net reproductivity of asymptomatic cases is larger than that of clinical cases, it is possible to show that there could exist a backward bifurcation even when $\theta^* \leq 1$. This situation could occur if the duration of infection of the asymptomatic case is much longer, because it does not necessarily need clinical treatment.

Next consider an epidemic model of measles with fluctuation of the immunity level for vaccinees. We again assume that there are two sorts of infectious states. The host population is divided into five subpopulations: the completely susceptible population, the vaccinated population, the recovered population with complete immunity, the classical infectious population for measles, and the subclinical infectious population for measles. Different from the assumption of the Kermack–McKendrick reinfection model, the recovered individuals have complete immunity and no susceptibility, and instead, the vaccinated individuals have partial susceptibility (according to the waning of immunity) depending on the duration since vaccination. By (re)infection, some of the vaccinated individuals develop subclinical infection, and the immunity level of the remaining vaccinated individuals is boosted to the level of newly vaccinated individuals. That is, the boosting effect is expressed by the “reset” of local time to zero for vaccinated individuals. Kishida ([15]) investigated this kind of reinfection model, and he found that multiple endemic steady states can exist under subcritical reproduction number. If we take into account subclinical infection, the coverage of immunization to eradicate the disease must be larger than the critical proportion of immunization calculated from the standard SIR model neglecting the subclinical cases. An introduction of imperfect vaccination would make it difficult to eradicate measles, although it can reduce the number of clinical cases.

References

- [1] R. Águas, L. J. White, R. W. Snow and M. G. M. Gomes (2008), Prospects for malaria eradication in Sub-Saharan Africa, *PLoS ONE*, Vol. 3, Issue 3, e1767.
- [2] D. Breda, O. Diekmann, W. F. de Graaf, A. Pugliese and R. Vermiglio (2012), On the formulation of epidemic models (an appraisal of Kermack and McKendrick), *J. Biol. Dyn.*, Vol.6, Suppl. 2: 103-117.
- [3] O. Diekmann and R. Montijn (1982), Prelude to Hopf bifurcation in an epidemic model: Analysis of a characteristic equation associated with a nonlinear Volterra integral equation, *J. Math. Biol.* 14, 117-127.
- [4] O. Diekmann and S. A. van Gils (1984), Invariant manifolds for Volterra integral equations of convolution type, *J. Diff. Equ.* 54: 139-180.
- [5] O. Diekmann, J. A. P. Heesterbeek and J. A. J. Metz (1990), On the definition and the computation of the basic reproduction ratio R_0 in models for infectious diseases in heterogeneous populations, *J. Math. Biol.* 28: 365-382.
- [6] O. Diekmann, J. A. P. Heesterbeek and T. Britton (2013), *Mathematical Tools for Understanding Infectious Disease Dynamics*, Princeton University Press, Princeton and Oxford.
- [7] M. G. Gomes, L. J. White and G. F. Medley (2004), Infection, reinfection, and vaccination under suboptimal immune protection: epidemiological perspectives, *J. Theor. Biol.* 228: 539-549.
- [8] M. G. Gomes, L. J. White and G. F. Medley (2005), The reinfection threshold, *J. Theor. Biol.* 236: 111-113.
- [9] H. Inaba (2001), Kermack and McKendrick revisited: The variable susceptibility model for infectious diseases, *Japan J. Indust. Appl. Math.* 18(2): 273-292.
- [10] H. Inaba (2012), On a new perspective of the basic reproduction number in heterogeneous environments, *J. Math. Biol.* 65: 309-348.
- [11] H. Inaba (2016), Endemic threshold analysis for the Kermack–McKendrick reinfection model, *Josai Mathematical Monographs* vol. 9, 105-133.
- [12] W. O. Kermack and A. G. McKendrick (1927), Contributions to the mathematical theory of epidemics I, *Proceedings of the Royal Society* 115A: 700-721. (reprinted in *Bulletin of Mathematical Biology* 53(1/2): 33-55, 1991)
- [13] W. O. Kermack and A. G. McKendrick (1932), Contributions to the mathematical theory of epidemics II. The problem of endemicity, *Proceedings of the Royal Society* 138A: 55-83. (reprinted in *Bulletin of Mathematical Biology* 53(1/2): 57-87, 1991)

- [14] W. O. Kermack and A. G. McKendrick (1933), Contributions to the mathematical theory of epidemics III. Further studies of the problem of endemicity, *Proceedings of the Royal Society* 141A: 94-122. (reprinted in *Bulletin of Mathematical Biology* 53(1/2): 89-118, 1991)
- [15] M. Kishida (2010), A mathematical model for measles with waning of immunity, boosting and subclinical infection, MA thesis, Graduate School of Mathematical Sciences, University of Tokyo. [in Japanese]
- [16] P. Magal, C. C. McCluskey and G. F. Webb (2010), Lyapunov functional and global asymptotic stability for an infection-age model, *Applicable Analysis* 89(7): 1109-1140.
- [17] J. A. J. Metz and O. Diekmann (1986), *The Dynamics of Physiologically Structured Populations*, Lecture Notes in Biomathematics 68, Springer-Verlag: Berlin.
- [18] M. Safan, H. Heesterbeek and K. Dietz (2006), The minimum effort required to eradicate infections in models with backward bifurcation, *J. Math. Biol.* 53: 703-718.