Epidemic dynamics with a time-varying susceptibility due to repeated infections

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\textbf{ABSTRACT}

In this paper, we consider the impact of heterogeneous susceptibility on disease transmission dynamics, using a simple mathematical model formulated by a system of ordinary differential equations. Our model describes a time-varying immunity level, which is enhanced by reinfection and diminished by waning immunity. Through mathematical analysis, we show that unexpected outbreaks, called delayed outbreaks, occur even when the basic reproduction number is less than one. A reallocation of susceptibility at the individual level, by repeated infections, in the host population induces delayed outbreaks.

\section{1. Introduction}

In many mathematical models for infectious disease transmission dynamics, such as the standard SIR models \cite{1,5,16}, susceptibility is assumed to be lost after recovery, as it is assumed that individuals establish permanent immunity to the disease. The assumption that immunity is maintained after recovery is relaxed in the paper \cite{17,18}. In \cite{17,18}, the authors consider reinfection of recovered individuals, assuming that recovered individuals have susceptibility to the disease, see also \cite{12,13} for mathematical analysis of the Kermack–McKendrick reinfection model formulated as a system of partial differential equations. Reinfection models, formulated by a system of ordinary differential equations, have been studied in \cite{7–9,14}. In the mathematical model studied in \cite{8,14} recovered individuals are assumed to have partial susceptibility to the disease, thus reinfection of recovered individuals is possible. It is shown that the disease transmission dynamics qualitatively change from epidemic (outbreaks of a disease) to endemic (persistence of a disease), when the basic reproduction number crosses the reinfection threshold.

In these studies, the susceptible population is assumed to be a homogeneous population: individuals in the susceptible population are equally susceptible to the disease. After recovery from infection, every individual is assumed to obtain the same degree of susceptibility, thus the recovered population is also considered as a homogeneous population,
with respect to susceptibility at the individual level. However, the degree of susceptibility an individual obtains after recovery from infection varies among individuals [19].

We are interested in the disease transmission dynamics influenced by the change of susceptibility at the individual level through repeated infections. In this paper, we expand the mathematical model studied in [14], that focuses on the difference of susceptibility against first and second infections. It assumes that susceptibility is constant among hosts if the number of exposures is same. In this paper, we analyse the impact of heterogeneity of susceptibility even if the number of exposures is the same. To this end, we construct a parsimonious mathematical model describing the heterogeneity of susceptibility. In our model, there is no distinction between susceptible hosts and recovered hosts like ‘S’ and ‘R’ classes in the standard SIR model. Hosts are classified into different compartments by their degree of susceptibility. After an infection, susceptibility can change resulting in the reallocation of compartments. To keep the mathematical analysis tractable, we consider a simple nonlinear system of ordinary differential equations. Our simple mathematical model is sufficient to show an unexpected outbreak, called a delayed outbreak [19], when the basic reproduction number is less than one. Delayed outbreaks are unexpected outbreaks where the infective population increases with a certain time delay, even though it initially decreases, since the basic reproduction number is less than one. In addition to the delayed outbreak, our model can capture common epidemiological dynamics: disease extinction, epidemic (sudden outbreaks of a disease), and endemic (persistence of a disease) cases [4]. In this paper, disease extinction refers to the epidemiological dynamics that the infective population monotonically decreases and eventually tends to 0.

Variation in susceptibility to the disease has been studied in the literature, see [2,11,15,20] and references therein. In [15], the author studies a general epidemic model that features an arbitrary distribution of susceptibility in the host population. The threshold type dynamics, with respect to the basic reproduction number, holds, as the susceptible population monotonically decreases, during the course of an epidemic, due to the permanent immunity assumption. If the disease does not confer permanent immunity, the susceptible population does not necessarily decrease over time. A more susceptible subpopulation may increase and the change of distribution of susceptibility, due to reinfection, may trigger a disease outbreak. We would like to consider such a condition that induces disease outbreak due to heterogeneous susceptibility, using a simple mathematical model. Analysing a simple reinfection epidemic model, we show that (i) the heterogeneity of susceptibility, (ii) initial value of infected population size, which is not small, and (iii) reinfection, induce a new type of epidemic dynamic, called delayed outbreak [19].

The paper is organized as follows. In Section 2, we introduce a simple mathematical model, allowing reduction and enhancement of susceptibility. We discuss the threshold conditions for the initial growth of the infective population and the existence of the endemic equilibrium. In Section 3, we numerically plot streamlines of the vector field given by the model equations. The vector field suggests bistability of the disease-free equilibrium and the endemic equilibrium. In Section 4, we analyse the mathematical model. We study the transient behaviour and the asymptotic behaviour of the solution of the model. In Section 5, we classify the disease transmission dynamics in parameter planes. In Section 6, we introduce the model studied by Katriel [14] and discuss its relationship to the model studied in this paper. In Section 7, we summarize the disease transmission dynamics including a new classification of disease dynamics.
2. Epidemic model with reduction and enhancement in susceptibility

For a simple exposition, we assume that in the host population there are two different susceptible subpopulations with different degrees of susceptibility. We denote by $S_1(t)$ and $S_2(t)$ densities of the first and second susceptible populations at time $t$, respectively. Denote by $\sigma_1$ and $\sigma_2$ the susceptibility of individuals in the first and second susceptible subpopulations, respectively (\(0 < \sigma_1, \sigma_2 \leq 1\)). Denote by $I(t)$ the density of the infective population at time $t$. We consider the following mathematical model

\[
S_1'(t) = -\beta \sigma_1 S_1 I + \gamma \theta I, \\
S_2'(t) = -\beta \sigma_2 S_2 I + \gamma (1 - \theta) I, \\
I'(t) = \beta \sigma_1 S_1 I + \beta \sigma_2 S_2 I - \gamma I.
\]

Parameter $\beta$ is the transmission coefficient and $\gamma$ is the recovery rate. Infective individuals, upon recovery from an infection, obtain susceptibility $\sigma_1$ with probability $\theta \in [0, 1]$ and susceptibility $\sigma_2$ with probability $1 - \theta$.

Let us here mention special cases of the model (1). For the case that $\sigma_1 = \sigma_2$, susceptible individuals in $S_1$ and $S_2$ are equally susceptible to the disease. Such a model is called an SIS type model, see Chapter 10 in [4]. If we denote by $S(t)$ as the total susceptible population, i.e. $S(t) = S_1(t) + S_2(t)$, for the case that $\sigma_1 = \sigma_2 = 1$, from (1) we obtain the following equations

\[
S'(t) = -\beta SI + \gamma I, \\
I'(t) = \beta SI - \gamma I.
\]

For (2), it is well known (see e.g. Chapter 10 in [4]) that

- if $\frac{\beta}{\gamma} \leq 1$ then the disease-free equilibrium attracts all positive solutions and
- if $\frac{\beta}{\gamma} > 1$ then the endemic equilibrium ($\frac{\gamma}{\beta}, 1 - \frac{\gamma}{\beta}$) attracts all positive solutions.

Thus the parameter $\beta/\gamma$ can be seen as a threshold parameter, which determines the qualitative dynamics.

The mathematical model studied in [14] corresponds to the model (1) with $\theta = 0$. In [14], it is assumed that susceptibility is reduced, from $\sigma_1$ to $\sigma_2$, after recovery from infection, thus the possibility of enhancement of susceptibility is not taken into account.

Thus, in this paper, without loss of generality, we assume that

\[0 < \sigma_2 < \sigma_1 \leq 1\] (3)

and that $1 \geq \theta > 0$.

For the model (1), we consider the following initial condition

\[S_j(0) = S_{j0} \geq 0, \quad j \in \{1, 2\}, \quad I(0) = I_0 > 0\]
with $\sum_{j=1}^2 S_{j0} + I_0 = 1$. From (1) one can easily see that $\sum_{j=1}^2 S_j(t) + I(t) = 1$ holds for $t \geq 0$. Thus we analyse the model (1) in the following invariant set

$$
\left\{ (S_1, S_2, I) \in \mathbb{R}_+^3 : \sum_{j=1}^2 S_j + I = 1 \right\}.
$$

(4)

Define

$$
\mathcal{R}_0 := \frac{\beta}{\gamma} (\sigma_1 S_{10} + \sigma_2 S_{20}).
$$

(5)

We call $\mathcal{R}_0$ defined as in (5) the basic reproduction number. We show that $\mathcal{R}_0$ determines the initial growth of the infective population. We write $I'(0^+)$ for the right derivative of $I$ at $t = 0$. Since

$$
I'(0^+) = \gamma I(0) (\mathcal{R}_0 - 1)
$$

(6)

holds, one can immediately see that the following result holds.

**Lemma 1:** It holds that

$$
\mathcal{R}_0 > 1 \iff I'(0^+) > 0,
$$

$$
\mathcal{R}_0 = 1 \iff I'(0^+) = 0,
$$

$$
\mathcal{R}_0 < 1 \iff I'(0^+) < 0.
$$

Therefore, if $\mathcal{R}_0 > 1$ then $I(t)$ initially increases, while if $\mathcal{R}_0 < 1$ then $I(t)$ initially decreases.

We now show that the model (1) has an endemic equilibrium. Let us define

$$
R_1 = \frac{\beta \sigma_1}{\gamma}, \quad R_2 = \frac{\beta \sigma_2}{\gamma}.
$$

Then nonnegative equilibria of the susceptible populations $S_1$ and $S_2$ are respectively given as

$$
\bar{S}_1 = \frac{\theta}{R_1}, \quad \bar{S}_2 = \frac{1 - \theta}{R_2}.
$$

(7)

Denote by $\bar{I}$ the endemic equilibrium of the infective population $I$. We have the following result for the existence of the endemic equilibrium.

**Proposition 1:** It holds that

$$
\bar{I} = 1 - \frac{\theta}{R_1} - \frac{1 - \theta}{R_2}.
$$

(8)

$\bar{I} > 0$ if and only if

$$
\frac{\theta}{R_1} + \frac{1 - \theta}{R_2} < 1.
$$

(9)
Proof: In the invariant set given as in (4), the endemic equilibrium can be found by \( \bar{T} = 1 - \sum_{j=1}^{2} \bar{S}_j \). Thus we obtain (8) from (7). It is easy to see that the endemic equilibrium is positive if and only if (9) holds.

An important remark is that the condition (9) in Proposition 1 for the existence of the endemic equilibrium is irrespective of the condition for the initial growth of the infective population. The existence condition for the endemic equilibrium (9) can be expressed in terms of \( R_0 \) as

\[
R_0 > \left( \frac{\theta}{\sigma_1} + \frac{1 - \theta}{\sigma_2} \right) (\sigma_1 S_{10} + \sigma_2 S_{20})
\]

from (5) and the endemic equilibrium for the infective population is expressed as

\[
\bar{T} = 1 - \frac{1}{R_0} \left( \frac{\theta}{\sigma_1} + \frac{1 - \theta}{\sigma_2} \right) (\sigma_1 S_{10} + \sigma_2 S_{20}).
\]

In general, the quantity on the right hand side of (10) is not equal to 1. Thus, for the model (1), \( R_0 = 1 \) is not a threshold condition for the existence of the endemic equilibrium.

3. Phase plane analysis in \((S_1, I)\)

In this section, we visualize phase portraits of the system (1). In the invariant set (4), \( S_2 = 1 - S_1 - I \) follows, thus the system (1) can be reduced to a two dimensional system of ordinary differential equations. Let

\[
\begin{align*}
f_1(S_1, I) &= -\beta \sigma_1 S_1 I + \gamma \theta I, \\
f_2(S_1, I) &= \beta \sigma_1 S_1 I + \beta \sigma_2 (1 - S_1 - I) I - \gamma I.
\end{align*}
\]

From (1) we have

\[
\begin{align*}
S_1'(t) &= f_1(S_1, I), \\
I'(t) &= f_2(S_1, I).
\end{align*}
\]

It is easy to see that \( S_1 \)-nullcline and \( I \)-nullcline are respectively given as \( S_1 = \theta / R_1 = \bar{S}_1 \) and

\[
I = \left( 1 - \frac{1}{R_2} \right) + \left( \frac{R_1}{R_2} - 1 \right) S_1.
\]

From 3, we have that \( R_1 > R_2 \). Let us consider the case that the endemic equilibrium exists (i.e. there is a unique intersection of \( S_1 \)-nullcline and \( I \)-nullcline) in the set \( \{(S_1, I) \in \mathbb{R}_+^2 : S_1 + I \leq 1\} \). Figure 1 shows qualitatively different phase portraits of the model (11) for two cases: \( R_1 > R_2 > 1 \) and \( R_1 > 1 > R_2 \). Figure 1(a) suggests that the endemic equilibrium attracts all solutions. On the other hand, Figure 1(b) suggests that the state \( I = 0 \) attracts some solutions, if the initial value of \( S_1 \) and \( I \) are sufficiently small. The difference arises due to the position of the \( I \)-nullcline as the change of the parameter \( R_2 \).
Figure 1. Streamlines of the vector fields by the right hand side of (11) and nullclines in the set \( \{(S_1, I) \in \mathbb{R}^2_+ : S_1 + I \leq 1\} \) for the cases \( R_1 > R_2 > 1 \) (left) and \( R_1 > 1 > R_2 \) (right). The intersection of the nullclines denotes the endemic equilibrium. In (right) some solutions are attracted to the extinction state \( I = 0 \). (left) Phase portraits of (11) for \( R_1 > R_2 > 1 \) and (right) Phase portraits of (11) for \( R_1 > 1 > R_2 \).

4. Mathematical analysis of the model

In this section, we analyse the dynamical behaviour of the model (1) in the invariant set (4). For a special case where \( S_{j0} = \bar{S}_j \) for \( j = \{1, 2\} \), it is obvious that \( I(t) = \bar{I} \) for \( t \geq 0 \). If either \( S_{10} = \bar{S}_1 \) or \( S_{20} = \bar{S}_2 \) holds, then the condition (9) implies that \( \lim_{t \to \infty} I(t) = \bar{I} \). Otherwise, \( \lim_{t \to \infty} I(t) = 0 \). Since the proof is standard, it is omitted.

Consider the case where \( S_{j0} \neq \bar{S}_j \) for \( j = \{1, 2\} \). Let us define

\[
x_j(t) := \frac{S_j(t) - \bar{S}_j}{S_{j0} - \bar{S}_j}, \quad j \in \{1, 2\},
\]

where \( \bar{S}_j, j \in \{1, 2\} \) are defined as in (7). Then we obtain the following system of ordinary differential equations

\[
x_j'(t) = -\beta \sigma_j x_j(t) I(t), \quad j \in \{1, 2\}, \quad (13a)
\]

\[
I'(t) = \beta I(t) \sum_{j=1}^{2} \sigma_j a_j x_j(t), \quad (13b)
\]

where

\[
a_j := S_{j0} - \bar{S}_j, \quad j \in \{1, 2\}. \quad (14)
\]

From the definition (12), \( x_j(0) = 1 \) for \( j \in \{1, 2\} \).

First we show an important lemma that is used in Theorems 1 and 2 to determine the asymptotic behaviour of the solution.
Lemma 2: (1) If $\bar{I} \leq 0$ then
\[ \lim_{t \to \infty} I(t) = 0. \] (15)
(2) If $\bar{I} > 0$ then either (15) or
\[ \lim_{t \to \infty} I(t) = \bar{I}. \] (16)

Proof: Since $x_j$ is a positive and decreasing function, $\lim_{t \to \infty} x_j(t)$ exists for $j \in \{1, 2\}$. It is easy to see that $\lim_{t \to \infty} I(t)$ also exists. First let us show that $\lim_{t \to \infty} I(t) = 0$ or $\lim_{t \to \infty} I(t) = \bar{I}$. Suppose that $\lim_{t \to \infty} x_j(t) > 0$, $j \in \{1, 2\}$ and $\lim_{t \to \infty} I(t) > 0$. Then from (13a) we obtain a contradiction to the boundedness of the solution. Therefore, it holds that either $\lim_{t \to \infty} x_j(t) = 0$, $j \in \{1, 2\}$ or $\lim_{t \to \infty} I(t) = 0$. From (19b), if $\lim_{t \to \infty} x_j(t) = 0$, $j \in \{1, 2\}$ then one has $\lim_{t \to \infty} I(t) = \bar{I}$. Thus, we see that either $\lim_{t \to \infty} I(t) = 0$ or $\lim_{t \to \infty} I(t) = \bar{I}$ holds. Since $I(t)$ is a positive function, if $\bar{I} < 0$, then $\lim_{t \to \infty} I(t) = \bar{I} < 0$ does not follow. Therefore, we obtain the conclusion. 

We define
\[ \xi := \frac{\sigma_2}{\sigma_1} \in (0, 1). \] (17)
and note that, from (8) and (14),
\[ I_0 + \sum_{j=1}^{2} a_j = \bar{I} \] (18)
follows. We introduce conservative quantities for the model (13) which reduces the number of dimensions of the system (13).

Lemma 3: It holds that
\[ x_2(t) = x_1(t)^\xi, \] (19a)
\[ I(t) + \sum_{j=1}^{2} a_j x_j(t) = \bar{I} \] (19b)
for $t \geq 0$.

Proof: From (13a), we get
\[ \frac{dx_1}{dx_2} = \frac{x_1}{\xi x_2}. \]
Then it is easy to see that (19a) follows. Next we differentiate the left hand side of (19b). From (13), we obtain
\[ \frac{d}{dt} \left( I(t) + \sum_{j=1}^{2} a_j x_j(t) \right) = 0, \]
thus, using (18),
\[ I(t) + \sum_{j=1}^{2} a_j x_j(t) = I_0 + \sum_{j=1}^{2} a_j = \bar{I}. \]

From Lemma 3, the trajectory \( t \mapsto (x_1(t), I(t)) \) in the \((x_1, I)\) plane is given by a function \( \tilde{I} : [0,1] \to \mathbb{R} \) defined as
\[ \tilde{I}(x_1) := \bar{I} - a_1 x_1 - a_2 x_2(x_1) = \bar{I} - a_1 x_1 - a_2 x_1^\xi. \] (20)
It follows that \( \tilde{I}(x_1(t)) = I(t), \ t \in \mathbb{R} \). One also sees that
\[ \frac{d\tilde{I}}{dx_1} = -(a_1 + \xi a_2 x_1^\xi - 1), \] (21)
follows. From (18), (20) and (21), it is straightforward to obtain the following lemma, whose proof we thus omit.

**Lemma 4:** It holds that
\[ \tilde{I}(0) = \bar{I}, \tilde{I}(1) = I_0 \]
and
\[ \tilde{I}'(1) = -(a_1 + \xi a_2), \]
\[ \tilde{I}'(0^+) = \begin{cases} +\infty, & a_2 < 0, \\ -a_1, & a_2 = 0, \\ -\infty, & a_2 > 0. \end{cases} \]

In the following we consider the transient and asymptotic behaviour of the solution of system (13). One can observe that, from (21), if \( a_j \geq 0 \) for \( j \in \{1, 2\} \) or \( a_j \leq 0 \) for \( j \in \{1, 2\} \) then \( I(t) \) is monotone on \( t \in \mathbb{R}^+ \). If \( a_1 \) and \( a_2 \) have different signs, \( \tilde{I} \) may have an extremum and \( I(t) \) is not necessary monotone.

Let \( a_2 \neq 0 \). Then, from (21), one sees that \( \tilde{I} \) has a unique extremum at \( x_1 = x_1^\ast \), where
\[ x_1^\ast = \left( -\frac{a_1}{a_2 \xi} \right)^{\frac{1}{\xi-1}}. \] (22)
The following result is a condition for \( \tilde{I} \) to have a unique extremum on \((0, 1)\).

**Lemma 5:** It holds that \( 0 < x_1^\ast < 1 \) if and only if either
\[ a_1 + a_2 \xi > 0, \ a_1 > 0 > a_2 \] (23)
or
\[ a_1 + a_2 \xi < 0, \ a_1 < 0 < a_2. \] (24)
It holds that \( \tilde{I} \) attains a unique maximum at \( x_1 = x_1^\ast \) if (23) holds and that \( \tilde{I} \) attains a unique minimum at \( x_1 = x_1^\ast \) if (24) holds.
Proof: From elementary calculations, it is easy to see that $0 < x_1^* < 1$ holds if and only if either (23) or (24) holds. From (21) one can compute that

$$\frac{d^2 \tilde{I}}{dx_1^2} = (1 - \xi) \xi a_2 x_1^{\xi-2}. $$

Thus if $a_2 < 0$ then $\tilde{I}$ is convex upward and if $a_2 > 0$ then $\tilde{I}$ is convex downward. Therefore, we obtain the conclusion.

From a direct computation one has

$$a_1 + a_2 \xi = \frac{1}{R_1} (R_0 - 1).$$

(25)

Thus, from Lemma 1, we obtain the following equivalent conditions

$$a_1 + a_2 \xi > 0 \iff R_0 > 1 \iff I'(0^+) > 0, \quad (26)$$

$$a_1 + a_2 \xi = 0 \iff R_0 = 1 \iff I'(0^+) = 0, \quad (27)$$

$$a_1 + a_2 \xi < 0 \iff R_0 < 1 \iff I'(0^+) < 0. \quad (28)$$

We now obtain the transient behaviour of the solution of the system (13).

Proposition 2: For the system (13) the following statements follow.

(1) Assume that $a_j \geq 0$ for $j \in \{1, 2\}$, so that $a_1 + a_2 \xi \geq 0$. Then $I(t)$ is monotonically increasing.

(2) Assume that $a_j \leq 0$ for $j \in \{1, 2\}$, so that $a_1 + a_2 \xi \leq 0$. Then $I(t)$ is monotonically decreasing.

(3) Assume that $a_1 > 0 > a_2$,

(a) so that $a_1 + a_2 \xi > 0$. Then $I(t)$ has a unique maximum.

(b) so that $a_1 + a_2 \xi \leq 0$. Then $I(t)$ is monotonically decreasing.

Proof: (1, 2) Since $x_j$, $j \in \{1, 2\}$ are positive functions, from (13b), one sees that $I$ is a monotone function on $t \in \mathbb{R}_+$, if $a_j$, $j \in \{1, 2\}$ have the same signs. Then it is easy to see that $I$ is a monotone increasing function if $a_j \geq 0$ for $j \in \{1, 2\}$ and is a monotone decreasing function if $a_j \leq 0$ for $j \in \{1, 2\}$.

(3) Assume $a_1 > 0 > a_2$. One has $I'(0^+) > 0$ if and only if $a_1 + a_2 \xi > 0$ from (26). From Lemma 5, it holds that $\tilde{I}'(x_1) = 0$ at $x_1 = x_1^* \in (0, 1)$ and that $\tilde{I}$ has a unique maximum at $x_1 = x_1^*$. On the other hand, one has $I'(0^+) \leq 0$ if and only if if $a_1 + a_2 \xi \leq 0$ from (28) and (27). From Lemma 5, $\tilde{I}$ does not have an extremum on $(0, 1)$. Thus $I$ is monotonically decreasing on $t \in \mathbb{R}_+$.

We now determine the asymptotic behaviour of the solution of the system (13).

Theorem 1: For the system (13) the following statements follow.

(1) Assume that $a_j \geq 0$ for $j \in \{1, 2\}$, so that $a_1 + a_2 \xi \geq 0$. Then $\lim_{t \to \infty} I(t) = \tilde{I}$. 

(2) Assume that \( a_j \leq 0 \) for \( j \in \{1, 2\} \), so that \( a_1 + a_2 \xi \leq 0 \). Then \( \lim_{t \to \infty} I(t) = \bar{T} \) if \( \bar{T} > 0 \) and \( \lim_{t \to \infty} I(t) = 0 \) if \( \bar{T} \leq 0 \).

(3) Assume that \( a_1 > 0 > a_2 \). Then \( \lim_{t \to \infty} I(t) = \bar{T} \) if \( \bar{T} > 0 \) and \( \lim_{t \to \infty} I(t) = 0 \) if \( \bar{T} \leq 0 \).

**Proof:** By the phase plane analysis due to Proposition 2, we see that \( I(t) \) is either a monotone function or convex upward. From Lemma 2 one can easily see that \( \lim_{t \to \infty} I(t) = \bar{T} \) if \( \bar{T}(0) = \bar{T} > 0 \) and \( \lim_{t \to \infty} I(t) = 0 \) if \( \bar{T}(0) = \bar{T} \leq 0 \). We note that, from (18), one sees that if \( a_j \geq 0 \) then \( \bar{T} > 0 \) follows. 

Finally we consider the case that \( a_2 > 0 > a_1 \) holds. From Lemma 5, in the \((x_1, I)\) plane, \( \bar{T} \) has a unique minimum at \( x_1 = x_1^* \), i.e.

\[
\bar{T}(x_1) \geq \tilde{T}(x_1^*), \quad x_1 \in [0, 1]
\]

if \( a_1 + a_2 \xi \leq 0 \). We denote by \( I^* = \tilde{T}(x_1^*) \) the unique minimum. We obtain the transient dynamics of the solution of the model (13). Here we see that the epidemic curve can increase after attaining a local minimum point.

**Proposition 3:** Let us assume that \( a_2 > 0 > a_1 \). For the system (13) the following statements follow.

1. If \( a_1 + \xi a_2 \geq 0 \) then \( I(t) \) is monotonically increasing.
2. If \( a_1 + \xi a_2 < 0 \) then the following statements follow.
   a. Suppose that \( \bar{T} \leq 0 \) holds. Then \( I(t) \) is monotonically decreasing.
   b. Suppose that \( \bar{T} > 0 \) holds.
      i. If \( I^* \leq 0 \), then \( I(t) \) is monotonically decreasing.
      ii. If \( I^* > 0 \), then \( I(t) \) has a unique minimum.

**Proof:** (1) If \( a_1 + a_2 \xi \geq 0 \) then \( I'(0^+) > 0 \), from (26) and (27). From Lemma 5, \( \bar{T} \) does not have an extremum on \((0, 1)\). Thus \( I \) is monotonically increasing on \( t \in \mathbb{R}_+ \).

(2) If \( a_1 + a_2 \xi < 0 \) then \( I'(0^+) < 0 \), see (28). From Lemma 5, it holds that \( \bar{T}(x_1) = 0 \) at \( x_1 = x_1^* \in (0, 1) \) and that \( \bar{T} \) has a unique minimum at \( x_1 = x_1^* \). (a) Suppose that \( \bar{T} \leq 0 \). It then follows that \( I^* \leq \bar{T} \leq 0 \). Recall that \( I(t) \) is a positive function. Therefore, \( I(t) \) is monotonically decreasing on \( t \in \mathbb{R}_+ \). (b) Suppose that \( \bar{T} > 0 \). We consider the two cases where \( I^* \leq 0 \) and \( I^* > 0 \). If \( I^* \leq 0 \) then, similar to the proof of the statement (a), we see that \( I(t) \) is monotonically decreasing on \( t \in \mathbb{R}_+ \). If \( I^* > 0 \), then from the graph of the function \( \bar{T} \), one sees that \( I(t) \) has a unique minimum. 

For \( a_2 > 0 > a_1 \), we determine the asymptotic behaviour of the solution of the system (13).

**Theorem 2:** Let us assume that \( a_2 > 0 > a_1 \). For the system (13) the following statements follow.

1. If \( a_1 + \xi a_2 \geq 0 \) then \( \lim_{t \to \infty} I(t) = \bar{T} \).
2. If \( a_1 + \xi a_2 < 0 \) then the following statements follow.
(a) Suppose that \( I \leq 0 \) holds. Then \( \lim_{t \to \infty} I(t) = 0 \).
(b) Suppose that \( I > 0 \) holds.
   (i) If \( I^* \leq 0 \), then \( \lim_{t \to \infty} I(t) = 0 \).
   (ii) If \( I^* > 0 \), then \( \lim_{t \to \infty} I(t) = I \).

**Proof:** By the phase plane analysis with Proposition 3, one can easily obtain the conclusion. Assume that \( a_1 + \xi a_2 \geq 0 \). Then \( a_1 + a_2 > a_1 + \xi a_2 \geq 0 \). From (18), one sees that \( I > 0 \) follows. □

From the direct computation using (20),

\[
I^* = I - a_1 x_1^* - a_2 (x_1^*)^\xi = I_0 + a_1 (1 - x_1^*) + a_2 \left( 1 - (x_1^*)^\xi \right).
\]

One sees that

\[
a_1 x_1^* + a_2 (x_1^*)^\xi = a_1 \left( -\frac{a_1}{a_2^\xi} \right)^\frac{1}{\xi - 1} + a_2 \left( -\frac{a_1}{a_2^\xi} \right)^\frac{\xi}{\xi - 1}
\]

\[
= a_1 \left( -\frac{a_1}{a_2^\xi} \right)^\frac{1}{\xi - 1} \left( 1 - \frac{1}{\xi} \right)
\]

\[
> 0.
\]

Therefore, we get

\[
I^* = I_0 + a_1 + a_2 - a_1 \left( \frac{1}{\xi} \right) \left( -\frac{a_1}{a_2^\xi} \right)^\frac{1}{\xi - 1}.
\]

One can express \( I^* \) in terms of \( R_1 \) and \( R_2 \) as

\[
I^* = 1 - \frac{\theta}{R_1} - \frac{1 - \theta}{R_2} - \left( S_{10} - \frac{\theta}{R_1} \right) \left( 1 - \frac{R_1}{R_2} \right) \left( -\frac{R_1 S_{10} - \theta}{R_2 S_{20} - (1 - \theta)} \right)^\frac{R_1}{R_2 - R_1}.
\]

The formula shows that \( I^* \) depends on the initial condition.

### 5. Qualitative classification of disease transmission dynamics with reinfection

In Section 4, we analyzed the model (13) using the parameters \( a_1 \) and \( a_2 \). In this section, we classify the disease transmission dynamics in the \((a_1, a_2)\) parameter plane, treating \( a_1 \) and \( a_2 \) as free parameters in \(-1 \leq a_j \leq 1, j \in \{1, 2\}\). In Figure 2, we visualize parameter regions considered in Propositions 2 and 3. Then we show that Figure 3 shows qualitatively different types of disease transmission dynamics in the \((a_1, a_2)\) parameter plane. Since \( a_1 \) and \( a_2 \) are composite parameters defined as in (14), some parameter regions are not admissible in Figures 2 and 3. To understand the disease transmission dynamics in terms of the original parameters, we apply the parameter transformation (14) back to Figure 3 to obtain the classification in the \((R_1, R_2)\) parameter plane in Figure 4.
Figure 2. Parameter regions in Propositions 2 and 3 are visualized in (left) and (right), respectively. The shaded region in (right) depicts the parameter region such that $I^* > 0$ holds. (left) Parameter regions in Propositions 2 for $a_j \geq 0$, $a_j \leq 0$ ($j \in \{1, 2\}$) and $a_1 > 0 > a_2$ and (right) Parameter regions in Propositions 3 for $a_1 > 0 > a_2$.

Figure 3. Classification of disease transmission dynamics in $(a_1, a_2)$ parameter plane. The line $l_{R_0=1}$ (the threshold condition $R_0 = 1$) and the line $l_{EE}$, where $I = 0$ are plotted. Regions (i), (ii) and (iii) denote the endemic, epidemic and disease extinction parameter regions, respectively. In region (iv) the disease is endemic even if $R_0 \leq 1$ (delayed outbreak). (left) Initial condition $I_0 = 0.1$ and (right) initial condition $I_0 \downarrow 0$.

From direct computations (see (25) and (18)) we have

$$R_0 = 1 \iff a_1 + \xi a_2 = 0,$$

$$I = 0 \iff I_0 + a_1 + a_2 = 0.$$
Figure 4. Classification of disease transmission dynamics in \((R_1, R_2)\) parameter plane. The straight line with negative slope is \(l_{R_0=1}\) (the threshold condition \(R_0 = 1\)) and the rounded curve is \(l_{EE}\), where \(\bar{I} = 0\). Regions (i), (ii) and (iii) denote the endemic, epidemic and disease extinction parameter regions, respectively. In region iv) the disease is endemic even if \(R_0 < 1\). The parameter values are \(\theta = 0.7\), \(S_{10} = 0.5\), \(S_{20} = 0.491\) and \(I(0) = 0.009\).

Thus the condition \(R_0 = 1\) and the condition for the existence of the endemic equilibrium \(\bar{I} = 0\) are respectively expressed as the following two lines

\[
\begin{align*}
l_{R_0=1} : & a_1 + \xi a_2 = 0, \\
l_{EE} : & I_0 + a_1 + a_2 = 0
\end{align*}
\]

in the \((a_1, a_2)\) parameter plane, fixing \(\xi\) and \(I_0\).

In Figure 2, we plot the line \(l_{R_0=1}\) and \(l_{EE}\) in the \((a_1, a_2)\) parameter plane. It is shown that \(R_0 > 1\) holds in the region above the line, \(l_{R_0=1}\), and that the endemic equilibrium exists (i.e. \(I > 0\)) in the region above the line \(l_{EE}\). In Figure 2, we also indicate each parameter region considered in Proposition 2 and 3.

Applying Theorems 1 and 2, we can determine the asymptotic behaviour of the solution in each parameter region. In Theorem 1, it is shown that \(\lim_{t \to \infty} I(t) = \bar{I}\) in the region above the line \(l_{EE}\) and that \(\lim_{t \to \infty} I(t) = 0\) in the region below the line \(l_{EE}\) (for the case that \(a_j \geq 0\), \(a_j \leq 0\) \(j \in \{1, 2\}\) and \(a_1 > 0 > a_2\)). Theorem 2 classifies the parameter region \(a_1 > 0 > a_2\). In the region above the line \(l_{R_0=1}\), \(\lim_{t \to \infty} I(t) = \bar{I}\) follows (Theorem 2 (1)). In the region below the line \(l_{R_0=1}\), different asymptotic behaviours occur. It is shown that in the region below the line \(l_{EE}\), \(\lim_{t \to \infty} I(t) = 0\) follows (Theorem 2 (2)(a)). The region enclosed by the lines \(l_{R_0=1}\) and \(l_{EE}\) is separated into two regions, according to the sign of \(I^*\). In particular, the shaded region in Figure 2(a) denotes the region where \(I^* > 0\). From Theorem 2 (2)(b), in the shaded region \(\lim_{t \to \infty} I(t) = \bar{I}\) follows while, in the region, corresponding to the case of Proposition 3 (2)(b)(i), \(\lim_{t \to \infty} I(t) = 0\) follows.
Summarizing these results, we can classify the parameter region into four regions; region (i), (ii), (iii) and (iv) as shown in Figure 3(a).

The parameter region (i), corresponding to the endemic case, consists of the following two parts

\[ \text{region (ia)} = \{ (a_1, a_2) : a_1 + \xi a_2 > 0, \ a_2 \geq 0 \} , \]
\[ \text{region (ib)} = \{ (a_1, a_2) : I = I_0 + a_1 + a_2 > 0, \ a_2 < 0 \} . \]

In the region (i) \( \lim_{t \to \infty} I(t) = \bar{I} \) follows. One sees that \( I(t) \) monotonically increases in the region (ia) and that \( I(t) \) has a peak in the region (ib).

The parameter region (ii), corresponding to the epidemic case, is defined as follows.

\[ \text{region (ii)} = \{ (a_1, a_2) : a_1 + \xi a_2 > 0, \ I = I_0 + a_1 + a_2 \leq 0 \} . \]

It is shown that \( I(t) \) has a unique peak and \( \lim_{t \to \infty} I(t) = 0 \). Here \( R_0 > 1 \) holds and no endemic equilibrium exists.

The disease is extinct if the model parameter values are in the region (iii). The region (iii) consists of the following two parts

\[ \text{region (iii)} = \{ (a_1, a_2) : a_1 + \xi a_2 \leq 0, \ I = I_0 + a_1 + a_2 \leq 0 \} , \]
\[ \text{region (iiib)} = \begin{cases} (a_1, a_2) : a_1 + \xi a_2 \leq 0, \\ I = I_0 + a_1 + a_2 > 0, \\ I^* \leq 0 \end{cases} . \]

In the region (iii) \( I \) monotonically decreases and \( \lim_{t \to \infty} I(t) = 0 \) follows. We note that in the region (iiib) the endemic equilibrium exists and \( R_0 \leq 1 \) holds. Since \( I^* \leq 0 \) holds in the region (iii), the disease is extinct, according to Theorem 2.

We find that in region (iv) disease outbreak occurs. Here \( I(t) \) has a unique minimum and that \( I \) eventually tends to the endemic equilibrium. Thus outbreak occurs with a certain time delay. We note that in the region (iv) the endemic equilibrium exists and \( R_0 \leq 1 \) holds. The region (iv) is given as

\[ \text{region (iv)} = \begin{cases} a_1 < 0 < a_2, \\ (a_1, a_2) : a_1 + \xi a_2 \leq 0, \\ I^* > 0 \end{cases} . \]

The condition \( a_1 < 0 < a_2 \) is equivalent to

\[ S_{10} < \bar{S}_1 \land S_{20} > \bar{S}_2 . \]

Since \( S_1 \) increases while \( S_2 \) decreases, the effective reproduction number

\[ R(t) = \frac{\beta}{\gamma} (\sigma_1 S_1(t) + \sigma_2 S_2(t)) \]

may nonmonotonically vary with respect to time \( t \) and indeed it exceeds one with time delay in region (iv). It is suggested that the increase of susceptibility due to the reallocation
Figure 5. Numerical illustrations of epidemic curve using the parameter sets located in the region (i) (panel (a)), (ii) (panel (b)), (iii) (panel (c)) and (iv) (panel (d)), respectively. The parameter values are $\beta = 2.0$, $\theta = 0.7$, $\gamma = 1.0/1.5$, $\sigma_1 = 0.4$ for panel (A), $0.6333$ for panel (b), $0.2667$ for panel (c), $0.4$ for panel (d), $\sigma_2 = 0.3333$ for panel (a), $0.1333$ for panel (b), $0.25$ for panels (c) and (d). The values of $R_1$ and $R_2$ are $1.2$ and $1.0$ for panel (a), $1.9$ and $0.4$ for panel (b), $0.8$ and $0.75$ for panel (a), $1.2$ and $0.75$ for panel (d). Initial conditions are $I(0) = 0.009$, $S_1(0) = 0.5$ and $S_2(0) = 0.491$.

Figure 6. Delayed outbreak disappears if $I_0$ is small, although the values of $R_1 = 1.2$ and $R_2 = 0.75$ are in the region (iv) when $I_0 = 0.009$ (see Figure 4). The parameter values are the same as Figure 5(d) except the initial conditions, $\beta = 2.0$, $\sigma_1 = 0.4$, $\sigma_2 = 0.25$, $\theta = 0.7$, $\gamma = 1.0/1.5$, $S_1(0) = 0.5$, $S_2(0) = 0.49999$ and $I_0 = 0.00001$.

...of susceptibility by reinfection may trigger disease outbreak. $I^* > 0$ is a condition such that a unique minimum point of $I(t)$ is positive. The region (iv) exists in the parameter plane for a positive $I_0 > 0$ and disappears in the limiting case $I_0 \downarrow 0$ (see Figures 3(b) and 6).
From (14) we have
\[ a_1 = S_{10} - \frac{\theta}{R_1}, \]
\[ a_2 = S_{20} - \frac{1 - \theta}{R_2}. \]

Fixing \( \theta, S_{10} \) and \( S_{20} \) we can obtain the classification of the disease transmission dynamics in the \((R_1, R_2)\) parameter plane, see Figure 4. Here we assume that \( R_1 > R_2 \) from (3). We plot the corresponding regions in the \((R_1, R_2)\) plane in Figure 4.

6. No enhancement of susceptibility

Here we discuss the relationship of disease transmission dynamics generated by our model (1) and the model studied in [14]. In [14] the author analyses the reinfection epidemic model, which is (1) with \( \theta = 0 \). In this case, no enhancement of susceptibility is assumed. It is shown that the epidemic dynamics qualitatively change from epidemic case to endemic case as the basic reproduction number crosses the so called reinfection threshold.

Let us set \( \sigma_1 = 1 \) and \( \sigma_2 = \sigma < 1 \) in (1) for comparison. The author in [14] studies the following system of ordinary differential equations.

\[
\begin{align*}
\dot{S}_1(t) &= -\beta S_1 I, \\
\dot{S}_2(t) &= -\beta \sigma S_2 I + \gamma I, \\
\dot{I}(t) &= \beta S_1 I + \beta \sigma S_2 I - \gamma I.
\end{align*}
\]

Here we regard the \( R \)-compartment in the model in [14] as the second susceptible population. The disease transmission dynamics of (31) is classified in terms of

\[
R_0 = \frac{\beta}{\gamma} (S_{10} + \sigma S_{20})
\]

and

\[
R_1 = \frac{\beta}{\gamma}.
\]

We have the following theorem from [14].

**Theorem 3:** For the model (31) the following statements hold.

1. Let \( R_1 > \frac{1}{\sigma} \). Then

\[
\lim_{t \to \infty} (S_1(t), S_2(t), I(t)) = \left( 0, \frac{1}{R_1 \sigma}, 1 - \frac{1}{R_1 \sigma} \right).
\]

2. Let \( R_1 \leq 1/\sigma \) holds. Then \( \lim_{t \to \infty} I(t) = 0 \) and,
(a) If \( R_0 > 1 \), then \( I(t) \) has a unique maximum at \( t = t^* \in \mathbb{R}_+ \) and \( I \) increases for \( 0 \leq t \leq t^* \) and decreases for \( t > t^* \).

(b) If \( R_0 \leq 1 \), then \( I(t) \) monotonically decreases on \( t \in \mathbb{R}_+ \).

In the limiting case that \( I_0 \downarrow 0 \) and \( S_{02} \downarrow 0 \) (thus \( S_{01} \uparrow 1 \)),

\[
\lim_{S_{01} \uparrow 1, \ S_{02} \downarrow 0} R_0 = R_1 = \frac{\beta}{\gamma}.
\]

Let us vary \( R_1 \) as a bifurcation parameter. From Lemma 1, \( R_1 \leq 1 \) implies that the disease is extinct, while \( R_1 > 1 \) implies that the infective population initially increases. Theorem 3 suggests that, in the model (31), the SIR-like threshold type behaviour occurs if \( R_1 < 1/\sigma \).

If \( R_1 \leq 1 \) then the disease is extinct and if \( 1 < R_1 < 1/\sigma \) then the disease is epidemic. When \( R_1 \) exceeds the threshold \( 1/\sigma \) then the disease becomes endemic from epidemic, thus qualitative change of the disease transmission dynamics occurs. The threshold \( 1/\sigma \) is called the reinfection threshold \([7,13,14]\).

For the case \( \theta = 0 \), from (7) one sees that \( S_1 = 0 \) i.e. there is no positive equilibrium for \( S_1 \). Therefore, one always has \( a_1 \geq 0 \). Let us focus on the parameter region \( \{(a_1, a_2) : a_1 \geq 0\} \) that consists of the three regions (i), (ii) and (iii) (see Figure 2(a) (A)). As shown in the previous section, the endemic case occurs when the endemic equilibrium exists (the region (i)). The line \( a_1 + \xi a_2 = 0 \) separates the region, where no endemic equilibrium exists, into two parts: epidemic and extinction cases. In particular, from Figure 2(a), one clearly sees that region (iv) disappears for this special case. In other words, enhancement of susceptibility (\( \theta > 0 \)) is responsible for the existence of the region (iv), where a delayed outbreak occurs.

### 7. Discussion

In this paper, we formulate transmission dynamics taking into account varying levels of immune protection due to reinfection. Our model includes the standard epidemic SIR and SIS models. Indeed, our model captures both epidemic and endemic cases, which are the common classifications for epidemiological dynamics of the SIR and SIS models. Introducing heterogeneity of susceptibility, we find that the model exhibits a delayed outbreak that does not fall into the common classification of disease dynamics. We show that it is possible that the epidemic curve initially decreases, but eventually increases and tends to an endemic equilibrium. In the standard SIR and SIS epidemic models, the initial condition does not qualitatively change the disease transmission dynamics, except that the basic reproduction number crosses 1. In the model (1), the initial condition of the infected population size is an important factor to induce a delayed outbreak. Our analysis reveals that (i) the heterogeneity of susceptibility, (ii) initial value of infected population size, which is not small, and (iii) reinfection induced delayed outbreak.

From Figures 3 and 4, one sees that there is a parameter region where the endemic equilibrium exists and the basic reproduction number is less than 1. The phenomenon is similar to some epidemic models that exhibit backward bifurcation of the endemic equilibrium ([3,6,10]). It is shown that unstable and stable endemic equilibria can coexist, when the basic reproduction number is less than 1 in the models studied in [3,6,10]. The structure of the endemic equilibrium induces bistability of the disease-free equilibrium and the
endemic equilibrium. Although, the endemic equilibrium is unique in the model (1), we find a similar bistable behaviour in Theorem 2 (2)(b). Note that $I^*$ depends on the initial condition (see (30)). Solutions with initial conditions such that $I^* > 0$ tend to the endemic equilibrium, while solutions with initial conditions such that $I^* \leq 0$ tend to a disease-free equilibrium, see also Figures 5(d) and 6. The vector fields in Figure 1(b) clearly show the bistable behaviour. Taking into account the demographic process in the model (1), we expect that backward bifurcation of the endemic equilibrium occurs. Mathematical analysis of the model with demographic process is left for our future work.

Disease transmission dynamics of the standard SIS and SIR models are equivalent to special cases of our model. If we set $\sigma_1 = \sigma_2$ in the model (1), susceptible individuals are equally susceptible and the model (1) is equivalent to the standard SIS epidemic model (2). If $\sigma_1 = \sigma_2$ then $\xi = 1$ follows. From (21), one sees that $I$ does not have an extremum and is monotone. Thus the delayed outbreak does not occur in the homogeneous setting. Moreover, in the $(a_1, a_2)$ parameter plane, the lines $a_1 + a_2 \xi = a_1 + a_2 = 0$ and $I_0 + a_1 + a_2 = 0$ are parallel. Therefore, region (iii) disappears and the epidemic case also does not occur in this setting. Regarding the SIR model, the dynamics with the parameter region below the line $I_0 + a_1 + a_2 = 0$ is equivalent with the dynamics described by the standard SIR model (without demography) which does not admit the endemic equilibrium. Indeed our model also has the threshold property with respect to the basic reproduction number. The boundary between epidemic case and extinction case in our model is $R_0 = 1$ as in the standard SIR model.

To understand what kinds of factors induce a delayed outbreak, this paper analyses a simple model with an assumption, the susceptibility posterior to an infection is independent with the immune status prior to infection. However, the complex dependencies between susceptibilities prior and posterior to an infection have been observed, e.g. the increase of immune protection level by re-vaccination and the increase of susceptibility by reinfection (antibody dependent enhancement). A model which takes into account the dependency between susceptibilities prior and posterior infection is required to understand delayed outbreak under complex conditions.

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