THE SPATIALLY HETEROGENEOUS DIFFUSIVE RABIES MODEL AND ITS SHADOW SYSTEM

YUXIN ZHANG
College of Mathematical Sciences
Harbin Engineering University
Harbin, Heilongjiang 150001, China

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ABSTRACT. In this paper, we consider a class of spatially heterogeneous reaction diffusion rabies model which was used to describe population dynamics of the rabies epidemic disease observed in Europe. The dynamics of both the original non-degenerate reaction-diffusion system and its corresponding shadow system are investigated in great details. Firstly, we prove that under certain conditions, the in-time solutions of both the original non-degenerate reaction-diffusion system and its shadow system exist globally and remain uniformly bounded. Secondly, we are capable of showing that the shadow system is the nice approximations for the original non-degenerate reaction-diffusion system when the diffusion rate $d_R$ of the infectious rabid individuals (R) is sufficiently large. This implies that the dynamics of the shadow system can say as much as possible about the dynamics of the original system when $d_R$ is sufficiently large. Finally, we characterize the basic reproduction number for the shadow system, and study the stability/instability of the disease-free steady state.

1. Introduction. Rabies is a zoonotic disease which is transmitted from animals to humans and caused by the rabies virus of the Lyssavirus genus, within the family Rhabdoviridae. The virus is transmitted in the saliva of rabid animals and generally enters the body via infiltration of virus-laden saliva from a rabid animal into a wound (e.g. scratches), or by direct exposure of mucosal surfaces to saliva from an infected animal (e.g. bites). Both animal and human rabies can be totally prevented through vaccination and postexposure immunization. However, according to [13], approximately 59,000 people die of rabies each year, mainly in rural areas of Asia and Africa, where domestic and stray dogs are playing an important role in contributing to human infection. Fooks et al. [11] indicated that, in the 21st century, rabies is still one of the most feared of all the infectious diseases and a serious threat to public health. Subsequently, a better understanding of the spatial spread of the rabies diseases is necessary if we are to find reliable methods to control the spread of the disease.

Mathematical modeling of rabies plays a crucial role toward designing effective strategies to prevent and control the disease. To describe the population dynamics of
the rabies among fox observed in Europe, Anderson et al. [4] pioneered a deterministic, compartmental model consisting of susceptible, infected but noninfectious, and infectious rabid individuals. Following [4], Murray et al. [27] considered a partially degenerate reaction-diffusion model by introducing the effect of spatial dispersal of rabid foxes. For this epidemic model, Murray et al. showed that the partially degenerate system may have a traveling wave, which consists of the rabies front, in which the largest number of foxes die from the disease; Wang and Zhao [38] characterized the basic reproduction number \( R_0 \) in terms of the principle eigenvalue of an elliptic problem, and discussed the influence of spatial heterogeneity and population mobility on disease transmission. Besides, the fox rabies has motivated quite a few research articles, see, for example, [3, 33, 42].

In reality, it has been found that a certain proportion of foxes recover from rabies and develop immunity to the epidemic. Based on this fact, Murray and Seward [26] introduced an immune class into the model of [27]. In this paper, we are concerned with the extended rabies model in which fox population is divided into four classes. The diffusive rabies model of our concerns takes in the form of

\[
\begin{align*}
\frac{\partial S}{\partial t} &= d_S \Delta S + (a - b) \left(1 - \frac{N}{K}\right) S + a^* Z - \beta RS, \quad \text{in } \Omega \times (0, T), \\
\frac{\partial I}{\partial t} &= d_I \Delta I + \beta RS - \sigma I - \left[b + (a - b) \frac{N}{K}\right] I, \quad \text{in } \Omega \times (0, T), \\
\frac{\partial R}{\partial t} &= d_R \Delta R + \sigma I - \alpha R - \mu R - \left[b + (a - b) \frac{N}{K}\right] R, \quad \text{in } \Omega \times (0, T), \\
\frac{\partial Z}{\partial t} &= d_Z \Delta Z + \mu R + (a - a^*) Z - \left[b + (a - b) \frac{N}{K}\right] Z, \quad \text{in } \Omega \times (0, T), \\
\partial_\nu S &= \partial_\nu I = \partial_\nu R = \partial_\nu Z = 0, \quad \text{on } \partial \Omega \times (0, T), \\
(S, I, R, Z)(x, 0) &= (S_0, I_0, R_0, Z_0)(x), \quad \text{in } \Omega,
\end{align*}
\]

where \( \Omega \) is an open bounded domain in \( \mathbb{R}^n \), \( 1 \leq n \leq 3 \), with smooth boundary \( \partial \Omega \) and its unit outer normal \( \nu \). Here \( S \) is the density of susceptible foxes, \( I \) is the density of infected but noninfectious foxes, \( R \) is the density of rabid foxes, \( Z \) is the density of immune foxes, \( N = S + I + R + Z \) is the total fox population, and \( d_S, d_I, d_R, d_Z \) are positive constants representing diffusion coefficients. \( \{0, T\} \) is the maximal interval for existence, with \( T \leq \infty \). The parameters \( a, a^*, b, K, \sigma, \alpha, \mu \) are positive constants, \( a, a^* \) are the birth rates, \( b \) is the intrinsic death rate, \( K \) is the environmental carrying capacity, \( \sigma \) is the per capita rate of infected foxes turning into infectious, \( \alpha \) is the case fatality rate of rabid foxes, \( \mu \) is the per capita rate of rabid foxes recovering to develop immunity. It is natural to assume that \( a > b \) and \( 0 \leq a^* < a \). In particular, if immune foxes are assumed to have only susceptible progeny then \( a^* = a \), if immune foxes are assumed to have only immune progeny then \( a^* = 0 \). The disease transmission coefficient \( \beta \) is dependent of the spatial variable \( x \), furthermore, \( \beta(x) \) is assumed to be strictly positive and twice continuously differentiable on \( \overline{\Omega} \). The initial value functions \( S_0(x) \geq 0 (\neq 0), I_0(x) \geq 0 (\neq 0), R_0(x) \geq 0 (\neq 0), Z_0(x) \geq 0 (\neq 0) \) are assumed to be continuous on \( \overline{\Omega} \), and satisfy the compatibility conditions on the boundary, say, \( \partial_\nu S_0 = \partial_\nu I_0 = \partial_\nu R_0 = \partial_\nu Z_0 = 0 \).

In the existing literatures, a common assumption is that \( d_S = d_I = d_Z = 0 \) and \( d_R > 0 \), since it was argued in [26, 27] that, compared with the susceptible individuals, the infected but non-infectious individuals and the immune individuals, the rabid individuals are more likely to wander randomly due to the particular characteristics of the rabies disease. Then, the random wandering of \( S, I \) and \( Z \)
were neglected. However, in reality, all the individuals should have their random wandering. Therefore, it is reasonable to assume that all the diffusion coefficients are positive, although in practice \(d_R\) is sufficiently large. For the special case when \(d_R\) is sufficiently large, one method to study the dynamics of the system is to consider its shadow system, a limiting system of system (1) as \(d_R \to \infty\) (see, e.g., [19, 24, 28]). If, under certain conditions, the shadow system is a nice approximation to the original system, then we can use the shadow system to say as much as possible about the dynamics of the original system. Sending \(d_R \to \infty\) in (1), and noticing that \(S, I, R, Z\) are all uniformly bounded with respect to \(d_R\) (This will be proved in Theorem 1.1), we formally have \(R(x,t) \to \xi(t)\), for some smooth function \(\xi(t)\).

Integrating the \(R\)-equation of (1) with respect to \(x\) over \(\Omega\), and dividing by \(|\Omega|\), the measure of \(\Omega\), then in the limit of \(d_R \to \infty\), we obtain the following shadow system of system (1):

\[
\begin{align*}
\frac{\partial S}{\partial t} &= d_S \Delta S + r \left( 1 - \frac{S + I + \xi + Z}{K} \right) S + a^* Z - \beta \xi S, \quad \text{in } \Omega \times (0, T), \\
\frac{\partial I}{\partial t} &= d_I \Delta I + \beta \xi S - \sigma I - \left[ b + \frac{r(S + I + \xi + Z)}{K} \right] I, \quad \text{in } \Omega \times (0, T), \\
\frac{\partial \xi}{\partial t} &= \frac{\sigma}{|\Omega|} \int_{\Omega} I dx - (a + b + \mu) \xi - \frac{r \xi}{K|\Omega|} \int_{\Omega} (S + I + \xi + Z) dx, \quad \text{in } (0, T), \\
\frac{\partial Z}{\partial t} &= d_Z \Delta Z + \mu \xi + (a - a^*) Z - \left[ b + \frac{r(S + I + \xi + Z)}{K} \right] Z, \quad \text{in } \Omega \times (0, T), \\
\frac{\partial}{\partial \nu} S &= \frac{\partial}{\partial \nu} I = \frac{\partial}{\partial \nu} Z = 0, \quad \text{on } \partial \Omega \times (0, T), \\
S(x, 0) &= S_0(x), \quad I(x, 0) = I_0(x), \quad \xi(0) = \xi_0, \quad Z(x, 0) = Z_0(x) \quad \text{in } \Omega,
\end{align*}
\]

where \(r := a - b, \quad \overline{R}_0 = \int_{\Omega} R_0(x) dx / |\Omega|, \quad [0, T)\) is the maximal interval for existence, with \(T \leq \infty\).

The concept of the "shadow system" was first proposed by Keener [17] in 1978. Since then, it has been extensively studied, and most of the research focuses on the existence of non-constant steady states (see, e.g., [14, 15, 22, 23, 24, 28, 29, 32, 40]), the stability and the instability of the non-constant positive steady states (see, e.g., [10, 22, 24, 28, 29, 31, 40]), the Hopf bifurcations (see, e.g., [28, 39]), the compact attractors and the existence of monotone solutions (see, e.g., [12, 18]), the global existence and boundedness, finite time blow-ups of the in-time solutions (see, e.g., [9, 19, 21]), the spectra of the linear diffusion operators related to the shadow system (see, e.g., [20]), and the dynamics of the stochastic shadow system (see, e.g., [41]).

By investigating the global existence and finite time blow-up of the in-time solutions, Li and Ni [21] observed there may be wide discrepancies between dynamics of the original reaction-diffusion systems and that of their shadow systems. Motivated by this result, we shall consider the global existence of the in-time solutions of (1) and (2) so as to compare the dynamics of the original reaction-diffusion system with that of its shadow system. To that end, we assume that \(a, a^*, b, K, \beta, \sigma, \alpha, \mu\) are all spatially dependent. Furthermore, we impose the following assumption:

\[\text{(A1) } a(x), a^*(x), b(x), K(x), \beta(x), \sigma(x), \alpha(x), \mu(x) \text{ are strictly positive, twice continuously differentiable on } \overline{\Omega}.\]

For the sake of stating the following results, we introduce some notations. Denote by \(\|u\|_p := (\int_{\Omega} |u|^p dx)^{1/p}\) the norm of \(L^p(\Omega)\) with \(1 \leq p < \infty\), by \(\|u\|_\infty := \text{ess sup}_{x \in \Omega} |u(x)|\) the norm of \(L^\infty(\Omega)\) (the supremum norm when \(u \in C(\overline{\Omega}, \mathbf{R})\)).
For $\gamma = (\gamma_1, \ldots, \gamma_n)$, $|\gamma| = \gamma_1 + \cdots + \gamma_n$ and $x = (x_1, \ldots, x_n)$, define $D^\gamma u := \partial^{|\gamma|}u/\partial x_1^{\gamma_1}\cdots\partial x_n^{\gamma_n}$. Then, denote by $W^k_p(\Omega)$ the space of any function $u(x)$, such that $D^\gamma u \in L^p(\Omega)$ for $|\gamma| \leq k$.

The global well-posedness result of (1) is stated as follows.

**Theorem 1.1.** Let $(A_1)$ hold and $1 \leq n \leq 3$. Suppose that $S_0, I_0, R_0, Z_0 \in W^2_2(\Omega) \cap C(\Omega, R)$, and that

1. for $x \in \Omega$, $S_0(x) \geq 0(\neq 0)$, $I_0(x) \geq 0(\neq 0)$, $R_0(x) \geq 0(\neq 0)$, $Z_0(x) \geq 0(\neq 0)$;
2. for $x \in \partial \Omega$, $(\partial_\nu S_0(x), \partial_\nu I_0(x), \partial_\nu R_0(x), \partial_\nu Z_0(x)) = (0, 0, 0, 0)$.

Then, system (1) has a unique nonnegative global solution $(S, I, R, Z)(x, t)$ such that

$$0 \leq S(x, t) \leq c_1, \quad 0 \leq I(x, t) \leq c_4, \quad 0 \leq R(x, t) \leq c_2, \quad 0 \leq Z(x, t) \leq c_3$$

(3) for $(x, t) \in \Omega \times [0, \infty)$, where $c_1, c_2, c_3$ and $c_4$ are positive constants independent of $d_R$.

While for the shadow system, we are capable of establishing global existence and boundedness of nonnegative smooth solutions. Our result reads as follows.

**Theorem 1.2.** Let $(S^\infty(x, t), I^\infty(x, t), \xi(t), Z^\infty(x, t))$ be the nonnegative smooth solution of (2) defined on $\Omega \times [0, T)$. Suppose that $(A_1)$ holds and $1 \leq n \leq 3$. Then,

$$0 \leq S^\infty(x, t) \leq c_1, \quad 0 \leq I^\infty(x, t) \leq c_4, \quad 0 \leq \xi(t) \leq c_2, \quad 0 \leq Z(x, t) \leq c_3$$

(4) for $(x, t) \in \Omega \times [0, T)$, where $c_1, c_2, c_3$ and $c_4$ are defined as in Theorem 1.1. Furthermore, $T = \infty$.

Further, we shall use the idea of [19] to show that $(S^\infty, I^\infty, \xi, Z^\infty)$ will be a nice approximation to $(S, I, R, Z)$ when $d_R$ is sufficiently large, where $(S, I, R, Z)$ and $(S^\infty, I^\infty, \xi, Z^\infty)$ are the nonnegative smooth solutions of the original non-degenerate reaction-diffusion system and the shadow system respectively. When $a, a^*, b, K, \sigma, \alpha, \mu$ are positive constants, and $\beta(x)$ is strictly positive and twice continuously differentiable on $\Omega$, the result is stated as follows.

**Theorem 1.3.** Let $(S, I, R, Z)(x, t)$ and $(S^\infty(x, t), I^\infty(x, t), \xi(t), Z^\infty(x, t))$ be the nonnegative global smooth solution of (1) and (2), respectively. Suppose that $d_S \geq 2r/\lambda_1$, $d_R \geq r/\lambda_1$ and $d_Z \geq 2r/\lambda_1$, where $\lambda_1$ is the smallest positive eigenvalue of $-\Delta$ in $\Omega$ subject to the homogeneous Neumann boundary condition. Then, for any fixed $T > 0$, there exists a positive constant $\tilde{C}(T)$ independent of $d_R$, such that for any $t \in [T(d_R), T]$,

$$\|S - S^\infty(t)\|_\infty + \|(I - I^\infty)(t)\|_\infty + \|(R - \xi)(t)\|_\infty + \|(Z - Z^\infty)(t)\|_\infty \leq \frac{\tilde{C}(T)}{\sqrt{d_R}}$$

(5)

where

$$T(d_R) := \max \left\{ \log(d_R\|\nabla R_0\|_2^2)/(2\lambda_1 d_R), 0 \right\}, \quad n = 1,$$

$$\max \left\{ \log(d_R\|\Delta R_0\|_2^2)/(\lambda_1 d_R), 0 \right\}, \quad n = 2, 3.$$
Lemma 2.1. We just need to establish a priori estimate for the nonnegative solution.

2. The global existence of (1) and (2). In this section, we shall consider the global existence and boundedness of the nonnegative in-time solutions of system (1) and (2). The existence and uniqueness of a nonnegative local solution to (1) can be obtained by employing Lemma A.1 (in Appendix). To show the global existence, we just need to establish a priori estimate for the nonnegative solution.

**Lemma 2.2.** Suppose that (A1) holds. Let \((S(x,t), I(x,t), R(x,t), Z(x,t))\) be the nonnegative classical solution of (1) defined on \(\Omega \times [0, T)\). Then, there exist positive constants \(c_1, c_2, c_3, c_4\), such that

\[
0 \leq S(x,t) \leq c_1, \quad 0 \leq R(x,t) \leq c_2, \quad 0 \leq Z(x,t) \leq c_3
\]

for \((x, t) \in \Omega \times [0, T)\).

**Proof.** For any given \(0 < T' < T\), in view of the definition of the classical solutions (Lemma A.1 in Appendix), we have \(S, I, R, Z \in C(\mathcal{Q}_T) \times C^2_1(Q_T)\). Here \(C^2_1(Q_T)\) denotes the space of any function \(u(x,t)\), such that \(D_1^2 D_2^k u \in C(Q_T)\) for \(|\gamma| + 2k \leq 2\), where \(Q_T := \Omega \times [0, T]\), for \(T' \in (0, \infty)\). Since \(S, I, R\) and \(Z\) are nonnegative for any \(x, t \in \Omega \times [0, T']\), by virtue of the upper-lower solution method, we obtain

\[
0 \leq S(x,t) \leq c_1 := \max \left\{ \|S_0\|_{L^\infty(\Omega)}, \sup_{x \in \Omega} K(x), \sup_{x \in \Omega} \left\{ a^*(x)K(x)/r(x) \right\} \right\},
\]

\[
0 \leq R(x,t) \leq c_2 := \max \left\{ \|R_0\|_{L^\infty(\Omega)}, \sup_{x \in \Omega} \left\{ \sigma(x)K(x)/r(x) \right\} \right\},
\]

\[
0 \leq Z(x,t) \leq c_3 := \max \left\{ \|Z_0\|_{L^\infty(\Omega)}, \sup_{x \in \Omega} \left\{ \mu(x)K(x)/r(x) \right\}, \sup_{x \in \Omega} K(x) \right\}
\]

for \((x, t) \in \Omega \times [0, T')\). Since \(c_1, c_2, c_3\) are independent of \(T'\), the assertion follows by the arbitrariness of \(T'\).

In order to establish an \(L^\infty\) priori estimate for \(I\), we shall employ the Sobolev embedding theorem \(W^1_p(\Omega) \to L^\infty(\Omega)\) for \(p > n\). Then, it remains to estimate the \(L^p\) norm of \(I\) and \(\nabla I\) for some \(p > n\).

**Lemma 2.2.** Suppose that (A1) holds and \(p > 2\). Let \((S, I, R, Z)(x,t)\) be the nonnegative solution of (1) defined on \(\Omega \times [0, T)\). Furthermore, suppose that \(S(., t), I(., t), R(., t), Z(., t) \in W^2_p(\Omega)\) for any \(t \in [0, T)\). Then, there exists a positive constant \(C(p, d_1)\), such that

\[
\|I(., t)\|_p \leq C(p, d_1)
\]

for any \(0 \leq t < T\).

**Proof.** Let us multiply both sides of the \(I\)-equation in (1) by \(pI^{p-1}\) and integrate with respect to \(x\) over \(\Omega\). Setting \(V := I^{p/2}\), by \(r = a - b\), we have

\[
\frac{d}{dt}(\|V\|_2^2) + p \int_{\Omega} (\sigma + b)V^2 dx + p \int_{\Omega} \frac{r}{K} N I^{p-1} dx
\]

\[
= -\frac{4d_I(p-1)}{p} \|\nabla V\|_2^2 + p \int_{\Omega} \beta R S I^{p-1} dx
\]

(8)
for any $0 \leq t < T$.

Let $l := (p-1)/p$. It then follows from (6) that
\[ p \int_{\Omega} \beta RSI^{p-1} dx \leq p c_1 c_2 \int_{\Omega} \beta V^2 dx. \]

For any $q > 1$, applying Hölder’s inequality with indices $q/(q-1)$ and $q$ to the integral on the right hand side, one has
\[ p \int_{\Omega} \beta RSI^{p-1} dx \leq p c_1 c_2 \|\beta\|_{q/(q-1)} \|V^2\|_q \]
\[ \leq p c_1 c_2 |\Omega|^{\frac{q-1}{q}} \sup_{x \in \Omega} \beta(x) (\|V\|_{2q})^{2l}. \tag{9} \]

Let us choose $q$ such that $1 < lq < 3$. This can be achieved due to $0 < l < 1$ and $q > 1$. Then, by Interpolation theorem ([1], or (86) in Appendix), there exists a positive constant $c > 0$ independent of $V$, such that
\[ \|V\|_{2q} \leq c \|V\|_{W_2^1(\Omega)} \|V\|_2^{1-\theta}, \tag{10} \]
where $0 < \theta < 1$. Substituting (10) into (9) gives
\[ p \int_{\Omega} \beta RSI^{p-1} dx \leq c p c_1 c_2 |\Omega|^{\frac{q-1}{q}} \sup_{x \in \Omega} \beta(x) (\|V\|_{W_2^1(\Omega)} \|V\|_2^{1-\theta})^{2l} \]
\[ \leq c p c_1 c_2 |\Omega|^{\frac{q-1}{q}} \sup_{x \in \Omega} \beta(x) \left( \|V\|_{2q}^2 + \|\nabla V\|_{2q}^{2\theta} \|V\|_2^{2(1-\theta)} \right), \tag{11} \]
where $c$ denotes a generic constant. For any $\varepsilon > 0$, Young’s inequality leads to
\[ c p c_1 c_2 |\Omega|^{\frac{q-1}{q}} \sup_{x \in \Omega} \beta(x) \|\nabla V\|_{2q}^{2\theta} \|V\|_2^{2(1-\theta)} \]
\[ \leq \theta \varepsilon \|\nabla V\|_2^2 + (1 - \theta \varepsilon) \left( c p c_1 c_2 |\Omega|^{\frac{q-1}{q}} \sup_{x \in \Omega} \beta(x) \right) \varepsilon^{-1} \frac{\|V\|_2^{2(1-\theta)}}{\theta \varepsilon}. \tag{12} \]

Let us discard a nonnegative term on the left hand side of (8), and substitute (11) and (12) into (8). Recalling $l = (p-1)/p$, it then follows by taking $\varepsilon = 4d_I/\theta$ that
\[ \frac{d}{dt} (\|V\|_2^2) + p \inf_{x \in \Omega} (\sigma(x) + b(x)) \|V\|_2^2 \leq -4d_I \|\nabla V\|_2^2 + p \int_{\Omega} \beta RSI^{p-1} dx \]
\[ \leq c'_1 p' \|V\|_2^2 + c'_2 p' \|V\|_2^{2(1-\theta)}, \]
where
\[ p' := p \inf_{x \in \Omega} (\sigma(x) + b(x)), \quad c'_1 := \frac{c p c_1 c_2}{p'} |\Omega|^{\frac{q-1}{q}} \sup_{x \in \Omega} \beta(x), \]
\[ c'_2 := \frac{1 - l\theta}{p'} \left( c p c_1 c_2 |\Omega|^{\frac{q-1}{q}} \sup_{x \in \Omega} \beta(x) \right) \varepsilon^{-1} \frac{\theta}{4d_I}. \]

Let $\zeta(t) := \|V(.,t)\|_2^2$. For any $0 < t < T$, we have
\[ \frac{d\zeta}{dt} + p' \zeta \leq c'_1 p' \zeta^4 + c'_2 p' \zeta^{4(1-\theta)}. \]
For $0 < t \leq t' \leq t'' < T$, let us multiply both sides of last inequality by $e^{p't}$, and integrate with respect to $t$ from 0 to $t'$. This gives

$$\zeta(t') \leq \zeta(0) + c'_1 \left( \sup_{[0,t'']} \zeta \right)^l + c'_2 \left( \sup_{[0,t'']} \zeta \right)^{(1-l)\theta}.$$

It follows that

$$\sup_{[0,t'']} \zeta \leq \zeta(0) + c'_1 \left( \sup_{[0,t'']} \zeta \right)^l + c'_2 \left( \sup_{[0,t'']} \zeta \right)^{(1-l)\theta}. \quad (13)$$

Introduce notations

$$h := \sup_{[0,t'']} \zeta(t), \quad \theta_1 := \min \left\{ l, \frac{l(1-\theta)}{1-l\theta} \right\}, \quad \theta_2 := \max \left\{ l, \frac{l(1-\theta)}{1-l\theta} \right\},$$

where $0 < \theta_1 \leq \theta_2 < 1$ since $0 < l, \theta < 1$. Then, (13) can be rewritten as

$$h \leq \zeta(0) + c'_1 h^{\theta_1} + c'_2 h^{\theta_2}. \quad (14)$$

Assume that $h > 1$, otherwise, we have $h \leq 1$. It then follows from (14) that

$$h \leq \zeta(0) + 2(c'_1 + c'_2)h^{\theta_2-1}h.$$

If $h > [3(c'_1 + c'_2)]^{1/(1-\theta_2)}$, we have $h \leq 3\zeta(0)$. Otherwise, we have $h \leq [3(c'_1 + c'_2)]^{1/(1-\theta_2)}$.

Based on the discussion above, it can be concluded that

$$h < 1 + 3\zeta(0) + [3(c'_1 + c'_2)]^{1/(1-\theta_2)}.$$

Recalling the definitions of $h$, $\zeta$, $c'_1$, $c'_2$, we conclude that there exists a positive constant $C(p, d_I)$ such that

$$\|I(\cdot, t)\|_p \leq C(p, d_I)$$

for any $0 \leq t < T$, where $C(p, d_I)$ depends on $p$, $d_I$, $c_1$, $c_2$, $\|I_0\|_p$ and $|\Omega|$.

Let $g(x, t, I) := \beta RS - (rNI/K)$. Then the following result follows from Lemma 2.2 immediately.

**Corollary 1.** Let all the assumptions in Lemma 2.2 be satisfied. Then, for any $p > 2$, there exists a positive constant $C(p, d_I)$, such that

$$\|g(t, I)\|_p \leq C(p, d_I) \quad (15)$$

for any $0 \leq t < T$.

**Proof.** Note that $N = S + I + R + Z$. A straightforward computation shows that

$$\|g(t, I)\|_p = \|\beta RS - \frac{r(S + I + R + Z)I}{K} \|_p$$

$$\leq \|\beta RS\|_p + \sup_{x \in \Omega} \left( \frac{r(x)}{K(x)} \right) \|S + R + Z\|_p + \sup_{x \in \Omega} \left( \frac{r(x)}{K(x)} \right) \||I|\|_p^2.$$  

Then (15) follows from Lemma 2.1 and Lemma 2.2 immediately.

For $p > 2$, following [16, 25], we define the operator $A : D(A) \to L^p(\Omega)$ by

$$Au := -d_I \Delta u + (\sigma + b)u, \quad (16)$$

where

$$D(A) = \{ u \in W^2_p(\Omega) ; \partial u/\partial \nu = 0 \text{ on } \partial \Omega \}.$$
Clearly, \(-A\) is the generator of the holomorphic semigroup \(e^{-At}\). Let us denote by \(\mu_1\) the principle eigenvalue of \(A\). It is straightforward to calculate that \(\mu_1 = \sigma + b\). The following statement is obtained in [25].

**Proposition 1.** Let operator \(A\) be defined as above. Then, we have

1. \(\|\nabla e^{-tA}\|_p \leq ce^{-\mu_1 t}((dt)^{-1/2} + 1)\);
2. \(\|e^{-tA} I\|_p \leq ce^{-\mu_1 t}((\|I\|_p + \|I\|_p^{1/2}\|A I\|_p^{1/2})\), for \(u \in D(A)\),

where \(c > 0\) is a constant independent of \(t\), \(d_1\), and \(\|\cdot\|_p\) denotes the norm in \(L^p(\Omega)\).

Let \((S(x,t), I(x,t), R(x,t), Z(x,t))\) be the solution of (1) defined on \(\Omega \times [0, T)\). Then by the definition of \(g(\cdot, t, I)\) and (16), \(I(\cdot, t)\) can be written as

\[
I(t) = e^{-tA}I_0 + \int_0^t e^{-(t-t')A} g(\tau, I(\tau)) d\tau.
\]

**Lemma 2.3.** Let all the assumptions in Lemma 2.2 be satisfied. Then, for \(p > 2\), there exists a positive constant \(C(p, d_1)\), such that

\[
\|\nabla I(t)\|_p \leq C(p, d_1)
\]

for any \(0 \leq t < T\).

**Proof.** By Proposition 1 and (17), we have

\[
\|\nabla I(t)\|_p \leq ce^{-\mu_1 t}((\|I_0\|_p + \|I_0\|_p^{1/2}\|A I_0\|_p^{1/2})
+ \int_0^t ce^{-\mu_1 (t-\tau)}((d_1(t-\tau))^{-1/2} + 1)||g(\tau, I(\tau))||_p d\tau
\]

for \(0 \leq t < T\). As a result, by integration one can obtain the estimate

\[
\|\nabla I(t)\|_p \leq c((\|I_0\|_p + \|I_0\|_p^{1/2}\|A I_0\|_p^{1/2}) + \frac{cC(p, d_1)\pi}{\sqrt{d_1\mu_1}} + \frac{cC(p, d_1)}{\mu_1},
\]

where (15) has been used. This implies (18) holds.

We now complete the proof of Theorem 1.1.

**Proof of Theorem 1.1.** Firstly, we show that system (1) has a unique nonnegative classical solution defined on \(\Omega \times [0, T)\), for some \(T = T(S_0, I_0, R_0, Z_0) \leq \infty\). We shall use Lemma A.1 in Appendix to prove it. To that end, we define

\[
F_1(x, u_1, u_2, u_3, u_4) := ru_1 - r(u_1 + u_2 + u_3 + u_4)u_1/K + a^* u_4 - \beta u_1 u_3,
\]

\[
F_2(x, u_1, u_2, u_3, u_4) := \beta u_1 u_3 - (\sigma + b)u_2 - r(u_1 + u_2 + u_3 + u_4)u_2/K,
\]

\[
F_3(x, u_1, u_2, u_3, u_4) := \sigma u_2 - (\alpha + b + \mu)u_3 - r(u_1 + u_2 + u_3 + u_4)u_3/K,
\]

\[
F_4(x, u_1, u_2, u_3, u_4) := \mu u_3 + (a - a^* - b)u_4 - r(u_1 + u_2 + u_3 + u_4)u_4/K.
\]

Let \(d_1 = d_2 = d_1, d_3 = d_R, d_4 = d_Z, u_1 = S, u_2 = I, u_3 = R, u_4 = Z, u_{1,0}(x) = S_0(x), u_{2,0}(x) = I_0(x), u_{3,0}(x) = R_0(x), u_{4,0}(x) = Z_0(x)\). Then, system (1) can be rewritten in the form of (69).

For \(i = 1, 2, 3, 4\), by (A1), \(F_i(x, u_1, u_2, u_3, u_4) \geq 0\) whenever \((u_1, u_2, u_3, u_4) \in \mathbb{R}_+^4\) and \(u_i = 0\), furthermore, \(F_i(x, u_1, u_2, u_3)\) is 2-times continuously differentiable with respect to \(x\), \(u_1\), \(u_2\), \(u_3\), and \(u_4\). Note that \(u_{i,0} \in C(\overline{\Omega}, \mathbb{R})\) and \(u_{i,0}(x) \geq 0\).

Thus, by Lemma A.1, (1) has a unique nonnegative classical solution \((S, I, R, Z) := (u_1, u_2, u_3, u_4)\) defined on \(\Omega \times [0, T)\), for some \(T = T(S_0, I_0, R_0, Z_0) \leq \infty\). Furthermore, It follows from the proof of [35, Theorem 7.3.1] that \(S(\cdot, t), I(\cdot, t), R(\cdot, t)\) and \(Z(\cdot, t) \in W^{2,2}_0(\Omega)\) for any \(0 < t < T\).
Since \( n < 4 \), Sobolev imbedding theorem allows us to conclude that \( W^1_4(\Omega) \rightarrow L^\infty(\Omega) \). This implies there exists a generic constant \( c > 0 \), such that
\[
||I(t)||_\infty \leq c(||I(t)||_4 + ||\nabla I(t)||_4).
\]
Then, by (7) and (18), we conclude there exists a positive constant \( c_4 \), such that
\[
0 \leq I(x,t) \leq c_4
\]
for \( (x,t) \in \Omega \times [0,T) \). Hence, together with Lemma 2.1, one obtains (3). Subsequently, Lemma A.1 implies \( T = \infty \).

Let \((S^\infty(x,t), I^\infty(x,t), \xi(t), Z^\infty(x,t))\) be the nonnegative smooth solution of the shadow system (2) defined on \( \Omega \times [0,T) \). Then by the same procedure as that for the original reaction-diffusion system, we can prove the boundedness of the nonnegative smooth solution to the shadow system. This implies the nonnegative smooth solution exists for all time \( t > 0 \). The proof of Theorem 1.2 is omitted as it parallels the proof of Lemma 2.1, Lemma 2.2 and Lemma 2.3.

3. Some lemmas. In this section, we present three lemmas which will be used in next section. To that end, we assume that the solutions of (1) and (2) are sufficiently smooth.

**Lemma 3.1.** Let \((S(x,t), I(x,t), R(x,t), Z(x,t))\) be the nonnegative global smooth solution of (2). If \( d_S \geq 2r/\lambda_1 \), \( d_R \geq r/\lambda_1 \) and \( d_Z \geq 2r/\lambda_1 \), then there exist positive constants \( c_5 \) and \( c_6 \) independent of \( d_R \), such that for any \( t > 0 \),
\[
||\nabla S(\cdot,t)||_2, \ ||\nabla I(\cdot,t)||_2, \ ||\nabla R(\cdot,t)||_2, \ ||\nabla Z(\cdot,t)||_2 \leq c_5, \nonumber
\]
\[
||\Delta S(\cdot,t)||_2, \ ||\Delta I(\cdot,t)||_2, \ ||\Delta R(\cdot,t)||_2, \ ||\Delta Z(\cdot,t)||_2 \leq c_6,
\]
where \( \lambda_1 \) is the smallest positive eigenvalue of \(-\Delta \) in \( \Omega \) subject to the homogeneous Neumann boundary condition.

**Proof.** We first show that there exists a constant \( c_5 > 0 \) independent of \( d_R \), such that
\[
||\nabla S(\cdot,t)||_2, \ ||\nabla I(\cdot,t)||_2, \ ||\nabla R(\cdot,t)||_2, \ ||\nabla Z(\cdot,t)||_2 \leq c_5\nonumber
\]
for any \( t > 0 \).

Multiplying the \( S \)-equation of (1) by \( \Delta S \) and integrating with respect to \( x \) over \( \Omega \), we obtain
\[
\frac{1}{2} \frac{d}{dt}(||\nabla S||^2_2) + d_S ||\Delta S||^2_2 + r \int_{\Omega} (2S + I + R + Z)|\nabla S|^2 dx + \int_{\Omega} \beta(x) R |\nabla S|^2 dx
\]
\[
= r||\nabla S||^2_2 - r \int_{\Omega} S(\nabla(I + R + Z) \cdot \nabla S) dx + a^* \int_{\Omega} \nabla Z \cdot \nabla S dx
\]
\[
- \int_{\Omega} \beta(x) S(\nabla R \cdot \nabla S) dx - \int_{\Omega} S R (\nabla \beta \cdot \nabla S) dx.
\]
\[
(21)
\]
It follows from Hölder’s inequality that
\[
\frac{1}{2} \frac{d}{dt}(||\nabla S||^2_2) + d_S ||\Delta S||^2_2 - r||\nabla S||^2_2
\]
\[
\leq r ||S||_2 ||\nabla(I + R + Z)||_4 ||\nabla S||_4 + ||a^*||_2 ||\nabla Z||_4 ||\nabla S||_4
\]
\[
+ ||\beta(x)||_2 ||\nabla R||_4 ||\nabla S||_4 + ||SR||_2 ||\nabla \beta||_4 ||\nabla S||_4.
\]
\[
(22)
\]
where we have discarded some nonnegative terms on the left hand side of (21).
By Gagliardo-Nirenberg inequality (Lemma D.1 in Appendix), there exists a constant $c > 0$, such that
\[
\|\nabla S\|_4 \leq c \|S\|_{W^2_2}^\theta \|S\|_{L^2}^{1-\theta},
\]
\[
\|\nabla (I + R + Z)\|_4 \leq c \|I + R + Z\|_{W^2_2}^\theta \|I + R + Z\|_{L^2}^{1-\theta},
\]
where $0 < \theta < 1$. Moreover, by the elliptic estimate ((82) in Appendix), there exists a constant $c > 0$, such that
\[
\|S\|_{W^2_2} \leq c (\|\Delta S\|_2 + \|S\|_2),
\]
\[
\|I + R + Z\|_{W^2_2} \leq c (\|\Delta(I + R + Z)\|_2 + \|I + R + Z\|_2).
\]

Then, by (3), (23) and (24), we have
\[
\|\nabla S\|_4 \leq c \|\Delta S\|_2 + \|S\|_2 \|S\|_2^{1-\theta}
\]
\[
\leq c \left(\|\Delta S\|_2 + c_1 \sqrt{|\Omega|}\right)^\theta \left(c_1 \sqrt{|\Omega|}\right)^{1-\theta},
\]
\[
\|\nabla (I + R + Z)\|_4 \leq c \left(\|\Delta I + \Delta R + \Delta Z\|_2 + \|I + R + Z\|_2\right)^\theta \|I + R + Z\|_2^{1-\theta}
\]
\[
\leq c \left(\|\Delta I\|_2 + \|\Delta R\|_2 + \|\Delta Z\|_2 + (c_2 + c_3 + c_4) \sqrt{|\Omega|}\right)^\theta
\]
\[
\times \left((c_2 + c_3 + c_4) \sqrt{|\Omega|}\right)^{1-\theta},
\]
where $c$ denotes a generic positive constant.

Hence, for any $\delta > 0$, we have
\[
\frac{r}{K} \|S\|_2 \|\nabla (I + R + Z)\|_4 \|\nabla S\|_4 \leq \rho_1 \rho_2,
\]
where
\[
\rho_1 := \left(\|\Delta I\|_2 + \|\Delta R\|_2 + \|\Delta Z\|_2 + (c_2 + c_3 + c_4) \sqrt{|\Omega|}\right)^\theta \left(\|\Delta S\|_2 + c_1 \sqrt{|\Omega|}\right)^{\theta \delta},
\]
\[
\rho_2 := \frac{cc_1 r}{K} \sqrt{|\Omega|} \left((c_2 + c_3 + c_4) \sqrt{|\Omega|}\right)^{1-\theta} \left(c_1 \sqrt{|\Omega|}\right)^{1-\theta} \delta^{-\theta}.
\]

It follows from Young’s inequality that $\rho_1 \rho_2 \leq \theta \rho_1^{1/\theta} + (1-\theta) \rho_2^{1/(1-\theta)}$. Since $0 < \theta < 1$, we have
\[
\frac{r}{K} \|S\|_2 \|\nabla (I + R + Z)\|_4 \|\nabla S\|_4 \leq \delta \left(\|\Delta I\|_2 + \|\Delta R\|_2 + \|\Delta Z\|_2 + (c_2 + c_3 + c_4) \sqrt{|\Omega|}\right) \left(\|\Delta S\|_2 + c_1 \sqrt{|\Omega|}\right)
\]
\[
+ \delta^{-\frac{\theta}{r-\theta}} \left(\frac{cc_1 r}{K} \sqrt{|\Omega|}\right)^{\frac{1}{1-\theta}} c_1 (c_2 + c_3 + c_4) |\Omega|
\]
\[
= \delta \|\Delta I\|_2 + \|\Delta R\|_2 + \|\Delta Z\|_2 \|\Delta S\|_2 + \delta (c_2 + c_3 + c_4) \sqrt{|\Omega|} \|\Delta S\|_2
\]
\[
+ \delta c_1 (c_2 + c_3 + c_4) |\Omega| + \delta c_1 \sqrt{|\Omega|} (\|\Delta I\|_2 + \|\Delta R\|_2 + \|\Delta Z\|_2)
\]
\[
+ \delta^{-\frac{\theta}{r-\theta}} \left(\frac{cc_1 r}{K} \sqrt{|\Omega|}\right)^{\frac{1}{1-\theta}} c_1 (c_2 + c_3 + c_4) |\Omega|.
\]

Let $u := (S, I, R, Z)$. We define
\[
\|\nabla u\|_2 = \|\nabla S\|_2 + \|\nabla I\|_2 + \|\nabla R\|_2 + \|\nabla Z\|_2,
\]
\[
\|\Delta u\|_2 = \|\Delta S\|_2 + \|\Delta I\|_2 + \|\Delta R\|_2 + \|\Delta Z\|_2,
\]
\[
\|\nabla (\Delta u)\|_2 = \|\nabla (\Delta S)\|_2 + \|\nabla (\Delta I)\|_2 + \|\nabla (\Delta R)\|_2 + \|\nabla (\Delta Z)\|_2.
\]
Again using Young’s inequality, we have
\[
\frac{r}{K} \|S\|_2 \|\nabla(I + R + Z)\|_4 \|\nabla S\|_4 \\
\leq 2\delta\|\Delta u\|^2_2 + \delta^{-\rho} \left(\frac{\varepsilon c_1 r}{\alpha}\sqrt{|\Omega|}\right)^{\frac{1}{\rho^2}} c_1 (c_2 + c_3 + c_4) |\Omega| \\
+ \frac{\delta}{2} \left(3c_1^2 + (c_2 + c_3 + c_4)^2 + 2c_1 (c_2 + c_3 + c_4)\right) |\Omega|.
\] (25)

Define
\[
M := \max_{0 \leq |\eta| \leq 2} \{ |D^\gamma \beta(x)| : x \in \Omega \}. 
\] (26)

Then, similar to (25), we obtain
\[
\|a^*\|_2 \|\nabla Z\|_4 \|\nabla S\|_4 \leq \delta \|\Delta u\|^2_2 + \frac{\delta}{2} (c_1 + c_3)^2 |\Omega| + \left(\delta^{-\rho} ca^* \sqrt{|\Omega|}\right)^{\frac{1}{\rho^2}} c_1 c_3 |\Omega|, \\
\|\beta S\|_2 \|\nabla R\|_4 \|\nabla S\|_4 \leq \delta \|\Delta u\|^2_2 + \frac{\delta}{2} (c_1 + c_2)^2 |\Omega| + \left(\delta^{-\rho} c c_1 M \sqrt{|\Omega|}\right)^{\frac{1}{\rho^2}} c_1 c_2 |\Omega|, \\
\|SR\|_2 \|\nabla \beta\|_4 \|\nabla S\|_4 \leq \frac{\delta}{2} \|\Delta u\|^2_2 + \frac{\delta}{2} (1 + c_1 |\Omega|^{\frac{1}{2}}) + \left(\delta^{-\rho} c c_1 c_2 M |\Omega|^{\frac{1}{2}}\right)^{\frac{1}{\rho^2}} c_1 |\Omega|^{\frac{1}{2}}. 
\] (27)

Substituting (25) and (27) into (22) gives
\[
\frac{1}{2} \frac{d}{dt} \left(\|\nabla S\|^2_2 \right) + d_s \|\Delta S\|^2_2 - r \|\nabla S\|^2_2 \leq \frac{9\delta}{2} \|\Delta u\|^2_2 + c_3 \delta + c_4 \delta^{-\rho},
\] (28)

where \(c_3\) and \(c_4\) are positive constants depending on \(c_1, c_2, c_3, c_4, |\Omega|\).

Analogously, we obtain that
\[
\frac{1}{2} \frac{d}{dt} \left(\|\nabla I\|^2_2 \right) + d_l \|\Delta I\|^2_2 \leq \frac{9\delta}{2} \|\Delta u\|^2_2 + c_5 \delta + c_6 \delta^{-\rho}, \\
\frac{1}{2} \frac{d}{dt} \left(\|\nabla R\|^2_2 \right) + d_R \|\Delta R\|^2_2 \leq 3\delta \|\Delta u\|^2_2 + c_7 \delta + c_8 \delta^{-\rho}, \\
\frac{1}{2} \frac{d}{dt} \left(\|\nabla Z\|^2_2 \right) + d_Z \|\Delta Z\|^2_2 - r \|\nabla Z\|^2_2 \leq 3\delta \|\Delta u\|^2_2 + c_9 \delta + c_{10} \delta^{-\rho},
\] (29)

where \(c_5, \ldots, c_{10}\) are positive constants depending on \(c_1, c_2, c_3, c_4, |\Omega|\). Here we have used \(a - b = r\).

Adding (28) and (29) together, we obtain
\[
\frac{1}{2} \frac{d}{dt} \left(\|\nabla u\|^2_2 \right) + d_s \|\Delta S\|^2_2 + d_l \|\Delta I\|^2_2 + d_R \|\Delta R\|^2_2 + d_Z \|\Delta Z\|^2_2 \\
- r \|\nabla S\|^2_2 - r \|\nabla Z\|^2_2 \leq 15\delta \|\Delta u\|^2_2 + (c_3 + c_5 + c_7 + c_9) \delta + (c_4 + c_6 + c_8 + c_{10}) \delta^{-\rho}. 
\] (30)

By [5, Lemma A1] ((83) in Appendix), we have
\[
\lambda_1 \|\nabla S\|^2_2 \leq \|\Delta S\|^2_2, \quad \lambda_1 \|\nabla Z\|^2_2 \leq \|\Delta Z\|^2_2, \quad \lambda_1 \|\nabla u\|^2_2 \leq \|\Delta u\|^2_2.
\] (31)

It follows from \(d_s \geq 2r/\lambda_1 \) and \(d_Z \geq 2r/\lambda_1 \) that
\[
\frac{r}{\lambda_1} \|\Delta S\|^2_2 \leq d_s \|\Delta S\|^2_2 - r \|\nabla S\|^2_2, \quad \frac{r}{\lambda_1} \|\Delta Z\|^2_2 \leq d_Z \|\Delta Z\|^2_2 - r \|\nabla Z\|^2_2.
\] (32)
Since $d_R \geq r/\lambda_1$, substituting (32) into (30) yields
\[
\frac{1}{2} \frac{d}{dt}(\|\nabla u\|_2^2) + \frac{\min\{\lambda_1 d_I, r\}}{\lambda_1} \|\Delta u\|_2^2 - 15\delta \|\Delta u\|_2^2 \\
\leq (c'_4 + c'_5 + c'_6 + c'_9)\delta + (c'_4 + c'_6 + c'_8 + c'_{10})\delta^{-\frac{\theta}{2}}.
\]
By (31), choosing $\delta = \min\{\lambda_1 d_I, r\}/30\lambda_1$, we have
\[
\frac{1}{2} \frac{d}{dt}(\|\nabla u\|_2^2) + \frac{1}{2} \min\{\lambda_1 d_I, r\} \|\nabla u\|_2^2 \\
\leq (c'_4 + c'_5 + c'_6 + c'_9)\delta + (c'_4 + c'_6 + c'_8 + c'_{10})\delta^{-\frac{\theta}{2}}.
\]
Then, by Gronwall’s inequality,
\[
\|\nabla u\|_2^2 \leq \|\nabla u_0\|_2^2 + \frac{c'_4 + c'_5 + c'_6 + c'_9}{15\lambda_1}
\]

\[
+ 2(c'_4 + c'_6 + c'_8 + c'_{10})(30\lambda_1)^{\frac{\theta}{2}} \min\{\lambda_1 d_I, r\}^{-\frac{\theta}{2}},
\]
where $\|\nabla u_0\|_2^2 = \|\nabla S_0\|_2^2 + \|\nabla I_0\|_2^2 + \|\nabla R_0\|_2^2 + \|\nabla Z_0\|_2^2$. Defining
\[
c'_8 := \|\nabla u_0\|_2^2 + \frac{c'_4 + c'_5 + c'_6 + c'_9}{15\lambda_1}
\]

\[
+ 2(c'_4 + c'_6 + c'_8 + c'_{10})(30\lambda_1)^{\frac{\theta}{2}} \min\{\lambda_1 d_I, r\}^{-\frac{\theta}{2}},
\]
we conclude that (20) holds for any $(x, t) \in \Omega \times [0, \infty)$.

We next show that there exists a positive constant $c_6$ independent of $d_R$, such that
\[
\|\Delta S(\cdot, t)\|_2, \quad \|\Delta I(\cdot, t)\|_2, \quad \|\Delta R(\cdot, t)\|_2, \quad \|\Delta Z(\cdot, t)\|_2 \leq c_6
\]
for $t \in [0, \infty)$.

Differentiating the S-equation of (1) with respect to $x$, we have
\[
\nabla \left( \frac{\partial S}{\partial t} \right) = d_s \nabla (\Delta S) + r \nabla S - \frac{r}{K} \nabla [(S + I + R + Z)S] + a^s \nabla Z - \nabla (\beta R S).
\]
Let us multiply (34) by $\nabla (\Delta S)$ and integrate with respect to $x$ over $\Omega$. This gives
\[
\frac{1}{2} \frac{d}{dt}(\|\Delta S\|_2^2) + d_s \|\nabla (\Delta S)\|_2^2 - r \|\Delta S\|_2^2
\]
\[
= \frac{r}{K} \int_\Omega S(\nabla N \cdot \nabla (\Delta S))dx + \frac{r}{K} \int_\Omega N(\nabla S \cdot \nabla (\Delta S))dx - a^s \int_\Omega \nabla Z \cdot \nabla (\Delta S)dx
\]
\[
+ \int_\Omega \beta R (\nabla S \cdot \nabla (\Delta S))dx + \int_\Omega \beta S (\nabla R \cdot \nabla (\Delta S))dx + \int_\Omega S R (\nabla \beta \cdot \nabla (\Delta S))dx.
\]

(35)

By Hölder’s inequality and Young’s inequality, for any $\delta > 0$, we have
\[
\frac{r}{K} \int_\Omega |S(\nabla N \cdot \nabla (\Delta S))| \; dx \leq \frac{r}{K} \|S\|_4 \|\nabla N\|_4 \|\nabla (\Delta S)\|_2
\]
\[
\leq \frac{1}{25} \left( \frac{r^2}{K^2} \|S\|_4^2 \|\nabla N\|_4^2 \right) + \frac{\delta}{2} \|\nabla (\Delta S)\|_2^2.
\]

(36)

Similar to (25), by (3), (23), (24) and $N = S + I + R + Z$, we have
\[
\frac{r^2}{K^2} \|S\|_4^2 \|\nabla N\|_4^2 \leq 8\delta^2 \|\Delta u\|_2^2 + 2c'_{11}\delta^2 + 2c'_{12}\delta^{-\frac{\theta}{2}}.
\]
where \( c'_{12} := c'_{12}(c_1, c_2, c_3, c_4, |\Omega|) \) are positive constants. Substituting the above inequality into (36) yields

\[
\frac{r}{K} \int_{\Omega} |S(\nabla N \cdot \nabla (\Delta S))| \, dx \leq 4\delta \|\Delta u\|_2^2 + c'_{11} \delta + c'_{12} \delta^{-\frac{1+\theta}{1-\theta}} + \frac{\delta}{2} \|\nabla (\Delta S)\|_2^2. \tag{37}
\]

We derive the estimates of the right hand of (35) term by term. Combining them together yields

\[
\frac{1}{2} \frac{d}{dt}(\|\Delta S\|_2^2) + d_S \|\nabla (\Delta S)\|_2^2 - r \|\Delta S\|_2^2 \\
\leq 6\delta \|\Delta u\|_2^2 + c''_1 \delta + c''_2 \delta^{-\frac{1+\theta}{1-\theta}} + \frac{3(c_1 c_2 M)^2|\Omega|}{2\delta} + 3\delta \|\nabla (\Delta S)\|_2^2, \tag{38}
\]

where \( c''_1 := c''_1(c_1, c_2, c_3, c_4, |\Omega|) \) and \( c''_2 := c''_2(c_1, c_2, c_3, c_4, |\Omega|) \) are positive constants.

Similarly, we have

\[
\frac{1}{2} \frac{d}{dt}(\|\Delta I\|_2^2) + d_I \|\nabla (\Delta I)\|_2^2 \\
\leq 5\delta \|\Delta u\|_2^2 + c''_0 \delta + c''_1 \delta^{-\frac{1+\theta}{1-\theta}} + 3\delta \|\nabla (\Delta I)\|_2^2 + 3(c_1 c_2 M)^2|\Omega|/\delta, \tag{39}
\]

where \( c''_0, \ldots, c''_1 \) are positive constants depending on \( c_1, c_2, c_3, c_4, |\Omega| \).

Since \( \int_{\Omega} \Delta S \, dx = \int_{\Omega} \Delta I \, dx = \int_{\Omega} \Delta R \, dx = \int_{\Omega} \Delta Z \, dx = 0 \), the Poincaré inequality ((48) in Appendix) leads to

\[
\lambda_1 \|\Delta S\|_2^2 \leq \|\nabla (\Delta Z)\|_2^2, \quad \lambda_1 \|\Delta Z\|_2^2 \leq \|\nabla (\Delta Z)\|_2^2, \quad \lambda_1 \|\Delta u\|_2^2 \leq \|\nabla (\Delta u)\|_2^2. \tag{40}
\]

Let us add (38) and (39) together. By (40), \( d_S \geq 2r/\lambda_1, d_I \geq r/\lambda_1 \) and \( d_Z \geq 2r/\lambda_1 \), we have

\[
\frac{1}{2} \frac{d}{dt}(\|\Delta u\|_2^2) + \frac{1}{\lambda_1} \min\{\lambda_1 d_I, r\} \|\nabla (\Delta u)\|_2^2 \\
\leq \delta \left( \frac{21}{\lambda_1} + 3 \right) \|\nabla (\Delta u)\|_2^2 + c''_1 \delta + c''_0 \delta^{-\frac{1+\theta}{1-\theta}} + 3(c_1 c_2 M)^2|\Omega| \delta^{-1},
\]

where \( c''_0 = c''_1 + c''_0 + c''_1 + c''_0 + c''_0 + c''_0 \). Taking \( \delta = \min\{\lambda_1 d_I, r\}/(6\lambda_1 + 42) \) yields

\[
\frac{1}{2} \frac{d}{dt}(\|\Delta u(t)\|_2^2) + \frac{1}{2} \min\{\lambda_1 d_I, r\} \|\Delta u(t)\|_2^2 \leq c''_0 \delta + c''_0 \delta^{-\frac{1+\theta}{1-\theta}} + 3(c_1 c_2 M)^2|\Omega| \delta^{-1}.
\]

By Gronwall’s inequality, we have

\[
\|\Delta u(t)\|_2^2 \leq \|\Delta u(0)\|_2^2 + \frac{c''_0}{3\lambda_1 + 21} + 2c''_0 (6\lambda_1 + 42) \frac{1+\theta}{1-\theta} (\min\{\lambda_1 d_I, r\})^{-\frac{1+\theta}{1-\theta}} \\
+ 12(c_1 c_2 M)^2|\Omega|((3\lambda_1 + 21)(\min\{\lambda_1 d_I, r\})^{-2},
\]

where \( c''_0 := c''_0(c_1, c_2, c_3, c_4, |\Omega|) \) and \( c''_1 := c''_1(c_1, c_2, c_3, c_4, |\Omega|) \) are positive constants.
where } \|\Delta u(0)\|_2^2 = \|\Delta S_0\|_2^2 + \|\Delta I_0\|_2^2 + \|\Delta R_0\|_2^2 + \|\Delta Z_0\|_2^2 \). Thus, (33) holds, where 
\[ c_6^2 := \|\Delta u(0)\|_2^2 + \frac{c_6^2}{3\lambda_1 + 21} + 2c_6''(6\lambda_1 + 42) \frac{1}{2}(\min\{\lambda_1 d_I, r\})^{-\frac{\alpha}{1+b}} + 12(c_1 c_2 M)^2 |\Omega| (3\lambda_1 + 21) (\min\{\lambda_1 d_I, r\})^{-2} \] 

By the same procedure as in the proof of Lemma 3.1, we can obtain the following result.

**Lemma 3.2.** Let \((S^\infty(x,t), I^\infty(x,t), \xi(t), Z^\infty(x,t))\) be the nonnegative global smooth solution of (2). If \(d_S \geq 2r/\lambda_1\), \(d_R \geq r/\lambda_1\) and \(d_Z \geq 2r/\lambda_1\), then there exist positive constants \(c_7\) and \(c_8\) independent of \(d_R\), such that for any \(t > 0\),
\[
\|\nabla S^\infty(\cdot,t)\|_2, \|\nabla I^\infty(\cdot,t)\|_2, \|\nabla Z^\infty(\cdot,t)\|_2 \leq c_7,
\|
abla S^\infty(\cdot,t)\|_2, \|\Delta I^\infty(\cdot,t)\|_2, \|\Delta Z^\infty(\cdot,t)\|_2 \leq c_8.
\]

(41)

Set \( \mathcal{R} := \int_\Omega R dx/|\Omega| \). Integrating the \(R\)-equation in (1) with respect to \(x\) over \(\Omega\), we have
\[
 \frac{d\mathcal{R}}{dt} = \frac{\sigma}{|\Omega|} \int_\Omega I dx - \frac{\alpha + b + \mu}{|\Omega|} \int_\Omega R dx - \frac{r}{K|\Omega|} \int_\Omega N R dx. \tag{42}
\]

**Lemma 3.3.** Suppose that all the conditions in Lemma 3.1 are satisfied. Then, there exist positive constants \(\bar{c}_1 = \bar{c}_1(S_0, I_0, R_0, Z_0)\) and \(T(d_R, \infty)\), such that for \(t \in [T(d_R, \infty), \infty)\),
\[
\|R(x,t) - \mathcal{R}(t)\|_{L^\infty(\Omega)} \leq \bar{c}_1 \sqrt{\frac{1}{d_R}}, \tag{43}
\]
where \(\mathcal{R}(t) := \frac{1}{|\Omega|} \int_\Omega R(x,t) dx\) and \(T(d_R)\) is defined as in Theorem 1.3.

**Proof.** Define \( \bar{R} := R - \mathcal{R} \). By \(\|\nabla \bar{R}(t)\|_2 = \|\nabla R(t)\|_2, \|\Delta \bar{R}(t)\|_2 = \|\Delta R(t)\|_2\), Sobolev embedding theorem \((\text{Appendix})\), together with elliptic estimates, we have
\[
\|\bar{R}(t)\|_2^2 \leq \begin{cases} c(\|R(t)\|_2^2 + \|\nabla R(t)\|_2^2), & n = 1, \\ c(\|\bar{R}(t)\|_2^2 + \|\Delta \bar{R}(t)\|_2^2), & n = 2, 3, \end{cases} \tag{44}
\]
where \(c\) denotes a generic constant.

Subtracting (42) from the \(R\)-equation in (1) leads to the equation for \(\bar{R}\),
\[
\frac{\partial \bar{R}}{\partial t} = d_R \Delta \bar{R} + \sigma (I - T) - (\alpha + b + \mu) \bar{R} - \frac{r}{K} \left( N R - \frac{1}{|\Omega|} \int_\Omega N R dx \right) \tag{45}
\]
with the homogeneous Neumann boundary condition
\[
\frac{\partial \bar{R}}{\partial \nu} = 0, \quad \text{on} \quad \partial \Omega \times (0, \infty),
\]
which is obtained from \(\partial R/\partial \nu = 0\).

We multiply both sides of (45) by \(\bar{R}\) and integrate with respect to \(x\) over \(\Omega\). This yields
\[
\frac{1}{2} \frac{d}{dt} (\|\bar{R}\|_2^2) + d_R \|\nabla \bar{R}\|_2^2 + (\alpha + b + \mu) \|\bar{R}\|_2^2 + \frac{r}{K} \int_\Omega N(\bar{R})^2 dx = \sigma \int_\Omega (I - T) \bar{R} dx - \frac{r}{K} \int_\Omega N \bar{R} dx,
\]
where we have used \(\int_{\Omega} \tilde{R}(x,t)dx = 0\) and \(R = \bar{R} + \tilde{R}\). Then, for any \(\delta > 0\), by (3) and Young’s inequality, we have

\[
\frac{1}{2} \frac{d}{dt} \left( \| \tilde{R} \|^2 \right) + dR \| \nabla \tilde{R} \|^2 + (\alpha + b + \mu) \| \tilde{R} \|^2 \\
\leq \frac{1}{2\delta} \left( \sigma^2 \| I - T \|^2 + \frac{\gamma^2}{K^2} \| N \| \tilde{R} \|^2 \right) + \delta \| \tilde{R} \|^2 \\
\leq \frac{1}{2\delta} \left( \sigma^2 c_4^2 + c_5^2 (c_1 + c_2 + c_3 + c_4)^2 \right) |\Omega| + \delta \| \tilde{R} \|^2.
\]

According to the Poincaré inequality, we have

\[
\lambda_1 \| \tilde{R} \|^2 \leq \| \nabla \tilde{R} \|^2 = \| \nabla \bar{R} \|^2.
\]

Then, taking \(\delta = \alpha + b + \mu\) yields

\[
\frac{1}{2} \frac{d}{dt} \left( \| \tilde{R} \|^2 \right) + \lambda_1 dR \| \tilde{R} \|^2 \leq \frac{(\sigma^2 c_4^2 + c_5^2 (c_1 + c_2 + c_3 + c_4)^2/K^2))|\Omega|}{2(\alpha + b + \mu)}.
\]

Hence, the application of Gronwall’s inequality leads to

\[
\| \tilde{R}(t) \|^2 \leq \| \tilde{R}(0) \|^2 e^{-2\lambda_1 dR t} + \frac{c'''}{dR},
\]

where \(c''' = (\sigma^2 c_4^2 + c_5^2 (c_1 + c_2 + c_3 + c_4)^2/K^2))|\Omega|/(2\lambda_1 (\alpha + b + \mu))\).

Similar to (47), we obtain that

\[
\| \nabla \tilde{R}(t) \|^2 \leq \| \nabla \tilde{R}(0) \|^2 e^{-2\lambda_1 dR t} + \frac{c'''}{dR},
\]

and

\[
\| \Delta \tilde{R}(t) \|^2 \leq \| \Delta \tilde{R}(0) \|^2 e^{-\lambda_1 dR t} + \frac{c'''}{dR},
\]

where \(c'''\) and \(c''''\) are positive constants depending on \(c_1, \cdots, c_5\).

If \(n = 1\), then by (44), (46), (47) and (48), we have

\[
\| \tilde{R}(t) \|^2 \leq c \left( \| \tilde{R}(0) \|^2 e^{-2\lambda_1 dR t} + \| \Delta \tilde{R}(0) \|^2 e^{-\lambda_1 dR t} + \frac{c'''}{dR} \right) \\
\leq c \left( \frac{1}{\lambda_1} + 1 \right) \| \Delta \tilde{R}(0) \|^2 e^{-\lambda_1 dR t} + \frac{c'''}{dR}.
\]

If \(n = 2, 3\), then by (31), (44), (46), (47) and (49), we have

\[
\| \tilde{R}(t) \|^2 \leq c \left( \| \tilde{R}(0) \|^2 e^{-2\lambda_1 dR t} + \| \Delta \tilde{R}(0) \|^2 e^{-\lambda_1 dR t} + \frac{c'''}{dR} \right) \\
\leq c \left( \frac{1}{\lambda_1} + 1 \right) \| \Delta \tilde{R}(0) \|^2 e^{-\lambda_1 dR t} + \frac{c'''}{dR}.
\]

For \(n = 1\), we define

\[
T(dR) = \begin{cases} 
0, & dR \| \nabla \tilde{R}(0) \|^2 \leq 1, \\
\log(dR \| \nabla \tilde{R}(0) \|^2) / (2\lambda_1 dR), & dR \| \nabla \tilde{R}(0) \|^2 > 1.
\end{cases}
\]

And for \(n = 2, 3\), we define

\[
T(dR) = \begin{cases} 
0, & dR \| \Delta \tilde{R}(0) \|^2 \leq 1, \\
\log(dR \| \Delta \tilde{R}(0) \|^2) / (\lambda_1 dR), & dR \| \Delta \tilde{R}(0) \|^2 > 1.
\end{cases}
\]

Then, for \(t \geq T(dR)\), one can check that (43) holds. \(\square\)
4. Approximations of shadow system to the original system for large $d_R$. 

In this section, we turn to the proof of Theorem 1.3. Set 
$$
\hat{S} := S - S^\infty, \quad \hat{I} := I - I^\infty, \quad \hat{R} := R - \xi, \quad \hat{Z} := Z - Z^\infty.
$$

Recalling (1), (2) and (42), we subtract the equations for $S^\infty$, $I^\infty$, $\xi$, $Z^\infty$ from the equations for $S$, $I$, $R$, $Z$ respectively. By $R - \xi = \hat{R} + \hat{R}$ and $\int_\Omega \hat{R} dx = 0$, we have 
\[
\frac{d\hat{S}}{dt} = d_S \Delta \hat{S} + r \hat{S} - A_1 \hat{S} - \frac{r}{K} \hat{S} \hat{I} - \left( \frac{r}{K} S + \beta(x) S^\infty \right) \left( \hat{R} + \hat{R} \right) + \left( a^* - \frac{r}{K} S \right) \hat{Z},
\]
\[
\frac{d\hat{I}}{dt} = d_I \Delta \hat{I} + \left( \beta(x) R - \frac{r}{K} I \right) \hat{S} - A_2 \hat{I} + \left( \beta(x) S^\infty - \frac{r}{K} I \right) \left( \hat{R} + \hat{R} \right) - \frac{r}{K} I \hat{Z},
\]
\[
\frac{d\hat{R}}{dt} = \frac{\sigma}{|\Omega|} \int_\Omega \hat{I} dx - \frac{r}{K} I \int_\Omega \left( R \hat{S} + \hat{R} \hat{R} + R \hat{Z} + A_3 \left( \hat{R} + \hat{R} \right) \right) dx - (\alpha + b + \mu) \hat{R},
\]
\[
\frac{d\hat{Z}}{dt} = d_Z \Delta \hat{Z} - \frac{r}{K} Z \hat{S} - \frac{r}{K} Z \hat{I} + \left( \mu - \frac{r}{K} Z \right) \left( \hat{R} + \hat{R} \right) + a \hat{Z} - A_4 \hat{Z}
\]
(50) 

for any $x \in \Omega$, $0 < t < \infty$, where 
\[
A_1 = \left( r(S^\infty + I^\infty + \xi + Z^\infty + S) + \beta R K \right) / K,
\]
\[
A_2 = \left( (\sigma + b) K + r(S^\infty + I^\infty + \xi + Z^\infty + I) \right) / K,
\]
\[
A_3 = S^\infty + I^\infty + \xi + Z^\infty + R,
\]
\[
A_4 = \left( (a^* + b) K + r(S^\infty + I^\infty + \xi + Z^\infty + Z) \right) / K.
\]

Equation (50) is equipped with the homogeneous Neumann boundary conditions 
\[
\partial_\nu \hat{S} = \partial_\nu \hat{I} = \partial_\nu \hat{Z} = 0, \quad \text{on } \partial \Omega \times (0, \infty),
\]
(51) 

and the initial conditions are given by 
$$
\hat{S}(x, 0) = 0, \quad \hat{I}(x, 0) = 0, \quad \hat{R}(0) = 0, \quad \hat{Z}(x, 0) = 0, \quad \text{in } \Omega.
$$

Step 1. Let us multiply the equations in (50) by $\hat{S}$, $\hat{I}$, $\hat{R}$, $\hat{Z}$, and integrate with respect to $x$ over $\Omega$ respectively. By the boundary conditions (51), we have 
\[
\frac{1}{2} \frac{d}{dt} \left( \|\hat{S}\|^2_2 \right) + d_S \|\nabla \hat{S}\|^2_2 + \int_\Omega A_1(\hat{S})^2 dx = g_1(\hat{u}),
\]
\[
\frac{1}{2} \frac{d}{dt} \left( \|\hat{I}\|^2_2 \right) + d_I \|\nabla \hat{I}\|^2_2 + \int_\Omega A_2(\hat{I})^2 dx = g_2(\hat{u}),
\]
\[
\frac{1}{2} \frac{d}{dt} \left( \|\hat{R}\|^2_2 \right) + (\alpha + b + \mu) \|\hat{R}\|^2_2 + \int_\Omega A_3(\hat{R})^2 dx = g_3(\hat{u}),
\]
\[
\frac{1}{2} \frac{d}{dt} \left( \|\hat{Z}\|^2_2 \right) + d_Z \|\nabla \hat{Z}\|^2_2 + \int_\Omega A_4(\hat{Z})^2 dx = g_4(\hat{u}),
\]
(53) 

Proof of Theorem 1.3. We divide the proof into four steps.

Step 1. Let us multiply the equations in (50) by $\hat{S}$, $\hat{I}$, $\hat{R}$, $\hat{Z}$, and integrate with respect to $x$ over $\Omega$ respectively. By the boundary conditions (51), we have 
\[
\frac{1}{2} \frac{d}{dt} \left( \|\hat{S}\|^2_2 \right) + d_S \|\nabla \hat{S}\|^2_2 + \int_\Omega A_1(\hat{S})^2 dx = g_1(\hat{u}),
\]
\[
\frac{1}{2} \frac{d}{dt} \left( \|\hat{I}\|^2_2 \right) + d_I \|\nabla \hat{I}\|^2_2 + \int_\Omega A_2(\hat{I})^2 dx = g_2(\hat{u}),
\]
\[
\frac{1}{2} \frac{d}{dt} \left( \|\hat{R}\|^2_2 \right) + (\alpha + b + \mu) \|\hat{R}\|^2_2 + \int_\Omega A_3(\hat{R})^2 dx = g_3(\hat{u}),
\]
\[
\frac{1}{2} \frac{d}{dt} \left( \|\hat{Z}\|^2_2 \right) + d_Z \|\nabla \hat{Z}\|^2_2 + \int_\Omega A_4(\hat{Z})^2 dx = g_4(\hat{u}),
\]
where
\[ g_1(\hat{u}) := r \| \hat{S} \|_2^2 - \int_\Omega \left( \frac{r}{K} S + \beta(x) S_\infty \right) \hat{R} S dx - \int_\Omega \left( \frac{r}{K} S + \beta(x) S_\infty \right) \hat{R} \hat{S} dx \]
\[ - \frac{r}{K} \int_\Omega S \hat{S} \hat{S} dx + \int_\Omega \left( a^* - \frac{r}{K} S \right) \hat{Z} \hat{S} dx, \]
\[ g_2(\hat{u}) := \int_\Omega \left( \beta(x) R - \frac{r}{K} I \right) \hat{S} \hat{I} dx + \int_\Omega \left( \beta(x) S_\infty - \frac{r}{K} I \right) \hat{R} \hat{I} dx - \frac{r}{K} \int_\Omega I \hat{Z} \hat{I} dx \]
\[ + \int_\Omega \left( \beta(x) S_\infty - \frac{r}{K} I \right) \hat{R} \hat{I} dx, \]
\[ g_3(\hat{u}) := \sigma \int_\Omega \hat{I} \hat{R} dx - \frac{r}{K} \int_\Omega S_\infty + I_\infty + \xi + Z_\infty + R \hat{R} \hat{R} dx \]
\[ - \frac{r}{K} \int_\Omega R \left( \hat{S} + \hat{I} + \hat{Z} \right) \hat{R} dx, \]
\[ g_4(\hat{u}) := a \| \hat{Z} \|_2^2 - \frac{r}{K} \int_\Omega Z \hat{S} \hat{Z} dx - \frac{r}{K} \int_\Omega Z \hat{I} \hat{Z} dx + \int_\Omega \left( \mu - \frac{r}{K} Z \right) \left( \hat{R} + \hat{R} \right) \hat{Z} dx. \]

By (3), (4), (26), Hölder’s inequality and Young’s inequality, we have
\[ |g_1(\hat{u})| \leq r \| \hat{S} \|_2^2 + \frac{r}{K} \| S \|_\infty \| \hat{I} \|_2 \| \hat{S} \|_2 + \left( \frac{r}{K} \| S \|_\infty + \| \beta(x) S_\infty \|_\infty \right) \| \hat{R} \|_2 \| \hat{S} \|_2 \]
\[ + \left( \frac{r}{K} \| S \|_\infty + \| \beta(x) S_\infty \|_\infty \right) \| \hat{R} \|_2 \| \hat{S} \|_2 + \left( a^* + \frac{r}{K} \| S \|_\infty \right) \| \hat{Z} \|_2 \| \hat{S} \|_2 \]
\[ \leq \left( r + \frac{a^*}{2} + 2 c_1 r + c_1 M \right) \| \hat{S} \|_2^2 + \frac{c_1 r}{2K} \| \hat{I} \|_2^2 + \frac{1}{2} \left( c_1 M + \frac{c_1 r}{K} \right) \| \hat{R} \|_2^2 \]
\[ + \frac{1}{2} \left( a^* + \frac{c_1 r}{K} \right) \| \hat{Z} \|_2^2 + \frac{1}{2} \left( c_1 M + \frac{c_1 r}{K} \right) \| \hat{R} \|_2^2. \]

Similar to the inequality above, we can derive the estimates of $|g_2(\hat{u})|$, $|g_3(\hat{u})|$ and $|g_4(\hat{u})|$ respectively. Adding these inequalities, by (52) and (53), we have
\[ \frac{1}{2} \frac{d}{dt} \left( \| \hat{u} \|_2^2 \right) \leq C \left( \| \hat{u} \|_2^2 + \| \hat{R} \|_2^2 \right), \]
where $C$ is a positive constant independent of $d_R$ and is to be chosen sufficiently large.

By $\| \hat{u}(0) \|_2^2 = 0$, (47) and Gronwall’s inequality, we have
\[ \| \hat{u}(t) \|_2^2 \leq \left( \frac{C \| \hat{R}(0) \|_2^2}{\lambda_1 d_R + C} + \frac{c_1'}{d_R} \right) e^{2Ct}, \]
which implies that
\[ \| \hat{u}(t) \|_2^2 \leq \frac{\tilde{c}_2(t)}{d_R}, \]
where $\tilde{c}_2(t) := \left( \frac{C \| \hat{R}(0) \|_2^2}{\lambda_1} + c_1' \right) e^{2Ct}$. 
Step 2. To derive the uniform estimate for $\|\nabla \tilde{u}(t)\|_2$.

Similar to (21), we have

$$\frac{1}{2} \frac{d}{dt} \left( \|\nabla \tilde{S}\|^2 + ds \|\Delta \tilde{S}\|^2 - r \|\nabla \tilde{S}\|^2_2 + \int_{\Omega} \left( \frac{r}{K} (N^\infty + S) + \beta R \right) |\nabla \tilde{S}|^2 dx \right) = g_5(\tilde{u}, \nabla \tilde{u}),$$

$$\frac{1}{2} \frac{d}{dt} \left( \|\nabla \tilde{I}\|^2 + d_I \|\Delta \tilde{I}\|^2 + (\sigma + b) \|\nabla \tilde{I}\|^2_2 + \frac{r}{K} \int_{\Omega} (N^\infty + I) |\nabla \tilde{I}|^2 dx \right) = g_6(\tilde{u}, \nabla \tilde{u}),$$

$$\frac{1}{2} \frac{d}{dt} \left( \|\nabla \tilde{Z}\|^2 + dx_0 \|\Delta \tilde{Z}\|^2 - r \|\nabla \tilde{Z}\|^2_2 + a^* \|\nabla \tilde{Z}\|^2_2 + \frac{r}{K} \int_{\Omega} (N^\infty + Z) |\nabla \tilde{Z}|^2 dx \right) = g_7(\tilde{u}, \nabla \tilde{u}),$$

where $N^\infty = S^\infty + I^\infty + \xi + Z^\infty$.

$g_5(\tilde{u}, \nabla \tilde{u})$

$$= - \frac{r}{K} \int_{\Omega} \tilde{S} (\nabla (S^\infty + I^\infty + Z^\infty + S) \cdot \nabla \tilde{S}) dx - \int_{\Omega} \beta (\tilde{R} + \tilde{R}) (\nabla S^\infty \cdot \nabla \tilde{S}) dx$$

$$- \int_{\Omega} \beta \tilde{S} (\nabla R \cdot \nabla \tilde{S}) dx - \int_{\Omega} \frac{r}{K} S + \beta S^\infty (\nabla \tilde{R} \cdot \nabla \tilde{S}) dx - \int_{\Omega} \tilde{R} \tilde{S} (\nabla \beta \cdot \nabla \tilde{S}) dx$$

$$- \frac{r}{K} \int_{\Omega} (\tilde{R} + \tilde{R} + \tilde{Z}) (\nabla S \cdot \nabla \tilde{S}) dx + \int_{\Omega} \frac{r}{K} \tilde{S} (\nabla \tilde{Z} \cdot \nabla \tilde{S}) dx$$

and

$g_6(\tilde{u}, \nabla \tilde{u})$

$$= \int_{\Omega} \left( \beta S^\infty - \frac{r}{K} \right) (\nabla \tilde{R} \cdot \nabla \tilde{I}) dx - \frac{r}{K} \int_{\Omega} I (\nabla \tilde{Z} \cdot \nabla \tilde{I}) dx + \int_{\Omega} \beta \tilde{S} (\nabla R \cdot \nabla \tilde{I}) dx$$

$$- \frac{r}{K} \int_{\Omega} (\tilde{S} + \tilde{I} + \tilde{R} + \tilde{R} + \tilde{Z}) (\nabla I \cdot \nabla \tilde{I}) dx + \int_{\Omega} \left( \beta R - \frac{r}{K} \right) (\nabla \tilde{S} \cdot \nabla \tilde{I}) dx$$

$$- \frac{r}{K} \int_{\Omega} \tilde{I} (\nabla (S^\infty + I^\infty + Z^\infty) \cdot \nabla \tilde{I}) dx + \int_{\Omega} \beta (\tilde{R} + \tilde{R}) (\nabla S^\infty \cdot \nabla \tilde{I}) dx$$

$$+ \int_{\Omega} \tilde{R} \tilde{S} (\nabla \beta \cdot \nabla \tilde{I}) dx + \int_{\Omega} S^\infty \tilde{R} (\nabla \beta \cdot \nabla \tilde{I}) dx + \int_{\Omega} S^\infty \tilde{R} (\nabla \beta \cdot \nabla \tilde{I}) dx,$$

and

$g_7(\tilde{u}, \nabla \tilde{u})$

$$= - \frac{r}{K} \int_{\Omega} Z (\nabla \tilde{S} \cdot \nabla \tilde{I}) dx - \frac{r}{K} \int_{\Omega} (\tilde{S} + \tilde{I} + \tilde{R} + \tilde{R} + \tilde{Z}) (\nabla Z \cdot \nabla \tilde{I}) dx$$

$$- \frac{r}{K} \int_{\Omega} \tilde{Z} (\nabla (S^\infty + I^\infty + Z^\infty) \cdot \nabla \tilde{I}) dx + \frac{r}{K} \int_{\Omega} \tilde{Z} (\nabla \tilde{I} \cdot \nabla \tilde{Z}) dx$$

$$+ \int_{\Omega} \left( \mu - \frac{r}{K} \right) (\nabla \tilde{R} \cdot \nabla \tilde{Z}) dx.$$

Suppose that $u \in W^2_2(\Omega) \cap C^1(\overline{\Omega}, \mathbb{R})$ satisfies $\partial u / \partial n = 0$ for $x \in \partial \Omega$. By the Gagliardo-Nirenberg inequality, the elliptic estimate and Young's inequality, we have

$$\|\nabla u\|_4 \leq c(\|u\|_2 + \|\Delta u\|_2), \quad (56)$$
where \( c > 0 \) denotes a generic constant. Then, it follows from (3), (4), (19) and (41) that
\[
\|\nabla (S^\infty + I^\infty + Z^\infty + S)\|_4 \\
\leq c (\|\Delta (S^\infty + I^\infty + Z^\infty + S)\|_2 + \|S^\infty + I^\infty + Z^\infty + S\|_2) \\
\leq c \left( c_6 + 3c_8 + (2c_1 + c_3 + c_4)\sqrt{|\Omega|} \right).
\] (57)

By Interpolation theorem ((86) in Appendix), together with Young’s inequality, we have
\[
\|\hat{S}\|_4 \leq c \|\hat{S}\|_{W^{n/4}_2(\Omega)} \|\hat{S}\|_2^{1-(n/4)} \leq c \left( \|\hat{S}\|_2 + \|\nabla \hat{S}\|_2 \right)
\] (58)
for \( n \leq 3 \).

Hence, by (57), (58) and Young’s inequality, we have
\[
\left| \frac{r}{K} \int_{\Omega} \hat{S} (\nabla (S^\infty + I^\infty + Z^\infty + S) \cdot \nabla \hat{S}) \, dx \right| \\
\leq \frac{r}{K} \|\hat{S}\|_4 \|\nabla (S^\infty + I^\infty + Z^\infty + S)\|_4 \|\nabla \hat{S}\|_2 \\
\leq \frac{cr}{K} \left( c_6 + 3c_8 + (2c_1 + c_3 + c_4)\sqrt{|\Omega|} \right) \left( \|\hat{S}\|_2 + \|\nabla \hat{S}\|_2 \right) \|\nabla \hat{S}\|_2 \\
\leq \frac{cr}{2K} \left( c_6 + 3c_8 + (2c_1 + c_3 + c_4)\sqrt{|\Omega|} \right) \left( \|\hat{S}\|_2^2 + 3\|\nabla \hat{S}\|_2^2 \right).
\] (59)

Repeating the same procedure, similar to (54), we have
\[
\frac{1}{2} \frac{d}{dt} \left( \|\nabla \tilde{u}(t)\|_2^2 \right) \leq |g_5(\tilde{u}, \nabla \tilde{u})| + |g_6(\tilde{u}, \nabla \tilde{u})| + |g_7(\tilde{u}, \nabla \tilde{u})| \\
\leq C \left( \|\tilde{u}\|_2^2 + \|\nabla \tilde{u}\|_2^2 + \|\tilde{R}\|_2^2 + \|\nabla \tilde{R}\|_2^2 \right),
\]
where the positive constant \( C \) is defined as in (54). Here we have used \( \nabla \tilde{R} = \nabla R \).

Note that \( \|\nabla \tilde{u}(0)\|_2^2 = 0 \). By (47), (48) and (55), we have
\[
\|\nabla \tilde{u}(t)\|_2^2 \leq \left( \frac{C\|\tilde{R}(0)\|_2^2}{\lambda_1 d_R} + \frac{C\|\nabla R_0\|_2^2}{\lambda_1 d_R} + \frac{c_1'' + c_2''}{d_R} \right) e^{2Ct} + \frac{2C t c_2(t)}{d_R},
\]
which implies that
\[
\|\nabla \tilde{u}(t)\|_2^2 \leq \tilde{c}_3(t) \frac{d}{d_R},
\] (60)
where \( \tilde{c}_3(t) := \left( \frac{C\|\tilde{R}(0)\|_2^2}{\lambda_1} + \frac{C\|\nabla R_0\|_2^2}{\lambda_1} + c_1'' + c_2'' \right) e^{2Ct} + 2C t c_2(t) \).

**Step 3.** To derive the uniform estimate for \( \|\Delta \tilde{u}(t)\|_2 \).

Let us act “\( \Delta \)” operator on both sides of \( \tilde{S} \)-equation, multiply the induced equation by \( \Delta \tilde{S} \), and integrate with respect to \( x \) over \( \Omega \). In consequence, we have
\[
\frac{1}{2} \frac{d}{dt} \left( \|\Delta \tilde{S}\|_2^2 \right) + d_s \|\nabla (\Delta \tilde{S})\|_2^2 + \frac{r}{K} \int_{\Omega} (S^\infty + I^\infty + \xi + Z^\infty + S)(\Delta \tilde{S})^2 \, dx \\
= r \|\Delta \tilde{S}\|_2^2 - 2 \frac{r}{K} \int_{\Omega} \Delta \tilde{S} (\nabla (S^\infty + I^\infty + Z^\infty + S) \cdot \nabla \tilde{S}) \, dx - \int_{\Omega} \Delta (\beta R \tilde{S}) \Delta \tilde{S} \, dx \\
+ \int_{\Omega} \left( a^* - \frac{r}{K}\tilde{S} \right) \Delta \tilde{Z} \Delta \tilde{S} \, dx - \int_{\Omega} S^\infty \tilde{R} \Delta \beta \Delta \tilde{S} \, dx - \int_{\Omega} \beta \tilde{R} \tilde{S} \Delta S^\infty \Delta \tilde{S} \, dx.
\]
where

\[
\Delta (\beta R \hat{S}) = R \Delta \beta + \beta R \Delta \hat{S} + \beta \hat{S} \Delta R + 2\beta \left( \nabla R \cdot \nabla \hat{S} \right) + 2R \left( \nabla \beta \cdot \nabla \hat{S} \right) + 2\hat{S} (\nabla \beta \cdot \nabla R),
\]

\[
\Delta (\beta S_\infty \tilde{R}) = S_\infty \tilde{R} \Delta \beta + \beta S_\infty \Delta \tilde{R} + \beta \tilde{R} \Delta S_\infty + 2\beta \left( \nabla S_\infty \cdot \nabla \tilde{R} \right) + 2S_\infty \left( \nabla \beta \cdot \nabla \tilde{R} \right) + 2\tilde{R} (\nabla \beta \cdot \nabla S_\infty).
\]

For \( n = 2, 3 \), it follows from elliptic estimates ((82) in Appendix) and Sobolev inequality ((85) in Appendix) that

\[
\|S\|_\infty \leq c (\|\Delta S\|_2 + \|S\|_2).
\]

Then, similar to (59), we have

\[
\left| \frac{2r}{K} \int_\Omega \Delta \hat{S} \left( \nabla (S_\infty + I_\infty + Z_\infty + S) \cdot \nabla \hat{S} \right) \, dx \right| \leq \frac{2r}{K} \|\Delta \hat{S}\|_2 \|\nabla (S_\infty + I_\infty + Z_\infty + S)\|_4 \|\nabla \hat{S}\|_4 \leq \frac{cr}{K} \left( (2c_1 + c_3 + c_4) \sqrt{\Omega} + c_6 + 3c_8 \right) \left( \|\hat{S}\|_2^2 + 3\|\Delta \hat{S}\|_2^2 \right),
\]

and

\[
\left| \int_\Omega S_\infty \tilde{R} \Delta \beta \Delta \hat{S} \, dx \right| \leq \|S_\infty \tilde{R}\|_\infty \|\Delta \beta\|_2 \|\Delta \hat{S}\|_2 \leq 3c_1 \sqrt{\frac{1}{M}} \left( \|\tilde{R}\|_2^2 + \|\Delta \tilde{R}\|_2^2 + 2\|\Delta \hat{S}\|_2^2 \right),
\]

where we have used (26), (56), (57) and (62).

Carrying out the same procedure for each term on the right hand side of (61), by \( \Delta R = \Delta \tilde{R} \), we have

\[
\frac{1}{2} \frac{d}{dt} \left( \|\Delta \hat{S}(t)\|_2^2 \right) \leq C \left( \|\tilde{u}\|_2^2 + \|\Delta \tilde{u}\|_2^2 + \|\tilde{R}\|_2^2 + \|\Delta R\|_2^2 \right).
\]

One also can obtain the similar inequality for \( \|\Delta \tilde{t}(t)\|_2^2 \) and \( \|\Delta \hat{Z}(t)\|_2^2 \). Adding them together leads to

\[
\frac{1}{2} \frac{d}{dt} \left( \|\Delta \tilde{u}(t)\|_2^2 \right) \leq C \left( \|\tilde{u}\|_2^2 + \|\Delta \tilde{u}\|_2^2 + \|\tilde{R}\|_2^2 + \|\Delta R\|_2^2 \right),
\]

where the constant \( C \) is defined as in (54).

Note that \( \|\Delta \tilde{u}(0)\|_2^2 = 0 \). By (47), (49) and (55), we have

\[
\|\Delta \tilde{u}(t)\|_2^2 \leq \left( \frac{C\|\tilde{R}(0)\|_2^2}{\lambda_1 d_R + C} + \frac{2C\|\Delta R(0)\|_2^2}{\lambda_1 d_R + 2C} + \frac{c_1'' + c_3''}{d_R} \right) e^{2Ct} + \frac{2Ct\tilde{c}(t)}{d_R}.
\]
which indicates that
\[ \| \Delta \tilde{u}(t) \|_2^2 \leq \frac{\tilde{c}_4(t)}{d_R}, \tag{63} \]
where \( \tilde{c}_4(t) := \left( c_1 \| \tilde{R}(t) \|_{L_1}^2 + 2c_1 \| \Delta \tilde{R} \|_{L_1}^2 + c_1'' + c_2'' \right) e^{2Ct} + 2Ct \tilde{c}_2(t) \). By \( R - \xi = \tilde{R} + \tilde{\xi} \), we have \( \| R - \xi \|_\infty \leq \| \tilde{R}(t) \|_\infty + \| \tilde{\xi}(t) \|_\infty \). Then, from the Sobolev embedding theorem and the elliptic estimate,
\[ \| \tilde{u}(t) \|_\infty \leq \begin{cases} c (\| \tilde{u} \|_2 + \| \nabla \tilde{u} \|_2 + \| \tilde{R} \|_\infty), \quad n = 1, \\ c (\| \tilde{u} \|_2 + \| \Delta \tilde{u} \|_2 + \| \tilde{R} \|_\infty), \quad n = 2, 3, \end{cases} \]
where \( \| \tilde{u}(t) \|_\infty := \| S - S^\infty \|_\infty + \| I - I^\infty \|_\infty + \| R - \xi \|_\infty + \| Z - Z^\infty \|_\infty \).

If \( n = 1 \), then by (43), (55) and (60), we have
\[ \| \tilde{u}(t) \|_\infty \leq \frac{c \left( \sqrt{c_2(T)} + \sqrt{c_3(T)} \right) + \tilde{c}_1}{\sqrt{d_R}} \]
for \( t \in [T(d_R), T] \), where \( T > 0 \) is any fixed constant.

If \( n = 2, 3 \), then by (43), (55) and (63), we have
\[ \| \tilde{u}(t) \|_\infty \leq \frac{c \left( \sqrt{c_2(T)} + \sqrt{c_4(T)} \right) + \tilde{c}_1}{\sqrt{d_R}} \]
for \( t \in [T(d_R), T] \), where \( T > 0 \) is any fixed constant. So far, we can conclude that (5) holds.

**Remark 1.** Suppose that (A1) is satisfied. If we replace the positive constants \( a, a^*, b, K, \sigma, \alpha \) and \( \mu \) with the spatially dependent functions \( a(x), a^*(x), b(x), K(x), \sigma(x), \alpha(x) \) and \( \mu(x) \) respectively, then Theorem 1.3 is still valid.

5. **Dynamics of the shadow system.** In this section, we consider the dynamics of the shadow system (2) by characterizing the basic reproduction number \( R_0 \) in the framework of [8, 37, 38]. To that end, we assume that the susceptible foxes become infected at the general incidence rate \( f(x, S, \xi) \). Namely, \( \beta(x)S \xi \) is replaced by \( f(x, S, \xi) \) in (2). For any \( x \in \Omega \), \( f(x, S, \xi) \) is supposed to satisfy:

(\text{H}_1) \quad f(x, S, \xi) = 0 \text{ whenever } S = 0 \text{ or } \xi = 0;

(\text{H}_2) \quad f(x, S, \xi) \geq 0 \text{ whenever } S \geq 0 \text{ and } \xi \geq 0;

(\text{H}_3) \quad f(x, S, \xi) \text{ is 2-times continuously differentiable with respect to } x, S \text{ and } \xi;

(\text{H}_4) \quad f_S(x, S, 0) = 0 \text{ whenever } S > 0, \text{ and } f_\xi(x, S, \xi) \geq 0(\neq 0) \text{ whenever } S, \xi \geq 0.

Clearly, \( \beta(x)S \xi \) is one of the prototypes of \( f(x, S, \xi) \) satisfying the aforementioned conditions.

By (\text{H}_1), system (2) admits a disease-free equilibrium \((K, 0, 0, 0)\). Linearizing the \( I \)-equation and \( \xi \)-equation around \((K, 0, 0, 0)\), we can obtain
\[
\begin{cases}
\frac{\partial I}{\partial t} = d_1 \Delta I - (\sigma + b + r)I + \frac{\partial f}{\partial \xi}(x, K, 0)\xi, \quad x \in \Omega, \ t > 0, \\
\frac{\partial \xi}{\partial t} = \frac{\sigma}{|\Omega|} \int_\Omega I dx - (\alpha + b + \mu + r)\xi, \quad t > 0, \\
\frac{\partial n}{\partial t} = 0, \quad x \in \partial \Omega, \ t > 0.
\end{cases}
\]
By (H3) and (H4), $f_{\xi}(:, K, 0) \in C(\overline{\Omega}, \mathbb{R})$ and for any $x \in \overline{\Omega}$, $f_{\xi}(x, K, 0) \geq 0(\neq 0)$. Following [37, 38], we consider the following linearized system without reinfection:

\[
\begin{align*}
\frac{\partial I}{\partial t} &= d_I \Delta I - (\sigma + b + r)I, & x \in \Omega, t > 0, \\
d_{\xi} &= \frac{\sigma}{|\Omega|} \int_{\Omega} I d\xi - (\alpha + b + \mu + r)\xi, & t > 0, \\
\partial_{\nu} I &= 0, & x \in \partial\Omega, t > 0.
\end{align*}
\]

(64)

Set

\[
X := \{\phi = (\phi_1(x), \phi_2) : \phi_1 \in C(\overline{\Omega}, \mathbb{R}), \phi_2 \in \mathbb{R}\},
\]

\[
X^+ := \{\phi \in X : \phi_1(x) \geq 0, \phi_2 \geq 0\}.
\]

Let $T(t)$ be the solution semigroup generated by (64) on $X$. Define

\[
F(x) := \begin{pmatrix}
0 & f_{\xi}(x, K, 0) \\
0 & 0
\end{pmatrix},
\]

where the entries in $F(x)$ denote the input rate of newly infected individuals.

Let $\phi \in X$ be the distribution of initial infection. Define

\[
L(\phi)(x) := \int_0^\infty F(x)T(t)\phi dt = F(x) \int_0^\infty T(t)\phi dt.
\]

By [8, 37, 38], the basic reproduction number of the shadow system (2) is given by the spectral radius of $L$, namely,

\[
R_0 := r(L).
\]

**Theorem 5.1.** Suppose that (H1)-(H4) hold. Then, the following conclusions hold true:

1. The basic reproduction number of the shadow system (2) is given by

\[
R_0 = \frac{\sigma \int_\Omega f_{\xi}(x, K, 0)dx}{(\sigma + b + r)(\alpha + b + \mu + r)|\Omega|}. \tag{65}
\]

2. If $R_0 < 1$, then the disease-free steady state $(K, 0, 0, 0)$ is asymptotically stable for (2).

**Proof.** 1. For $\phi := (\phi_1, \phi_2) \in X$, we define

\[
B(\phi)(x) := \begin{pmatrix}
d_I \Delta \phi_1(x) - (\sigma + b + r)\phi_1(x) \\
\frac{\sigma}{|\Omega|} \int_{\Omega} \phi_1(x)dx - (\alpha + b + \mu + r)\phi_2
\end{pmatrix}.
\]

From Theorem B.2 in Appendix, $T(t)$ is a positive semigroup in the sense that $T(t)X^+ \subseteq X^+$ for all $t \geq 0$. Since $B$ is the generator of the semigroup $T(t)$ on $X$, in view of [36, Theorem 3.12], $B$ is a resolvent-positive operator. A similar argument shows that $\Phi := B + F$ is a resolvent-positive operator.

Let $\lambda \in \sigma(B)$ denote the spectral value of $B$ in $\Omega$ subject to the homogenous Neumann boundary condition. For brevity, we define $B_1 := d_I \Delta - (\sigma + b + r)$. Then, either $\lambda \in \sigma(B_1)$ or $\lambda = -(\alpha + b + \mu + r)$. Since $s(B_1) := \sup\{Re\lambda : \lambda \in \sigma(B_1)\} = -(\alpha + b + r) < 0$, we have $s(B) < 0$.

Thus, it follows from [36, Theorem 3.12] that $L = -FB^{-1}$, where $-B^{-1}\phi = \int_0^\infty T(t)\phi dt$ for $\phi := (\phi_1(x), \phi_2) \in X$. Then, a direct computation leads to

\[
L(\phi)(x) = \left(\frac{\sigma \int_\Omega f_{\xi}(x, K, 0)\phi_1(x)dx}{(\alpha + b + \mu + r)(\sigma + b + r)|\Omega|} + \frac{f_{\xi}(x, K, 0)}{\alpha + b + \mu + r}\phi_2, 0\right)^T.
\]
Define $Y := \{ \phi \in X : \phi_2 = 0 \}$. Then, $L(X) \subset Y$. Let $L_Y$ be the restriction of $L$ to $Y$. Then, $L_Y$ is a linear operator on $Y$, and for any $\phi \in Y$,

$$L_Y(\phi)(x) = \left( \frac{\sigma f_\xi(x, K, 0)}{(\alpha + b + \mu + r)(\alpha + b + r)|\Omega|} \int_\Omega \phi_1(x)dx, \quad 0 \right)^T,$$

and for all integers $m \geq 1$,

$$L^m_Y(\phi)(x) = \left( \int_\Omega f_R(x, K, 0)dx \int_\Omega \phi_1(x)dx, \quad 0 \right)^T,$$

with $R_0$ defined in (65). Then, $r(L_Y) = R_0$. For $m \geq 2$, by $L^m = L^{m-1}_Y L$, we have $||L^m_Y|| \leq ||L^{m-1}_Y|| ||L||$. Hence, $r(L) = r(L_Y) = R_0$. Therefore, $R_0$ is the basic reproduction number.

2. Since $B, \Phi = B + F$ are resolvent-positive operators, $s(B) < 0$ and $F$ is a positive linear operator, by [36, Theorem 3.5], $s(\Phi)$ has the same sign as $r(-FB^{-1}) - 1 = R_0 - 1$.

The linearized system of system (2) around $(K, 0, 0, 0)$ is given by

$$\begin{align*}
\frac{\partial S}{\partial t} &= d_S \Delta S - r S - r I - (r + f_\xi(x, K, 0)) \xi + (a^* - r) Z, \quad x \in \Omega, \ t > 0, \\
\frac{\partial I}{\partial t} &= d_I \Delta I - (\sigma + b + r) I + f_\xi(x, K, 0) \xi, \quad x \in \Omega, \ t > 0, \\
\frac{d \xi}{dt} &= \frac{\sigma}{|\Omega|} \int_\Omega I dx - (\alpha + b + \mu + r) \xi, \quad t > 0, \\
\frac{\partial Z}{\partial t} &= d_Z \Delta Z + \mu \xi - a^* Z, \quad x \in \Omega, \ t > 0, \\
\frac{\partial \nu}{\partial t} &= \partial_{\nu} S = \partial_{\nu} I = \partial_{\nu} Z = 0, \quad x \in \partial \Omega, \ t > 0,
\end{align*}$$

(66)

with its corresponding linear operator defined on Banach space $C(\Omega, \mathbb{R}) \times C(\Omega, \mathbb{R}) \times \mathbb{R} \times C(\Omega, \mathbb{R})$:

$$\tilde{\Phi}(\phi_1, \phi_2, \phi_3, \phi_4) := \begin{pmatrix}
d_S \Delta \phi_1 - r \phi_1 - r \phi_2 - (r + f_\xi(x, K, 0)) \phi_3 + (a^* - r) \phi_4 \\
d_I \Delta \phi_2 - (\sigma + b + r) \phi_2 + f_\xi(x, K, 0) \phi_3 \\
\frac{\sigma}{|\Omega|} \int_\Omega \phi_2 dx - (\alpha + b + \mu + r) \phi_3 \\
\partial_\nu \phi_4 + \mu \phi_3 - a^* \phi_4
\end{pmatrix}.$$

We consider the eigenvalues of $\Phi$ and $\tilde{\Phi}$ subject to the homogeneous Neumann boundary conditions. Note that every nonnegative spectral value of $\tilde{\Phi}$ is also a spectral value of operator $\Phi$. By $R_0 < 1$, we have $s(\Phi) < 0$, and then $s(\tilde{\Phi}) < 0$. Let $Q(t)$ be the solution semigroup of system (66). It then follows from [36, Theorem 3.14] that $\omega(Q) = s(\tilde{\Phi}) < 0$. Therefore, by [7, Theorem 2.1], we conclude that $(K, 0, 0, 0)$ is asymptotically stable for (2).

In the case $f(x, S, \xi) = \beta(x) S \xi$, we establish instability results concerning system (2) in the following theorem.

**Theorem 5.2.** If $R_0 > 1$, then there exists $\varepsilon_0 > 0$ such that any positive solution of (2) satisfies $\limsup_{t \to \infty} \|(S(\cdot, t), I(\cdot, t), \xi(t), Z(\cdot, t)) - (K, 0, 0, 0)\|_\infty \geq \varepsilon_0$. 

Proof. For any given \( \varepsilon \in (0, K) \), we consider the eigenvalue problem of

\[
\begin{aligned}
d_t \Delta \phi_1 & - (\sigma + b) \phi_1 - \frac{r(K + 4\varepsilon)}{K} \phi_1 + \beta(x)(K - \varepsilon) \phi_2 = \lambda \phi_1, & \quad x \in \Omega, \\
\sigma \int_{\Omega} \phi_1 dx & - (\alpha + b + \mu) \phi_2 - \frac{r(K + 4\varepsilon)}{K} \phi_2 = \lambda \phi_2, & \quad x \in \Omega, \\
\partial_n \phi_1 & = 0, & \quad x \in \partial \Omega.
\end{aligned}
\]

(67)

By Lemma C.1 (in Appendix C), (67) has its principle eigenvalue \( \lambda^* \) and the corresponding positive eigenfunction \( \phi^*_\varepsilon > 0 \) on \( \overline{\Omega} \). In particular, when \( \varepsilon = 0 \),

\[
\lambda^* = \frac{-(\sigma + 2b + 2r + \alpha + \mu) + \sqrt{(\sigma - \alpha - \mu)^2 + 4\overline{\beta}k\sigma}}{2},
\]

where \( \overline{\beta} := \frac{1}{|\Omega|} \int_{\Omega} \beta(x)dx \).

Since \( R_0 > 1 \), we have \( \lambda^* > 0 \). Since \( \lim_{\varepsilon \to 0} \lambda^*_\varepsilon = \lambda^* > 0 \), we can fix \( \varepsilon_0 \) sufficiently small, such that \( \lambda^*_\varepsilon_0 > 0 \). To reach a contradiction, we assume that there exists a positive solution \( (S, I, \xi, Z) \) of (2) such that

\[
\limsup_{t \to \infty} \|(S, I, \xi, Z) - (K, 0, 0, 0)\|_\infty < \varepsilon_0.
\]

(68)

Then, there exists a sufficiently large \( t_0 > 0 \), such that for all \( t \geq t_0 \),

\[
\begin{aligned}
\frac{\partial I}{\partial t} & \geq d_t \Delta I - (\sigma + b)I - \frac{r(K + 4\varepsilon_0)}{K} I + \beta(x)(K - \varepsilon_0)\xi, \\
\frac{d\xi}{dt} & \geq \frac{\sigma}{|\Omega|} \int_{\Omega} I dx - (\alpha + b + \mu)\xi - \frac{r(K + 4\varepsilon_0)}{K} \xi,
\end{aligned}
\]

Since \( (I(\cdot, t_0), \xi(t_0)) \gg 0 \) in \( X \), we can choose a sufficiently small \( \rho > 0 \) such that \( (I(\cdot, t_0), \xi(t_0)) \geq \rho \phi^*_\varepsilon_0 \). One can verify that \( \rho e^{\lambda^*_\varepsilon_0(t-t_0)} \phi^*_\varepsilon_0 \) is a solution of the following linear system:

\[
\begin{aligned}
\frac{\partial I}{\partial t} & = d_t \Delta I - (\sigma + b)I - \frac{r(K + 4\varepsilon_0)}{K} I + \beta(x)(K - \varepsilon_0)\xi, & \quad x \in \Omega, \ t > t_0, \\
\frac{d\xi}{dt} & = \frac{\sigma}{|\Omega|} \int_{\Omega} I dx - (\alpha + b + \mu)\xi - \frac{r(K + 4\varepsilon_0)}{K} \xi, & \quad t > t_0, \\
\partial_n I & = 0, & \quad x \in \partial \Omega, \ t > t_0.
\end{aligned}
\]

Then, by Theorem B.2 (in Appendix B), we have

\[
(I(\cdot, t), \xi(t)) \geq \rho e^{\lambda^*_\varepsilon_0(t-t_0)} \phi^*_\varepsilon_0, \quad x \in \Omega, \ t \geq t_0.
\]

Hence, \( I(x, t) \) and \( \xi(t) \) approach \( \infty \) as \( t \to \infty \), which is a contradiction to (68). \( \square \)

A. Appendix. Consider the following reaction-diffusion system

\[
\begin{aligned}
\frac{\partial u_i}{\partial t} & = d_i \Delta u_i + F_i(x, u_1, \ldots, u_m), & \quad \text{in } \Omega \times (0, \infty), \\
\partial_n u_i & = 0, & \quad \text{on } \partial \Omega \times (0, \infty), \\
u_i(x, 0) & = \phi_i(x), & \quad \text{in } \Omega, \\
i & = 1, 2, \ldots, m,
\end{aligned}
\]

(69)

where \( d_i > 0(i = 1, \ldots, m) \) are constants. Let \( u := (u_1, \ldots, u_m) \), \( F := (F_1, \ldots, F_m) \) and \( \phi := (\phi_1, \ldots, \phi_m) \), \( X_i = C(\Omega, \mathbb{R}) \) with the usual supremum norm, and \( X^+_i \)
the cone of nonnegative functions in \( X_i \). Define \( \|u\|_{\infty} := \sum_{i=1}^{m} \|u_i\|_{\infty} \) for \( u = (u_1, \ldots, u_m) \in \prod_{i=1}^{m} X_i \).

We summarize Theorem 3.1 and Corollary 3.2 of [35, Chapter 7] as follows.

**Lemma A.1.** Suppose that \( F : \bar{\Omega} \times \mathbb{R}^m \rightarrow \mathbb{R}^m \) is \( C^2 \) continuous in \((x,u)\) and satisfies \( F_i(x,u) \geq 0 \) whenever \( x \in \bar{\Omega}, u \in \mathbb{R}^m \) and \( u_i = 0 \). Then, for each \( \phi \in \prod_{i=1}^{m} X_i^+ \), (69) has a unique noncontinuable mild solution \( u(t) = u(t,\phi) \in \prod_{i=1}^{m} X_i^+ \) defined on \([0,T]\), where \( T = T(\phi) \leq \infty \). Furthermore, the following properties hold:

1. \( u(x,t) = [u(t)](x) \) is a classical solution of (69), in the sense that \( D_1u_i, D_2u_i, \ D_2^2u_i \) exist and are continuous for \( x,t \in \Omega \times (0,T) \). Furthermore, the derivatives \( D_1u_i \) are continuous on \( \bar{\Omega} \times (0,T) \), and \( u_i \) is continuous on \( \Omega \times [0,T) \).

2. If \( T < \infty \), then \( \|u(t)\|_{\infty} \rightarrow \infty \) as \( t \rightarrow T \).

**B. Appendix.** In this section, we state and prove comparison principle which is needed in the proofs of Theorems 5.1 and 5.2. For any fixed \( T > 0 \), we consider the following general linear system:

\[
\begin{align*}
\frac{\partial I}{\partial t} &= d_1 \Delta I + a_{11}(x,t)I + a_{12}(x,t)\xi, \quad \text{in } \Omega \times (0,T], \\
\frac{d\xi}{dt} &= \frac{a_{21}(t)}{\|\Omega\|} \int_{\Omega} I(x,t)dx + a_{22}(t)\xi, \quad \text{in } (0,T], \\
\partial_{\nu} I &= 0, \quad \text{on } \partial\Omega \times (0,T],
\end{align*}
\]

where \( a_{11}(x,t) \), \( a_{12}(x,t) \) are bounded on \( \overline{Q}_T \), \( a_{21}(t) \), \( a_{22}(t) \) are bounded on \([0,T]\). For simplicity, we introduce the following notations:

\[
\begin{align*}
\mathcal{L}_1 I := \frac{\partial I}{\partial t} - d_1 \Delta I, \quad \mathcal{L}_2 \xi := \frac{d\xi}{dt}, \quad T(t) := \frac{1}{|\Omega|} \int_{\Omega} I(x,t)dx.
\end{align*}
\]

**Lemma B.1.** Let \( \partial\Omega \in C^2 \), \( I(x,t) \in C(\overline{Q}_T) \cap C^{2,1}(Q_T) \) and \( \xi(t) \in C([0,T]) \). Assume that the following conditions hold:

1. \( a_{12}(x,t) \geq 0 \) for \( (x,t) \in Q_T \), \( a_{21}(t) \geq 0 \) for \( t \in (0,T] \);
2. \( \mathcal{L}_1 I - a_{11} I - a_{12} \xi < 0 \) for \( (x,t) \in Q_T \), \( \mathcal{L}_2 \xi - a_{21} \xi - a_{22} \xi < 0 \) for \( t \in (0,T] \);
3. For any \( x \in \Omega \), \( I(x,0) < 0 \), \( \xi(0) < 0 \);
4. For \( (x,t) \in \partial\Omega \times (0,T], \partial_{\nu} I(x,t) \leq 0 \).

Then, we have

\[
I(x,t) < 0 \text{ on } \overline{Q}_T, \quad \xi(t) < 0 \text{ in } (0,T].
\]

**Proof.** Let \( I(x,t) = I_1(x,t)e^{\eta t}, \xi(t) = \xi_1(t)e^{\eta t} \), where \( \eta > 0 \) is arbitrarily chosen. Then, by condition 2, we have

\[
\mathcal{L}_1 I_1 + \tilde{a}_{11} I_1 - a_{12} \xi_1 < 0 \text{ in } Q_T, \quad \mathcal{L}_2 \xi_1 - a_{21} \xi_1 + a_{22} \xi_1 < 0 \text{ in } (0,T].
\]

(71) where \( \tilde{a}_{11}(x,t) = \eta - a_{11}(x,t) \) and \( \tilde{a}_{22}(t) = \eta - a_{22}(t) \). Since \( a_{11}(x,t) \) is bounded on \( \overline{Q}_T \), we can choose sufficiently large \( \eta \) such that \( \tilde{a}_{11}(x,t) > 0 \) for \( x,t \in \overline{Q}_T \).

Since \( \xi_1(t) \in C([0,T]) \) with \( \xi_1(0) = \xi(0) < 0 \) and \( I_1(x,t) \in C(\overline{Q}_T) \) with \( I_1(x,0) = I(x,0) < 0 \) for \( x \in \Omega \), there exists a \( \rho > 0 \), such that \( \xi_1(t) < 0 \) and \( I_1(x,t) < 0 \) for \( x,t \in \overline{Q}_\rho \).
Define
\[ \Lambda := \{ t : t \leq T, \xi_1(s) < 0 \text{ and } I_1(x, s) < 0, \forall x \in \overline{\Omega}, 0 \leq s < t \} . \]

Then \( t^* = \sup \Lambda \) exists and \( 0 < t^* \leq T \). It follows from the definition of \( \Lambda \) that
\[ \xi_1(t) \leq 0 \text{ on } [0, t^*], \quad I_1(x, t) \leq 0 \text{ on } \overline{Q}_t. \tag{72} \]

We are now proving that (70) holds by using the contradiction arguments.

**Case 1.** Suppose that \( \xi_1(t^*) = 0 \). Thus, it follows from the definition of \( t^* \) that \( \xi_1(t) < 0 \) for \( 0 \leq t < t^* \). Then, \( \xi_1(t^*) \geq 0 \). Together with (72) and \( a_{21}(t) \geq 0 \) for \( t \in (0, T] \), we obtain that
\[ [\mathcal{L}_2\xi_1 - a_{21}I_1 + \bar{a}_{22}\xi_1]_{t^*} \geq 0, \]
which contradicts with the second inequality of (71).

**Case 2.** Suppose there exists \( x^* \in \Omega \) such that \( I_1(x^*, t^*) = 0 \). By the definition of \( t^* \), we have \( I_1(x, t) < 0 \) for \( (x, t) \in \overline{\Omega} \times [0, t^*) \). Then, it implies that \( I_1(x, t) \) reaches its maximum at \( (x^*, t^*) \) in \( Q_{t^*} \). Hence,
\[ \frac{\partial I_1(x^*, t^*)}{\partial t} \geq 0, \quad \Delta I_1(x^*, t^*) \leq 0. \]

By (72) and \( a_{12}(x, t) \geq 0 \) for \( (x, t) \in Q_T \), we then obtain
\[ [\mathcal{L}_1I_1 + \bar{a}_{11}I_1 - a_{12}\xi_1]_{(x^*, t^*)} \geq 0, \]
which is a contradiction to the first inequality of (71).

**Case 3.** Suppose there exists \( x^* \in \partial\Omega \) such that \( I_1(x^*, t^*) = 0 \). Note that \( I_1(x, t) < 0 \) for \( (x, t) \in \overline{\Omega} \times [0, t^*) \) and \( I_1(x, t^*) < 0 \) for \( x \in \Omega \). Then, it follows that \( I_1(x, t) < 0 = I_1(x^*, t^*) \) in \( Q_{t^*} \). Since \( a_{12}(x, t) \geq 0 \) for \( (x, t) \in Q_T \), by (71) and (72), we have
\[ \frac{\partial I_1}{\partial t} - d_t \Delta I_1 + \bar{a}_{11}I_1 \leq \mathcal{L}_1I_1 + \bar{a}_{11}I_1 - a_{12}\xi_1 < 0 \text{ in } Q_{t^*}. \]

By Hopf boundary lemma ([34]), we have \( \partial_n I(x^*, t^*) > 0 \), which contradicts with condition 4.

So far, we can conclude that, \( I(x, t) < 0 \) for \( (x, t) \in \overline{Q}_T \) and \( \xi(t) < 0 \) for \( t \in (0, T] \).

By Lemma B.1, we can get the following theorem:

**Theorem B.2.** Assume \( \partial \Omega \in C^2 \), \( a_{12}(x, t) \geq 0 \) for \( (x, t) \in Q_T \), \( a_{21}(t) \geq 0 \) for \( t \in (0, T] \). Let \( I(x, t) \in C(\overline{Q}_T) \cap C^2(\Omega) \), \( \xi(t) \in C([0, T]) \) and satisfy
\[ \mathcal{L}_1I - a_{11}I - a_{12}\xi \leq 0 \text{ in } Q_T, \quad \mathcal{L}_2\xi - a_{21}\mathcal{T} - a_{22}\xi \leq 0 \text{ in } (0, T]. \tag{73} \]

Suppose that \( I(x, 0) \leq 0 \) for \( x \in \overline{\Omega} \), \( \xi(0) \leq 0 \) and \( \partial_n I(x, t) \leq 0 \) for \( (x, t) \in \partial\Omega \times (0, T] \). Then, we have
\[ I(x, t) \leq 0 \text{ on } \overline{Q}_T, \quad \xi(t) \leq 0 \text{ in } (0, T]. \tag{74} \]

**Proof.** Since \( a_{11}(x, t), a_{12}(x, t) \) are bounded on \( \overline{Q}_T \), \( a_{21}(t), a_{22}(t) \) are bounded on \( [0, T] \), there exists \( \delta > 0 \) such that \( \delta - a_{11} - a_{12} > 0 \) for \( i = 1, 2 \) for \( x \in \overline{\Omega} \) and \( 0 < t \leq T \). Let \( I_1(t, x) = I(x, t) - \varepsilon e^{\delta t} \) and \( \xi_1(t) = \xi(t) - \varepsilon e^{\delta t} \), where \( \varepsilon > 0 \) is arbitrarily chosen. It follows from (73) that
\[ \mathcal{L}_1I_1 - a_{11}I_1 - a_{12}\xi_1 = \mathcal{L}_1I - a_{11}I - a_{12}\xi - \varepsilon e^{\delta t} \leq 0, \]
\[ \mathcal{L}_2\xi_1 - a_{21}\mathcal{T} - a_{22}\xi_1 = \mathcal{L}_2\xi - a_{21}\mathcal{T} - a_{22}\xi - \varepsilon e^{\delta t} \leq 0. \]
In addition, \( I_1^*(x, 0) < 0 \) on \( \Omega \) and \( \xi_1^*(0) < 0 \). In view of Lemma B.1, we have
\[ I_1^*(x, t) < 0 \] on \( \partial \Omega \), \( \xi_1^*(t) < 0 \) in \( (0, T) \).
Then, letting \( \varepsilon \to 0 \), we can obtain (74), which completes the proof. \( \square \)

C. Appendix. We study the following elliptic eigenvalue problem:
\[
\begin{cases}
d_1 \Delta \phi(x) + a_{11} \phi(x) + a_{12}(x) \eta = \lambda \phi(x), & \text{in } \Omega, \\
\frac{a_{21}}{|\Omega|} \int_{\Omega} \phi(x) dx + a_{22} \eta = \lambda \eta, & \text{in } \Omega, \\
\partial_n \phi = 0, & \text{on } \partial \Omega,
\end{cases}
\] (75)
where \( d_1, a_{11}, a_{21}, a_{22} \) are nonzero constants, while \( a_{12}(x) \in C(\Omega, \mathbb{R}) \) is a spatially dependent function, which is not identically zero.

**Lemma C.1.** Suppose that \( a_{21} > 0 \) and for any \( x \in \Omega, a_{12}(x) \geq 0 (\neq 0) \). Then,
\[ \lambda^* := a_{11} + a_{22} + \sqrt{(a_{11} - a_{22})^2 + 4a_{21}a_{12}} \]
is a geometrically simple eigenvalue of (75) with a strongly positive eigenfunction \((\phi(x), \eta)\), where \( a_{12} := \frac{1}{|\Omega|} \int_{\Omega} a_{12}(x) dx \).

**Proof.** Let \( \lambda \) be the eigenvalue of (75) and \((\phi(x), \eta)\) be the corresponding eigenfunction. If \( \int_{\Omega} \phi(x) dx = 0 \), then integrating the first equation of (75) over \( \Omega \) and using boundary condition yields \( \eta \int_{\Omega} a_{12}(x) dx = 0 \). Since \( a_{12} \in C(\Omega, \mathbb{R}) \), \( a_{12}(x) \geq 0 \) and \( a_{12}(x) \neq 0 \), we have \( \int_{\Omega} a_{12}(x) dx \neq 0 \). It follows that \( \eta = 0 \). Therefore, \( \lambda \) is an eigenvalue of the following elliptic problem
\[
\begin{cases}
d_1 \Delta \phi(x) + a_{11} \phi(x) = \lambda \phi(x), & \text{in } \Omega, \\
\partial_n \phi = 0, & \text{on } \partial \Omega.
\end{cases}
\]
Thus, \( \lambda = \lambda_i := -d_1 \mu_i + a_{11}, i = 0, 1, 2, \ldots \), where \( 0 = \mu_0 < \mu_1 < \cdots < \mu_n < \cdots \) are the eigenvalues of \(-\Delta\) with homogeneous Neumann boundary condition. In particular, \( \eta = 0 \) implies that \((\phi(x), \eta)\) can never be strongly positive.

If \( \int_{\Omega} \phi(x) dx \neq 0 \), then we can obtain that \( \eta \neq 0 \) and \( \lambda \neq a_{22} \). Thus, a direct computation gives
\[ \eta = \frac{a_{21}}{(\lambda - a_{22}) |\Omega|} \int_{\Omega} \phi(x) dx. \] (76)
Substituting (76) into the first equation of (75), and consider the elliptic problem
\[
\begin{cases}
d_1 \Delta \phi(x) + a_{11} \phi(x) + \frac{a_{21}a_{12}(x)}{(\lambda - a_{22}) |\Omega|} \int_{\Omega} \phi(x) dx = \lambda \phi(x), & \text{in } \Omega, \\
\partial_n \phi = 0, & \text{on } \partial \Omega.
\end{cases}
\] (77)
Integrating the first equation of (77) over \( \Omega \) and using the fact that \( \int_{\Omega} \phi(x) dx \neq 0 \), we have
\[ a_{11} + \frac{a_{21}}{(\lambda - a_{22}) |\Omega|} \int_{\Omega} a_{12}(x) dx = \lambda. \] (78)
Solving (78), we have
\[ \lambda^\pm := a_{11} + a_{22} \pm \sqrt{(a_{11} - a_{22})^2 + 4a_{21}a_{12}}. \] (79)
If \( \lambda = \lambda^- \) holds. We assume that it is the eigenvalue of (75) and let \( (\phi^-(x), \eta^-) \) is the eigenfunction corresponding to \( \lambda^- \). Since \( \eta^- \neq 0 \), without loss of generality, we may assume that \( \eta^- > 0 \). Rewrite the second equation of (75) as follows:

\[
\frac{a_{21}}{|\Omega|} \int_\Omega \phi^-(x)dx = (\lambda^- - a_{22})\eta^-.
\]

By (79), \( \lambda^- - a_{22} < 0 \). This together with \( a_{21} > 0 \), implies that \( \int_\Omega \phi^-(x)dx < 0 \). Hence, \( \phi^-(x) \) can never be a positive function in \( \Omega \).

If \( \lambda = \lambda^+ \) holds. Then, it is clear \( \lambda^+ - a_{11} > 0 \). Suppose \( \int_\Omega \phi(x)dx = 1 \), by the standard elliptic regularity theory, we conclude (77) has a unique solution denoted by \( \phi^+(x) \). Let

\[
\eta^+ := \frac{a_{21}}{(\lambda^+ - a_{22})|\Omega|} \int_\Omega \phi^+(x)dx.
\]

It follows that \( \lambda^+ \) is the eigenvalue of (75) with the corresponding eigenfunction \( (\phi^+(x), \eta^+) \).

Since \( \int_\Omega \phi^+(x)dx > 0 \) and \( a_{12}(x) \geq 0 \) for \( x \in \overline{\Omega} \), it follows from (77) that

\[
\begin{cases}
-d_I \Delta \phi^+(x) + (\lambda^+ - a_{11})\phi^+(x) \geq 0, & \text{in } \Omega, \\
\partial_\nu \phi^+(x) = 0, & \text{on } \partial \Omega.
\end{cases}
\]

According to the strong maximum principle, we have \( \phi^+_I(x) > 0 \) for \( x \in \Omega \). This implies that

\[
\lambda^* := \lambda^+ = \frac{a_{11} + a_{22} + \sqrt{(a_{11} - a_{22})^2 + 4a_{21}a_{12}}}{2}
\]

is an eigenvalue of (75) with a strongly positive eigenfunction \( (\phi^+(x), \eta^+) \).

We now show that \( \lambda_* \) is geometrically simple. Suppose that \( (\phi(x), \eta) \) and \( (\phi^*(x), \eta^*) \) are two different eigenfunctions of the eigenvalue \( \lambda^* \). Then, we have (75)|\( \lambda = \lambda^* \) and

\[
\begin{cases}
d_I \Delta \phi^*(x) + a_{11}\phi^*(x) + a_{12}(x)\eta^* = \lambda^*\phi^*(x), & \text{in } \Omega, \\
\frac{a_{21}}{|\Omega|} \int_\Omega \phi^*(x)dx + a_{22}\eta^* = \lambda^*\eta^*, & \text{in } \Omega, \\
\partial_\nu \phi^*(x) = 0, & \text{on } \partial \Omega.
\end{cases}
\]

By the second equations of (75) and (80), we have

\[
\eta/\eta^* = \frac{\int_\Omega \phi(x)dx}{\int_\Omega \phi^*(x)dx} =: \tau > 0.
\]

Then, we have \( \eta = \tau \eta^* \). Multiplying the first equation of (75)|\( \lambda = \lambda^* \) by \( \tau \), and using the first equation of (80) to subtract it, we have

\[
d_I \Delta (\phi^*(x) - \tau \phi(x)) + (a_{11} - \lambda^*)(\phi^*(x) - \tau \phi(x)) = 0, \quad \text{in } \Omega.
\]

(81)

Since \( \lambda^* > a_{11} \), we can conclude from (81) and the homogeneous Neumann boundary conditions that \( \phi^*(x) \equiv \tau \phi(x) \). Hence, we have \( (\phi^*(x), \eta^*) \equiv \tau(\phi(x), \eta) \), which implies that \( \lambda_* \) is geometrically simple.
D. Appendix. We state the following well-known results which have been frequently used in our proof.

**Lemma D.1.** (30) Let \( \Omega \subset \mathbb{R}^n \) be a bounded domain with smooth boundary. Fix \( 1 \leq q, r \leq \infty \), the natural numbers \( k \) and \( j \). Suppose that for a real number \( \theta \) and \( j/k \leq \theta \leq 1 \), \( 1/p = j/n + \theta(1/r - k/n) + (1 - \theta)/q \). Then, for any \( u \in L^p(\Omega) \) with \( D^k u \in L^q(\Omega) \), we have \( D^j u \in L^r(\Omega) \), and there exist positive constants \( c = c(n, k, j, q, r, \theta) \) and \( c' = c'(n, k, j, q, r, \theta) \) depending on \( \Omega \), such that \( \| D^j u \|_r \leq c(n, k, j, q, r, \theta) \| D^k u \|_q \| u \|_{L^\theta} + c'(n, k, j, q, r, \theta) \| u \|_s \), where \( s > 0 \) is arbitrarily chosen. In particular, if \( 1 \leq n \leq 3 \) and \( (p, j, k, r, q, s) = (4, 1, 2, 2, 2, 2) \), we have \( \| \nabla u \|_4 \leq k_1 \| u \|_{W^2_{2}(\Omega)} \| u \|_{2}^{1 - \theta} \), where \( k_1 = k_1(n) := (c + c')n \) and \( \theta = (4 + n)/8 \).

**Lemma D.2.** The following conclusions hold true:

1. (2) Let \( \Omega \) be bounded and \( \partial \Omega \subset C^2 \). Then, there exists a \( k_2 > 0 \), independent of \( u \), such that,
   \[
   \| u \|_{W^2_{2}(\Omega)} \leq k_2(\| \Delta u \|_2 + \| u \|_2),
   \]
   for \( u \in W^2_{2}(\Omega) \cap C^1(\Omega) \) satisfying \( \partial_{\nu} u = 0 \) on \( \partial \Omega \).

2. (5) Suppose that \( u \in W^2_{2}(\Omega) \), with \( \partial_{\nu} u = 0 \) on \( \partial \Omega \). Then
   \[
   \lambda_1 \| \nabla u \|_2^2 \leq \| \Delta u \|_2^2.
   \]

3. (6) Let \( \Omega \) be a bounded domain with Lipschitz boundary. Then, for \( u \in W^2_{2}(\Omega) \), satisfying \( \partial_{\nu} u = 0 \) on \( \partial \Omega \),
   \[
   \lambda_1 \| u - \overline{u} \|_2^2 \leq \| \nabla u \|_2^2, \quad \text{with } \overline{u} := \frac{1}{|\Omega|} \int_{\Omega} u(x)dx.
   \]

4. (1) Let \( \Omega \) be a domain in \( \mathbb{R}^n \), \( j \geq 0 \) and \( k \geq 1 \) be integers and \( 1 \leq p < \infty \). Suppose that \( \Omega \) satisfies the strong local Lipschitz condition. If \( kp > n \), let \( W^p_{k}(\Omega) \rightarrow C^{j}(\Omega) \), where \( 0 < \lambda \leq k(1/p) \); and if \( n = (k - 1)p \),
   \[
   W^p_{k}(\Omega) \rightarrow C^{j}(\Omega), \quad 0 < \lambda < 1.
   \]
   In particular, if \( n = 1 \) and \( (k, p, j) = (1, 2, 0) \), then \( W^2_{2}(\Omega) \rightarrow C^{0}(\Omega) \), where \( 0 < \lambda \leq 1/2 \); If \( n = 2 \) and \( (k, p, j) = (2, 2, 0) \), then \( W^2_{2}(\Omega) \rightarrow C^{0}(\Omega) \), where \( 0 < \lambda < 1 \); If \( n = 3 \) and \( (k, p, j) = (2, 2, 0) \), then \( W^2_{2}(\Omega) \rightarrow C^{0}(\Omega) \), where \( 0 < \lambda \leq 1/2 \). Hence, there exists a constant \( c > 0 \), such that
   \[
   \| u \|_{\infty} \leq \left\{ \begin{array}{ll}
   c' \| u \|_{W^2_{2}(\Omega)}, & n = 1, \\
   c \| u \|_{W^2_{2}(\Omega)}, & n = 2, 3.
   \end{array} \right.
   \]

5. (1) Let \( \Omega \) be a domain in \( \mathbb{R}^n \) satisfying the cone condition. If \( kp > n \), let \( p \leq q \leq \infty \); if \( kp = n \), let \( p \leq q < \infty \); if \( kp < n \), let \( p \leq q \leq \infty \). Then there exists a constant \( k_3 > 0 \) depending on \( k, n, p, q \) and the dimensions of the cone \( C \) providing the cone condition for \( \Omega \), such that for all \( u \in W^k_{p}(\Omega) \),
   \[
   \| u \|_q \leq k_3 \| u \|_{W^k_{p}(\Omega)} \| u \|_{1-\theta}^\theta, \quad \text{where } \theta = n/(kp) - n/(kq).
   \]
   In particular, if \( n \leq 3 \) and \( k = 1, p = 2, 2 \leq q \leq 6 \), then
   \[
   \| u \|_q \leq k_3 \| u \|_{W^k_{2}(\Omega)} \| u \|_2^{1-\theta},
   \]
   where \( 0 < \theta < 1 \).

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E-mail address: xyz.j18153.com