ASYMPTOTIC BEHAVIOUR OF THE SOLUTIONS TO A VIRUS DYNAMICS MODEL WITH DIFFUSION

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Abstract. Asymptotic behaviour of the solutions to a basic virus dynamics model is discussed. We consider the population of uninfected cells, infected cells, and virus particles. Diffusion effect is incorporated there. First, the Lyapunov function effective to the spatially homogeneous part (ODE model without diffusion) admits the $L^1$ boundedness of the orbit. Then the pre-compactness of this orbit in the space of continuous functions is derived by the semigroup estimates. Consequently, from the invariant principle, if the basic reproductive number $R_0$ is less than or equal to 1, each orbit converges to the disease free spatially homogeneous equilibrium, and if $R_0 > 1$, each orbit converges to the infected spatially homogeneous equilibrium, which means that the simple diffusion does not affect the asymptotic behaviour of the solutions.

1. Introduction. A considerable number of studies have been made on virus dynamics. A lot of research results are obtained by mathematical models that assume spatial homogeneity. To consider the interaction among many agents, it is natural to start with ordinary differential equations, which assume the spatial homogeneity. However, diffusion effect may cause a change of qualitative behaviour of solutions. Therefore, models incorporating diffusion effect also should be discussed. For examples, Prüss, Zacher, and Schnaubelt [9] and Wang, Yang, and Kuniya [14] incorporate the spatial movement of some agents into their models.

In this paper, we consider the asymptotic behaviour of the solutions of the virus dynamics model with diffusion

\begin{align}
\frac{\partial u_1}{\partial t} &= d_1 \Delta u_1 + \lambda - mu_1 - \beta u_1 u_3, \\
\frac{\partial u_2}{\partial t} &= d_2 \Delta u_2 + \beta u_1 u_3 - au_2, \\
\frac{\partial u_3}{\partial t} &= d_3 \Delta u_3 + au_2 - bu_3,
\end{align}

(1)

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in a bounded domain $\Omega \subset \mathbb{R}^n$, where $u_1(x,t)$, $u_2(x,t)$, and $u_3(x,t)$ stand for the population density of uninfected cells, that of infected cells, and that of viruses, respectively, at the time $t$ and at the point $x \in \Omega$. We assume that the boundary $\partial \Omega$ is smooth, and impose the Neumann boundary condition

$$\frac{\partial u}{\partial \nu} = 0 \text{ on } \partial \Omega,$$

where $\nu$ is the outer unit normal vector on $\partial \Omega$, and $u = (u_1, u_2, u_3)$. In the initial condition

$$u(x,0) = u_0(x) \text{ in } \Omega,$$

we assume that $u_0 = (u_{0,1}, u_{2,0}, u_{3,0}) \in C^2(\overline{\Omega}; \mathbb{R}^3)$, $\partial u_0/\partial \nu|_{\partial \Omega} = 0$, and each component of $u_0$ is non-negative and not identically equal to zero.

Equation (1) is obtained by incorporating the diffusion terms to the ordinary differential equation (ODE) model

$$\frac{du_1}{dt} = \lambda - mu_1 - \beta u_1 u_3,$$
$$\frac{du_2}{dt} = \beta u_1 u_3 - au_2,$$
$$\frac{du_3}{dt} = aru_2 - bu_3,$$

with which Nowak and Bangham [8] considers the persistent infection of HIV. Thus, uninfected cells are produced at a constant rate $\lambda$, have a death rate $m$, and become infected at a rate $\beta u_3$. The death rates of infected cells and viruses are denoted, respectively, by $a$ and $b$. Each infected cell releases $r$ virus particles when it bursts.

Equation (4) has two equilibria $u^\diamond = (u_1^\diamond, 0, 0)$ and $u^* = (u_1^*, u_2^*, u_3^*)$, where

$$u_1^\diamond = \frac{\lambda}{m}, \quad u_1^* = \frac{b}{r \beta}, \quad u_2^* = \frac{bm}{ar \beta} (R_0 - 1), \quad u_3^* = \frac{m}{\beta} (R_0 - 1).$$

Here, $R_0 = r \beta \lambda / (bm)$ is the basic reproduction number[1]. The equilibrium $u^\diamond$ is the disease free state. The equilibrium $u^*$ is the interior equilibrium, whose elements are all positive, if and only if $R_0 > 1$.

We put

$$\Phi(s) = s - \log s - 1 \quad (s > 0).$$

For Equation (4), Korobeinikov [6] proposes the Lyapunov functions

$$U(u) = u_1^\diamond \Phi \left( \frac{u_1}{u_1^\diamond} \right) + u_2 + \frac{1}{r} u_3$$

for $u^\diamond$, and

$$V(u) = u_1^* \Phi \left( \frac{u_1}{u_1^*} \right) + u_2^* \Phi \left( \frac{u_2}{u_2^*} \right) + \frac{u_3^*}{r} \Phi \left( \frac{u_3}{u_3^*} \right)$$

for $u^*$, and proves global stability of $u^\diamond$ if $R_0 \leq 1$, and that of $u^*$ if $R_0 > 1$.

We put $f(u) = (f_1(u), f_2(u), f_3(u))$ and

$$f_1(u) = \lambda - mu_1 - \beta u_1 u_3,$$
$$f_2(u) = \beta u_1 u_3 - au_2,$$
$$f_3(u) = aru_2 - bu_3.$$
The derivatives $\dot{U}_4$ and $\dot{V}_4$ along the solutions to (4) are, respectively,

$$\dot{U}_4(u) = \nabla U(u) \cdot f(u) = mu_1^* \left( 2 - \frac{u_1}{u_1^*} - \frac{u_3}{u_1} \right) + \frac{b}{r} (R_0 - 1)u_3,$$

and

$$\dot{V}_4(u) = \nabla V(u) \cdot f(u) = mu_1^* \left( 2 - \frac{u_1}{u_1^*} - \frac{u_1^*}{u_1} \right) + au_2^* \left( 3 - \frac{u_1^*}{u_1} - \frac{u_2u_3^*}{u_5u_3} - \frac{u_1u_2^*u_3}{u_1^*u_2u_3} \right).$$

(9)

(10)

By the inequality on arithmetic and geometric means, the right-hand side of $\dot{U}_4(u)$ is non-positive for any $u_1, u_3 > 0$ if $R_0 \leq 1$, and similarly, the right-hand side of $\dot{V}_4(u)$ is non-positive for any $u_1, u_2, u_3 > 0$ and $u_1^*, u_2^*, u_3^* > 0$. We shall use these relations in Sections 2 and 5.

We consider the asymptotic behaviour of the solution to (1), (2), and (3), mainly using the method in Latos, Suzuki, and Yamada [7]. Note that the spatially homogeneous steady solutions to (1) are $u(x,t) = u^\circ$ and $u(x,t) = u^*$. We can use the Lyapunov functions (6) and (7) to show that, as $t \to \infty$, each solution $u(\cdot, t)$ to (1) converges in $C(\overline{\Omega}; \mathbb{R}^3)$ to the spatially homogeneous equilibrium solution $u(x,t) = u^\circ$ if $R_0 \leq 1$, and to $u(x,t) = u^*$ if $R_0 > 1$.

**Theorem 1.1.** Let $u = (u_1, u_2, u_3)$ be the solution to (1), (2), and (3). Then it holds that

$$u(\cdot, t) \to \hat{u} \text{ in } C(\overline{\Omega}; \mathbb{R}^3) \text{ as } t \to \infty,$$

(11)

where $\hat{u} = u^\circ$, the disease free spatially homogeneous equilibrium, if $R_0 \leq 1$, and $\hat{u} = u^*$, the infected spatially homogeneous equilibrium, if $R_0 > 1$.

Here, the Lyapunov functions play two roles. First, they establish the $L^1$ bound of the orbit. Second, they provide the omega limit argument by the pre-compactness of the orbit in $C(\overline{\Omega}; \mathbb{R}^3)$. For this property to show, we use the semigroup estimates and the standard parabolic regularity.

This paper is composed of seven sections and two appendices. Sections 2, 3, and 4 are devoted to the $L^1$, $L^p$, and $W^{2,p}$ a priori estimates, respectively, and Theorem 1.1 is proven in Section 5. Section 6 shows some results of numerical simulations. Section 7 is a discussion, and the positivity of the solution and the semigroup estimate used for the proof are stated in Appendixes A and B, respectively. Henceforth, $\|v\|_p = \|v(\cdot)\|_{L^p(\Omega)}$ denotes the standard $L^p$ norm of the function $v = v(x)$ ($x \in \Omega$).

2. $L^1$ bound of the solution. Having assumed the smooth initial value, we have unique existence of the classical solution local-in-time, which is extended to global-in-time if we can derive a priori bound on its $L^\infty$ norm. In this section we show the following proposition.

**Proposition 2.1.** The solution $u = (u_i(x,t))$ to (1), (2), and (3) is $L^1$-bounded, that is, there exists a positive constant $C_1$ such that

$$\|u_i(\cdot, t)\|_1 \leq C_1 \quad (t > 0; i = 1, 2, 3).$$

(12)
and

$$\mathcal{V}(u) = \mathcal{V}(u)(t) = \int_{\Omega} V(u(x,t)) \, dx$$  \hspace{1cm} (13)$$

along the classical solution $u = u(x,t)$ to (1), (2), and (3), defined on $\overline{\Omega} \times [0, T]$ for some $T > 0$. This use is justified by the positivity of the solution assured by the following proposition.

**Proposition 2.2.** Let initial function $u_0$ satisfy $u_{i0}(x) \geq 0$ and $u_{i0} \neq 0$ on $\overline{\Omega}$, for $i = 1, 2, 3$. Then it holds that

$$u_i(x,t) > 0 \quad (x \in \overline{\Omega}, \, 0 < t \leq T; \, i = 1, 2, 3).$$

**Proof.** The reaction terms $f_1, f_2, \text{ and } f_3$ defined by (8) satisfy

$$f_1(0, u_2, u_3) = \lambda > 0, \quad f_2(u_1, 0, u_3) = \beta u_1 u_2 \geq 0, \quad f_3(u_1, u_2, 0) = aru_2 \geq 0$$

for $u_1, u_2, u_3 \geq 0$, which implies $u_i(x,t) > 0$ in $\overline{\Omega} \times (0, T]$ from the assumption, by Proposition A.1 in Appendix (i = 1, 2, 3).

We note that the spatially homogeneous steady solutions to Equation (1) coincide with the equilibria of the corresponding ODE model (4). First we consider the case $R_0 \leq 1$.

**Proposition 2.3.** Suppose $R_0 \leq 1$, and let $u = (u_i(x,t))$ be the solution to (1), (2), and (3). Then there exists a positive constant $C_2$ such that

$$\left\| \Phi \left( \frac{u_1(\cdot, t)}{u_i^0} \right) \right\|_1 \leq C_2, \quad \|u_2(\cdot, t)\|_1 \leq C_2, \quad \|u_3(\cdot, t)\|_1 \leq C_2 \quad (t > 0).$$

**Proof.** For $U(u)$ defined by (12), the derivative $\dot{U}(u)$ along the solution to (1) satisfies

$$\dot{U}(u) = \frac{d}{dt} \int_{\Omega} U(u(x,t)) \, dx$$

$$= \int_{\Omega} \frac{\partial}{\partial t} \left\{ u_1(x,t) - u_1^0 \log u_1(x,t) - u_1^0 \right\} + u_2(x,t) + \frac{1}{r} u_3(x,t) \right\} \, dx$$

$$= \int_{\Omega} \left\{ \left( 1 - \frac{u_1^0}{u_1} \right) \{ d_1 \Delta u_1(x,t) + f_1(u(x,t)) \} \right. \right. \right.$$

$$+ \{ d_2 \Delta u_2(x,t) + f_2(u(x,t)) \} + \frac{1}{r} \{ d_3 \Delta u_3(x,t) + f_3(u(x,t)) \} \right\} \, dx$$

$$= \int_{\Omega} \left\{ \left( 1 - \frac{u_1^0}{u_1} \right) d_1 \Delta u_1 + d_2 \Delta u_1 + \frac{d_3}{r} \Delta u_3 \right\} \, dx + \int_{\Omega} \dot{U}(u) \, dx.$$ 

Hence it holds that

$$\dot{U}(u) = - \int_{\Omega} \frac{d_1 u_1^0}{u_1^0} |\nabla u_1|^2 \, dx + \int_{\Omega} \dot{U}(u) \, dx$$

by Green’s formula and the Neumann condition (2). Here, $\dot{U}(4)$ stands for the right-hand side of (9), and hence the last term of the right-hand side on (14) is non-positive. We thus end up with

$$\dot{U}(u) = \frac{d}{dt} \int_{\Omega} U(u(x,t)) \, dx \leq 0.$$  \hspace{1cm} (15)
Hence there exists a constant $C_3$ that satisfies
\[
\int_{\Omega} U(u(x,t)) \, dx = \int_{\Omega} \left\{ u_1^\alpha \Phi \left( \frac{u_1(x,t)}{u_1^\alpha} \right) + u_2(x,t) + \frac{1}{r} u_3(x,t) \right\} \, dx 
\leq C_3 \quad (t > 0).
\]
This proves the proposition because $\Phi(s) \geq 0$ and $u_2, u_3 > 0$. \hfill \qed

In the case $R_0 > 1$, we have a similar result.

**Proposition 2.4.** Suppose $R_0 > 1$, and let $u = (u_i(x,t))$ be the solution of (1) and (2), and (3). Then there exists a positive constant $C_4$ such that
\[
\left\| \Phi \left( \frac{u_i(\cdot,t)}{u_i^*} \right) \right\|_{L_1} \leq C_4 \quad (t > 0; i = 1, 2, 3).
\]

**Proof.** For $\mathcal{V}(u)$ defined by (13), its derivative along the solution of (1) becomes
\[
\dot{\mathcal{V}}(1)(u) = \frac{d}{dt} \int_{\Omega} V(u(x,t)) \, dx 
\]
\[
= \int_{\Omega} \left\{ \left( 1 - \frac{u_1^*}{u_1} \right) (d_1 \Delta u_1 + f_1(u)) + \left( 1 - \frac{u_2^*}{u_2} \right) (d_2 \Delta u_2 + f_2(u)) \right. 
\]
\[
+ \frac{1}{r} \left( 1 - \frac{u_3^*}{u_3} \right) (d_3 \Delta u_3 + f_3(u)) \left\} dx 
\]
\[
= \int_{\Omega} \left\{ \left( 1 - \frac{u_1^*}{u_1} \right) d_1 \Delta u_1 + \left( 1 - \frac{u_2^*}{u_2} \right) d_2 \Delta u_2 + \frac{1}{r} \left( 1 - \frac{u_3^*}{u_3} \right) d_3 \Delta u_3 \right\} \, dx 
\]
\[
+ \int_{\Omega} \dot{\mathcal{V}}(4)(u) \, dx 
\]
\[
= -\int_{\Omega} \left\{ \frac{d_1 u_1^2}{u_1^*} |\nabla u_1|^2 + \frac{d_2 u_2^*}{u_2^*} |\nabla u_2|^2 + \frac{d_3 u_3^*}{r u_3^*} |\nabla u_3|^2 \right\} \, dx + \int_{\Omega} \dot{\mathcal{V}}(4)(u) \, dx \tag{16}
\]
by Green's formula and the Neumann condition (2). Here, $\dot{\mathcal{V}}(4)$ stands for the right-hand side of (10), and hence the last term on the right-hand side on (16) is non-positive. We thus end up with
\[
\dot{\mathcal{V}}(1)(u) = \frac{d}{dt} \int_{\Omega} V(u(x,t)) \, dx \leq 0. \tag{17}
\]
Hence there exists a constant $C_5$ that satisfies
\[
\int_{\Omega} V(u(x,t)) \, dx = \int_{\Omega} \left\{ u_1^\alpha \Phi \left( \frac{u_1}{u_1^\alpha} \right) + u_2 \Phi \left( \frac{u_2}{u_2^*} \right) + \frac{u_3^*}{r} \Phi \left( \frac{u_3}{u_3^*} \right) \right\} \, dx 
\leq C_5 \quad (t > 0).
\]
Since $\Phi(s) \geq 0$, this proves the proposition. \hfill \qed

To complete the proof of Proposition 2.1, we note the following proposition.

**Proposition 2.5.** Any function $v = v(x) > 0$ on $\Omega$ satisfies
\[
\|v\|_1 \leq 2\|\Phi(v)\|_1 + s_0|\Omega|,
\]
where $|\Omega|$ denotes the volume of $\Omega$, and $s_0$ is the root of $\Phi(s/2) = \log 2$ with $s > 2$. 

Proof. The equation $\Phi(s/2) = \log 2$ has the unique root $s = s_0$ in $\{s \mid s > 2\}$, because $\Phi(s)$ is strictly increasing in $\{s \mid s \geq 1\}$, $\Phi(1) = 0$, and $\lim_{s \to +\infty} \Phi(s) = +\infty$. By the monotonicity of $\Phi(s)$ in $\{s \mid s \geq 1\}$, $\Phi(s/2) > \log 2$ if $s > s_0$. On the other hand, by the definition (5), we have
\[
\Phi\left(\frac{s}{2}\right) - \log 2 = \Phi\left(\frac{s}{2}\right) - \frac{s}{2}.
\]
Hence $\Phi\left(\frac{s}{2}\right) - \frac{s}{2}$ if and only if $\Phi\left(\frac{s}{2}\right) > \log 2$. Thus we have \[\Phi\left(\frac{s}{2}\right) > \frac{s}{2} \text{ for } s > s_0.\]
(18)

Given $v = v(x) > 0$, let $\Omega_1 = \{x \in \Omega \mid v(x) > s_0\}$, $\Omega_2 = \Omega \setminus \Omega_1$. Then (18) implies
\[
\|v\|_1 = \|v\|_{L^1(\Omega_1)} + \|v\|_{L^1(\Omega_2)} \leq \|2\Phi(v)\|_{L^1(\Omega_1)} + s_0|\Omega_2| \\
\leq 2\|\Phi(v)\|_1 + s_0|\Omega|.
\]

We are ready to give the following proof, regardless of the value $R_0$.

Proof of Proposition 2.1. If
\[
\left\| \Phi\left(\frac{u_i(\cdot,t)}{u_i^*}\right) \right\|_1 \leq C_6 \quad (t > 0),
\]
Proposition 2.5 implies
\[
\left\| \frac{u_i(\cdot,t)}{u_i^*} \right\|_1 \leq 2C_6 + s_0|\Omega|,
\]
and hence
\[
\|u_i(\cdot,t)\|_1 \leq 2u_i^*C_6 + u_i^*s_0|\Omega| \quad (t > 0).
\]
Then Propositions 2.3 and 2.4 prove the proposition. □

3. $L^p$ bound of the solution. The $L^1$ bound of the solution is improved to $L^p$ bound of the solution for $1 \leq p < \infty$, including its derivatives by the method of Latos, Suzuki, and Yamada [7]. In this section, we show the following proposition.

Proposition 3.1. Let $u = (u_i(x,t))$ be the solution to (1), (2), and (3). Then for any $p$ ($1 \leq p < \infty$), there exists a constant $C_7$ such that
\[
\|u_i(\cdot,t)\|_p \leq C_7 \quad (t > 0; i = 1, 2, 3).
\]

The first observation is the following proposition.

Proposition 3.2. Let $u = (u_i(x,t))$ be the solution to (1), (2), and (3). Given $1 \leq q < \infty$, assume
\[
\|u_1(\cdot,t)\|_q \leq C_8 \quad (t > 0)
\]
with a constant $C_8$. Then, for each $p \in [q, \infty)$, satisfying
\[
\frac{1}{p} > \frac{1}{q} - \frac{2}{n},
\]
(19)
we have a constant $C_9$ such that
\[
\|u_1(\cdot,t)\|_p \leq C_9 \quad (t > 0).
\]
Proof. Let \( \bar{u}_1 = \bar{u}_1(x,t) \) be the solution to
\[
\frac{\partial \bar{u}_1}{\partial t} = \left( d_1 \Delta - \frac{m}{2} \right) \bar{u}_1 + \lambda - \frac{m}{2} u_1, \quad \frac{\partial \bar{u}_1}{\partial \nu} \bigg|_{\partial \Omega} = 0, \quad \bar{u}_1(x,0) = u_{1,0}(x).
\]
Then, \( v_1 = \bar{u}_1 - u_1 \) satisfies
\[
\frac{\partial v_1}{\partial t} - d_1 \Delta v_1 + \frac{m}{2} v_1 > 0, \quad \frac{\partial v_1}{\partial \nu} \bigg|_{\partial \Omega} = 0, \quad v_1(x,0) = 0,
\]
by \( u_1, u_3 > 0 \), and hence it follows that \( v_1(x,t) > 0 \) from the strong maximum principle. Thus we obtain
\[
0 < u_1(x,t) < \bar{u}_1(x,t) \quad (t > 0, x \in \overline{\Omega}).
\]
Henceforth, \( \Delta \) is provided with the Neumann boundary condition. Let \( L = d_1 \Delta - m/2 \). Then it holds that
\[
\bar{u}_1(\cdot, t) = e^{tL} u_{1,0} + \int_0^t e^{(t-s)L} \left( \lambda - \frac{m}{2} u_1 \right)(\cdot, s) \, ds,
\]
which yields
\[
\| \bar{u}_1(\cdot, t) \|_p \leq \| e^{tL} u_{1,0} \|_p + \int_0^t \left\| e^{(t-s)L} \left( \lambda - \frac{m}{2} u_1 \right)(\cdot, s) \right\|_p \, ds \tag{21}
\]
for \( p \geq 1 \). Here, \( e^{tL} u_{1,0} \) is the solution to \( \partial u/\partial t = d_1 \Delta u - (m/2) u \) with the initial value \( u_{1,0} \). Therefore, we have \( \| e^{tL} u_{1,0} \|_p \leq \| u_{1,0} \|_p \). Now we use the semigroup estimate (Proposition B.1 in Appendix),
\[
\| e^{tL} w \|_p \leq C_{10} e^{-\frac{n}{m} r} \max \left\{ 1, \left( d_1 r \right)^{-\frac{1}{2}} \left( \frac{1}{m} - \frac{1}{p} \right) \right\} \| w \|_q,
\]
to deduce
\[
\int_0^t \left\| e^{(t-s)L} \left( \lambda - \frac{m}{2} u_1 \right)(\cdot, s) \right\|_p \, ds \\
\leq \int_0^t C_{10} e^{-\frac{n}{m} (t-s)} \max \left\{ 1, \left( (t-s) d_1 \right)^{-\frac{1}{2}} \left( \frac{1}{m} - \frac{1}{p} \right) \right\} \left\| \left( \lambda - \frac{m}{2} u_1 \right)(\cdot, s) \right\|_q \, ds \\
\leq C_{10} \sup_{s > 0} \left\| \left( \lambda - \frac{m}{2} u_1 \right)(\cdot, s) \right\|_q \int_0^t e^{-\frac{n}{m} r} \max \left\{ 1, \left( d_1 r \right)^{-\frac{1}{2}} \left( \frac{1}{m} - \frac{1}{p} \right) \right\} \, dr. \tag{22}
\]
If
\[
-\frac{n}{2} \left( \frac{1}{q} - \frac{1}{p} \right) > -1
\]
which is equivalent to (19), the last integral on the right-hand side of (22) is bounded in \( t > 0 \). Since \( \| \lambda - (m/2) u_1 \|_q \leq \lambda \| \Omega \|^{1/q} + (m/2) \| u_1 \|_q \), the assumption, \( \| u_1(\cdot, t) \|_q < C_8 \) for \( t > 0 \), and inequalities (20) and (21) prove the proposition. \( \square \)

Corollary 3.3. Assume that for an integer \( l \) (0 \( \leq l \leq n-2 \)), there exists a constant \( C_{11} \) such that
\[
\| u_l(\cdot, t) \|_{\frac{n}{n-l}} \leq C_{11} \quad (t > 0).
\]
If \( l < n - 2 \), then there exists a constant \( C_{12} \) such that
\[
\| u_1(\cdot, t) \|_{\frac{n}{n-(l+1)}} \leq C_{12} \quad (t > 0).
\]
If \( l = n - 2 \), then for any \( p \) (1 \( \leq p < \infty \)), there exists a constant \( C_{13} \) such that
\[
\| u_1(\cdot, t) \|_p \leq C_{13} \quad (t > 0).
\]
Proof. If \( l < n - 2 \), we take
\[
p = \frac{n}{n - (l + 1)}, \quad q = \frac{n}{n - l}.
\]
Then it holds that
\[
\frac{1}{p} = \frac{n - l - 1}{n} > \frac{n - l - 2}{n} = \frac{n - l}{n} - \frac{2}{n} = \frac{1 - 2}{n},
\]
and hence, by Proposition 3.2, there exists a constant \( C_{12} \) such that \( \|u_1(\cdot, t)\|_p \leq C_{12} \) for \( t > 0 \).

If \( l = n - 2 \) we take \( q = n/(n - (n - 2)) = n/2 \), which means \( 1/q - 2/n = 0 \). Then the conclusion of Proposition 3.2 holds for any \( p \geq 1 \), and we obtain the result.

**Corollary 3.4.** For any \( p \geq 1 \), there exists a constant \( C_{14} \) such that
\[
\|u_1(\cdot, t)\|_p \leq C_{14} \quad (t > 0).
\]
**Proof.** By Proposition 2.1, the assumption in Corollary 3.3 holds for \( l = 0 \). Thus repeating the use of Corollary 3.3 proves the corollary.

Now we turn to the estimates on \( u_2 \) and \( u_3 \).

**Proposition 3.5.** Let \( u = (u_1(x, t), u_2(x, t), u_3(x, t)) \) be the solution to \( (1), (2), \) and \( (3) \), and \( 1 \leq q < \infty \). If \( l < n - 2 \), then for any \( p \geq q \) with \( (19) \), i.e.,
\[
\frac{1}{p} > \frac{1}{q} - \frac{2}{n},
\]
we have a constant \( C_{16} \) such that
\[
\|u_3(\cdot, t)\|_p \leq C_{16} \quad (t > 0).
\]
Similarly, if \( l = n - 2 \), then for any \( p \geq q \) with \( (19) \) we have a constant \( C_{18} \) such that
\[
\|u_2(\cdot, t)\|_p \leq C_{18} \quad (t > 0).
\]
**Proof.** The proof is similar to that of Proposition 3.2, because we have
\[
\begin{align*}
  u_3(\cdot, t) &= e^{t(d_3\Delta - b)}u_{3,0} + \int_0^t e^{(t-s)(d_3\Delta - b)}aru_2(\cdot, s)\,ds, \\
  u_2(\cdot, t) &= e^{t(d_2\Delta - a)}u_{2,0} + \int_0^t e^{(t-s)(d_2\Delta - a)}\beta u_1 u_3(\cdot, s)\,ds.
\end{align*}
\]
by \( (1), (2), \) and \( (3) \).

**Corollary 3.6.** Assume that for an integer \( l \) (\( 0 \leq l \leq n - 2 \)), there exists a constant \( C_{19} \) such that
\[
\|u_2(\cdot, t)\|_{\frac{n}{n-l+1}} \leq C_{19}, \quad \|u_3(\cdot, t)\|_{\frac{n}{n-l+1}} \leq C_{19} \quad (t > 0).
\]
If \( l < n - 2 \), then there exists a constant \( C_{20} \) such that
\[
\|u_2(\cdot, t)\|_{\frac{n}{n-l+1}} \leq C_{20}, \quad \|u_3(\cdot, t)\|_{\frac{n}{n-l+1}} \leq C_{20} \quad (t > 0).
\]
If \( l = n - 2 \), then for any \( p \) (\( 1 \leq p < \infty \)), there exists a constant \( C_{21} \) such that
\[
\|u_2(\cdot, t)\|_p \leq C_{21}, \quad \|u_3(\cdot, t)\|_p \leq C_{21} \quad (t > 0).
\]
Inequality (24) thus arises for $q_L v$ in this section. Henceforth, for the vector valued function $W$.

Corollary 3.7. For any $C$ for some $C_{23}$, hence noting 

$$\frac{n-l}{n} = \frac{1}{n} + \frac{n-(l+1)}{n}$$

and the Hölder inequality, we obtain 

$$\|u_1 u_3(\cdot, t)\|_{\frac{n}{n-l}} \leq \|u_1(\cdot, t)\|_n \|u_3(\cdot, t)\|_{\frac{n}{n-l}} \leq C_{23}C_{22}.$$ 

Inequality (24) thus arises for $q = n/(n-l)$, and, therefore, Proposition 3.5 implies 

$$\|u_2(\cdot, t)\|_{\frac{n}{n-l}} \leq C_{24} \quad (t > 0),$$

for some $C_{24}$.

If $l = n - 2$, then, by Proposition 3.5, (23) for $q = n/(n-l) = n/2$ implies that for any $p (1 \leq p < \infty)$, there exists a constant $C_{25}$ such that 

$$\|u_3(\cdot, t)\|_p \leq C_{25} \quad (t > 0).$$

Using this inequality for $p = n$, the Hölder inequality, and Corollary 3.4, we have 

$$\|u_1 u_3(\cdot, t)\|_2 \leq \|u_1(\cdot, t)\|_n \|u_3(\cdot, t)\|_n \leq C_{23}C_{25} \quad (t > 0).$$

Thus, by Proposition 3.5 again, each $p (1 \leq p < \infty)$ admits $C_{26}$ such that 

$$\|u_2(\cdot, t)\|_p \leq C_{26} \quad (t > 0).$$

This completes the proof. \qed

Corollary 3.7. For any $p (1 \leq p < \infty)$, there exists a constant $C_{27}$ such that 

$$\|u_2(\cdot, t)\|_p \leq C_{27}, \quad \|u_3(\cdot, t)\|_p \leq C_{27} \quad (t > 0).$$

Proof. By Proposition 2.1 and Corollary 3.6, the result follows exactly as in Corollary 3.4. \qed

Corollaries 3.4 and 3.7 are summarized as Proposition 3.1.

4. $W^{2,p}$ bound of the solution. We apply the other form of semigroup estimates in this section. Henceforth, for the vector valued function $v = (v_1, v_2, \ldots, v_n)$, its $L^p$ norm is denoted by $\|v\|_p = \|v_1\|_p + \|v_2\|_p + \cdots + \|v_n\|_p$.

Proposition 4.1. Let $u = (u_i(x, t))$ be the solution of (1), (2), and (3). Then for each $p (1 \leq p < \infty)$, there exists a constant $C_{28}$ such that 

$$\|\nabla u_i(\cdot, t)\|_p \leq C_{28} \quad (t > 0; \ i = 1, 2, 3).$$

Proof. By Equation (1), we get 

$$\|\nabla u_1(\cdot, t)\|_p \leq \|\nabla e^{(t(1)\Delta - m)}u_{1,0}\|_p + \int_0^t \|\nabla e^{(t-s)(1)\Delta - m)}(\lambda - \beta u_1 u_3)(\cdot, s)\|_p \, ds.$$  

(26)

We may assume $1 < p < \infty$. Then it holds that 

$$\|\nabla e^{(t(1)\Delta - m)}u_{1,0}\|_p \leq C_{29} \|e^{(t(1)\Delta - m)}u_{1,0}\|_{W^{1,p}} \leq C_{30} \|\Delta^{1/2}e^{(t(1)\Delta - m)}u_{1,0}\|_p$$ 

$$= C_{30}e^{(t(1)\Delta - m)}\Delta^{1/2}u_{1,0}\|_p \leq C_{30}\|\Delta^{1/2}u_{1,0}\|_p \leq C_{30}\|u_{1,0}\|_{W^{1,p}} \leq C_{31}$$
by \( u_{1,0} \in C^2(\mathcal{Q}) \).

From the other semigroup estimate (Proposition B.2 and Remark B.3 in Appendix), on the other hand, it follows that
\[
\|\nabla e^{\tau(d_1 \Delta - m)} w\|_p \leq C_{32} e^{-\tau r} \max\{1, (d_1 r)^{-1/2}\} \|w\|_p,
\]
and hence
\[
\int_0^t \|\nabla e^{(t-s)(d_1 \Delta - m)} (\lambda - \beta u_1 u_3)(\cdot, s)\|_p ds \leq C_{32} \sup_{s>0} \|\nabla (\lambda - \beta u_1 u_3)(\cdot, s)\|_p \int_0^t e^{-\tau r} \max\{1, (d_1 r)^{1/2}\} dr.
\]

Here, by the Hölder inequality we obtain
\[
\|\nabla (\lambda - \beta u_1 u_3)(\cdot, s)\|_p \leq \|\lambda\|_p + |\beta| \cdot \|u_1 u_3(\cdot, s)\|_p.
\]
Then, by Proposition 3.1 (replaced \( p \) by \( 2p \)), (26) proves the proposition for \( i = 1 \). Using (25), we can similarly prove it for \( i = 2, 3 \).

Now we consider the derivatives of the second order.

**Proposition 4.2.** Let \( u = (u_i(x, t)) \) be the solution to (1), (2), and (3). Then for each \( p \) (\( 1 \leq p < \infty \)), there exists a constant \( C_{33} \) such that
\[
\|\nabla^2 u_i(\cdot, t)\|_p \leq C_{33} \quad (t > 0; \ i = 1, 2, 3).
\]

**Proof.** By Equation (1), we have
\[
\|\Delta u_i(\cdot, t)\|_p \leq \|\Delta e^{(t-s)(d_1 \Delta - m)} u_{1,0}\|_p + \int_0^t \|\Delta e^{(t-s)(d_1 \Delta - m)} (\lambda - \beta u_1 u_3)\|_p ds.
\]

Here we may assume \( 1 < p < \infty \). The first term of the right-hand side is estimated as
\[
\|\Delta e^{(t-s)(d_1 \Delta - m)} u_{1,0}\|_p = \|e^{(t-s)(d_1 \Delta - m)} \Delta u_{1,0}\|_p \leq C_{34} \quad (t > 0),
\]
using \( u_{1,0} \in D(\Delta) \). For the second term, we use Proposition B.2 to deduce
\[
\|\Delta e^{(t-s)(d_1 \Delta - m)} (\lambda - \beta u_1 u_3)\|_p \leq C_{35} e^{-m(t-s)} \max \left\{1, (t-s)^{-1/2} \right\} \|\Delta (\lambda - \beta u_1 u_3)(\cdot, t)\|_p.
\]

Then, by Remark B.3 in Appendix, the Hölder inequality, and Proposition 3.1 and 4.1, we have for some \( C_{36} \) and \( C_{37} \),
\[
\|\Delta (\lambda - \beta u_1 u_3)(\cdot, t)\|_p \leq C_{36} \|\nabla (\lambda - \beta u_1 u_3)(\cdot, t)\|_p \leq C_{36} \beta(\|u_3(\cdot, t)\|_{2p} \|\nabla u_1(\cdot, t)\|_{2p} + \|u_1(\cdot, t)\|_{2p} \|\nabla u_3(\cdot, t)\|_{2p}) \leq C_{37}.
\]

This proves
\[
\|\Delta u_i(\cdot, t)\|_p \leq C_{38} \quad (t > 0)
\]
for \( i = 1 \). Then inequality (27) for \( u_1 \) follows from the elliptic estimate. The other inequalities for \( u_2 \) and \( u_3 \) can be shown similarly. \( \Box \)
5. **Proof of Theorem 1.1.** First, we derive an $L^\infty$ bound of the solution.

**Proposition 5.1.** For each solution $u = (u_i(x,t))$ to (1), (2), and (3), there exists a constant $C_{39}$ such that
\[
\|u_i(\cdot,t)\|_\infty + \|\nabla u_i(\cdot,t)\|_\infty \leq C_{39} \quad (t > 0, \ i = 1, 2, 3).
\]

*Proof.* By Morrey’s theorem (Gilbarg and Trudinger [4], Corollary 7.11 and its notes), we have $W^{1,p}(\Omega) \subset C^{1-n/p}(\overline{\Omega})$ with the continuous imbedding. By Propositions 3.1 and 4.1 for $p > n$, it holds that
\[
\|u_i(\cdot,t)\|_\infty \leq C_{40} \quad (t > 0, \ i = 1, 2, 3).
\]

By Proposition 4.2, $u_i(\cdot,t)$ is bounded in $W^{2,p}(\Omega)$ for any $p \geq 1$ (See Remark B.3), and hence $\nabla u_i(\cdot,t)$ is bounded in $W^{1,p}(\Omega)$. Thus, by Morrey’s theorem again, we obtain
\[
\|\nabla u_i(\cdot,t)\|_\infty \leq C_{41} \quad (t > 0, \ i = 1, 2, 3).
\]

□

From the above a priori estimate, the solution $u = (u_i(x,t))$ to (1), (2), (3) is global-in-time. Now we can use the invariance principle to study its asymptotic behaviour under the presence of the Lyapunov function (Henry [5, Theorem 4.3.4]), noting the following proposition.

**Proposition 5.2.** The orbit $u = (u_i(\cdot,t))$ created by the solution to (1), (2), (3) is pre-compact in $C(\overline{\Omega}; \mathbb{R}^3)$.

*Proof.* By Proposition 5.1, the family $\{u_i(\cdot,t)\}$ is uniformly bounded and equicontinuous on $\overline{\Omega}$. Therefore, the Arzelà-Ascoli theorem implies the result. □

Proposition 5.2 implies that the omega limit set $\omega((u_i,0))$ is nonempty, compact, invariant under the flow defined by (1)-(2), and is connected (Henry [5, Theorem 4.3.3]). Furthermore, the Lyapunov function is constant on this set. We are thus ready to complete the following proof.

*Proof of Theorem 1.1.* First, we take the case $R_0 > 1$. We put, with $\mathcal{V}$ defined by (13),
\[
E_1 = \{v \in C(\overline{\Omega}; \mathbb{R}^3) | \dot{V}_1(v) = 0\}.
\]

Take $\tilde{u}_0 = (\tilde{u}_i,0) \in \omega((u_i,0))$, and let $\tilde{u} = (\tilde{u}_i(x,t))$ be the solution to (1)-(2) with the initial value $\tilde{u}_0$. Then, it holds that $\tilde{u}(.\cdot,t) \in \omega((u_i,0))$ and hence $\tilde{u}_0 \in E_1$. Thus we obtain $\omega((u_i,0)) \subset E_1$, and hence $\tilde{u}(.\cdot,t) \in E_1$, which means
\[
\int_\Omega |\nabla \tilde{u}_i(\cdot,t)|^2 \, dx = 0 \quad (i = 1, 2, 3), \quad \int_\Omega \dot{V}_1(\tilde{u}(x,t)) \, dx = 0.
\]

By the first equality, $\tilde{u}_i(x,t)$ is spatially homogeneous, and hence $\tilde{u}(t) = (\tilde{u}_i(x,t))$ satisfies (4). By the last equality and (10), we get
\[
2 - \frac{\ddot{\tilde{u}}_1}{\tilde{u}_1} - \frac{\dot{u}_1^2}{u_1} = 0, \quad 3 - \frac{\ddot{\tilde{u}}_2}{\tilde{u}_1} - \frac{\dot{u}_2 u_1^2}{u_2 u_3} - \frac{\ddot{\tilde{u}}_3}{u_1 u_2 u_3} = 0
\]
for $\tilde{u}_i = \tilde{u}_i(t)$, which yields
\[
\frac{\ddot{\tilde{u}}_1}{\tilde{u}_1} = \frac{u_1^*}{\dot{u}_1}, \quad \frac{\ddot{\tilde{u}}_2}{\tilde{u}_1} = \frac{u_1^* u_3^*}{\dot{u}_2}, \quad \frac{\ddot{\tilde{u}}_3}{u_1^* u_2 u_3} = \frac{\ddot{\tilde{u}}_3}{\dot{u}_1 u_2 u_3}.
\]
Hence we have
\[ \tilde{u}_1(t) \equiv u_1^*, \quad \frac{\tilde{u}_2(t)}{u_2^*} = \frac{\tilde{u}_3(t)}{u_3^*}. \]
Since \( \tilde{u}_1(t) \) is independent of \( t \), the first equation in (4) shows that \( \tilde{u}_3(t) \) is also a constant. Hence \( \tilde{u}_2(t) \) is so. Thus we obtain \((\tilde{u}_1,0,\tilde{u}_2,0,\tilde{u}_3,0) \equiv (u_1^*,u_2^*,u_3^*)\), and therefore, \( \omega((u_1,0,u_2,0,u_3,0)) = \{u^*=(u_1^*,u_2^*,u_3^*)\} \). This means (11) for the case \( R_0 > 1 \).

Assuming the other case \( R_0 \leq 1 \), we put, with \( \mathcal{U} \) defined by (12),
\[ E_0 = \{v \in C(\Omega;\mathbb{R}^3)|\mathcal{U}((t)=0)\}. \]
It holds that \( \omega((u_4,0)) \subset E_0 \) similarly. Given \((\tilde{u}_1,0,0,0,0) \in \omega((u_4,0))\), we take the solution to (1)-(2) with the initial value \((\tilde{u}_1,0,0,0,0)\), denoted by \( \tilde{u} = (\tilde{u}_1(\cdot, t)) \). Then it holds that \( \tilde{u} = \tilde{u}_1(\cdot, t) \in \omega((u_4,0)) \subset E_0 \), and hence
\[ \int_{\Omega} (\nabla \tilde{u}_1(\cdot, t))^2 \, dx = 0, \quad \int_{\Omega} \tilde{U}_1(\tilde{u}(x, t)) \, dx = 0. \]
Thus we obtain \( \nabla \tilde{u}_1(x, t) \equiv 0 \) for \( t > 0 \), which implies, by the first equation of (1), \( \nabla \tilde{u}_1(\cdot, t) \equiv 0 \). Hence, by the third equation of (1), it holds that \( \nabla \tilde{u}_2(x, t) \equiv 0 \). Hence \( \tilde{u} = (\tilde{u}_1(\cdot, t)) \) is spatially homogeneous, and satisfies (4).

By (9), on the other hand, we get \( 2 - \frac{\tilde{u}_1(t)}{u_1^*} - \frac{u_2^*}{u_1^*} = 0 \) which yields
\[ \frac{\tilde{u}_1(t)}{u_1^*} = \frac{u_2^*}{u_1^*}. \]
Therefore it holds that \( \tilde{u}_1(t) \equiv u_1^* \). Since \( \tilde{u}_3(t) \) is constant, \( \tilde{u}_3(t) \) and \( \tilde{u}_2(t) \) are so by the first and the third equations of (1), respectively. Thus we obtain \( \omega((u_4,0)) = \{u^*\} \) and hence (11) for \( R_0 \leq 1 \).

6. Numerical simulations. In this section, we show some results of numerical simulations. The simulations were carried out with the Crank-Nikolson method, and confirmed with the explicit method (Smith [11, Chapter 2]).

We consider the case \( n = 1 \) and \( \Omega = \{x|0 < x < 10\} \). We set
\[ d_1 = 0.1, d_2 = 0.1, d_3 = 1.0. \]
The other parameter values are based on those used in Bonhoeffer et al. [1]:
\[ \lambda = 1.0 \times 10^7, m = 0.1, \beta = 5.0 \times 10^{-10}, a = 0.5, r = 20.0, b = 5.0. \]  
For the parameter values (28), we have
\[ u^*(1.0 \times 10^8, 0, 0), u^*(5.0000 \times 10^8, -8.0000 \times 10^7, -1.6000 \times 10^8), \]
and \( R_0 = 0.2 \). Thus the solutions converge to \( u^* \) as \( t \to \infty \).

To depict the solutions tending to the spatially homogeneous equilibrium, we set the initial functions that fluctuate:
\[ u_{i,0}(x) = 5.0 \times 10^8 \psi_1(x), u_{2,0}(x) = 8.0 \times 10^8 \psi_1(x), u_{3,0}(x) = 2.0 \times 10^8 \psi_1(x), \]
where \( \psi_1(x) = \{2 + \cos(4\pi x/10)\}/3 \), which oscillates between \( 1/3 \) and 1. The graph of \( u_i(x, t) \)’s, for this initial condition, are shown in Figure 1. For each \( u_i \)’s, the spatial heterogeneity becomes smaller as time elapses, and \( u_i(x, t) \) is almost spatially homogeneous at \( t = 8 \). Once the solution of (1) becomes almost spatially homogeneous, we can expect that its dynamics is governed by (4) and that the solution converges to \( u^* \).
To show the graphs for $R_0 > 1$, we change the value $\beta$ to $\beta = 5.0 \times 10^{-8}$. The other parameter values are the same as the previous case. For these parameter values, we have

$$u^*(1.0 \times 10^8, 0, 0), u^*(5.0000 \times 10^6, 1.9000 \times 10^7, 3.8000 \times 10^7),$$

and $R_0 = 20.0$. Thus the solutions converges to $u^*$ as $t \to \infty$.

We consider a situation where a small amount of viruses invade the middle of $\Omega$. Hence we set

$$u_{1,0}(x) = 1.0 \times 10^8, u_{2,0}(x) = 0, u_{3,0}(x) = 100.0 \times \psi_2(x - 5),$$

where $\psi_2(x) = \exp(-1/(1 - x^2))$ for $-1 < x < 1$, and $\psi_2(x) = 0$ otherwise.

In Figure 2, each graph of $u_i(x,t)$'s is shown from two view angles. The values of $u_i$'s drastically change from $t = 3$ to $t = 5$, and during this time interval, the spatial heterogeneity also changes drastically. After the period, each $u_i$ becomes almost spatially homogeneous, and $u_i(-,t)$ converges to $u^*_i$ as $t \to \infty$ ($i = 1, 2, 3$).

In Figure 2, the graphs of $u_i(x,t)$'s seem flat for $0 \leq t \leq 2$ and for $6 \leq t \leq 15$, and it might be expected that $u_i(x,t)$'s are spatially homogeneous during these periods.
However it may be due to the large ranges of values $u_i(x, t)$'s. In Figure 3, we divide the graph of $u_3(x, t)$ (Figure 2 (c)) into three time intervals, $[0, 2.1]$, $[2.1, 6.0]$, and $[6.0, 15.0]$. Figure 3 (a) shows that $u_3(x, t)$ is not spatially homogeneous at least for $1.5 \leq t \leq 2$. On the other hand, Figure 3 (c) shows that $u_3(x, t)$ is almost spatially homogeneous for $6 \leq t \leq 15$. Then we can expect that the dynamics is governed by (4) and the solution converges to the spatially homogeneous equilibrium $u^*$.

![Figure 3](image.png)

Figure 3. The graphs of $u_3$: In the case $R_0 > 1$. We divide Figure 2 (c) into three parts: (a) $0 \leq t \leq 2.1$, (b) $2.1 \leq t \leq 6.0$, and (c) $6.0 \leq t \leq 15.0$.

7. **Concluding remarks.** In Section 2 we confirmed that Lyapunov function used for the ODE model induces $L^1$ bound of the solution for the corresponding PDE system incorporating the diffusion. This structure is quite common to virus dynamics models. The proof of the compactness of orbits (from $L^1$ bound to $W^{2,p}$ bound), on the other hand, depends on the reaction terms in our argument, which, however, is applicable also to many other models. Then, the invariance principle of the omega limit set implies the convergence of the spatially inhomogeneous solution to the spatially homogeneous equilibrium. We shall discuss these points in a forthcoming paper, treating other virus dynamics models.

The function $\Phi(s)$ in (5) is different from the entropy density effective to the thermodynamical model, $\Phi(s) = s(\log s - 1) + 1$, which guarantees the Csiszár-Kullback inequality

$$\|g - G\|_1 \leq 4M \int_\Omega G\Phi \left( \frac{g}{G} \right) \, dx$$

valid to $0 < g, G \in L^1(\Omega)$ with $\|g\|_1 = \|G\|_1 = M$. It is now well-known that this inequality can be a basis to infer the exponential convergence of the spatially inhomogeneous solution to the spatially homogeneous equilibrium in $L^1$ norm (see [2]).

Without (29), however, the convergence (11) is exponential, thanks to the theory of linearization. In fact, in the case of $R_0 > 1$, for example, the ODE theory has revealed that the stationary solution $u^* = (u_1^*, u_2^*, u_3^*)$ is linearly asymptotically stable for the ODE part. This means that the eigenvalues of the linearized matrix

$$A = \begin{pmatrix}
-m - \beta u_3^* & 0 & -\beta u_1^* \\
\beta u_3^* & -a & \beta u_1^* \\
0 & ar & -b
\end{pmatrix}$$

lie in the left-half space on the complex plane,

$$\text{Re } \sigma(A) < -\delta,$$

(30)
where \( \sigma(A) \) denotes the spectrum of \( A \) and \( \delta > 0 \). If \( u = (u_i(x,t)) \) is the solution to (1), (2), and (3), we obtain
\[
\frac{\partial \tilde{u}}{\partial t} = (L + A)(\tilde{u}) + F(\tilde{u}) \tag{31}
\]
for \( \tilde{u} = (\tilde{u}_i(x,t)) \) with \( \tilde{u}_i = u_i - u_i^* \), where
\[
L = \begin{pmatrix}
  d_1 \Delta & 0 & 0 \\
  0 & d_2 \Delta & 0 \\
  0 & 0 & d_3 \Delta
\end{pmatrix}, \quad F(\tilde{u}) = \begin{pmatrix}
  -\tilde{u}_1 \tilde{u}_3 \\
  \tilde{u}_1 \tilde{u}_3 \\
  0
\end{pmatrix}.
\]

Here we recall that \( \Delta \) is provided with the Neumann boundary condition.

Regarding that the solution \( u \) approaches to the equilibrium \( u^* \), we take the linear part of (31),
\[
\frac{\partial v}{\partial t} = Lv + Av, \quad v|_{t=0} = v_0.
\]
Since \( (Lv, v) \leq 0 \) for \( v \in D(L) \), it holds that
\[
\frac{1}{2} \frac{d}{dt} \|v\|_2^2 \leq -\delta \|v\|_2^2
\]
and hence \( \|v(\cdot,t)\|_2 \leq \|v_0\|_2 e^{-\delta t} \). Regarding \( LA = AL \), we obtain
\[
\|L^2v(\cdot,t)\|_2 \leq \|L^2v_0\|_2 e^{-\delta t}
\]
for any \( \gamma > 0 \), in particular, \( \|v(\cdot,t)\|_{\infty} \leq Ce^{-\delta t} \). The exponential decay of \( \|\tilde{u}(\cdot,t)\|_{\infty} \) as \( t \to \infty \) now follows from this linear theory[15, Theorem 6.10].

Appendix A. Positivity of the solution. Let \( u = (u_i(x,t)) \) \( (x \in \overline{\Omega}, 0 < t \leq T) \) be a classical solution to the system of reaction-diffusion equations
\[
\frac{\partial u_i}{\partial t} = d_i \Delta u_i + f_i(u_1, u_2, \ldots, u_N), \quad (x \in \Omega \subset \mathbb{R}^n, 0 < t \leq T; i = 1, 2, \ldots, N), \tag{32}
\]
with the initial-boundary condition
\[
u_i|_{t=0} = u_{i,0}(x), \quad \frac{\partial u_i}{\partial t} \bigg|_{\partial \Omega} = 0, \quad i = 1, 2, \ldots, N, \tag{33}
\]
where \( f_i : \mathbb{R}_+^N \to \mathbb{R}_+^N \) \( (i = 1, 2, \ldots, N) \) are smooth functions. Then we obtain the following proposition.

Proposition A.1. If \( f_i \) \( (i = 1, 2, \ldots, N) \) satisfy
\[
f_i(u_1, \ldots, u_{i-1}, 0, u_{i+1}, \ldots, u_N) \geq 0
\]
for \( u_1, \ldots, u_{i-1}, u_{i+1}, \ldots, u_N \geq 0 \), and if the solution \( u = (u_i(x,t)) \) to (32) satisfies \( u_{i,0} \geq 0 \) and \( u_{i,0} \neq 0 \) on \( \Omega \) for each \( i \), then it holds that
\[
u_i(x,t) > 0, \quad (x \in \overline{\Omega}, 0 < t \leq T; i = 1, 2, \ldots, N).
\]

For the proof we put \( G_i(u) = -u_i \) \( (i = 1, 2, \ldots, N) \) for \( u = (u_1, u_2, \ldots, u_N) \), and take the first quadrant with boundary,
\[
K = \bigcap_{i=1}^N \{ u | G_i(u) \leq 0 \}.
\]
Since
\[
dG_i(u) = \sum_{j=1}^N \frac{\partial G_i}{\partial u_j} f_j(u) = -f_i(u),
\]
if \( f_i(u) \leq 0 \) for \( u \in K \) satisfying \{ \{ u \mid G_i(u) = 0 \} \), then it holds that \( dG_i(u) \leq 0 \).

Hence, if \( f_i(u_1, \ldots, u_{i-1}, 0, u_{i+1}, \ldots, u_N) \geq 0 \) for \( i = 1, 2, \ldots, N \), the first quadrant \( K \) is an invariant region \([12, \text{Theorem 14.11}]\). The strong maximum principle now guarantees the proposition.

### Appendix B. Semigroup estimates.

We state estimates for the semigroup generated by the realization of the Laplacian in \( L^p(\Omega) \) \((1 \leq p < \infty)\) under the Neumann boundary condition. We assume that the spatial domain \( \Omega \) is bounded in \( \mathbb{R}^n \), and its boundary is smooth.

The following estimate follows from Lemma 3 in Part I in Rothe \([10]\).

**Proposition B.1.** Assume \( 1 \leq q \leq p \leq \infty \). Then there exists a constant \( C \) such that

\[
\| e^{t\Delta} u \|_p \leq C \max \left\{ 1, t^{-\frac{\alpha}{2}} \left( \frac{\alpha}{2} - \frac{1}{q} \right) \right\} \| u \|_q \quad (t > 0).
\]

We consider another semigroup estimate. The domain of the fractional power \((-\Delta)^\alpha\) is the Sobolev space \( W^{2\alpha,p}(\Omega) \) if \( 0 \leq \alpha < (p + 1)/(2p) \), and \( W^{2\alpha,p}_N(\Omega) \) if \( (p + 1)/(2p) < \alpha \leq 1 \), where \( W^{2\alpha,p}_N(\Omega) \) is the Sobolev space with the Neumann boundary condition.\([15, \text{Theorem 16.11}]\). Moreover, for some \( C \) it holds that

\[
\| (-\Delta)^\alpha e^{t\Delta} \|_{B(L^p(\Omega), L^p(\Omega))} \leq Ct^{-\alpha} \quad (t > 0),
\]

where \( \| \cdot \|_{B(L^p(\Omega), L^p(\Omega))} \) is the norm for the bounded linear operators on \( L^p(\Omega) \). Thus, if we note that \((-\Delta)^\alpha e^{t\Delta} u = (-\Delta)^\alpha e^{(t/2)\Delta} e^{(t/2)\Delta} u\), Proposition B.1 implies the following proposition.

**Proposition B.2.** Assume \( 1 \leq q \leq p \leq \infty \) and \( \alpha \geq 0 \). Then there exists a constant \( C \) such that

\[
\| (-\Delta)^\alpha e^{t\Delta} u \|_p \leq C \max \left\{ 1, t^{-\frac{\alpha}{2}} \left( \frac{\alpha}{2} - \frac{1}{q} \right)^{-\alpha} \right\} \| u \|_q \quad (t > 0).
\]

**Remark B.3.** There exists a positive constant \( C \) such that

\[
C^{-1} \| v \|_{W^1,p(\Omega)} \leq \| (-\Delta)^{1/2} v \|_p \leq C \| v \|_{W^1,p(\Omega)},
\]

\[
C^{-1} \| v \|_{W^2,p(\Omega)} \leq \| \Delta v \|_p \leq C \| v \|_{W^2,p(\Omega)} (v \in W^{2,p}_N(\Omega)).
\]

For the proof of these inequalities, see, for example, Theorem 16.11 in Yagi \([15]\).

By the first inequalities and Poincaré’s inequality (Evans \([3, \text{Section 5.6}]\)), the left hand side of (34) can be replaced by \( \| \nabla e^{t\Delta} u \|_p \) if \( \alpha = 1/2 \).

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**REFERENCES**

[1] S. Bonhoeffer, R. M. May, G. M. Shaw and M. A. Nowak, Virus dynamics and drug therapy, Proc. Natl. Acad. Sci. USA, 94 (1997), 6971–6976.

[2] J. A. Carrillo, A. Jüngel, P. A. Markowich, G. Toscani and A. Untertritter, Entropy dissipation methods for degenerate parabolic problems and generalized Sobolev inequalities, Monatsh. Math., 133 (2001), 1–82.

[3] C. L. Evans, Partial Differential Equations, American Mathematical Society, Providence, 1998.

[4] D. Gilbarg and N. S. Trudinger, Elliptic Partial Differential Equations of Second Order, 2nd edition, Springer-Verlag, New York, 1983.

[5] D. Henry, Geometric Theory of Semilinear Parabolic Equations, Lecture Notes in Mathematics, Springer-Verlag, New York, 1981.
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[6] A. Korobeinikov, Global properties of basic virus dynamics models, Bull. Math. Biol., 66 (2004), 879–883.

[7] E. Latos, T. Suzuki and Y. Yamada, Transient and asymptotic dynamics of a prey-predator system with diffusion, Math. Methods Appl. Sci., 35 (2012), 1101–1109.

[8] M. A. Nowak and C. R. M. Bangham, Population dynamics of immune responses to persistent viruses, Science, 272 (1996), 74–79.

[9] J. Prüss, R. Zacher and R. Schnaubelt, Global asymptotic stability of equilibria in models for virus dynamics, Math. Model. Nat. Phenom., 3 (2008), 126–142.

[10] F. Rothe, Global Solutions of Reaction-Diffusion Systems, Lecture Notes in Mathematics, Springer-Verlag, New York, 1984.

[11] G. D. Smith, Numerical Solution of Partial Differential Equations—Finite Difference Methods, 3rd edition, Oxford University press, Oxford, 1985.

[12] J. Smoller, Shock Waves and Reaction-Diffusion Equations, 2nd edition, Springer-Verlag, New York, 1994.

[13] H. Tanabe, Equations of Evolution, Pitman, London, 1979.

[14] J. Wang, J. Yang and T. Kuniya, Dynamics of a PDE viral infection model incorporating cell-to-cell transmission, J. Math. Anal. Appl., 444 (2016), 1542–1564.

[15] A. Yagi, Abstract Parabolic Evolution Equations and Their Applications, Springer-Verlag, New York, 2010.

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