The Asymptotic Behavior of Solutions of the Buffered Bistable System

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Abstract

In this paper, we study a model for calcium buffering with bistable nonlinearity. We present some results on the stability of equilibrium states and show that there exists a threshold phenomenon in our model. In comparing with the model without buffers, we see that stationary buffers cannot destroy the asymptotic stability of the associated equilibrium states and the threshold phenomenon. Moreover, we also investigate the propagation property of solutions with initial data being a disturbance of one of the stable states which is confined to a half-line. We show that the more stable state will eventually dominate the whole dynamics and that the speed of this propagation (or invading process) is positive.

Key Words: calcium, buffer, bistable, threshold, propagation

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1 Introduction

It is known that the intra-cellular space of an oocyte can become an excitable medium when the concentration of the inositol (1,4,5)-trisphosphate (IP_3) is increased [47, 27, 5, 20, 30]. Like the other excitable systems (e.g., Belousov-Zhabotinsky reaction and FitzHugh-Nagumo model), oocytes can generate a well-known set of wave patterns including target waves, spirals waves, traveling pulses, and traveling fronts [33, 23, 52, 56, 30]. However, regarding the wave patterns, there is a crucial difference between mature and immature *Xenopus* oocytes. This may be due to the following facts. In immature *Xenopus* oocytes, target and spiral waves can be observed when the IP_3 concentration is elevated [47, 27, 5, 20]. On the other hand, the fertilization calcium (Ca^{2+}) wave in mature *Xenopus* oocytes propagates across the intra-cellular space like a tide (front), moving at a speed of $5-10$ μms^{-1} with basal cytosolic calcium concentration ($[Ca^{2+}]_{\mathrm{cyt}}$) of the order of $0.2-0.3$ μM in front of the wave and $1.3-2.0$ μM in its wake [40, 9, 64]. Therefore, it seems that the cytoplasm of mature *Xenopus* oocytes can support two alternative stable physiological Ca^{2+} concentrations, which is unusual since prolonged high $[Ca^{2+}]_{\mathrm{cyt}}$ are toxic in most of cell types [33, 23, 52, 56]. Furthermore, experimental observation also shows the existence of a threshold of the Ca^{2+} concentration below which additions of Ca^{2+} cannot trigger a wave [40, 64]. This kind of threshold behavior is indeed a hallmark of *bistability*. Thus, it is quite interesting to understand what mechanism can cause such phenomena.

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Actually, existing experimental evidence and many modeling studies suggest the following cellular mechanism for Ca^{2+} waves in mature oocytes and other cell types [6, 65, 66, 5, 31, 40, 42, 29, 21, 58, 22, 9, 23, 64]. Binding of stimuli (e.g., sperm) to the receptors in the plasma membrane results in the production of IP_3. Then the IP_3 diffuses rapidly and binds to the IP_3R (which is the IP_3 receptor and acts as a IP_3/Ca^{2+}-mediated Ca^{2+} channel) on the membrane of the internal Ca^{2+} store ER (endoplasmic reticulum). Hence the IP_3 (Ca^{2+}) activates the IP_3R channel, through which Ca^{2+} can be released from ER into cytosol. Note that there are two other components of the Ca^{2+} flux across the ER membrane, i.e., direct leak through the membrane of ER and Ca^{2+} uptake by sarco- and endoplasmic reticulum Ca^{2+}-ATPase (SERCA) pumps. Thus if the released Ca^{2+} diffuses to neighboring ER, it will initiate further Ca^{2+} release from there via the so-called Ca^{2+}-induced Ca^{2+} release (CICR). Repetition of this process can then generate an advancing wave front of Ca^{2+} concentration.

Finally, for physiological function of the fertilization Ca^{2+} wave, we recall the following fact [56] that the cell divisions initiating development of *Xenopus* oocytes begin only after the fertilization Ca^{2+} wave has propagated across the entire cell. Moreover, the eggs of many species, from frog and starfish to hamster and human, exhibit propagating Ca^{2+} wave upon fertilization [39, 64].

2 The Mathematical Model

Before stating the model for Ca^{2+} waves, we make some comments and assumptions on ER and IP_3R. Although ER has very complicated irregular geometry [61], for simplicity, we will assume that it is a homogeneous, continuous medium [21, 64, 51]. Also the Ca^{2+} concentration in ER is $2-3$ orders of magnitude greater than that in the cytosol. Therefore, it may be plausible to assume that the Ca^{2+} capacity of ER is infinity everywhere [64, 59, 51, 52, 56]. Next, we will discuss the features of the regulation of the Ca^{2+} channel IP_3R. Actually, the key features of the regulation of IP_3R by IP_3 and Ca^{2+} have been found and included in many modeling studies [6, 19, 43, 14, 65, 66, 42, 29, 23, 64, 52, 56, 30]. They include the well-known bell-shaped dependence of the channel opening on $[Ca^{2+}]_{\mathrm{cyt}}$, which implies that Ca^{2+} can activate as well as inactivate the channel opening. Hence this fact suggests that we should include a gating variable for the gated opening of the IP_3R in the model. However, we will follow [21, 59, 51, 56] to assume that the dynamics of Ca^{2+} in cytosol are much slower than the gating variable for Ca^{2+} inactivation of the IP_3R (more discussion on this assumption will be given in section 6). Hence we will only include the Ca^{2+} concentration of the cytosol in the model below, and so the Ca^{2+} concentration in ER and the gating variable for the IP_3R will not enter the governing equation. Note that we will also assume that the IP_3 concentration is uniform and constant [52, 56, 59].

Now we can state the model for Ca^{2+} waves. First, we use a simplified version of the Li and Rinzel model [29] by Smith, Pearson, and Keizer [52, 56, 59, 51] with an assumption that Ca^{2+} buffers being absence. We will take Ca^{2+} buffers into account later. When combined with Ca^{2+} diffusion [4, 16, 11], the model takes the following form:

$$\frac{\partial u}{\partial t} = D\frac{\partial^2 u}{\partial x^2} + f(u), \tag{2.1}$$

where u denotes the concentration of free cytosolic Ca^{2+}, $D > 0$ is the diffusion coefficient of the free cytosolic Ca^{2+}, and $f(u) = J_{\mathrm{channel}} + J_{\mathrm{pump}} + J_{\mathrm{leak}}$ is the rate of change of $[Ca^{2+}]_{\mathrm{cyt}}$ due to fluxes through the IP_3R, SERCA pumps, and direct leak at each space point. Here $f(u)$ takes the bistable nonlinearity. Since we will only concern the qualitative properties of (2.1), for simplicity, in this paper we shall only consider the typical example

$$f(u) = u(1-u)(u-a)$$

for some $a \in (0,1)$. We remark that the bistability is suggested by experimental observations [10, 18, 44, 40, 26, 9, 64] and is caused by the release and uptake properties of ER [9, 64]. Furthermore, the three zeros of f have the following interpretation in biology: the state 0 represents a stable resting state at basal Ca^{2+} concentration of the cytosol, the state 1 is a stable resting point at high Ca^{2+} concentration of the cytosol, while the state a is unstable and corresponds to a threshold for CICR. For more details on the biological motivation and interpretation of this model, the reader is referred to Chapter 5 and 8 of Fall et al.'s book [52, 56], Keener and Sneyd's book [23], and references therein.

Although the model (2.1) shares many similarities with other excitable systems (e.g., the simplified version of the FitzHugh-Nagumo model), the study of Ca^{2+} waves still has some other crucial differences. The most important one among them should be the existence of Ca^{2+} buffers. In fact, a large fraction of cytosolic Ca^{2+} (around 99%) is bound to large Ca^{2+}-binding proteins, called Ca^{2+} buffers [1, 36]. Not only do these buffers restrict the diffusion of free Ca^{2+}, they also affect the kinetics of Ca^{2+} release and uptake [63], and thus they would be expected to have an important effect on the properties of Ca^{2+} dynamics [1].

A simple way to model calcium buffering is to assume that Ca^{2+} interacts with buffers according to the following reaction scheme

$$\mathrm{Ca}^{2+} + \mathrm{B}_i \rightleftharpoons \mathrm{Ca}^{2+}\mathrm{B}_i, \quad i = 1, \cdots, n, \tag{2.2}$$

where B_i and $\mathrm{Ca}^{2+}\mathrm{B}_i$ denote the unbound and bound forms of the ith buffer, respectively [63, 59, 60]. Let v_i denote the concentration $[\mathrm{B}_i]$ of the ith buffer and b_0^i denote the total amount of the ith buffer. Note that $b_0^i = [\mathrm{B}_i] + [\mathrm{Ca}^{2+}\mathrm{B}_i]$. We shall assume that b_0^i is a constant at each spatial point for all $t > 0$. It follows from the law of mass action [23] that the rate of change of u due to buffering is given by

$$\frac{du}{dt} = \sum_{i=1}^{n} [k_-^i (b_0^i - v_i) - k_+^i u v_i], \tag{2.3}$$

where the positive constants k_+^i and k_-^i denote the forward and reverse rate constants of the ith reaction (2.2), respectively. Hence if we assume that the space dimension of the cell is one, and let $D_i \geq 0$, $i = 1, \cdots, n$, be the diffusion coefficient of the ith buffer, then we have the following buffered reaction-diffusion system:

$$\frac{\partial u}{\partial t} = D\frac{\partial^2 u}{\partial x^2} + f(u) + \sum_{i=1}^{n} [k_-^i (b_0^i - v_i) - k_+^i u v_i], \ (x,t) \in \mathbf{R} \times (0, \infty), \tag{2.4}$$

$$\frac{\partial v_i}{\partial t} = D_i \frac{\partial^2 v_i}{\partial x^2} + k_-^i (b_0^i - v_i) - k_+^i u v_i, \ (x,t) \in \mathbf{R} \times (0, \infty), \ i = 1, \cdots, n. \tag{2.5}$$

For numerical studies including Ca^{2+} buffers, see, for examples, [8, 21, 38, 49]. Regarding the analytical works on buffers, we mention the well-known *rapid buffer approximation* (RBA). More precisely, if we assume that the buffer has fast kinetics (relative to the other reactions in the model), then we can reduce the full buffered model to a single quasilinear parabolic equation in which the effective diffusion coefficient of free cytosolic Ca^{2+} now depends on the Ca^{2+} concentration (see Wagner and Keizer [63] and Smith [54]). This approximation has been widely used in many recent works. For example, Sneyd et al. [59] and Slepchenko et al. [51] have used this approximation to consider the associated properties of traveling waves in the buffered bistable system. See also Neher [34, 35, 37]), Smith [53], Smith et al. [55], etc.

3 Main Results

Intuitively, it is clear that the associated properties of the model (2.1) should not be affected by the presence of infinitely slow buffers (buffers with very slow kinetics). For infinitely fast buffers (buffers with very fast kinetics), we can use the RBA to reduce the model (2.4)-(2.5) to one single quasilinear equation, which is more easier to deal with. However, what will happen if the buffer is neither infinitely slow nor fast? Therefore, by considering the whole system (2.4)-(2.5), it is the main purpose of this paper to study to what extent the (immobile) buffers can retain the properties of the model (2.1).

First, we set some notation:

$$\begin{aligned}
&\kappa_i(u) := k_-^i b_0^i/(k_+^i u + k_-^i) \ \text{ for } \ i = 1, \cdots, n,\\
&\mathbf{b_0} = (b_0^1, \cdots, b_0^n) := (\kappa_1(0), \cdots, \kappa_n(0)),\\
&\mathbf{b_1} = (b_1^1, \cdots, b_1^n) := (\kappa_1(a), \cdots, \kappa_n(a)),\\
&\mathbf{b_2} = (b_2^1, \cdots, b_2^n) := (\kappa_1(1), \cdots, \kappa_n(1)),\\
&\mathbf{v}(x,t) := (v_1(x,t), \cdots, v_n(x,t)).
\end{aligned}$$

Also, for two vectors $\mathbf{c} = (c_1, \cdots, c_n)$ and $\mathbf{d} = (d_1, \cdots, d_n)$, the symbol $\mathbf{c} < \mathbf{d}$ means $c_i < d_i$ for $i = 1, \cdots, n$, and $\mathbf{c} \le \mathbf{d}$ means $c_i \le d_i$ for $i = 1, \cdots, n$. Moreover, let $(u(x,t), \mathbf{v}(x,t))$ denote a classical solution of (2.4)-(2.5) with the initial data $u(\cdot, 0) \in [0,1]$ and $\mathbf{v}(\cdot, 0)) \in [\mathbf{b_2}, \mathbf{b_0}]$ on $\mathbf{R}$. If there is no ambiguity, we will also let $u(x,t)$ denote a classical solution of (2.1) with the initial data $u(\cdot, 0) \in [0,1]$ on $\mathbf{R}$. In the sequel, we will assume that *all of the buffers are stationary (immobile)*, i.e., $D_i = 0$ for $i = 1, \cdots, n$.

Now, we turn to the analysis of the model (2.4)-(2.5). First, experimental observations [9, 64] that the Ca^{2+} wave propagates as a front implies that the cytoplasm of mature *Xenopus* oocyte can support the existence of two alternative stable $[Ca^{2+}]_{cyt}$, i.e., exhibit the unusual property of the *bistability*. Hence, it would be interesting to investigate how the buffers affect the stability of these two physiological states of $[Ca^{2+}]_{cyt}$. In fact, Aronson and Weinberger [3, 2] have showed the attraction basin for the physiological states of $[Ca^{2+}]_{cyt}$, 0 and 1, of the model (2.1) (i.e., the model (2.4)-(2.5) without buffers) as follows:

(P1) *Let $a \in (0,1)$. If $u(x,0) \in [0,a]$ for all $x \in \mathbf{R}$ and $u(\cdot,0) \not\equiv a$, then $\lim_{t\to+\infty} u(x,t) = 0$ uniformly for x in bounded subsets of $\mathbf{R}$.*

(P2) *Let $a \in (0,1)$. If $u(x,0) \in [a,1]$ for all $x \in \mathbf{R}$ and $u(\cdot,0) \not\equiv a$, then $\lim_{t\to+\infty} u(x,t) = 1$ uniformly for x in bounded subsets of $\mathbf{R}$.*

Since $[Ca^{2+}]_{cyt}$ is initially at the basal state 0, we may think of $u(\cdot,0)$ as the initial stimulus (e.g., a micro-injection of Ca^{2+}). Hence (P1)-(P2) imply that in the absence of buffers, if $u(\cdot,0)$ is smaller than the threshold of CICR (a) everywhere, then $[Ca^{2+}]_{cyt}$ will return to its basal state 0 eventually; however, if $u(\cdot,0)$ is higher than the threshold of CICR (a) over the whole cytosol, then $[Ca^{2+}]_{cyt}$ will ultimately go to the unusual elevated Ca^{2+} concentration 1.

On the other hand, if we take the buffers into account, then we need to focus on the model (2.4)-(2.5). This leads to one question: What are the reasonable concentrations of the buffers to accompany these two stable physiological states of $[Ca^{2+}]_{cyt}$, 0 and 1? Indeed, (2.3) tells us that if $[Ca^{2+}]_{cyt}$ is at the state 0 (1, resp.) and in equilibrium with the buffers, then the concentration of the unbound form of the ith buffer, $[B_i]$, $i = 1, \cdots, n$, must take the value b_0^i (b_2^i, resp.). In fact, a quick calculation reveals that $(0, \mathbf{b_0})$ and $(1, \mathbf{b_2})$ are the solutions of (2.4)-(2.5). Also, note that when $[Ca^{2+}]_{cyt}$ is at the stable elevated state 1, the concentrations of the bound forms of the buffers are $\mathbf{b_0} - \mathbf{b_2}$. Furthermore, we can see that these two states, $(0, \mathbf{b_0})$ and $(1, \mathbf{b_2})$, are stable with respect to (2.4)-(2.5) and that their attraction basins are given in the following two properties:

(Q1) *Let* $a \in (0,1)$. *If* $u(x,0) \in [0,a]$, $v_i(x,0) \in [b_1^i, b_0^i]$ *for all* $x \in \mathbf{R}$, $i = 1, \cdots, n$, *and* $u(\cdot,0) \not\equiv a$, *then* $\lim_{t\to+\infty}(u(x,t), \mathbf{v}(x,t)) = (0, \mathbf{b_0})$ *uniformly for* x *in bounded subsets of* $\mathbf{R}$.

(Q2) *Let* $a \in (0,1)$. *If* $u(x,0) \in [a,1]$, $v_i(x,0) \in [b_2^i, b_1^i]$ *for all* $x \in \mathbf{R}$, $i = 1, \cdots, n$, *and* $u(\cdot,0) \not\equiv a$, *then* $\lim_{t\to+\infty}(u(x,t), \mathbf{v}(x,t)) = (1, \mathbf{b_2})$ *uniformly for* x *in bounded subsets of* $\mathbf{R}$.

Note that the buffers consist of two kinds: one is already in the cell (endogenous buffer), the other is added experimentally (exogeneous buffer). We let B_i, $i = 1, \cdots, m$, be the unbound form of the ith endogenous buffer, and B_j, $j = m+1, \cdots, n$, the unbound form of the jth exogeneous buffer. Note that initially, $[\mathrm{Ca}^{2+}]_{\mathrm{cyt}}$ stays at the stable basal state 0 at each space point, and so the concentration of the unbound form of the ith endogenous buffer, $[\mathrm{B}_i]$, $i = 1, \cdots, m$, must take the value b_0^i in order to be in equilibrium with Ca^{2+} over the whole cytosol. Hence (Q1) suggests that if the initial concentration of the unbound form of the jth exogeneous buffer, $[\mathrm{B}_j]$, $j = m+1, \cdots, n$, is in $[b_1^j, b_0^j]$ everywhere, and if the initial stimulus $u(\cdot,0)$ (e.g., a micro-injection of Ca^{2+}) is less than the threshold of CICR (a) at each space point, then $[\mathrm{Ca}^{2+}]_{\mathrm{cyt}}$ will eventually go back to its basal state 0 and the concentrations of the unbound forms of the buffers will return to their total concentrations of the buffers $\mathbf{b_0}$. Note that in order that Ca^{2+} with $[\mathrm{Ca}^{2+}] = a$ is in equilibrium with the jth buffer at a localized space point, $[\mathrm{B}_j]$ must take the value b_1^j by (2.3). (Q2) has a similar implication and we omit it.

Next, we will discuss the threshold behavior of the model (2.4)-(2.5). In fact, in mature *Xenopus* eggs, Ca^{2+} waves can not only be triggered by the entry of sperm, but also by a micro-injection of Ca^{2+}; and it is also reported that in order to initiate a Ca^{2+} wave in such a cell, the injected Ca^{2+} concentration must be greater than some threshold [40, 30]. Even more, similar observations have been found on oocytes of mouse and hamster [10, 44, 26, 18, 32]. Here comes one technical question: How can we observe such phenomena experimentally? Actually, in order to visualize the calcium dynamics, we need to inject a fluorescent indicator (e.g., Ca^{2+}-green dextran, BAPTA, and EGTA) into the cell, and these indicators are exactly the (exogeneous) Ca^{2+} buffers. Thus it would be interesting to see that in the presence of Ca^{2+} buffers, does a threshold in the magnitude/amount of the Ca^{2+} injection exist in order to initiate a Ca^{2+} wave?

Before answering this question, we need to take another point of view to think of the notion of a threshold. We will use Li's idea [30] to pursue this (see also [2, 3]). Indeed, it is known that a threshold exists in the one dimensional cell model (2.1), that is, a. However, this quantity only describes the value of $[\mathrm{Ca}^{2+}]_{\mathrm{cyt}}$ at each space point. Moreover, if the initial stimulus $u(x,0)$ (e.g., a micro-injection of Ca^{2+}) is greater than a at each space point, then the corresponding solution $u(x,t)$ of (2.1) ($[\mathrm{Ca}^{2+}]_{\mathrm{cyt}}$) will evolve into the stable elevated state 1, but not a wave. Therefore, the threshold may not be determined by the size of the injection current. However, a possible candidate could be the total Ca^{2+} content of the injection pipette. Mathematically, it means that the threshold may be determined by the L^1 norm of the initial stimulus $u(x,0)$. In fact, Aronson and Weinberger [3] have proved the following property of (2.4)-(2.5) without buffers (i.e. (2.1)):

(P3) *Let* $a \in (0,1)$. *There exist positive constants* $C = C(a)$ *and* $\sigma = \sigma(a)$ *such that* $u(x,t) = O(e^{-Ct})$ *uniformly for all* x *in* $\mathbf{R}$, *if* $\|u(\cdot,0)\|_1 := \int_{\mathbf{R}} u(x,0)dx < \sigma$.

Initially, in the absence of a stimulus, the cytosol, governed by (2.1), is at the stable basal state 0. Thinking of $u(\cdot,0)$ as the initial stimulus (e.g., a micro-injection of Ca^{2+}), (P3) states that in the absence of buffers, if the L^1 norm of $u(\cdot,0)$ (e.g., the total Ca^{2+} content of the injection pipette) is not sufficiently large, then the wave will not be triggered and the solution $u(x,t)$ of (2.1) ($[\mathrm{Ca}^{2+}]_{\mathrm{cyt}}$)

will decay exponentially fast to the basal state, which is zero in this case, as $t \to +\infty$. Interestingly, even in the presence of immobile buffers, we can have the following property:

(Q3) *Let $a \in (0,1)$. There exist positive constants C and σ depending on k_+^i, k_-^i, b_0^i, a such that $u(x,t) = O(e^{-Ct})$ and $v_i(x,t) = b_0^i + O(e^{-Ct})$ for $i = 1, \cdots, n$, uniformly for all x in $\mathbf{R}$, if $(u(x,0), \mathbf{v}(x,0)) = (\phi(x), \mathbf{b_0})$ on $\mathbf{R}$ with $\|\phi\|_1 := \int_{\mathbf{R}} \phi(x)dx < \sigma$.*

Note that the cytosol, mediated by (2.4)-(2.5), is initially at the basal state $(0, \mathbf{b_0})$. Thinking of $\phi(\cdot)$ as the initial stimulus (e.g., a micro-injection of Ca^{2+}), then (Q3) implies that in the presence of uniformly distributed buffers, a threshold of the L^1 norm of the initial stimulus $\phi(\cdot)$ (e.g., the total Ca^{2+} content of the injection pipette) to trigger a wave indeed exists; and this threshold may depend on the total concentration $\mathbf{b_0}$ and the kinetic properties of the buffers. Moreover, if the L^1 norm of $\phi(\cdot)$ (e.g., the total Ca^{2+} content of the injection pipette) is not bigger than such a threshold, then the cell will return to its basal state $(0, \mathbf{b_0})$ exponentially fast. This result appears to agree with the following experimental observations [10, 18, 44, 32, 40, 26, 30]: a localized increase in $[Ca^{2+}]_{cyt}$ to a high value introduced by a small amount of Ca^{2+} will only induce a localized transient, but not trigger a wave. We briefly discuss the assumption: Buffers are uniformly distributed at $t = 0$. As before, we let B_i, $i = 1, \cdots, m$, be the unbound form of the ith endogenous buffer, and B_j, $j = m+1, \cdots, n$, the unbound form of the jth exogeneous buffer. Since initially, the ith endogenous buffer should be in equilibrium with Ca^{2+} over the whole cytosol, and so $[B_i]$ must take the value b_0^i. Hence all of the endogenous buffers satisfy this assumption. Thus in order to fulfill this assumption, we only distribute the exogeneous buffers uniformly over the whole cell at $t = 0$.

The above discussion suggests the following problem: Does a highly localized increase in $[Ca^{2+}]_{cyt}$ (a Ca^{2+} spike) in a sufficiently large interval (area) evolve into a traveling front? To answer this, we firstly recall the following technical property from [2, 3, 7]:

Let $a \in (0, 1/2)$. Then there is a unique $\chi \in (a, 1)$ such that $\int_0^\chi f(q)dq = 0$. Also, for any given $\eta \in (\chi, 1)$, there exists a constant $d_\eta \in \mathbf{R}^+$ and a solution $q_\eta(x)$ of

$$Dq'' + f(q) = 0 \tag{3.6}$$

in $(-d_\eta, d_\eta)$ such that $0 = q_\eta(\pm d_\eta) < q_\eta(x) \leq \eta = q_\eta(0)$ for $x \in (-d_\eta, d_\eta)$ and $xq_\eta'(x) < 0$ for $x \in (-d_\eta, d_\eta) \setminus \{0\}$.

Now, we can give a partial answer to the above question. Indeed, for one dimensional cell with the absence of buffers, Aronson and Weinberger [3] have proved the following property for (2.1):

(P4) *Let $a \in (0, 1/2)$. If $u(x,0) \geq q_\eta(x - x_0)$ in $(x_0 - d_\eta, x_0 + d_\eta)$ for some $\eta \in (\chi, 1)$ and $x_0 \in \mathbf{R}$, then we have $\lim_{t\to+\infty} u(x,t) = 1$ uniformly for x in bounded subsets of $\mathbf{R}$.*

Thinking of $u(\cdot, 0)$ as the initial stimulus (e.g., a micro-injection Ca^{2+}) and d_η the size of the initial stimulus, then (P4) says that in the absence of buffers, if the magnitude and the size of a localized stimulus $u(\cdot, 0)$ is sufficiently large or $u(\cdot, 0)$ lies above the comparison function q_η, then $[Ca^{2+}]_{cyt}$, governed by (2.1), will evolve into another stable state 1. Furthermore, in the presence of buffers with one assumption on the initial data, we still can show a similar result as stated below.

(Q4) *Let $a \in (0, 1/2)$. If $u(x,0) \geq q_\eta(x - x_0)$ and $v_i(x,0) = \kappa_i(u(x,0))$, $i = 1, \cdots, n$, in $(x_0 - d_\eta, x_0 + d_\eta)$ for some $\eta \in (\chi, 1)$ and $x_0 \in \mathbf{R}$, then $\lim_{t\to+\infty}(u(x,t), \mathbf{v}(x,t)) = (1, \mathbf{b_2})$ uniformly for x in bounded subsets of $\mathbf{R}$.*

We discuss the constraint on the initial data $\mathbf{v}(\cdot, 0)$ of the buffers in (Q4). In fact, if the buffer B_i, $i = 1, \cdots, n$, has kinetics which are much faster than the time scale of the other Ca^{2+} reactions, then following Wagner and Keizer [63, 59], we may conclude that to a first order approximation, v_i satisfies the following:

$$v_i = k_-^i b_0^i / (k_+^i u + k_-^i) = \kappa_i(u).$$

Therefore, the initial constraint $v_i(x, 0) = \kappa_i(u(x, 0))$, $i = 1, \cdots, n$, is fulfilled by the buffers with fast kinetics. In particular, the popular fluorescent indicators in biological experiments, like fura-2 and Calcium Green, have such required properties [41]. We remark that by (Q3)-(Q4), we could expect that there is a threshold effect for the system (2.4)-(2.5). Hence, this not only generalizes (P3)-(P4), but also tells us that stationary buffers cannot destroy the threshold phenomenon.

Now, we briefly discuss Ca^{2+} waves of the system (2.4)-(2.5). Actually, a partial answer to the question of wave activity is given in [60] recently. Recall from [13] that for any $a \in (0, 1)$ there exists a stable monotone traveling wave solution u of (2.1) connecting the stable states 0 and 1 with speed c in the form $u(x, t) = U(x + ct)$. On the other hand, for $a \in (0, 1/2)$ it is shown in [60] that there exists a monotone traveling wave solution $(u, \mathbf{v})$, $\mathbf{v} := (v_1, \cdots, v_n)$, of the system (2.4)-(2.5) with speed $c_0 > 0$ in the form $u(x, t) = \mathcal{U}(x + c_0 t)$, $v_i(x, t) = \mathcal{V}_i(x + c_0 t)$, $i = 1, \cdots, n$, such that

$$(\mathcal{U}, \mathcal{V}_1, \cdots, \mathcal{V}_n)(-\infty) = (0, \mathbf{b}_0), \;\; (\mathcal{U}, \mathcal{V}_1, \cdots, \mathcal{V}_n)(+\infty) = (1, \mathbf{b}_2).$$

Moreover, this traveling wave solution is asymptotically stable in the sense that if a solution $(u, \mathbf{v})$ of (2.4)-(2.5) which vaguely resembles this traveling wave solution at the initial time, then there exists $x_0 \in \mathbf{R}$ such that

$$\lim_{t \to +\infty} |u(x, t) - \mathcal{U}(x + c_0 t + x_0)| = 0, \tag{3.7}$$

$$\lim_{t \to +\infty} |v_i(x, t) - \mathcal{V}_i(x + c_0 t + x_0)| = 0, \; i = 1, \cdots, n, \tag{3.8}$$

uniformly with respect to $x \in \mathbf{R}$. Therefore, we conclude that stationary buffers cannot eliminate the wave activity.

Finally, we want to investigate the propagation property for solutions of (2.4)-(2.5). In particular, we are interested in the case when the disturbance of the stable state which is initially confined to a half-line $(-\infty, x_0]$ for some $x_0 \in \mathbf{R}$. Inspired by work on the wave activity [3, 2, 25], we shall investigate the large time behavior of $u(\xi - st, t)$ and $v_i(\xi - st, t)$, $i = 1, \cdots, n$, as $t \to +\infty$ for small values of the wave speed s, where $u(x, t)$ and $v_i(x, t)$ solve (2.4)-(2.5). More precisely, we have the following propagation property.

(Q5) *Assume that $a \in (0, 1/2)$. Then there exists a positive constant $\hat{c}_0$ such that for any $s < \hat{c}_0$ we have $\lim_{t \to +\infty}(u(\xi - st), \mathbf{v}(\xi - st, t)) = (1, \mathbf{b_2})$ uniformly for ξ in $[\eta, +\infty)$ for all $\eta \in \mathbf{R}$, if $u(x, 0) = 1$, $\mathbf{v}(x, 0) = \mathbf{b_2}$ for all $x \geq x_0$ for some $x_0 \in \mathbf{R}$. A similar result holds for the case $a \in (1/2, 1)$.*

Note that the parameter s which appears in the above property represents the speed of propagation of a disturbance. We may also explain (Q5) as follows. Recall that $(0, \mathbf{b}_0)$ and $(1, \mathbf{b}_2)$ are two stable equilibrium states of the system (2.4)-(2.5). Then (Q5) tells us how these two stable states interact with each other. For example, when $a \in (0, 1/2)$, the state $(1, \mathbf{b}_2)$ is more stable than $(0, \mathbf{b}_0)$, it is natural to expect that the state $(1, \mathbf{b}_2)$ will eventually dominate the whole dynamics. On the other hand, when $a \in (1/2, 1)$, the state $(0, \mathbf{b}_0)$ is more stable than $(1, \mathbf{b}_2)$, the state $(0, \mathbf{b}_0)$ will eventually dominate. The property (Q5) shows that the speed of this propagation (or invading process) is positive. Note that this result could be comparable to those obtained by Aronson and Weinberger [3, 2] and Klaasen and Troy [25].

The main idea to prove (Q1)-(Q5) is to use the comparison principle by constructing suitable super and sub solutions. This idea is based on the works of Aronson and Weinberger [3], Hastings [17], Klaasen and Troy [24, 25], and Schonbek [50].

We now outline the structure of the remaining of this paper as follows. In Section 4, we shall develop a proposition of invariance region and a comparison principle for the system (2.4)-(2.5). Then the proofs of the main results (Q1)-(Q5) are given in Section 5, with all of the proofs of necessary technical lemmas being deferred to the appendix. Finally, a summary and discussion are given in Section 6.

4 Mathematical Preliminaries

Given positive constants k_+^i, k_-^i, $i = 1, \cdots, n$, we set

$$\begin{aligned} F(u, \mathbf{v}) &:= f(u) + \sum_{i=1}^{n} G_i(u, \mathbf{v}),\ f(u) := u(1-u)(u-a), \\ G_i(u, \mathbf{v}) &:= k_-^i b_0^i - (k_+^i u + k_-^i) v_i,\ i = 1, \cdots, n. \end{aligned}$$

By assuming that all of the buffers are immobile, we can rewrite (2.4)-(2.5) as the following system.

$$\frac{\partial u}{\partial t} = D\frac{\partial^2 u}{\partial x^2} + F(u, \mathbf{v}),\ (x,t) \in \mathbf{R} \times \mathbf{R}^+, \quad (\mathbf{R}^+ := (0, \infty)) \tag{4.1}$$

$$\frac{\partial v_i}{\partial t} = G_i(u, \mathbf{v}),\ (x,t) \in \mathbf{R} \times \mathbf{R}^+,\ i = 1, \cdots, n. \tag{4.2}$$

We remark that $G_i(u, \mathbf{v}) = 0$ if and only if $v_i = \kappa_i(u)$. We shall investigate the asymptotic behavior as $t \to +\infty$ of the solution of (4.1)-(4.2) with the initial data

$$u(x, 0) = \phi(x),\ v_i(x, 0) = \psi_i(x),\ i = 1, \cdots, n, \quad \text{for } x \in \mathbf{R}. \tag{4.3}$$

We will briefly discuss the existence of the classical solution of (4.1)-(4.3). In fact, if $\phi(x)$ and $\psi_i(x)$, $i = 1, \cdots, n$, are sufficiently smooth and satisfy that $0 \le \phi(x) \le 1$ and $b_2^i \le \psi_i(x) \le b_0^i$ for all $x \in \mathbf{R}$ and $i = 1, \cdots, n$, then a similar argument as in [46] shows that the problem (4.1)-(4.3) has a unique solution $(u(x,t), \mathbf{v}(x,t))$ of class C^3 on $\mathbf{R} \times [0, \infty)$. Note that $(u(x,t), \mathbf{v}(x,t))$ satisfies

$$\begin{aligned} u(x,t) &= \int_{\mathbf{R}} K(x,y,t)\phi(y)dy \\ &\quad + \int_0^t \int_{\mathbf{R}} K(x,y,t-s)F(u(y,s), \mathbf{v}(y,s))dyds, \end{aligned} \tag{4.4}$$

$$v_i(x,t) = \psi_i(x) + \int_0^t G_i(u(x,s), \mathbf{v}(x,s))ds, \tag{4.5}$$

where

$$K(x,y,t) := \frac{1}{2\sqrt{\pi D t}} e^{-(x-y)^2/(4Dt)}.$$

Suppose that ϕ and ψ_i, $i = 1, \cdots, n$, are uniformly Hölder continuous in $\mathbf{R}$ with exponent α for some $\alpha \in (0,1)$. From (4.4) and (4.5), using an iteration method of Evans and Shenk [12], regularity theory of parabolic equations (cf. [15]) and invariance region theory, we can show that there is a unique solution $(u, \mathbf{v})$ defined for all $t > 0$ such that $u \in C^{2,1}(\mathbf{R} \times \mathbf{R}^+) \cap C^0(\mathbf{R} \times [0, \infty))$, $v_i \in C^0(\mathbf{R} \times \mathbf{R}^+)$, and $v_{i,t} \in C^0(\mathbf{R} \times \mathbf{R}^+)$ for $i = 1, \cdots, n$, where the set $C^{2,1}(\mathbf{R} \times \mathbf{R}^+)$ consists of all functions that are once continuously differentiable in t and twice continuously differentiable in x for all $(x, t) \in \mathbf{R} \times \mathbf{R}^+$, and the set $C^0(\mathbf{R} \times [0, \infty))$ consists of continuous functions in $\mathbf{R} \times [0, \infty)$. Both here and below, for functions $g(x)$ and $h(x, t)$, a constant $\delta \in (0, 1)$, and a set $\Omega \subset \mathbf{R} \times [0, +\infty)$, we define

$$
\begin{aligned}
&|g|_0 \equiv \sup_{x \in \mathbf{R}} |g(x)|, \ [g]_\delta \equiv \sup_{x,y \in \mathbf{R},\, x \neq y} \{|g(x) - g(y)|/|x - y|^\delta\} \\
&C^\delta(\mathbf{R}) := \{g \in C^0(\mathbf{R}) \mid |g|_0 + [g]_\delta < \infty\}, \\
&[h]_{\delta;\Omega} \equiv \sup_{(x,t),(y,s) \in \Omega,\, (x,t) \neq (y,s)} \{|h(x, t) - h(y, s)|/(|x - y|^\delta + |t - s|^{\delta/2})\}, \\
&|h|_{0;\Omega} \equiv \sup_{(x,t) \in \Omega} |h(x, t)|, \ |h|_{\delta;\Omega} \equiv |h|_{0;\Omega} + [h]_{\delta;\Omega}, \\
&C^\delta(\Omega) := \{h \in C^0(\Omega) \mid |h|_{0;\Omega} + [h]_{\delta;\Omega} < \infty\}.
\end{aligned}
$$

Therefore, except otherwise stated, we shall assume that the initial data $\phi(x)$ and $\psi_i(x)$, $i = 1, \cdots, n$, are in $C^\alpha(\mathbf{R})$ for some $\alpha \in (0, 1)$.

First, we have the following proposition of invariance regions.

Proposition 1 *(Invariance Region) Let $(u, \mathbf{v})$ be a global solution of (4.1)-(4.2) with $0 \leq u(x, 0) \leq 1$ and $\mathbf{b}_2 \leq \mathbf{v}(x, 0) \leq \mathbf{b}_0$ for all $x \in \mathbf{R}$. Then the followings hold.*

(1) *$0 \leq u(x, t) \leq 1$ and $\mathbf{b_2} \leq \mathbf{v}(x, t) \leq \mathbf{b_0}$ for all $(x, t) \in \mathbf{R} \times \mathbf{R}^+$.*

(2) *If $0 \leq u(x, 0) \leq a$ and $\mathbf{b_1} \leq \mathbf{v}(x, 0) \leq \mathbf{b_0}$ for all $x \in \mathbf{R}$, then $0 \leq u(x, t) \leq a$ and $\mathbf{b_1} \leq \mathbf{v}(x, t) \leq \mathbf{b_0}$ for all $(x, t) \in \mathbf{R} \times \mathbf{R}^+$.*

(3) *If $a \leq u(x, 0) \leq 1$ and $\mathbf{b_2} \leq \mathbf{v}(x, 0) \leq \mathbf{b_1}$ for all $x \in \mathbf{R}$, then $a \leq u(x, t) \leq 1$ and $\mathbf{b_2} \leq \mathbf{v}(x, t) \leq \mathbf{b_1}$ for all $(x, t) \in \mathbf{R} \times \mathbf{R}^+$.*

Proof. We shall only consider the case when $0 \leq u(x, 0) \leq 1$ and $\mathbf{b_2} \leq \mathbf{v}(x, 0) \leq \mathbf{b_0}$ for all $x \in \mathbf{R}$, since the proof for the other two cases are similar. However, the proof follows from Theorem 14.11 on p.203 and Corollary 14.9 on p.202 of [57] (see also [48]). The outer normal conditions on the boundary of the set $\{(u, \mathbf{v}) \mid 0 \leq u \leq 1, b_2^i \leq v_i \leq b_0^i, i = 1, \cdots, n\}$ follow from the properties of F and G_i, $i = 1, \cdots, n$. $\square$

Throughout this paper, we shall always assume that the initial data $\phi(x)$ and $\psi_i(x)$, $i = 1, \cdots, n$, are in $[0, 1]$ and $[b_2^i, b_0^i]$, respectively.

The next proposition is a comparison theorem for the system (4.1)-(4.2).

Proposition 2 *(Comparison Principle) Let $(u_j, \mathbf{v}_j), j = 1, 2$, be the solution of (4.1)-(4.2) on $(\hat{a}, \hat{b}) \times \mathbf{R}^+$ with $0 \leq u_1(x, 0) \leq u_2(x, 0) \leq 1$ and $\mathbf{b_2} \leq \mathbf{v}_2(x, 0) \leq \mathbf{v}_1(x, 0) \leq \mathbf{b_0}$ for all $x \in \mathbf{R}$. If $\hat{a} \neq -\infty$, we assume that $0 \leq u_1(\hat{a}, t) \leq u_2(\hat{a}, t) \leq 1$ and $\mathbf{b_2} \leq \mathbf{v}_2(\hat{a}, t) \leq \mathbf{v}_1(\hat{a}, t) \leq \mathbf{b_0}$ for all $t > 0$; if $\hat{b} \neq +\infty$, we assume that $0 \leq u_1(\hat{b}, t) \leq u_2(\hat{b}, t) \leq 1$ and $\mathbf{b_2} \leq \mathbf{v}_2(\hat{b}, t) \leq \mathbf{v}_1(\hat{b}, t) \leq \mathbf{b_0}$ for all $t > 0$. Then the following statements hold.*

(1) *$u_1(x, t) \leq u_2(x, t)$ and $\mathbf{v}_2(x, t) \leq \mathbf{v}_1(x, t)$ for all $(x, t) \in (\hat{a}, \hat{b}) \times \mathbf{R}^+$.*

(2) *If $0 \leq u_1(x, 0) < u_2(x, 0) \leq 1$ for all $x \in (c, d) \subseteq (\hat{a}, \hat{b})$, then we have $u_1(x, t) < u_2(x, t)$ and $\mathbf{v}_2(x, t) < \mathbf{v}_1(x, t)$ for all $(x, t) \in (\hat{a}, \hat{b}) \times \mathbf{R}^+$.*

Proof. Set $\mathbf{v}_1 = (v_{11}, \cdots, v_{1n})$, $\mathbf{v}_2 = (v_{21}, \cdots, v_{2n})$, and $(\tilde{u}, \tilde{\mathbf{v}}) = (u_1 - u_2, \mathbf{v}_2 - \mathbf{v}_1)$. Then $(\tilde{u}, \tilde{\mathbf{v}})$ satisfies

$$L_1[\tilde{u}, \tilde{\mathbf{v}}] = F(u_1, \mathbf{v}_1) - F(u_2, \mathbf{v}_2) := [f_1(x,t)\tilde{u} - \sum_{i=1}^{n} f_{1i}(x,t)\tilde{v}_i], \tag{4.6}$$

$$L_{2i}[\tilde{u}, \tilde{\mathbf{v}}] = G_i(u_2, \mathbf{v}_2) - G_i(u_1, \mathbf{v}_1) := [-g_{2i}(x,t)\tilde{u} + \tilde{g}_{2i}(x,t)\tilde{v}_i], \ i = 1, \cdots, n, \tag{4.7}$$

together with the initial data

$$\tilde{u}(x,0) = u_1(x,0) - u_2(x,0), \ \tilde{v}_i(x,0) = v_{2i}(x,0) - v_{1i}(x,0), \ i = 1, \cdots, n,$$

where

$$\begin{aligned}
L_1[u, \mathbf{v}] &= u_t - Du_{xx}, \\
L_{2i}[u, \mathbf{v}] &= v_{i,t}, \\
f_1(x,t) &= F_u(\theta_1 u_1 + (1-\theta_1)u_2, \theta_1 \mathbf{v}_1 + (1-\theta_1)\mathbf{v}_2)(x,t), \\
f_{1i}(x,t) &= F_{v_i}(\theta_1 u_1 + (1-\theta_1)u_2, \theta_1 \mathbf{v}_1 + (1-\theta_1)\mathbf{v}_2)(x,t), \\
g_{2i}(x,t) &= G_{i,u}(\theta_{2i} u_1 + (1-\theta_{2i})u_2, \theta_{2i} \mathbf{v}_1 + (1-\theta_{2i})\mathbf{v}_2)(x,t), \\
\tilde{g}_{2i}(x,t) &= G_{i,v_i}(\theta_{2i} u_1 + (1-\theta_{2i})u_2, \theta_{2i} \mathbf{v}_1 + (1-\theta_{2i})\mathbf{v}_2)(x,t),
\end{aligned}$$

for some $\theta_1 = \theta_1(u_1, \mathbf{v}_1, u_2, \mathbf{v}_2) \in (0,1)$, $\theta_{2i} = \theta_{2i}(u_1, \mathbf{v}_1, u_2, \mathbf{v}_2) \in (0,1)$ and $i = 1, \cdots, n$.

We claim that the region $\{\tilde{u} \le 0, \tilde{v}_i \le 0, i = 1, \cdots, n\}$ is invariant under the flow (4.6)-(4.7). Indeed, from Proposition 1 and the definitions of F and G_i, it follows that

$$f_{1i}(x,t) < 0 \text{ and } g_{2i}(x,t) < 0 \ \text{ for all } (x,t) \in (\hat{a}, \hat{b}) \times [0, +\infty) \text{ and } i = 1, \cdots, n. \tag{4.8}$$

Also, note that $\tilde{u}(x,0) \le 0$ and $\tilde{\mathbf{v}}(x,0) \le 0$ for all $x \in (\hat{a}, \hat{b})$ with the correct inequalities on the boundary sets if $\hat{a} \neq -\infty$ or $\hat{b} \neq +\infty$. Therefore, for each $i = 1, \cdots, n$, by Theorem 14.11 of [57, p. 203] we have $\tilde{u}(x,t) \le 0$ and $\tilde{\mathbf{v}}(x,t) \le \mathbf{0}$ for all $(x,t) \in (\hat{a}, \hat{b}) \times [0, +\infty)$.

Now we turn to the proof of the second part. First, we claim that $\tilde{u}(x,t) < 0$ for all $(x,t) \in (\hat{a}, \hat{b}) \times \mathbf{R}^+$. By our assumption, it follows that

$$\tilde{u}(x,0) < 0 \ \text{ for all } x \in (c,d). \tag{4.9}$$

For contradiction, we suppose that there exist $x_1 \in (\hat{a}, \hat{b})$ and $t_1 > 0$ such that $\tilde{u}(x_1, t_1) = 0$. Choose a bounded interval $(a_1, b_1) \subset (\hat{a}, \hat{b})$ such that $a_1 < x_1 < b_1$ and $(a_1, b_1) \cap (c,d) \neq \emptyset$. Then we have $\tilde{u}(a_1, t) \le 0$, $\tilde{\mathbf{v}}(a_1, t) \le \mathbf{0}$ and $\tilde{u}(b_1, t) \le 0$, $\tilde{\mathbf{v}}(b_1, t) \le \mathbf{0}$ for all $t \in [0, t_1]$, and $\tilde{u}(x,0) \le 0$, $\tilde{\mathbf{v}}(x,0) \le \mathbf{0}$ for all $x \in [a_1, b_1]$. Although the diffusion coefficients of $\tilde{v}_i$ in our system is 0 for $i = 1, \cdots, n$, however, scrutinizing the proof of Theorem 13 in [45, pp. 189-190], we can conclude that $\tilde{u} \equiv 0$ on $[a_1, b_1] \times [0, t_1]$, a contradiction to (4.9). Therefore, we have $\tilde{u}(x,t) < 0$ for all $(x,t) \in (\hat{a}, \hat{b}) \times \mathbf{R}^+$.

Finally, we prove that $\tilde{\mathbf{v}}(x,t) < \mathbf{0}$ for all $(x,t) \in (\hat{a}, \hat{b}) \times \mathbf{R}^+$. Indeed, fix $i \in \{1, \cdots, n\}$ and for contradiction, we assume that there exist $x_2 \in (\hat{a}, \hat{b})$ and $t_2 > 0$ such that $\tilde{v}_i(x_2, t_2) = 0$. Since $\tilde{v}_i \le 0$ on $(\hat{a}, \hat{b}) \times [0, +\infty)$, we have $\tilde{v}_{i,t}(x_2, t_2) = \partial \tilde{v}_i / \partial t(x_2, t_2) \ge 0$. On the other hand, using the fact that $\tilde{u}(x_2, t_2) < 0$ and (4.7)-(4.8), it follows that

$$\begin{aligned}
\tilde{v}_{i,t}(x_2, t_2) &= -g_{2i}(x_2, t_2)\tilde{u}(x_2, t_2) + \tilde{g}_{2i}(x_2, t_2)\tilde{v}_i(x_2, t_2) \\
&< \tilde{g}_{2i}(x_2, t_2)\tilde{v}_i(x_2, t_2) = 0,
\end{aligned}$$

a contradiction. Thus we have $\tilde{v}_i(x,t) < 0$ for all $(x,t) \in (\hat{a}, \hat{b}) \times \mathbf{R}^+$. The proof is completed. □

We shall quote some results from [7] about solutions of the equation (3.6). These results will play a very important role in the proof of our theorems.

First, we define the functional

$$H(q) = \frac{1}{D} \int_0^q f(s)ds.$$

Note that

$$E[q](x) := \frac{1}{2}(q')^2(x) + H(q(x))$$

is constant along any trajectory of (3.6). Assume that $a \in (0, 1/2)$. Then there exists a unique positive number $\chi \in (a, 1)$ such that $H(\chi) = 0$. The trajectory through the regular point $(\chi, 0)$ in the phase plane (q, q') is the locus of points (q, q') satisfying $(q')^2/2 + H(q) = 0$. It is therefore a closed curve which intersects the q-axis at $(\chi, 0)$ and $(0, 0)$. We denote the corresponding solution as q_χ with $q_\chi(0) = \chi$. Moreover, for any given $\eta \in (\chi, 1)$, there exists a constant $d_\eta \in \mathbf{R}^+$ and a function $q_\eta(x)$ such that $q_\eta(x)$ is a solution of (3.6) in $(-d_\eta, d_\eta)$ such that $0 = q_\eta(\pm d_\eta) < q_\eta(x) \leq \eta = q_\eta(0)$ in $(-d_\eta, d_\eta)$ and $xq'_\eta(x) < 0$ for $x \in (-d_\eta, d_\eta) \setminus \{0\}$.

The following proposition is the main tool for our discussion.

Proposition 3 *Fix $l \in \{0, a\}$. Let q be a solution of (3.6) in $(\hat{a}, \hat{b})$ such that $l \leq q \leq 1$ in $(\hat{a}, \hat{b})$, where $-\infty \leq \hat{a} < \hat{b} \leq +\infty$. Here we assume that $q(\hat{a}) = l$, if $\hat{a} > -\infty$; and $q(\hat{b}) = l$, if $\hat{b} < +\infty$. Let $(u, \mathbf{v})$ be the solution of (4.1)-(4.2) with the initial values*

$$u(x, 0) = \begin{cases} q(x) & \text{in } (\hat{a}, \hat{b}), \\ l & \text{otherwise}, \end{cases} \quad \text{and} \quad v_i(x, 0) = \kappa_i(u(x, 0)),\ i = 1, \cdots, n.$$

Then $u(x, t+h) \geq u(x, t)$ and $\mathbf{v}(x, t+h) \leq \mathbf{v}(x, t)$ for all $(x, t) \in \mathbf{R} \times [0, +\infty)$ for any $h > 0$. Also, there exists a solution w of (3.6) in $\mathbf{R}$ with the property

$$w \geq q \ \text{ in } \ (\hat{a}, \hat{b}),\ w \in [l, 1] \ \text{ on } \ \mathbf{R} \tag{4.10}$$

such that

$$\lim_{t \to +\infty} u(x, t) = w(x), \quad \lim_{t \to +\infty} v_i(x, t) = \kappa_i(w(x)),\ i = 1, \cdots, n,$$

uniformly for x in any bounded interval of $\mathbf{R}$. Moreover, if $\tilde{w}$ is a solution of (3.6) with the property (4.10) and $\tilde{\sigma}_i(x) := \kappa_i(\tilde{w}(x))$, $i = 1, \cdots, n$, for all $x \in \mathbf{R}$, then we have $\tilde{w} \geq w$ and $\tilde{\sigma}_i \leq \sigma_i$ on $\mathbf{R}$ for $i = 1, \cdots, n$.

Proof. We assume that $\hat{a} > -\infty$ and $\hat{b} < +\infty$, since the other cases $\hat{a} > -\infty$ or $\hat{b} < +\infty$ can be handled in a similar way. By Proposition 1, we have $u(x, t) \in [l, 1]$ and $v_i(x, t) \in [b_2^i, \kappa_i(l)]$ for all $(x, t) \in \mathbf{R} \times [0, +\infty)$ and $i = 1, \cdots, n$. Set $\mathbf{p} := (p_1, \cdots, p_n)$, where $p_i(x) := \kappa_i(q(x))$, $i = 1, \cdots, n$. Note that $(q, \mathbf{p})$ and $(u, \mathbf{v})$ are solutions of (4.1)-(4.2) on $(\hat{a}, \hat{b}) \times \mathbf{R}^+$ such that $q(x) = u(x, 0)$, $\mathbf{p}(x) = \mathbf{v}(x, 0)$ for all $x \in (\hat{a}, \hat{b})$, and $l = q(\hat{a}) \leq u(\hat{a}, t)$, $l = q(\hat{b}) \leq u(\hat{b}, t)$, $v_i(\hat{a}, t) \leq p_i(\hat{a}) = \kappa_i(l)$, $v_i(\hat{b}, t) \leq p_i(\hat{b}) = \kappa_i(l)$ for all $t > 0$ and $i = 1, \cdots, n$. Then, by applying Proposition 2, we obtain that $u(x, t) \geq q(x)$ and $\mathbf{v}(x, t) \leq \mathbf{p}(x)$ for all $(x, t) \in (\hat{a}, \hat{b}) \times \mathbf{R}^+$. Therefore, for any $h > 0$ and each $i = 1, \cdots, n$, we have

$$u(x, h) \geq u(x, 0) \quad \text{and} \quad v_i(x, h) \leq v_i(x, 0) \ \text{ for all } \ x \in \mathbf{R}.$$

Apply Proposition 2 again, we conclude that for any $h > 0$ and each $i = 1, \cdots, n$,

$$u(x, t+h) \geq u(x, t) \quad \text{and} \quad v_i(x, t+h) \leq v_i(x, t) \quad \text{for all } \ (x, t) \in \mathbf{R} \times \mathbf{R}^+.$$

Noting that $u \le 1$ on $\mathbf{R} \times \mathbf{R}^+$, it follows that for each $x \in \mathbf{R}$, $u(x,t)$ is nondecreasing in t and bounded above, and so the limit $\lim_{t\to+\infty} u(x,t) = w(x)$ exists for all $x \in \mathbf{R}$. Clearly, (4.10) holds. Similarly, for each $x \in \mathbf{R}$ and $i = 1, \cdots, n$, $v_i(x,t)$ is nonincreasing and bounded below by b_2^i, and so the limit $\lim_{t\to+\infty} v_i(x,t) = \sigma_i(x)$ exists for all $x \in \mathbf{R}$.

Using the bounds of u and $\mathbf{v}$, by applying the interior L^p estimate (cf. Theorem 7.13 of [28, p. 172], for example) to (4.1) and Sobolev's embedding theorems, it is easy to show that there exists a positive constant c_1, depending only on D, k_+^i, k_-^i, $\mathbf{b_0}$, $|u(\cdot,0)|_\alpha$, such that

$$|u|_{\alpha;Q} \le c_1, \;\; Q := \mathbf{R} \times [0, +\infty). \tag{4.11}$$

Next, we claim that there exists c_2, determined by D, k_+^i, k_-^i, $\mathbf{b_0}$, $|u(\cdot,0)|_\alpha$, $|v_i(\cdot,0)|_\alpha$, such that

$$|v_i|_{\alpha;Q} \le c_2. \tag{4.12}$$

Indeed, fix $i \in \{1, \cdots, n\}$. Solving (4.2), we obtain that

$$v_i(x,t) = e^{-\int_0^t (k_+^i u(x,s) + k_-^i) ds} \psi_i(x) + k_-^i b_0^i \int_0^t e^{\int_t^s (k_+^i u(x,\tau) + k_-^i) d\tau} ds.$$

For $(x,t), (y,t) \in Q$ with $x \ne y$, we have

$$\begin{aligned}
|v_i(x,t) - v_i(y,t)| \;\; &\le \;\; |e^{-\int_0^t (k_+^i u(x,s)+k_-^i) ds} - e^{-\int_0^t (k_+^i u(y,s)+k_-^i) ds}|\psi_i(x) \\
&\quad + e^{-\int_0^t (k_+^i u(y,s)+k_-^i) ds} |\psi_i(x) - \psi_i(y)| \\
&\quad + k_-^i b_0^i \int_0^t |e^{\int_t^s (k_+^i u(x,\tau)+k_-^i) d\tau} - e^{\int_t^s (k_+^i u(y,\tau)+k_-^i) d\tau}| ds \\
&:= \;\; I + II + III.
\end{aligned}$$

Using $b_2^i \le \psi_i(x) \le b_0^i$ for all $x \in \mathbf{R}$, $[u]_{\alpha;Q} \le c_1$, and the inequality

$$|e^{-x_1} - e^{-x_2}| \le |x_1 - x_2| \;\; \text{for all } x_1, x_2 \ge 0,$$

it follows that

$$\begin{aligned}
I \;\; &\le \;\; |e^{-k_-^i t} (\int_0^t k_+^i u(x,s) ds - \int_0^t k_+^i u(y,s) ds)| \psi_i(x) \\
&\le \;\; c_1 k_+^i b_0^i t e^{-k_-^i t} |x - y|^\alpha
\end{aligned}$$

for all $t \ge 0$. For II, we have

$$II \le [\psi_i]_\alpha |x - y|^\alpha.$$

Similarly, we can estimate III as the following.

$$\begin{aligned}
III \;\; &\le \;\; k_-^i b_0^i \int_0^t e^{k_-^i (s-t)} k_+^i | \int_t^s (u(x,\tau) - u(y,\tau)) d\tau | ds \\
&\le \;\; c_1 k_+^i k_-^i b_0^i (\int_0^t (t-s) e^{k_-^i (s-t)} ds) |x - y|^\alpha \\
&\le \;\; c_1 k_+^i k_-^i b_0^i [(e^{-k_-^i t} + 1 + k_-^i t e^{-k_-^i t}) / (k_-^i)^2] |x - y|^\alpha.
\end{aligned}$$

From these estimates on I, II and III, we conclude that there exists c_2, determined by D, k_+^i, k_-^i, $\mathbf{b_0}$, $|u(\cdot,0)|_\alpha$, $|v_i(\cdot,0)|_\alpha$, such that

$$|v_i(x,t) - v_i(y,t)| \le c_2 |x - y|^\alpha \;\; \text{for all } \;(x,t), (y,t) \in Q \;\text{ and }\; i = 1, \cdots, n. \tag{4.13}$$

For $(x,t),(x,s)\in Q$, by applying the mean-value theorem to (4.2), there exists a constant which is still denoted by c_2, such that

$$|v_i(x,t)-v_i(x,s)|\le c_2|t-s| \;\text{ for all }\; (x,t),(x,s)\in Q \;\text{ and }\; i=1,\cdots,n. \tag{4.14}$$

Now, for all $(x,t),(y,s)\in Q$, from (4.13), (4.14), and the following inequality

$$\frac{|v_i(x,t)-v_i(y,s)|}{|x-y|^\alpha+|t-s|^{\alpha/2}}\le\frac{|v_i(x,t)-v_i(y,t)|}{|x-y|^\alpha}+\frac{|v_i(y,t)-v_i(y,s)|}{|t-s|^{\alpha/2}},$$

the claim (4.12) follows.

Therefore, (4.11), (4.12), and the Schauder estimates (see Theorem 5 of [15, p. 64]) imply that $[u]_{\alpha;Q}$, $|u_x|_{0;Q}$, $|u_{xx}|_{0;Q}$, $[u_{xx}]_{\alpha;Q}$, $|u_t|_{0;Q}$, and $[u_t]_{\alpha;Q}$ are bounded uniformly. Furthermore, from (4.2) and (4.12) it follows that $[v_i]_{\alpha;Q}$, $|v_{i,t}|_{0;Q}$, and $[v_{i,t}]_{\alpha;Q}$, $i=1,\cdots,n$, are also uniformly bounded. Then we can conclude that, for each bounded x interval, the t parameterized families of functions u, u_{xx}, u_t, v_i, $v_{i,t}$ are equicontinuous in x and hence converge uniformly to w, w_{xx}, 0, σ_i, 0, respectively, as $t\to\infty$. Thus w satisfies (3.6) and σ_i satisfies $\sigma_i=\kappa_i(w)$ for $i=1,\cdots,n$.

Finally, if $\tilde w$ is a solution of (3.6) with the property (4.10) and $\tilde\sigma_i(x)=\kappa_i(\tilde w(x))$, $i=1,\cdots,n$, then we have $\tilde w(x)\ge u(x,0)$ and $\tilde\sigma_i(x)\le v_i(x,0)$ for all $x\in\mathbf{R}$ and $i=1,\cdots,n$. Then, by applying Proposition 2, we obtain that $\tilde w(x)\ge u(x,t)$ and $\tilde\sigma_i(x)\le v_i(x,t)$ for all $(x,t)\in\mathbf{R}\times\mathbf{R}^+$ and $i=1,\cdots,n$. This implies that $\tilde w\ge w$ and $\tilde\sigma_i\le\sigma_i$ on $\mathbf{R}$ for $i=1,\cdots,n$. Thus the theorem follows. ∎

5 Proofs of Main Results

For reader's convenience, all of the proofs of lemmas in this section are deferred to the appendix.

5.1 Stability of the equilibrium state $(1,\mathbf{b_2})$

In this subsection, we determine the stability of the equilibrium state $(1,\mathbf{b_2})$ of (4.1)-(4.2) and obtain its attraction region.

Theorem 1 *Let $a\in(0,1)$ and $(u,\mathbf{v})$ be a solution of (4.1)-(4.2) satisfying that $u(x,0)\in[a,1]$, $v_i(x,0)\in[b_2^i,b_1^i]$ for all $x\in\mathbf{R}$ and $i=1,\cdots,n$, and $u(\cdot,0)\not\equiv a$. Then*

$$\lim_{t\to+\infty}(u(x,t),\mathbf{v}(x,t))=(1,\mathbf{b_2})$$

uniformly for x in bounded subsets of $\mathbf{R}$.

Proof. Since $u(\cdot,0)\not\equiv a$, by Proposition 2, we conclude that $u(x,t)>a$ and $\mathbf{v}(x,t)<\mathbf{b_1}$ for all $(x,t)\in\mathbf{R}\times\mathbf{R}^+$. Let $h>0$. Let $\epsilon\in(0,1-a)$ be sufficiently small such that $u(x,h)\ge a+\epsilon$ and $v_i(x,h)\le b_1^i-\epsilon$ for all $x\in[-\delta_1,\delta_1]$ and $i=1,\cdots,n$, where δ_1 is defined in Lemma 7.1 of the appendix. Then from Lemma 7.1 it follows that there exist a solution $q(x)$ of (3.6) and $\hat x\in(0,\delta_1)$ such that $q(x)\in(a,a+\epsilon]$ for all $x\in(-\hat x,\hat x)$ and $q(\pm\hat x)=a$. Then from Propositions 2 and 3 it follows that

$$\liminf_{t\to+\infty}u(x,t)\ge w(x) \;\text{ and }\; \limsup_{t\to+\infty}v_i(x,t)\le\sigma_i(x) \;\text{ for all }\; x\in\mathbf{R},$$

where $w(x)$ satisfies (3.6) in $\mathbf{R}$, $\sigma_i(x)=\kappa_i(w(x))$, $i=1,\cdots,n$, and $a\le q(x)\le w(x)\le1$, $b_2^i\le\sigma_i(x)\le\kappa_i(q(x))\le b_1^i$ for all $x\in(-\hat x,\hat x)$.

If we can show that $w\equiv1$ and $\sigma_i\equiv b_2^i$ for $i=1,\cdots,n$, then the proof is completed. Indeed, since $w(x)\in[a,1]$ and satisfies (3.6) for all $x\in\mathbf{R}$, it follows from the phase plane analysis that either $w\equiv a$ or 1. Since $w(0)\ge q(0)>a$, we must have $w\equiv1$, and so $\sigma_i\equiv b_2^i$ on $\mathbf{R}$ for $i=1,\cdots,n$. This completes the proof. ∎

5.2 Stability of the equilibrium state $(0, \mathbf{b_0})$

In this subsection, we derive the asymptotic stability of the equilibrium state $(0, \mathbf{b_0})$ of (4.1)-(4.2) as follows. Since the proof of the following theorem is similar to that of Theorem 1, we shall omit it.

Theorem 2 *Let $a \in (0,1)$ and $(u, \mathbf{v})$ be a solution of (4.1)-(4.2) satisfying that $u(x,0) \in [0,a]$, $v_i(x,0) \in [b_1^i, b_0^i]$ for all $x \in \mathbf{R}$ and $i = 1, \cdots, n$, and $u(\cdot, 0) \not\equiv a$, then*

$$\lim_{t \to +\infty} (u(x,t), \mathbf{v}(x,t)) = (0, \mathbf{b_0})$$

uniformly for x in bounded subsets of $\mathbf{R}$.

5.3 Threshold phenomenon

In this subsection, we mainly concern the threshold phenomenon for our system. For this, we first note that one can view the initial data $(u(x,0), \mathbf{v}(x,0))$ as a perturbation of either the equilibrium state $(1, \mathbf{b_2})$ or $(0, \mathbf{b_0})$. And we shall show that a disturbance $(u(x,0), \mathbf{v}(x,0))$ of the state $(0, \mathbf{b_0})$ which is not sufficiently large on a sufficiently large interval will eventually go to the state $(0, \mathbf{b_0})$, and so this implies that $(0, \mathbf{b_0})$ is asymptotically stable with respect to such perturbation. More precisely, we have the following theorem.

Theorem 3 *Let $a \in (0,1)$ and $(u, \mathbf{v})$ be the solution of (4.1)-(4.2) with the initial value $(\phi, \mathbf{b_0})$. Then there exist positive constants $C = C(k_+^i, k_-^i, b_0^i, a)$ and $\sigma = \sigma(k_+^i, k_-^i, b_0^i, a)$ such that*

$$u(x,t) = O(e^{-Ct}) \ \text{ and } \ v_i(x,t) = b_0^i + O(e^{-Ct}) \ \text{ for } \ i = 1, \cdots, n,$$

uniformly in $\mathbf{R}$, if $\|\phi\|_1 := \int_{\mathbf{R}} \phi(x)dx < \sigma$.

In order to prove Theorem 3, we first have the following lemma which is a weaker version of Theorem 2.

Lemma 5.1 *Let $(u(x,t), \mathbf{v}(x,t)) \in [0,1] \times [b_2^1, b_0^1] \times \cdots \times [b_2^n, b_0^n]$ be a solution of (4.1)-(4.2) on $\mathbf{R} \times [0, +\infty)$. If there exists $\gamma \in (0,a)$ such that $u(x,0) \in [0,\gamma]$ and $\mathbf{v}(x,0) \in [\kappa_1(\gamma), b_0^1] \times \cdots \times [\kappa_n(\gamma), b_0^n]$ for all $x \in \mathbf{R}$, then there exists a positive constant $C = C(k_+^i, k_-^i, b_0^i, a)$ such that*

$$u(x,t) = O(e^{-Ct}) \ \text{ and } \ v_i(x,t) = b_0^i + O(e^{-Ct}) \ \text{ for } \ i = 1, \cdots, n,$$

uniformly in $\mathbf{R}$.

Inspired by the idea of Schonbek [50], we can estimate the L^∞ norm of the solution $(u, \mathbf{v})$ of (4.1)-(4.2) by the L^1 norm of the initial condition. More precisely, we have the following lemma.

Lemma 5.2 *Let $(u, \mathbf{v})$ be the solution of (4.1)-(4.2) with the initial value $(\phi, \mathbf{b_0})$ at $t = 0$. Then there exists a positive constant C such that*

$$u(x,t) + \sum_{i=1}^{n} (b_0^i - v_i(x,t)) \le C\Big(\frac{1}{\sqrt{t}} + \sqrt{t} + e^{Ct} + \sqrt{t}e^{Ct} + t\sqrt{t}e^{Ct}\Big)\|\phi\|_1 \tag{5.1}$$

for all $(x,t) \in \mathbf{R} \times [0, +\infty)$, where $\|\phi\|_1$ is defined by $\|\phi\|_1 = \int_{\mathbf{R}} \phi(x)dx$.

Now, we are ready to prove Theorem 3.

Proof of Theorem 3. By Lemma 5.2, we have

$$u(x,1)+\sum_{i=1}^{n}(b_0^i - v_i(x,1)) \le C(2+3e^C)\|\phi\|_1 \quad \text{for all } \; x\in \mathbf{R},$$

where C is defined in Lemma 5.2. This implies that we can choose $\sigma > 0$ such that $u(x,1) < a/2$ and $v_i(x,1) > \kappa_i(a/2)$ for all $x \in \mathbf{R}$ and $i = 1, \cdots, n$, if $\|\phi\|_1 < \sigma$. Combining this with Lemma 5.1, the theorem follows. □

The following theorem shows us that $(u, \mathbf{v}) \equiv (1, \mathbf{b_2})$ is asymptotically stable with respect to some perturbation.

Theorem 4 *Let $a \in (0, 1/2)$ and $(u, \mathbf{v})$ be a solution of (4.1)-(4.2) on $\mathbf{R} \times \mathbf{R}^+$. If*

$$u(x,0) \ge q_\eta(x-x_0), \;\; v(x,0)=\kappa_i(u(x,0)), \; i=1,\cdots,n, \; in \;\; (x_0-d_\eta, x_0+d_\eta)$$

for some $\eta \in (\chi, 1)$ and for some x_0, then we have

$$\lim_{t\to+\infty} u(x,t)=1 \quad and \quad \lim_{t\to+\infty} v_i(x,t)=b_2^i, \; i=1,\cdots,n$$

for all $x \in \mathbf{R}$.

Proof. By Proposition 2, we may assume that $u(x, 0) = q_\eta(x - x_0)$. Then we apply Proposition 3 with $(q(x), p_1(x), \cdots, p_n(x)) = (q_\eta(x), \kappa_1(q_\eta(x)), \cdots, \kappa_n(q_\eta(x)))$. What left to prove is that $\tau \equiv 1$ on $\mathbf{R}$. However, this follows from the phase plane consideration (see also [3]). This completes the proof. □

Theorems 3 and 4 show the existence of a threshold phenomenon for the system (4.1)-(4.2). Therefore, stationary buffers cannot destroy the threshold phenomenon.

5.4 Propagation phenomenon

Recall that $(0, \mathbf{b}_0)$ and $(1, \mathbf{b}_2)$ are two stable states of the system (4.1)-(4.2). In this subsection, we shall investigate how these two stable states interact with each other. Recall from [60] that, under certain assumptions, for $a \in (0, 1/2)$ there exists a traveling wave solution $(u, \mathbf{v})$ of (4.1)-(4.2) with speed $c_0 > 0$ in the form $u(x, t) = \mathcal{U}(x + c_0t)$, $v_i(x, t) = \mathcal{V}_i(x + c_0t)$, $i = 1, \cdots, n$, such that

$$(\mathcal{U},\mathcal{V}_1,\cdots,\mathcal{V}_n)(-\infty)=(0,\mathbf{b}_0), \;\; (\mathcal{U},\mathcal{V}_1,\cdots,\mathcal{V}_n)(+\infty)=(1,\mathbf{b}_2).$$

Moreover, it is also shown [60] that this traveling wave solution is asymptotically stable in a certain sense (see (3.7) and (3.8) in section 3). Roughly speaking, under certain conditions on the initial data, a solution $(u, \mathbf{v})$ of (4.1)-(4.2) converges to a translation of this traveling wave solution as $t \to +\infty$. Note that the state $(1, \mathbf{b}_2)$ is more stable than the state $(0, \mathbf{b}_0)$, if $a \in (0, 1/2)$. Therefore, it is natural to expect that the state $(1, \mathbf{b}_2)$ will eventually dominate the whole dynamics. The existence of a traveling wave solution shows that this invading process is of positive speed.

Suppose that $(u, \mathbf{v})$ is a sufficiently smooth solution of (4.1)-(4.2) such that $u(x, 0) = 1$ and $\mathbf{v}(x, 0) = \mathbf{b_2}$ for all $x \ge x_0$ for some $x_0 \in \mathbf{R}$. No assumption is made on the behavior of $(u, \mathbf{v})$ for $x < x_0$, $t = 0$, except that $0 \le u \le 1$ and $\mathbf{b}_2 \le \mathbf{v} \le \mathbf{b}_0$ (as we always assume). *Suppose* that we can choose functions $(w_0(x), \mathbf{V}_0(x))$ with $w_0(x) \le u(x, 0)$ and $\mathbf{V}_0(x) \ge \mathbf{v}(x, 0)$, such that the conditions of Stability Theorem of [60] hold. Let $(w, \mathbf{V})$ be the solution of (4.1)-(4.2) with the initial data

$(w_0, \mathbf{V}_0)$. Then, by a comparison, we have $w(x,t) \le u(x,t) \le 1$ and $\mathbf{b}_2 \le \mathbf{v}(x,t) \le \mathbf{V}(x,t)$ for all $x \in \mathbf{R}$ and $t \ge 0$. Also, by the stability result of [60], there is a constant x_0, such that

$$|w(x,t) - \mathcal{U}(x + c_0 t + x_0)| \to 0, \ \ |\mathbf{V}_i(x,t) - \mathcal{V}_i(x + c_0 t + x_0)| \to 0$$

as $t \to +\infty$ uniformly for all $x \in \mathbf{R}$.

Now, given any $s < c_0$, for any $\xi \in \mathbf{R}$ we write

$$\begin{aligned} w(\xi - st, t) &= \mathcal{U}(\xi - st + c_0 t + x_0) + [w(\xi - st, t) - \mathcal{U}(\xi - st + c_0 t + x_0)], \\ V_i(\xi - st, t) &= \mathcal{V}_i(\xi - st + c_0 t + x_0) + [V_i(\xi - st, t) - \mathcal{V}_i(\xi - st + c_0 t + x_0)]. \end{aligned}$$

Then we obtain that

$$\lim_{t \to +\infty} (u(\xi - st, t), \mathbf{v}(\xi - st, t)) = (1, \mathbf{b_2}) \tag{5.2}$$

uniformly for $\xi \in [\eta, +\infty)$ for all $\eta \in \mathbf{R}$.

We remark that for $a \in (1/2, 1)$, by a similar argument as the case for $a \in (0, 1/2)$, we can show that there exists a traveling wave solution of the system (4.1)-(4.2). But, the stability of this traveling wave solution is still unknown.

However, without knowing the existence and stability of traveling wave solution, we shall prove in this subsection that (5.2) holds. For this, we introduce the moving coordinate $\rho = x + ct$ for some $c > 0$. Then the system (4.1)-(4.2) is reduced to the following system:

$$\frac{\partial u}{\partial t} = D\frac{\partial^2 u}{\partial \rho^2} - c\frac{\partial u}{\partial \rho} + F(u, \mathbf{v}), \tag{5.3}$$

$$\frac{\partial v_i}{\partial t} = -c\frac{\partial v_i}{\partial \rho} + G_i(u, \mathbf{v}), \ i = 1, \cdots, n. \tag{5.4}$$

We shall always assume in this subsection that the solution is sufficiently smooth.

Note that the associated steady state solutions $(q, \mathbf{p})$, $\mathbf{p} = (p_1, \cdots, p_n)$, of (5.3)-(5.4) satisfy the following ordinary differential equations:

$$Dq'' - cq' + F(q, \mathbf{p}) = 0, \tag{5.5}$$

$$-cp_i' + G_i(q, \mathbf{p}) = 0, \ \ i = 1, \cdots, n. \tag{5.6}$$

We shall consider the solution of (5.5)-(5.6) in $\mathbf{R}^+$ with

$$q(0) = 1, \ q'(0) = -\beta, \ p_i(0) = b_2^i, \ p_i'(0) = 0, \ i = 1, \cdots, n, \ c = \min\{\epsilon, \beta\}, \tag{5.7}$$

where $\beta > 0$ is a parameter and ϵ is a given fixed positive constant.

Then we have the following key lemma in this subsection.

Lemma 5.3 *Let $a \in (1/2, 1)$. Then for each $\epsilon > 0$ there exists $\beta = \beta(\epsilon) > 0$ such that the solution $(q, \mathbf{p})$ of (5.5)-(5.7) exists in $[0, \infty)$ and it satisfies*

(1) $0 < q < 1$ *and* $q' < 0$ *on* $(0, +\infty)$,

(2) $\mathbf{b_2} < \mathbf{p}(\rho) < \mathbf{b_0}$ *and* $\mathbf{p}' > \mathbf{0}$ *on* $(0, +\infty)$,

(3) $\lim_{\rho \to +\infty} (q(\rho), q'(\rho), \mathbf{p}(\rho)) = (0, 0, \mathbf{b_0})$.

With this key lemma, we can use the idea of Klaasen and Troy [25] to prove one of the main theorems of this subsection.

Theorem 5 *Let $a \in (1/2, 1)$. Suppose that $(u, \mathbf{v})$ is a sufficiently smooth solution of (4.1)-(4.2) such that $u(x, 0) = 0$ and $\mathbf{v}(x, 0) = \mathbf{b_0}$ for all $x \geq x_0$ for some $x_0 \in \mathbf{R}$. Then there exists a positive constant $\hat{c}_0$ such that for any $s < \hat{c}_0$ we have*

$$\lim_{t \to +\infty} (u(\xi - st, t), \mathbf{v}(\xi - st, t)) = (0, \mathbf{b_0})$$

uniformly for $\xi \in [\eta, +\infty)$ for all $\eta \in \mathbf{R}$.

Proof. First, under the assumptions of the theorem, it follows from Proposition 1 that $0 \leq u(x,t) \leq 1$ and $\mathbf{b_2} \leq \mathbf{v}(x,t) \leq \mathbf{b_0}$ for all $(x,t) \in \mathbf{R} \times \mathbf{R}^+$.

For each $\epsilon > 0$, let $c(\epsilon) := \min\{\epsilon, \beta(\epsilon)\}$, where $\beta(\epsilon)$ is the constant obtained in Lemma 5.3. Set $\hat{c}_0 := \sup_{\epsilon > 0}\{c(\epsilon)\}$.

Given $s < \hat{c}_0$. Choose $\epsilon > 0$ such that $s < c(\epsilon) < \hat{c}_0$. Let $\beta, q, \mathbf{p}, c$ be obtained in Lemma 5.3 corresponding to this ϵ. For this c, we define $\bar{u}(\rho, t) := u(\rho - ct, t)$ and $\bar{\mathbf{v}}(\rho, t) := \mathbf{v}(\rho - ct, t)$. Then $(\bar{u}, \bar{\mathbf{v}})$ satisfy (5.3)-(5.4) with the initial condition $(\bar{u}(\rho, 0), \bar{\mathbf{v}}(\rho, 0)) = (u(\rho, 0), \mathbf{v}(\rho, 0))$. Thus, if $\rho > x_0$, then $\bar{u}(\rho, 0) = 0 \leq q(\rho - x_0)$ and $\bar{\mathbf{v}}(\rho, 0) = \mathbf{b_0} \geq \mathbf{p}(\rho - x_0)$. Also, note that $\bar{u}(x_0, t) \leq 1 = q(x_0 - x_0)$ and $\bar{\mathbf{v}}(x_0, t) \geq \mathbf{b_2} = \mathbf{p}(x_0 - x_0)$ for all $t > 0$. Then an analogue comparison principle to Proposition 2 can be proved for the system (5.3)-(5.4). Therefore, we conclude that $\bar{u}(\rho, t) \leq q(\rho - x_0)$ and $\bar{\mathbf{v}}(\rho, t) \geq \mathbf{p}(\rho - x_0)$ for $\rho \geq x_0$ and $t > 0$.

Now, for $\xi \in \mathbf{R}$, let $\rho = \xi + (c - s)t$, then we have

$$\begin{aligned} 0 \leq u(\xi - st, t) = u(\rho - ct, t) = \bar{u}(\rho, t) \leq q(\rho - x_0), \\ \mathbf{p}(\rho - x_0) \leq \bar{\mathbf{v}}(\rho, t) = \mathbf{v}(\rho - ct, t) = \mathbf{v}(\xi - st, t) \leq \mathbf{b_0} \end{aligned}$$

for $\rho > x_0$ and $t > 0$. Noting that $\rho = \xi + (c - s)t \to +\infty$ as $t \to +\infty$, it follows that $q(\rho - x_0) \to 0$ and $\mathbf{p}(\rho - x_0) \to \mathbf{b_0}$ as $t \to +\infty$. Therefore, we have

$$\lim_{t \to +\infty} (u(\xi - st, t), \mathbf{v}(\xi - st, t)) = (0, \mathbf{b_0}).$$

Moreover, the convergence is uniform on $[\eta, +\infty)$ for any $\eta \in \mathbf{R}$. The theorem follows. □

Proceeding as in the proof of Lemma 5.3, we can prove the following lemma.

Lemma 5.4 *Let $a \in (0, 1/2)$. Then for each $\epsilon > 0$ there exists $\beta = \beta(\epsilon) > 0$ such that the solution $(q, q', \mathbf{p})$ of (5.5)-(5.6) with the following initial conditions*

$$q(0) = 0, \;\; q'(0) = \beta, \;\; p_i(0) = b_0^i, \;\; p_i'(0) = 0, \; i = 1, \cdots, n, \;\; c = \min\{\epsilon, \beta\},$$

exists in $[0, \infty)$ and it satisfies

(1) $0 < q < 1$ *and* $q' > 0$ *on* $(0, +\infty)$,

(2) $\mathbf{b_2} < \mathbf{p} < \mathbf{b_0}$ *and* $\mathbf{p}' < \mathbf{0}$ *on* $(0, +\infty)$,

(3) $\lim_{\rho \to +\infty}(q(\rho), q'(\rho), \mathbf{p}(\rho)) = (1, 0, \mathbf{b_2})$.

Then, by a similar argument, we have the following theorem.

Theorem 6 *Let $a \in (0, 1/2)$. Suppose that $(u, \mathbf{v})$ is a sufficiently smooth solution of (4.1)-(4.2) such that $u(x, 0) = 1$ and $\mathbf{v}(x, 0) = \mathbf{b_2}$ for all $x \geq x_0$ for some $x_0 \in \mathbf{R}$. Then there exists a positive constant $\hat{c}_0$ such that for any $s < \hat{c}_0$ we have*

$$\lim_{t \to +\infty} (u(\xi - st, t), \mathbf{v}(\xi - st, t)) = (1, \mathbf{b_2})$$

uniformly for $\xi \in [\eta, +\infty)$ for all $\eta \in \mathbf{R}$.

6 Summary and Discussion

In this paper, we consider the buffered bistable system (2.4)-(2.5) as a model for the fertilization Ca^{2+} wave, which is a simplified version of the Li and Rinzel model [29] by Smith, Pearson, and Keizer [52, 56, 59, 51] with an crucial improvement, i.e., the kinetics of the buffers are not necessarily fast with respect to the Ca^{2+} reactions. Our main concern is to study how the (immobile) buffers affect the properties of the model (2.1). For instance, can the addition of buffers eliminate wave activity? how much do buffers affect the stability properties of the associated steady states? Can the addition of buffers destroy the threshold phenomenon?

By constructing suitable super and sub solutions, we can prove that stationary buffers cannot destroy the asymptotic stability of the equilibrium states $u \equiv 0$ and $u \equiv 1$ of the bistable equation (2.1) without buffers. This implies that immobile buffers preserve the important feature of mature *Xenopus* eggs–a *bistable* physiological state of Ca^{2+} in the cytosol [9, 64, 40]. Moreover, if we view $u(\cdot, 0)$ as the initial stimulus (e.g., a micro-injection of Ca^{2+} into the cytosol) and its L^1 norm (e.g., the total Ca^{2+} content in the injection pipette) is not greater than some threshold, then even in the presence of uniformly distributed immobile exogeneous buffers (e.g., BAPTA and EGTA), the Ca^{2+} wave will not be triggered and $[Ca^{2+}]_{\mathrm{cyt}}$ will return to its basal state 0 exponentially fast. On the other hand, in the presence of immobile buffers with fast kinetics, we prove that for some localized initial stimulus on a sufficiently large region, $[Ca^{2+}]_{\mathrm{cyt}}$ will evolve into the stable elevated state 1. These results seem to be in good agreement with experimental observations: a calcium spike introduced by a tiny amount of Ca^{2+} only induces a localized transient, but not trigger a wave; however, if a spike with large enough size and magnitude may let $[Ca^{2+}]_{\mathrm{cyt}}$ evolve to the high Ca^{2+} concentration, even a wave [40, 51, 30]. Also note that these phenomena are visualized only by injecting the fluorescent indicators (e.g., fura-2) which are exactly Ca^{2+} buffers. Therefore, we could expect that even in the presence of immobile buffers, there is still a threshold effect for the system (2.1). Finally, we investigate the propagation property of solutions with initial data being a disturbance of one of the stable states which is confined to a half-line. We show that the more stable state will eventually dominate the whole dynamics and that the speed of this propagation (or invading process) is positive.

We remark that all of previous studies [59, 51, 56, 63] have made the assumption that buffers have very fast kinetics with respect to the other reactions, with which the RBA can be applied. On the other hand, in this study, neither the assumption that buffers have very fast kinetics nor the assumption that *buffers are in excess* is made (and so the so-called RBA and *excess buffer approximation* (EBA) [54] are not employed in our study). Hence, our results complement the previous studies [59, 51, 56, 63] partially, where the RBA have been employed.

In this paper, we only consider the case: all of the buffers are immobile. However, there are mobile endogenous buffers in the cytosol, even more, many indicator dyes are mobile (e.g., fura-2). Therefore, it seems to be crucial to know whether or not our results hold for mobile buffers. For example, if we apply our method to calculate the attraction basins for the two important physiological states, $(0, \mathbf{b_0})$ and $(1, \mathbf{b_2})$ of (2.4)-(2.5), it leads to the existence of non-constant equilibrium solutions of the following system:

$$D\frac{\partial^2 u}{\partial x^2} + f(u) + \sum_{i=1}^{n}[k_-^i(b_0^i - v_i) - k_+^i u v_i] = 0,\ x \in \mathbf{R}, \tag{6.1}$$

$$D_i\frac{\partial^2 v_i}{\partial x^2} + k_-^i(b_0^i - v_i) - k_+^i u v_i = 0,\ x \in \mathbf{R},\ i = 1, \cdots, n, \tag{6.2}$$

which is still open. The generalization of (Q4) to mobile buffers will also encounter the system (6.1)-(6.2). These will be left as our future study. On the other hand, for the existence of a traveling wave of (2.4)-(2.5) with mobile buffers, we may apply the method of Volpert et al. [62] to get the existence of a traveling wave with some assumptions on the kinetic properties of buffers. Combining this with our previous result [60], it shows that only mobile buffers can prevent the existence of waves. Moreover, if we assume that all of the buffers have fast kinetics, then the system (2.4)-(2.5) can be reduced to a single quasilinear equation via the so-called RBA. Along this line, the authors in [59, 51] have applied numerical methods to study the effect of one rapid mobile buffer on the traveling wave of the reduced system, and obtained many interesting relationships between the wave speed and the associated kinetic properties of the buffer. Although these numerical results in [59, 51] are only for one single mobile buffer and limited by the assumption of RBA, these results may provide a clue to our future analytical study of the system (2.4)-(2.5) on the relationships between the properties of traveling waves and the kinetic characteristics of multiple mobile buffers.

Although our results may suggest that the model (2.4)-(2.5) can explain the crucial bistable property, the threshold phenomena, and the propagation property of mature *Xenopus* eggs, there are some delicate phenomena (e.g., the shape and speed of the wave [9, 64, 30]) which cannot be understood with (2.4)-(2.5). This may be due to the limitations of the model (2.4)-(2.5) by the main facts that (1) they involve only one spatial dimension; (2) they do not include the gating variable for Ca^{2+} inactivation of the IP_3R explicitly [66, 29, 4, 64]; (3) they neglect the effect of Ca^{2+} depletion of the ER [21], i.e., the Ca^{2+} concentration in the ER is not necessarily infinite; (4) the influence of the inhomogeneity of parameters is not included (e.g., The inhomogeneous distribution of the ER, IP_3R, and SERCA pumps in the cell [61, 36, 64, 30]). By replacing the Ca^{2+} diffusion constant (D) with the effective diffusion constant in buffered medium and incorporating (2), Wagner et al. [64] have obtained a two-variable model which is based on De Young-Keizer model [66] and Li-Rinzel model [29]. Using such a model, Wagner et al. [64] have performed simulations to argue that bistability and inhomogeneities in the Ca^{2+} release properties are required to explain the shape and speed of the fertilization Ca^{2+} wave in the disk. Although their study can explain many delicate features of the shape and speed of the fertilization Ca^{2+} wave, they did not consider the effect of the buffers explicitly, which seems to be crucial [36]. By using one dimensional version of Wagner et al.'s model and including one mobile buffer with fast kinetics (thus RBA can be employed), Slepchenko et al. [51] found that there is a typical hysteresis loop in the wave speed dependence on the total buffer concentration. This raises an interesting question for our future study: Does such a loop also exist in the presence of buffers without fast kinetics? Finally, by incorporating (2), (3), and (4), Li [30] has modified Wagner et al.'s model to obtain a three-variable model without including the effect of buffers explicitly. By numerical simulation, Li [30] has discovered a new traveling front, called Tango waves. But the effect of buffers, even buffers with fast kinetics, on such a wave is still unknown.

7 Appendix

In this section, we collect the lemmas which are used in the proofs of main results. Also, we give the proofs of the lemmas stated in that section.

7.1 One Auxiliary Lemma

First, the following lemma can easily be proved by a phase plane analysis.

Lemma 7.1 *Let $a \in (0, 1)$.*

(1) *For any sufficiently small* $\epsilon \in (0, 1-a)$, *there exist* $\eta \in (a, a+\epsilon]$ *and* $\delta_1 > 0$, *with* $\delta_1 = \delta_1(\epsilon) \to 0$ *as* $\epsilon \to 0$, *such that* $q' < 0$ *on* $(0, x_\eta)$, $q' > 0$ *on* $(-x_\eta, 0)$, *and* $q(-x_\eta) = q(x_\eta) = a$ *for some* $x_\eta \in (0, \delta_1)$ *for any solution* q *of (3.6) with* $q(0) = \eta$ *and* $q'(0) = 0$. *Moreover, if we set* $p_i(x) = \kappa_i(q_i(x))$, $i = 1, \cdots, n$, *on* $[-x_\eta, x_\eta]$, *then we have* $p_i' > 0$ *on* $(0, x_\eta)$, $p_i' < 0$ *on* $(-x_\eta, 0)$, *and* $p_i(-x_\eta) = p_i(x_\eta) = \kappa_i(a)$.

(2) *For any sufficiently small* $\epsilon \in (0, a)$, *there exist* $\eta \in [a - \epsilon, a)$ *and* $\delta_1 > 0$, *with* $\delta_1 = \delta_1(\epsilon) \to 0$ *as* $\epsilon \to 0$, *such that* $q' > 0$ *on* $(0, x_\eta)$, $q' < 0$ *on* $(-x_\eta, 0)$, *and* $q(-x_\eta) = q(x_\eta) = a$ *for some* $x_\eta \in (0, \delta_1)$ *for any solution* q *of (3.6) with* $q(0) = \eta$ *and* $q'(0) = 0$. *Moreover, if we set* $p_i(x) = \kappa_i(q_i(x))$, $i = 1, \cdots, n$, *on* $[-x_\eta, x_\eta]$, *then we have* $p_i' < 0$ *on* $(0, x_\eta)$, $p_i' > 0$ *on* $(-x_\eta, 0)$, *and* $p_i(-x_\eta) = p_i(x_\eta) = \kappa_i(a)$.

7.2 Proof of Lemma 5.1.

In order to prove Lemma 5.1, we first prove the following lemma.

Lemma 7.2 *Let* $(u, \mathbf{v})$ *be the sufficiently smooth solution of (4.1)-(4.2) such that* $u_t(x, 0) \leq 0$, $v_{i,t}(x, 0) \geq 0$ *for all* $x \in \mathbf{R}$ *and* $i = 1, \cdots, n$. *Then* $u_t(x, t) \leq 0$, $v_{i,t}(x, t) \geq 0$ *for all* $(x, t) \in \mathbf{R} \times [0, +\infty)$ *and* $i = 1, \cdots, n$.

Proof. Define $b(x, t) = u_t(x, t)$ and $h_i(x, t) = -v_{i,t}(x, t)$, $i = 1, \cdots, n$, on $\mathbf{R} \times [0, +\infty)$. Then b and h_i satisfy the following system

$$\begin{aligned} b_t - Db_{xx} &= F_u(u, \mathbf{v})(x, t)b - \sum_{j=1}^{n} F_{v_j}(u, \mathbf{v})(x, t)h_j, \\ h_{i,t} &= -G_{i,u}(u, \mathbf{v})(x, t)b + G_{i,v_i}(u, \mathbf{v})(x, t)h_i, \end{aligned}$$

together with the initial data

$$b(x, 0) = u_t(x, 0) \leq 0 \quad \text{and} \quad h_i(x, 0) = -v_t(x, 0) \leq 0,$$

where $h_{i,t} = \partial h_i / \partial t$ for $i = 1, \cdots, n$. Recall that $F_{v_i}(u, \mathbf{v}) = -(k_+^i u + k_-^i) < 0$ and $G_{i,u}(u, \mathbf{v}) = -k_+^i v_i < 0$ for all $(u, \mathbf{v}) \in [0, 1] \times [b_2^1, b_0^1] \times \cdots \times [b_2^n, b_0^n]$ and $i = 1, \cdots, n$, and that $(u(x, t), \mathbf{v}(x, t)) \in [0, 1] \times [b_2^1, b_0^1] \times \cdots \times [b_2^n, b_0^n]$ for all $(x, t) \in \mathbf{R} \times [0, +\infty)$. Thus $F_{v_i}(u(x, t), \mathbf{v}(x, t)) < 0$ and $G_{i,u}(u(x, t), \mathbf{v}(x, t)) < 0$ for all $(x, t) \in \mathbf{R} \times [0, +\infty)$ and $i = 1, \cdots, n$. Combining this with the fact that $b(x, 0) \leq 0$ and $h_i(x, 0) \leq 0$ for all $x \in \mathbf{R}$ and $i = 1, \cdots, n$, it follows from Theorem 14.11 of [57, p. 203] that $b(x, t) \leq 0$ and $h_i(x, t) \leq 0$ for all $(x, t) \in \mathbf{R} \times [0, +\infty)$ and $i = 1, \cdots, n$. This completes the proof. $\square$

Proof of Lemma 5.1. Let $(\tilde{u}, \tilde{\mathbf{v}})$ be the solution of (4.1)-(4.2) with the initial conditions

$$\tilde{u}(x, 0) = \gamma \quad \text{and} \quad \tilde{v}_i(x, 0) = \kappa_i(\gamma), \ i = 1, \cdots, n, \quad \text{for all} \ \ x \in \mathbf{R}.$$

It is clear that $(\tilde{u}, \tilde{\mathbf{v}})$ is independent of x, and so we may set $\tilde{u}(x, t) := \tilde{u}(t)$ and $\tilde{v}_i(x, t) := \tilde{v}_i(t)$, $i = 1, \cdots, n$, on $\mathbf{R} \times [0, +\infty)$. Moreover, $(\tilde{u}, \tilde{\mathbf{v}})$ satisfies the following system

$$u_t = f(u) + \sum_{i=1}^{n} [k_-^i (b_0^i - v_i) - k_+^i u v_i], \ t \in (0, +\infty), \tag{7.1}$$

$$v_{i,t} = k_-^i (b_0^i - v_i) - k_+^i u v_i, \ t \in (0, +\infty), \ i = 1, \cdots, n, \tag{7.2}$$

with the initial data

$$u(0) = \gamma \text{ and } v_i(0) = \kappa_i(\gamma),\ i = 1, \cdots, n.$$

By Lemma 7.2, we have $\tilde{u}_t(t) \le 0$, $\tilde{v}_{i,t}(t) \ge 0$ for all $t \in [0, +\infty)$ and $i = 1, \cdots, n$. Using this fact and noting that $(\tilde{u}(t), \tilde{\mathbf{v}}(t)) \in [0,1] \times [b_2^1, b_0^1] \times \cdots \times [b_2^n, b_0^n]$ for all $t \in \mathbf{R}^+$, it follows that the limits $\bar{u} =: \lim_{t\to+\infty} \tilde{u}(t)$ and $\bar{v}_i =: \lim_{t\to+\infty} \tilde{v}_i(t)$, $i = 1, \cdots, n$, exist and satisfy that $\bar{u} \in [0, \gamma)$ and $\bar{v}_i \in [\kappa_i(\gamma), b_0^i]$ for $i = 1, \cdots, n$.

Next we claim that $\bar{u} = 0$ and $\bar{v}_i = b_0^i$ for $i = 1, \cdots, n$. Indeed, we may choose a sequence of $\{t_m\}_{m\in\mathbf{N}}$ such that $\lim_{m\to+\infty} t_m = +\infty$ and $\lim_{m\to+\infty} \tilde{u}'(t_m) = \lim_{m\to+\infty} \tilde{v}_i'(t_m) = 0$ for $i = 1, \cdots, n$. Evaluating (7.1)-(7.2) at $t = t_m$ and taking the limit, we obtain that

$$f(\bar{u}) = k_-^i(b_0^i - \bar{v}_i) - k_+^i \bar{u}\bar{v}_i = 0$$

for $i = 1, \cdots, n$. Recall that $\bar{u} \in [0, \gamma)$ and $\bar{v}_i \in [\kappa_i(\gamma), b_0^i]$ for $i = 1, \cdots, n$, this implies that $\bar{u} = 0$ and $\bar{v}_i = b_0^i$ for $i = 1, \cdots, n$. Therefore, $(\tilde{u}, \tilde{\mathbf{v}})$ tends to $(0, b_0^1, \cdots, b_0^n)$ as $t \to +\infty$. Moreover, since all the eigenvalues of the linearized system of (7.1)-(7.2) around the constant solution $(0, \mathbf{b_0})$ are negative, there exists a positive constant $C = C(k_+^i, k_-^i, b_0^i, a)$ such that $\tilde{u}(t) = O(e^{-Ct})$ and $\tilde{v}_i(t) = b_0^i + O(e^{-Ct})$ for $i = 1, \cdots, n$.

Note that $u(x,0) \le \tilde{u}(x,0)$ and $\mathbf{v}(x,0) \ge \tilde{\mathbf{v}}(x,0)$ for all $x \in \mathbf{R}$. Thus we can apply Proposition 2 to conclude that $u(x,t) \le \tilde{u}(x,t)$ and $\mathbf{v}(x,t) \ge \tilde{\mathbf{v}}(x,t)$ for all $(x,t) \in \mathbf{R} \times [0, +\infty)$. Noting that $u(x,t) \ge 0$ and $\mathbf{v}(x,t) \le \mathbf{b_0}$, for all $(x,t) \in \mathbf{R} \times [0, +\infty)$, we reach our conclusion. □

7.3 Proof of Lemma 5.2.

Set $W(x,t) = (u(x,t), \tilde{\mathbf{v}}(x,t)) = (u(x,t), (\mathbf{b_0} - \mathbf{v})(x,t))$ on $\mathbf{R} \times [0, +\infty)$. Then the components of W satisfy the following system

$$\frac{\partial u}{\partial t} = D\frac{\partial^2 u}{\partial x^2} + \tilde{F}(u, \tilde{\mathbf{v}}),\ (x,t) \in \mathbf{R} \times (0, +\infty), \tag{7.3}$$

$$\frac{\partial \tilde{v}_i}{\partial t} = \tilde{G}_i(u, \tilde{\mathbf{v}}),\ (x,t) \in \mathbf{R} \times (0, +\infty),\ i = 1, \cdots, n, \tag{7.4}$$

with the initial data

$$u(x,0) = \phi(x),\ \ \tilde{v}_i(x,0) = 0,\ x \in \mathbf{R},\ i = 1, \cdots, n, \tag{7.5}$$

where $\tilde{F}(u, \tilde{\mathbf{v}}) = f(u) + \sum_{i=1}^n [k_-^i \tilde{v}_i - k_+^i u(b_0^i - \tilde{v}_i)]$ and $\tilde{G}_i(u, \tilde{\mathbf{v}}) = -k_-^i \tilde{v}_i + k_+^i u(b_0^i - \tilde{v}_i)$ for $i = 1, \cdots, n$. Also, note that for all $(x,t) \in \mathbf{R} \times \mathbf{R}^+$, the components of W can be written as

$$u(x,t) = L(x,t) + \int_0^t \int_{\mathbf{R}} K(x,y,t-s)\tilde{F}(W(y,s))dyds, \tag{7.6}$$

$$\tilde{v}_i(x,t) = \int_0^t k_+^i e^{-k_-^i(t-s)} u(x,s)v_i(x,s)ds,\ i = 1, \cdots, n, \tag{7.7}$$

where

$$L(x,t) = \int_{\mathbf{R}} K(x,y,t)\phi(y)dy \text{ and } K(x,y,t) = \frac{1}{2\sqrt{\pi D t}} e^{-(x-y)^2/(4Dt)}.$$

By Proposition 1, we have that $0 \le u \le 1$ and $\mathbf{b_2} \le \mathbf{v} \le \mathbf{b_0}$ on $\mathbf{R} \times \mathbf{R}^+$. Therefore, the solution $W = (u, \tilde{\mathbf{v}})$ of (7.3)-(7.5) satisfies $0 \le u \le 1$ and $\mathbf{0} \le \tilde{\mathbf{v}} \le \mathbf{b_0} - \mathbf{b_2}$ on $\mathbf{R} \times \mathbf{R}^+$. It follows that there exists a constant $C = C(k_+^i, k_-^i, b_0^i, a)$ such that for all $(x,t) \in \mathbf{R} \times [0, +\infty)$ and each $i = 1, \cdots, n$, we have

$$|\tilde{F}(W(x,t))| \le C|W(x,t)| \text{ and } |k_+^i u(x,t)v_i(x,t)| \le C|W(x,t)|. \tag{7.8}$$

Both here and below, we define $|W(x,t)|$ by $|W(x,t)| := u(x,t) + \sum_{i=1}^{n} \tilde{v}(x,t)$. Throughout the proof of this lemma, C always denote a constant, which may be different from sentence to sentence, but they depend only on D, k_+^i, k_-^i, b_0^i, and a.

Thus, by (7.6), (7.7), and (7.8) we obtain that

$$\begin{aligned} |W(x,t)| &= u(x,t) + \sum_{i=1}^{n} \tilde{v}(x,t) \\ &\leq L(x,t) + C\int_0^t \int_{\mathbf{R}} K(x,y,t-s)|W(y,s)|dyds \\ &\quad + C\int_0^t |W(x,s)|ds \end{aligned} \tag{7.9}$$

for all $(x,t) \in \mathbf{R} \times [0,+\infty)$.

Now, we estimate the first two terms on the right-hand side of (7.9). For the first term, we have the following bound

$$L(x,t) \leq \frac{C}{\sqrt{t}}\|\phi\|_1 \tag{7.10}$$

for all $(x,t) \in \mathbf{R} \times \mathbf{R}^+$. To estimate the second term, we observe that

$$\int_0^t \int_{\mathbf{R}} K(x,y,t-s)|W(y,s)|dyds \leq C\int_0^t \int_{\mathbf{R}} \frac{|W(y,s)|}{\sqrt{t-s}}dyds \tag{7.11}$$

for all $(x,t) \in \mathbf{R} \times \mathbf{R}^+$.

If we can show that the right-hand side of (7.11) is bounded above by $C(\sqrt{t} + \sqrt{t}e^{Ct})\|\phi\|_1$ for all $t > 0$ for some positive constant C, then, by (7.10) and by applying the Gronwall's inequality to (7.9), we can obtain the desired inequality (5.1).

For this, we first estimate the L^1 norm of $|W(x,t)|$. More precisely, we claim that

$$\int_0^t \int_{\mathbf{R}} |W(y,s)|dyds \leq Ce^{Ct}\|\phi\|_1 \tag{7.12}$$

for all $t > 0$ for some positive constant C. Indeed, integrating (7.9) over $\mathbf{R} \times [0,t]$ yields that for each $t > 0$,

$$\begin{aligned} \int_0^t \int_{\mathbf{R}} |W(x,s)|dxds &\leq \int_0^t \int_{\mathbf{R}} L(x,s)dxds \\ &\quad + C\int_0^t \int_{\mathbf{R}} \int_0^s \int_{\mathbf{R}} K(x,y,s-\tau)|W(y,\tau)|dyd\tau dxds \\ &\quad + C\int_0^t \int_{\mathbf{R}} \int_0^s |W(x,\tau)|d\tau dxds \\ &\leq \int_0^t \int_{\mathbf{R}} \int_{\mathbf{R}} K(x,y,s)\phi(y)dydxds \\ &\quad + C\int_0^t \int_{\mathbf{R}} \int_0^s \int_{\mathbf{R}} K(x,y,s-\tau)|W(y,\tau)|dyd\tau dxds \\ &\quad + C\int_0^t \int_{\mathbf{R}} \int_0^s |W(x,\tau)|d\tau dxds \\ &= I(t) + II(t) + III(t). \end{aligned} \tag{7.13}$$

Note that $\int_{\mathbf{R}} K(x,y,t) = 1$ for all $t > 0$. Changing the order of integration in $I(t)$ and $II(t)$ and integrating over x first, it follows that

$$I(t) \leq t\|\phi\|_1 \text{ and } II(t) \leq C \int_0^t \int_0^s \int_{\mathbf{R}} |W(y,\tau)| dy d\tau ds$$

for all $t > 0$. Combing these two inequalities with (7.13), we obtain that

$$\int_0^t \int_{\mathbf{R}} |W(x,s)| dx ds \leq t\|\phi\|_1 + C \int_0^t \int_0^s \int_{\mathbf{R}} |W(x,\tau)| dx d\tau ds.$$

Thus the Gronwall's inequality gives the claim (7.12).

Now, we turn to estimate the right-hand side of (7.11). Using (7.9) and a similar argument as used in (7.13), we obtain that for each $t > 0$,

$$\begin{aligned}
\int_0^t \int_{\mathbf{R}} \frac{|W(x,s)|}{\sqrt{t-s}} dx ds &\leq \int_0^t \int_{\mathbf{R}} \int_{\mathbf{R}} \frac{K(x,y,s)\phi(y)}{\sqrt{t-s}} dy dx ds \\
&\quad + C \int_0^t \int_{\mathbf{R}} \int_0^s \int_{\mathbf{R}} \frac{K(x,y,s-\tau)|W(y,\tau)|}{\sqrt{t-s}} dy d\tau dx ds \\
&\quad + C \int_0^t \int_{\mathbf{R}} \int_0^s \frac{|W(x,\tau)|}{\sqrt{t-s}} d\tau dx ds \\
&= IV(t) + V(t) + VI(t).
\end{aligned} \tag{7.14}$$

We first estimate the bound for $IV(t)$. Changing the order of integration and integrating over x first, it follows that

$$IV(t) \leq C\sqrt{t}\|\phi\|_1$$

for all $t > 0$. For $V(t)$, we use Fubini's Theorem and (7.12) to obtain

$$\begin{aligned}
V(t) &\leq C \int_0^t \int_{\mathbf{R}} \int_0^s \int_{\mathbf{R}} \frac{K(x,y,s-\tau)|W(y,\tau)|}{\sqrt{t-s}} dy d\tau dx ds \\
&\leq C \int_0^t \int_0^s \int_{\mathbf{R}} \frac{|W(y,\tau)|}{\sqrt{t-s}} dy d\tau ds \\
&= C \int_0^t \int_{\mathbf{R}} \int_\tau^t \frac{|W(y,\tau)|}{\sqrt{t-s}} ds dy d\tau \\
&= C \int_0^t \int_{\mathbf{R}} \sqrt{t-\tau} |W(y,\tau)| dy d\tau \\
&\leq C\sqrt{t} \int_0^t \int_{\mathbf{R}} |W(y,\tau)| dy d\tau \leq C\sqrt{t} e^{Ct} \|\phi\|_1
\end{aligned}$$

for all $t > 0$. Similar arguments lead to the bound for $VI(t)$, i.e.,

$$\begin{aligned}
VI(t) &= C \int_0^t \int_{\mathbf{R}} \int_\tau^t \frac{|W(x,\tau)|}{\sqrt{t-s}} ds dx d\tau \\
&= C \int_0^t \int_{\mathbf{R}} \sqrt{t-\tau} |W(x,\tau)| dx d\tau \\
&\leq C\sqrt{t} \int_0^t \int_{\mathbf{R}} |W(x,\tau)| dx d\tau \\
&\leq C\sqrt{t} e^{Ct} \|\phi\|_1.
\end{aligned}$$

Combing these bounds for $IV(t)$, $V(t)$, and $VI(t)$, from (7.14) it follows that

$$\int_0^t \int_{\mathbf{R}} \frac{|W(x,s)|}{\sqrt{t-s}} dxds \le C(\sqrt{t} + \sqrt{t}e^{Ct})\|\phi\|_1.$$

This completes the estimate of the right-hand side of (7.11).

Finally, we use (7.10), (7.11), and (7.9) to get

$$|W(x,t)| \le C(\frac{1}{\sqrt{t}} + \sqrt{t} + \sqrt{t}e^{Ct})\|\phi\|_1 + C\int_0^t |W(x,s)|ds$$

for all $t > 0$. Then, by applying the Gronwall's inequality to the above inequality, we obtain that

$$|W(x,t)| \le C(\frac{1}{\sqrt{t}} + \sqrt{t} + e^{Ct} + \sqrt{t}e^{Ct} + t\sqrt{t}e^{Ct})\|\phi\|_1$$

for all $(x,t) \in \mathbf{R} \times \mathbf{R}^+$. This completes the proof. $\square$

7.4 Proof of Lemma 5.3.

In order to prove Lemma 5.3, we set

$$\tau = \rho/c, \quad \cdot = d/d\tau, \quad \theta = c^2/D, \quad \dot{q} = z. \tag{7.15}$$

Then we can rewrite (5.5)-(5.6) as the following first order system of differential equations

$$\dot{q} = z, \tag{7.16}$$

$$\dot{z} = \theta(z - F(q,\mathbf{p})), \tag{7.17}$$

$$\dot{p}_i = G_i(q,\mathbf{p}), \; i = 1,\cdots,n, \tag{7.18}$$

while the condition (5.7) becomes the following

$$q(0) = 1, \; z(0) = -c\beta, \; p_i(0) = b_2^i, \; \dot{p}_i(0) = 0, \; i = 1,\cdots,n, \; c = \min\{\epsilon,\beta\}. \tag{7.19}$$

Therefore, it remains to show the following lemma.

Lemma 7.3 *Let $a \in (1/2,1)$. Then for each $\epsilon > 0$ there exists $\beta = \beta(\epsilon) > 0$ such that the solution $(q,z,\mathbf{p})$ of (7.16)-(7.19) exists in $[0,\infty)$ and it satisfies*

(1) $0 < q < 1$ *and* $z < 0$ *on* $(0,+\infty)$,

(2) $\mathbf{b_2} < \mathbf{p}(\tau) < \mathbf{b_0}$ *and* $\dot{\mathbf{p}} > \mathbf{0}$ *on* $(0,+\infty)$,

(3) $\lim_{\tau\to+\infty}(q(\tau),z(\tau),\mathbf{p}(\tau)) = (0,0,\mathbf{b_0})$.

From now on we shall fix $\epsilon > 0$. We shall adapt the method used in [24, 17] (see also [60]) to prove Lemma 7.3. We denote the maximum existence interval of the solution of (7.16)-(7.19) for a given $\beta > 0$ by $[0,T)$, where $T = T(\beta) > 0$. Then we have

Lemma 7.4 *Let $(q,z,\mathbf{p})$ be the solution of (7.16)-(7.19) in $[0,T)$ for a given $\beta > 0$. Then $0 < q < 1$, $z < 0$, $\mathbf{b_2} < \mathbf{p} < \mathbf{b_0}$, and $\dot{\mathbf{p}} > \mathbf{0}$ for $\tau > 0$ near $\tau = 0$.*

This lemma implies that τ_0 and $\bar{q}$ in the following definition are well-defined.

Definition 1 *Let $(q, z, \mathbf{p})$ be the solution of (7.16)-(7.19) for a given $\beta > 0$. Let $\tau_0 = \tau_0(\beta)$ be the first zero of $\dot{q}$ if it exists; and set $\tau_0 = T$ if $\dot{q} < 0$ on $(0, T)$. We also set $\bar{q} := \bar{q}(\beta) = q(\tau_0(\beta))$ ($\bar{q}$ may be $-\infty$).*

By this definition and Lemma 7.4, we have the following lemma.

Lemma 7.5 *Let $(q, z, \mathbf{p})$ be the solution of (7.16)-(7.19) for a given $\beta > 0$. Then $q < 1$ and $z < 0$ on $(0, \tau_0)$.*

Since $\dot{q} < 0$ on $(0, \tau_0)$, we can express z and p_i, $i = 1, \cdots, n$, as functions of q for $q \in (\bar{q}, 1)$. Let $Z(q) = z(\tau(q))$ and $P_i(q) = p_i(\tau(q))$, $i = 1, \cdots, n$, for $q \in (\bar{q}, 1)$. Set $\mathbf{P} = (P_1, \cdots, P_n)$. Then Z and $\mathbf{P}$ satisfy the following equations

$$\dot{Z} := \frac{dZ}{dq} = \theta\left(1 - \frac{F(q, \mathbf{P})}{Z}\right), \tag{7.20}$$

$$\dot{P}_i := \frac{dP_i}{dq} = \frac{G_i(q, \mathbf{P})}{Z}, \; i = 1, \cdots, n, \tag{7.21}$$

for $q \in (\bar{q}, 1)$ with the *terminal* conditions

$$Z(1) = -c\beta, \quad \mathbf{P}(1) = \mathbf{b_2}. \tag{7.22}$$

Note that $Z(q) < 0$ for $q \in (\bar{q}, 1)$ and $Z(\bar{q}) = 0$ if $\bar{q}$ is finite.

Lemma 7.6 *Let $(q, z, \mathbf{p})$ be the solution of (7.16)-(7.19) for a given $\beta > 0$. Assume that $\bar{q} \geq 0$. Then we have $b_2^i < P_i(q) < \kappa_i(q)$ for all $q \in (\bar{q}, 1)$ and $i = 1, \cdots, n$. Moreover, $\dot{p}_i > 0$ on $(0, \tau_0)$ for $i = 1, \cdots, n$.*

Proof. Fix $i \in \{1, \cdots, n\}$. Noting that $q > 0$, $z = \dot{q} < 0$ on $(0, \tau_0)$, and $\dot{p}_i > 0$ on $(0, \hat{\tau})$ for some $\hat{\tau} > 0$, and using (7.18), we have $P_i(q) < \kappa_i(q)$ for all $q \in (\hat{q}, 1)$ for some $\hat{q} \in [\bar{q}, 1)$. We claim that $P_i(q) < \kappa_i(q)$ for all $q \in (\bar{q}, 1)$. Otherwise, there exists $q_1 > \bar{q}$ such that $P_i(q) < \kappa_i(q)$ for all $q \in (q_1, 1)$ and $P_i(q_1) = \kappa_i(q_1)$. Then, by (7.21), $\dot{P}_i(q_1) = 0$. Moreover, from (7.21) and Lemma 7.5 it follows that $\dot{P}_i < 0$ on $(q_1, 1)$. Hence $\ddot{P}_i(q_1) \leq 0$. On the other hand, differentiating (7.21) and using $\dot{P}_i(q_1) = 0$, we obtain

$$\ddot{P}_i(q_1) = -\frac{k_+^i P_i(q_1)}{Z(q_1)} > 0,$$

a contradiction. Therefore, we have $P_i(q) < \kappa_i(q)$ for all $q \in (\bar{q}, 1)$.

Combining this with the fact that $Z < 0$ on $(\bar{q}, 1)$, we have $\dot{P}_i < 0$ on $(\bar{q}, 1)$, and so $\dot{p}_i > 0$ on $(0, \tau_0)$. Moreover, from $P_i(1) = b_2^i$ it follows that $P_i(q) > b_2^i$ for all $q \in (\bar{q}, 1)$. This completes the proof. $\square$

Lemma 7.7 *Let $a \in (0, 1)$. Suppose that (5.5)-(5.7) has a solution $(q, \mathbf{p})$ for some $\beta > 0$ with $0 < q < 1$ and $q' < 0$ on $(0, +\infty)$. Then we have $a \in (1/2, 1)$.*

Proof. Multiplying (5.5) and (5.6) by q' and integrating them from 0 to $+\infty$, we get

$$-D\beta^2/2 - c\left[\int_0^{+\infty} (q')^2(\rho)d\rho - \sum_{i=1}^n \int_0^{+\infty} q'(\rho)p_i'(\rho)d\rho\right] = -\int_1^0 f(q)dq = (1 - 2a)/12.$$

By Lemma 7.6, $p_i'(\rho) = \dot{p}_i(\tau)/c > 0$ on $(0, +\infty)$ for $i = 1, \cdots, n$. Thus the left hand side of the above equation is negative. It follows that $a \in (1/2, 1)$. Hence the proof is completed. $\square$

Lemma 7.8 *There exists no solution $(q, z, \mathbf{p})$ of (7.16)-(7.19) satisfying that $q(\tau_0) = 0$, $\dot{q}(\tau_0) = 0$ and $\ddot{q}(\tau_0) \geq 0$ for some finite τ_0.*

Proof. Suppose that there is a solution $(q, z, \mathbf{p})$ of (7.16)-(7.19) such that $q(\tau_0) = 0$, $\dot{q}(\tau_0) = 0$ and $\ddot{q}(\tau_0) \geq 0$ for some finite τ_0 for some $\beta > 0$. Recall from Lemma 7.6 that $\dot{p}_i(\tau_0) \geq 0$ for $i = 1, \cdots, n$. Hence $\ddot{q}(\tau_0) \leq 0$, by (7.17), and so $\ddot{q}(\tau_0) = 0$. Therefore, using (7.17)-(7.18) and the definitions of F and G_i, $i = 1, \cdots, n$, it follows that $\dot{p}_i(\tau_0) = 0$ for $i = 1, \cdots, n$. This implies that $q \equiv 0$ and $p_i \equiv \kappa_i(0) = b_0^i$, $i = 1, \cdots, n$, on $[0, \tau_0]$, by the uniqueness theorem for the differential equations, a contradiction. This completes the proof. □

Now, we are ready to prove Lemma 7.3.

Proof of Lemma 7.3. We divide the proof into the following steps.

Step 1. We claim that $\bar{q} < a$ and $Z(a) \leq -c\beta - \theta(1-a)$ for any $\beta > 0$. Indeed, by Lemma 7.6 and Lemma 7.5, we have $G_i(q, \mathbf{P}(q)) > 0$ and $\dot{P}_i(q) < 0$ for all $q \in (\bar{q}, 1)$ and $i = 1, \cdots, n$, as long as $\bar{q} \geq 0$. Also, note that $f(q) > 0$ for all $q \in (a, 1)$. Combining these two facts with the definitions of F and G_i, $i = 1, \cdots, n$, we obtain that $F(q, \mathbf{P}(q)) > 0$ and $G_i(q, \mathbf{P}(q)) > 0$ for all $q \in (\max\{\bar{q}, a\}, 1)$ and $i = 1, \cdots, n$. Thus if $\bar{q} \geq a$, then using (7.20) and noting that $Z < 0$ on $(\bar{q}, 1)$, it follows that $\dot{Z} \geq \theta > 0$ on $(\bar{q}, 1)$. This implies that $Z(\bar{q}) < 0$, a contradiction. Therefore, we have $\bar{q} < a$.

Moreover, noting that $F(q, \mathbf{P}(q)) > 0$ and $Z(q) < 0$ for all $q \in [a, 1)$, and using (7.20) again, it follows that $\dot{Z} \geq \theta$ on $[a, 1)$. Hence $Z(a) \leq -c\beta - \theta(1-a)$.

Step 2. We claim that there exists a finite $\hat{\tau}$ such that $\dot{q} < 0$ on $(0, \hat{\tau}]$ and $q(\hat{\tau}) = 0$, if β is sufficiently large. By Lemma 7.6, we have $b_2^i < P_i(q) < \kappa_i(q)$ for all $q \in (\bar{q}, 1)$ and $i = 1, \cdots, n$, as long as $\bar{q} \geq 0$. Let

$$B = \sup\{\mid F(q, \mathbf{P}) \mid \mid 0 \leq q \leq 1, b_2^i \leq P_i \leq \kappa_i(q) \text{ for } i = 1, \cdots, n\}.$$

Choose β_0 such that $\beta_0 > \max\{2B/\epsilon, \epsilon\}$. Then we claim that $\bar{q}(\beta) < 0$ for all $\beta > \beta_0$. Suppose that $\bar{q} := \bar{q}(\tilde{\beta}) \geq 0$ for some $\tilde{\beta} > \beta_0$. Let $(Z_{\tilde{\beta}}, P_{\tilde{\beta},1}, \cdots, P_{\tilde{\beta},n})$ be the corresponding solution of (7.20)-(7.22). Note that the corresponding c is given by $\tilde{c} = \epsilon$. Then we have $Z_{\tilde{\beta}}(q) < -\epsilon\tilde{\beta}$ for all $q \in (\hat{q}, a]$ for some $\hat{q} \in (0, a)$ and $Z_{\tilde{\beta}}(\hat{q}) = -\epsilon\tilde{\beta}$, since $Z_{\tilde{\beta}}(a) \leq -\epsilon\tilde{\beta} - \tilde{\theta}(1-a)$, by *Step 1*, and $Z_{\tilde{\beta}}(q) = 0$ for some $q < a$. On the other hand, from (7.20) it follows that

$$\begin{aligned}
\dot{Z}_{\tilde{\beta}}(q) &= \tilde{\theta}\left(1 - \frac{F(q, \mathbf{P}_{\tilde{\beta}})}{Z_{\tilde{\beta}}}\right) \\
&\geq \tilde{\theta}(1 - B/(\epsilon\tilde{\beta})) \\
&> \tilde{\theta}/2
\end{aligned}$$

for all $q \in [\hat{q}, a]$. This implies that $Z_{\tilde{\beta}}(q) < -\epsilon\tilde{\beta} - \tilde{\theta}(1-a)$ for all $q \in [\hat{q}, a]$, a contradiction. Therefore, if $\beta > \beta_0$, we have $\bar{q} < 0$, and so $Z(q) < 0$ for all $q \in [0, 1)$. Hence there exists a finite $\hat{\tau}$ such that $\dot{q} < 0$ on $(0, \hat{\tau}]$ and $q(\hat{\tau}) = 0$.

Step 3. We show that there exists a sufficiently small $\beta > 0$ such that $\dot{q}(\tau_0) = 0$ and $q(\tau_0) \in (0, a)$ for some finite τ_0. If not, then there exists a sequence $\{\beta_j\}_{j \in \mathbf{N}}$ with $\lim_{j \to \infty} \beta_j = 0$ such that the corresponding solutions $(q_j, \mathbf{p}_j)$ of (7.16)-(7.19) satisfy that $\dot{q}_j < 0$ on $(0, \hat{\tau}_j)$ and $q_j(\hat{\tau}_j) = 0$ for some $\hat{\tau}_j$ ($\hat{\tau}_j$ may be infinite). Notice that $q_j(\tau) \searrow 0$ as $\tau \to \infty$, if $\dot{q}_j < 0$ and $q_j > 0$ in $(0, \infty)$. Here the fact $\bar{q} < a$ is used.

Let $\mathbf{P}_j = (P_{j,1}, \cdots, P_{j,n})$. Multiplying (7.20) with Z_j and integrating from 1 to q, we obtain

$$\frac{Z_j(q)^2}{2} = (c_j\beta_j)^2/2 + \theta_j \int_1^q (Z_j(s) - F(s, \mathbf{P}_j(s)))ds \tag{7.23}$$

for all $q \in [0,1]$. By Lemma 7.6, we have $b_2^i < P_{j,i}(q) \leq \kappa_i(q)$ for all $q \in [0,1]$ and $i = 1, \cdots, n$. Note that $Z_j(q) < 0$ for all $q \in (0,1)$. Thus if we let $A_j = \sup_{0 \leq q \leq 1} |Z_j(q)|$, then it follows from (7.23) that $A_j^2/2 \leq (c_j\beta_j)^2/2 + \theta_j(A_j + B)$. Using the definition of θ_j, this implies that

$$\lim_{j \to \infty} A_j = 0. \tag{7.24}$$

Solving (7.21) with an integration by parts, we obtain that

$$P_{j,i}(q) = \kappa_i(q) - \int_1^q \kappa_i'(\eta) \exp[-\int_\eta^q ([k_+^i s + k_-^i]/Z_j(s))ds]d\eta$$

for all $q \in [0,1]$ and $i = 1, \cdots, n$. Then it follows from (7.24) that

$$\lim_{j \to \infty} P_{j,i}(q) = \kappa_i(q) \tag{7.25}$$

uniformly for $q \in [0,1]$ for $i = 1, \cdots, n$. From (7.23) it follows that

$$\int_1^0 F(s, \mathbf{P}_j(s))ds \leq \int_1^0 Z_j(s)ds + D\beta_j^2/2. \tag{7.26}$$

Letting $j \to \infty$ in (7.26), using (7.24) and (7.25), we obtain that

$$\int_1^0 F(s, \kappa_1(s), \cdots, \kappa_n(s))ds = (2a-1)/12 \leq 0,$$

a contradiction to the fact that $a \in (1/2, 1)$.

Step 4. We reach the conclusion. Let $(q_\beta, z_\beta, \mathbf{p}_\beta)$ be the solution of (7.16)-(7.19) for a given $\beta > 0$. Define

$$\mathcal{P}_1 = \{\beta > 0 \mid \dot{q}_\beta < 0 \text{ on } (0, \hat{\tau}] \text{ and } q_\beta(\hat{\tau}) = 0 \text{ for some finite } \hat{\tau}\},$$
$$\mathcal{P}_2 = \{\beta > 0 \mid \dot{q}_\beta(\tau_0) = 0 \text{ for some } \tau_0 \in \mathbf{R}^+ \text{ and } q_\beta(\tau_0) \in [0,1)\}.$$

Then $\mathcal{P}_1$ is nonempty by *Step 2*. Clearly, $\mathcal{P}_1$ is open by continuous dependence on the parameter β. Also, $\mathcal{P}_2$ is nonempty by *Step 3*. For each $\beta \in \mathcal{P}_2$, let $\tau_0 = \tau_0(\beta)$ be the first zero of $\dot{q}_\beta$, then we have $\ddot{q}_\beta(\tau_0) \geq 0$. By Lemma 7.8 and *Step 1*, we have $q_\beta(\tau_0) \in (0,a)$. Next we claim that $\ddot{q}_\beta(\tau_0) > 0$. If not, then $\ddot{q}_\beta(\tau_0) = 0$. By (7.16)-(7.17), we have $F(q_\beta(\tau_0), \mathbf{p}_\beta(\tau_0)) = 0$. Also, recall from Lemma 7.6 that $\dot{p}_{\beta,i}(\tau_0) \geq 0$ for $i = 1, \cdots, n$. Combining these two facts with this fact that $f(u) < 0$ for $u \in (0,a)$, we obtain that $\dot{p}_{\beta,i_0}(\tau_0) > 0$ for some $i_0 \in \{1, \cdots, n\}$. From this, (7.17), and the definition of F, it follows that $d^3q_\beta/dt^3(\tau_0) = -\theta \sum_{i=1}^n F_{v_i}\dot{p}_{\beta,i}(\tau_0) > 0$, a contradiction to the definition of τ_0. Thus $\ddot{q}_\beta(\tau_0) > 0$ and this implies that $\mathcal{P}_2$ is open.

By *Step 2* and the above discussion, $\mathcal{P}_2$ is nonempty open set which is bounded above. Therefore, the number $\beta^* := \sup \mathcal{P}_2$ exists and $\beta^* \in (0,\infty) \setminus (\mathcal{P}_1 \cup \mathcal{P}_2)$. Let $(q_{\beta^*}, \mathbf{p}_{\beta^*})$ be the corresponding solution of (7.16)-(7.19) with this β^*. Then $\dot{q}_{\beta^*} < 0$ for all $\tau \in (0,+\infty)$ and $q_{\beta^*}(\tau) \to 0$ as $\tau \to +\infty$. Moreover, by Lemma 7.6, we have $\dot{p}_{\beta^*,i} > 0$ on $(0,+\infty)$ for $i = 1, \cdots, n$. Now we claim that $p_{\beta^*,i}(\tau) \to b_0^i$ as $\tau \to +\infty$ for $i = 1, \cdots, n$. Indeed, fix $i \in \{1, \cdots, n\}$, using Lemma 7.6 and noting that $q_{\beta^*} \in (0,1)$ on $(0,+\infty)$, we have $p_{\beta^*,i} \in (b_2^i, b_0^i)$ on $(0,+\infty)$. Using this fact and noting that $\dot{p}_{\beta^*,i} > 0$ on $(0,+\infty)$, it follows that there exists $l \in (b_2^i, b_0^i]$ such that $p_{\beta^*,i} \to l$ as $\tau \to +\infty$. Hence we can choose a sequence $s_1 < s_2 < \cdots < s_m < \cdots$ with $s_m \to +\infty$ as $m \to +\infty$ satisfying that $q_{\beta^*}(s_m) \to 0$, $p_{\beta^*,i}(s_m) \to l$ and $\dot{p}_{\beta^*,i}(s_m) \to 0$ as $m \to +\infty$. From this and (7.18) it follows that $l = b_0^i$. Hence the proof is completed. $\square$

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