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SPATIAL DYNAMICS FOR A MODEL OF EPIDERMAL WOUND HEALING

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Abstract. In this paper, we consider the spatial dynamics for a non-cooperative diffusion system arising from epidermal wound healing. We shall establish the spreading speed and existence of traveling waves and characterize the spreading speed as the slowest speed of a family of non-constant traveling wave solutions. We also construct some new types of entire solutions which are different from the traveling wave solutions and spatial variable independent solutions. The traveling wave solutions provide the healing speed and describe how wound healing process spreads from one side of the wound. The entire solution exhibits the interaction of several waves originated from different locations of the wound. To the best of knowledge of the authors, it is the first time that it is shown that there is an entire solution in the model for epidermal wound healing.

1. **Introduction.** In this paper, we study the spatial dynamics, including spreading speeds, traveling wave solutions and entire solutions of a non-cooperative reaction-diffusion systems arising from wound healing. Wound healing is complex and remains only partially understood, despite extensive research. Several reaction-diffusion models have been developed in Sherratt and Murray [22,23], Dale, Maini, Sherratt [3] and others to understand the biological process of epidermal wound healing through mathematical analysis and numerical simulations. We refer to Murray [18] for more detailed discussions and further references. The models consist of two conservation equations, one for the epithelial cell density per unit area ($u_1(x,t)$) and one for the concentration of the mitosis-regulating chemical ($u_2(x,t)$). There are two types of the chemicals, one in which the chemical activates mitosis and the other in which it inhibits it. The following simplified model was proposed

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in [18, 22] for the activator

$$\begin{aligned} \frac{\partial u_1}{\partial t} &= d_1 \Delta u_1 + s(u_2)u_1(2-u_1) - u_1 \\ \frac{\partial u_2}{\partial t} &= d_2 \Delta u_2 + b(h(u_1) - u_2) \end{aligned} \tag{1.1}$$

where $b > 0, \kappa \in (0, \frac{1}{2})$, $s(u_2) = \kappa u_2 + 1 - \kappa$ is the linearized function which reflects the chemical control of motosis. The term $s(u_2)u_1(2-u_1)$ is chosen so that, at $u_2 = 1$, the sum of it and the natural decay $-u_1$ is of logistic growth form, $u_1(1-u_2)$ [18]. Here $\kappa < \frac{1}{2}$ is a necessary condition as we shall see that the rate of change of u_1 of (3.19) must be positive, which is the linearization of (1.1) at the origin. The chemical production by the function $h(u_1) = \frac{u_1(1+\zeta^2)}{u_1^2+\zeta^2}, \zeta \in (0,1)$ reflects an appropriate cellular response to injury. The qualitative form of the solution of (1.1) in the linear phase is of a wave moving with constant shape and speed. Such a solution is amenable to analysis if we consider a one dimensional geometry rather than the two dimensional radially symmetric geometry. Mathematically, we look for a traveling wave solution of the form $u_1(x,t) = \phi_1(\xi), u_2(x,t) = \phi_2(\xi), \xi = x + ct$ where c is the wave speed, positive since here we consider waves moving to the left. In Section 3, we shall establish the existence of traveling waves as well as the results on the speed of propagation to (1.1). We also characterize the minimum speed as the slowest speed of a family of non-constant traveling wave solutions of (1.1). In addition, we construct some new types of entire solution which describe the interactions of traveling wave solutions. Traveling wave solutions and spreading speeds for reaction-diffusion equations have been studied by a number of researchers. Fisher [6] studied the nonlinear parabolic equation

$$w_t = w_{xx} + w(1-w). \tag{1.2}$$

for the spatial spread of an advantageous gene in a population and conjectured c^* is the asymptotic speed of propagation of the advantageous gene. His results show that (1.2) has a traveling wave solution of the form $w(x+ct)$ if only if $|c| \geq c^* = 2$. Kolmogorov, Petrowski, and Piscounov [11] proved the similar results with more general model. Those pioneering work along with the paper by Aronson and Weinberger [1,2] confirmed the conjecture of Fisher and establish the speeding spreads for nonlinear parabolic equations. Lui [17] established the theory of spreading speeds for cooperative recursion systems. In a series of papers, Weinberger, Lewis and Li [14, 15, 31] studied spreading speeds and traveling waves for more general cooperative recursion systems, and in particular, for quite general cooperative reaction-diffusion systems by analyzing of traveling waves and the convergence of initial data to wave solutions. However, mathematical challenges remain because many reaction-diffusion systems are not necessarily cooperative due to various biological or physical constraints. Thieme [25] showed that asymptotic spreading speed of integral equations with nonmonotone growth functions can still be obtained by constructing monotone functions. For a related nonmonotone integro-difference equation, Hsu and Zhao [10], Li, Lewis and Weinberger [16] extended the theory of spreading speed and established the existence of traveling wave solutions. The first author and Castillo-Chavez [27] prove that a class of nonmonotone integro-difference systems have spreading speeds and traveling wave solutions. Such an extension is largely based on the construction of two monotone operators with appropriate properties and fixed point theorems in Banach spaces. A similar method was also used in Ma [19] and the author [26] to prove the existence of traveling wave solutions of non-quasimonotone delayed nonlocal reaction-diffusion equations. Weinberger, Kawasaki and Shigesada [33] established the spreading speeds of propagation for a partially-cooperative system describing the interaction between ungulates and grass by employing comparison methods. In a recent paper [28], one of the authors studied traveling waves and spreading speeds of propagation for a class of non-cooperative reaction-diffusion systems and the model discussed in [33].

In addition to the traveling wave solutions and spreading speeds, another important issue in population and epidemic dynamics is the interaction between traveling wave solutions, see e.g., [4, 5]. Mathematically, this phenomenon can be described by a class of *entire solutions* that are defined for all space and time. From the viewpoint of biology and epidemiology, such entire solutions provide some new spread of epidemic and invasion ways of the species. In recent years, there are quite a few significant works devoted to the interaction of traveling waves and entire solutions for various monotone diffusion equations, see e.g., [7, 8, 13, 20, 29, 36] and the references cited therein. Recently, in [35], we studied the entire solutions for a class of non-cooperative reaction-diffusion systems with monostable nonlinearity and applied these results to some biological and epidemiological models. The traveling wave solutions provide the healing speed and describe how wound healing process spreads from one side of the wounded area. The entire solution exhibits the interaction of several waves (local repairing process) originated from different locations. The entire solution may better describe epidermal wound healing. To the best of knowledge of the authors, it is the first time that it is shown that there is an entire solution in the model for epidermal wound healing.

In this paper, we first state the general results on non-cooperative systems in [28, 35]. In Section 3 we apply the general result to obtain the spreading speed, minimal wave speed and entire solutions for the non-cooperative system (1.1). The main results for the epidermal wound healing model in this paper are summarized in Theorems 3.1. Finally we present simulations of traveling wave solutions of (1.1) and discuss biological implications of traveling wave solutions and entire solutions in Section 4.

2. **General results on non-cooperative systems.**

We begin with some notation. We shall use $R, k, k^{\pm}, f, f^{\pm}, r, u, v$ to denote vectors in $\mathbb{R}^N$ or N-vector valued functions , and x, y, ξ the single variable in $\mathbb{R}$. Let $u = (u_i), v = (v_i) \in \mathbb{R}^N$, we write $u \geq v$ if $u_i \geq v_i$ for all i; and $u \gg v$ if $u_i > v_i$ for all i. A vector u is positive if $u \gg 0$. For any $r = (r_i) \gg 0, r \in \mathbb{R}^N$ let

$$[0, r] = \{u : 0 \leq u \leq r, u \in \mathbb{R}^N\} \subseteq \mathbb{R}^N$$

and

$$\mathcal{C}_r = \{u = (u_i) : u_i \in C(\mathbb{R}, \mathbb{R}), 0 \leq u_i(x) \leq r_i \text{ for } x \in \mathbb{R},\ i = 1, ..., N\},$$

where $C(\mathbb{R}, \mathbb{R})$ is the set of all continuous functions from $\mathbb{R}$ to $\mathbb{R}$.

Consider the system of reaction-diffusion equations

$$u_t = Du_{xx} + f(u) \text{ for } x \in \mathbb{R},\ t \geq 0. \tag{2.3}$$

with

$$u(x, 0) = u_0(x) \text{ for } x \in \mathbb{R}, \tag{2.4}$$

where $u = (u_i),\ D = \text{diag}(d_1, d_2, ..., d_N), d_i > 0$ for $i = 1, ..., N$

$$f(u) = (f_1(u), f_2(u), ..., f_N(u)),$$

$u_0(x)$ is a bounded uniformly continuous function on $\mathbb{R}$. In this paper, by a solution we mean a continuous function u, which is twice continuously differentiable with respect to x or ξ and once continuously differentiable with respect to t, satisfies an appropriate system of equations.

In order to deal with non-cooperative system, we shall assume that there are two additional cooperative systems

$$u_t = Du_{xx} + f^+(u) \text{ for } x \in \mathbb{R},\ t \geq 0, \tag{2.5}$$

$$u_t = Du_{xx} + f^-(u) \text{ for } x \in \mathbb{R},\ t \geq 0, \tag{2.6}$$

where f^+ lies above and f^- below f. Such an assumption will enable us to make use of the corresponding results for cooperative systems in [17,31] to establish spreading speeds for (2.3).

(H_1) i. Assume that $D = \text{diag}(d_1, d_2, ..., d_N), d_i > 0$ for $i = 1, ..., N$. Let $k^+ = (k_i^+) \gg 0$ and $f : [0, k^+] \to \mathbb{R}^N$ be a continuous and twice piecewise continuously differentiable function. Assume that $\mathcal{C}_{k^+}$ is an invariant set of (2.3) in the sense that for any given $u_0 \in \mathcal{C}_{k^+}$, the solution of (2.3) with the initial condition u_0 exists and remains in $\mathcal{C}_{k^+}$ for $t \in [0, \infty)$.

ii. Let $0 \ll k^- = (k_i^-) \leq k = (k_i) \leq k^+$. Assume there exist continuous and twice piecewise continuously differentiable function $f^\pm = (f_i^\pm) : [0, k^+] \to \mathbb{R}^N$ such that for $u \in [0, k^+]$

$$f^-(u) \leq f(u) \leq f^+(u).$$

iii. $f(0) = f(k) = 0$ and there is no other positive equilibrium of f between 0 and k. $f^\pm(0) = f^\pm(k^\pm) = 0$. There is no other positive equilibrium of $f^\pm$ between 0 and $k^\pm$. f has finite number of equilibria in $[0, k^+]$.

iv. (2.5) and (2.6) are cooperative (i.e. $\partial_i f_j^\pm(u) \geq 0$ for $u \in [0, k^\pm], i \neq j$).

v. $f^\pm(u), f(u)$ have the same Jacobian matrix $f'(0)$ at $u = 0$.

Note that an entire solution of (2.3) is a classical solution defined for $(x, t) \in \mathbb{R}^2$. A traveling wave solution u of (2.3) is a special entire solution of the form $u = \phi(x + ct), u \in C(\mathbb{R}, \mathbb{R}^N)$.

It is clear that the characteristic equation for (2.3) with respect to the trivial equilibrium 0 can be represented by

$$\frac{1}{\lambda} A_\lambda \eta_\lambda = c\eta_\lambda, \tag{2.7}$$

where

$$A_\lambda = (a_\lambda^{i,j}) = \text{diag}(d_i\lambda^2) + f'(0).$$

The matrix $f'(0)$ has nonnegative off diagonal elements. In fact, there is a constant α such that $f'(0) + \alpha I$ has nonnegative entries, where I is the identity matrix.

Let

$$M(A) = \rho(A + \alpha I) - \alpha.$$

Here $A + \alpha I$ is irreducible and nonnegative, and $\rho(A + \alpha I)$ is the spectral radius of $A + \alpha I$. ([9,31])

We shall need the following assumption (H_2).

(H$_2$) Assume that A_λ with irreducible blocks is in block lower triangular form. Further assume that its first diagonal block has the positive principal eigenvalue $M(A_\lambda)$, and $M(A_\lambda)$ is strictly larger than the principal eigenvalues of all other irreducible diagonal blocks for $\lambda \geq 0$. In addition, assume that there is a positive eigenvector $\nu_\lambda = (\nu_\lambda^i) \gg 0$ of A_λ corresponding to $M(A_\lambda)$, and that ν_λ is continuous with respect to λ for $\lambda > 0$.

Let
$$\Phi(\lambda) = \frac{1}{\lambda} M(A_\lambda) > 0.$$
From the arguments of [17,28,32], there exist two numbers $c_* > 0$ and $\lambda_* > 0$ such that
$$c_* = \Phi(\lambda_*) = \inf_{\lambda > 0} \Phi(\lambda), \tag{2.8}$$
and for any $c > c_*$, there exists $\lambda_1 := \lambda_1(c) \in (0, \lambda_*)$ such that $\Phi(\lambda_1) = c$ and $\Phi(\lambda) < c$ for any $\lambda \in (\lambda_1, \lambda_*]$.

In addition to (H_1)-(H_2), we also need assumption (H_3) which guarantees that the nonlinearity does not display an Allee effect along the particular function $\nu_\lambda e^{-\lambda x}$.

(H$_3$) Assume that for any $\alpha > 0, \lambda \in [0, \lambda_*]$,
$$f^+(\alpha \nu_\lambda) \leq \alpha f'(0) \nu_\lambda, \ \text{ where } \ \nu_\lambda = (\nu_\lambda^i).$$

The following theorem on traveling wave solutions and spreading speed for general non-cooperative systems is from [28].

Theorem 2.1. *([28]) Assume* (H$_1$) $-$ (H$_3$) *hold. Then the following statements are valid:*

(i.) For any $u_0 \in \mathcal{C}_k$ with compact support, the solution $u(x,t)$ of (2.3) with (2.4) satisfies
$$\lim_{t\to\infty} \sup_{|x| \geq tc} u(x,t) = 0, \ \textit{for } c > c^*.$$
(ii.) For any vector $\omega \in \mathbb{R}^N, \omega \gg 0$, there is a positive R_ω with the property that if $u_0 \in \mathcal{C}_k$ and $u_0 \geq \omega$ on an interval of length $2R_\omega$, then the solution $u(x,t)$ of (2.3) with (2.4) satisfies
$$k^- \leq \liminf_{t\to\infty} \inf_{|x| \leq tc} u(x,t) \leq k^+, \ \textit{for } 0 < c < c^*.$$
(iii.) For each $c > c^*$ (2.3) admits a traveling wave solution $\phi(x+ct)$ such that $0 \ll \phi(\xi) \leq k^+, \xi \in \mathbb{R}$,
$$k^- \leq \liminf_{\xi\to\infty} \phi(\xi) \leq \limsup_{\xi\to\infty} \phi(\xi) \leq k^+$$
and
$$\lim_{\xi\to-\infty} \phi(\xi) e^{-\lambda_1(c)\xi} = \nu_{\lambda_1}. \tag{2.9}$$
If, in addition, (2.3) is cooperative in $\mathcal{C}_k$, then u is nondecreasing on $\mathbb{R}$.

(iv.) For $c = c^*$ (2.3) admits a nonconstant traveling wave solution $\phi(x+ct)$ such that $0 \leq \phi(\xi) \leq k^+, \xi \in \mathbb{R}$.

(v.) For $0 < c < c^*$ (2.3) does not admit a traveling wave solution $\phi(x+ct)$ with $\liminf_{\xi\to\infty} \phi(\xi) \gg 0$ and $\phi(-\infty) = 0$.

To obtain the results on entire solutions, we need a more stronger condition (H$_3$)$'$ as follows:

$(\mathrm{H}_3)'$: For any $n \in \mathbb{Z}^+$, $\alpha_1, \cdots, \alpha_n > 0$ and $\lambda_1, \cdots, \lambda_n \in [0, \lambda_*]$,

$$f^+(\alpha_1 v_{\lambda_1} + \cdots + \alpha_n v_{\lambda_n}) \le f'(0)(\alpha_1 v_{\lambda_1} + \cdots + \alpha_n v_{\lambda_n}).$$

For convenience, let $\phi_c^-(\xi)$ and $\Gamma^-(t)$ be the traveling wave solution and spatially independent solution of the lower auxiliary system (2.6), respectively. The existence of spatially independent solutions of such cooperative systems follows from [35, Lemma 2.12]. Further, we denote

$$\begin{aligned} u^-(x,t) &= \max\Big\{ \max_{1\le i\le l} \phi_{c_i}^-\big(x + c_i t + h_i\big), \\ &\qquad \max_{1\le j\le m} \phi_{c_j'}^-\big(-x + c_j' t + h_j'\big), \chi\Gamma^-(t+h)\Big\}, \\ \Pi^+(x,t) &= \sum_{i=1}^{l} v(\lambda_1(c_i)) e^{\lambda_1(c_i)(x+c_i t+h_i)} \\ &\quad + \sum_{j=1}^{m} v(\lambda_1(c_j')) e^{\lambda_1(c_j')(-x+c_j' t+h_j')} + v^* e^{\lambda^*(t+h)}. \end{aligned}$$

Here and in the sequel, $v^* = v_0$ and $\lambda^* = M(A_0)$.

From the argument of [35], we obtain the following result on the entire solutions for general non-cooperative systems.

Theorem 2.2. *([35]) Assume* (H_1), (H_2) *and* $(\mathrm{H}_3)'$ *hold. For any* $l, m \in \mathbb{N} \cup \{0\}$, $h_1, \cdots, h_l, h_1', \cdots, h_m'$, $h \in \mathbb{R}$, $c_1, \cdots, c_l, c_1', \cdots, c_m' > c_*$ *and* $\chi \in \{0,1\}$ *with* $l + m + \chi \ge 2$, *there exists an entire solution* $U_p(x,t)$ *of (2.3) such that*

$$u^-(x,t) \le U_p(x,t) \le \min\{k^+, \Pi^+(x,t)\} \text{ for } (x,t) \in \mathbb{R}^2, \tag{2.10}$$

where $p := p_{l,m,\chi} = (c_1, h_1, \cdots, c_l, h_l, c_1', h_1', \cdots, c_m', h_m', \chi h)$. *Furthermore, the following results hold.*

- *(i.)* $U_p(x,t) \gg 0$ *for* $(x,t) \in \mathbb{R}^2$ *and* $\lim_{t\to-\infty} \sup_{\|x\|\le A} \|U_p(x,t)\| = 0$ *for any* $A \in \mathbb{R}_+$.
- *(ii.) If* $\chi = 1$, *then* $\liminf_{t\to+\infty} \inf_{x\in\mathbb{R}} U_p(x,t) \ge k^-$ *and for every* $x \in \mathbb{R}$,
$$U_p(x,t) \sim v^* e^{\lambda^*(t+h)} \text{ as } t \to -\infty.$$
- *(iii.) If* $\chi = 0$, *then* $\liminf_{t\to+\infty} \inf_{\|x\|\le A} U_p(x,t) \ge k^-$ *for any* $A \in \mathbb{R}_+$ *and for every* $x \in \mathbb{R}^N$,
$$U_p(x,t) = O\big(e^{\vartheta(c_1,\cdots,c_l,c_1',\cdots,c_m')t}\big) \text{ as } t \to -\infty,$$
where $\vartheta(c_1, \cdots, c_l, c_1', \cdots, c_m') = \min_{1\le i\le l, 1\le j\le m} \{c_i\lambda_1(c_i), c_j'\lambda_1(c_j')\}$.

3. **Results on a model arising from epidermal wound healing.** In Section 3, we shall apply Theorems 2.1 and 2.2 to the model (1.1) arising from epidermal wound healing. This model is not cooperative because of the fact that $h(u_1)$ is not monotone. We shall establish the existence of traveling waves as well as the results on the speed of propagation to (1.1). We also characterize the spreading speed as the slowest speed of a family of non-constant traveling wave solutions of (1.1). In addition, we shall construct some new types of entire solutions which are different from the traveling wave solutions and spatial variable independent solutions. The spreading speed for (1.1) was discussed in [18, 23] based on numerical methods and singular perturbation techniques for several special cases, for example, $d_1 = 0$.

Our main result in this paper is Theorem 3.1.

Theorem 3.1. *Let d_1, d_2 be all positive numbers and $\kappa \in (0, \frac{1}{2})$, $\zeta \in (0,1)$,*

$$\frac{d_2}{d_1} < 2 + \frac{b}{1-2\kappa} \tag{3.11}$$

and

$$\frac{2\kappa h'(0)}{1-\kappa} \leq \begin{cases} 1 + \dfrac{1-2\kappa}{b} & \text{if } d_1 \geq d_2, \\ (2 - \dfrac{d_2}{d_1})\dfrac{1-2\kappa}{b} + 1, & \text{if } d_1 \leq d_2. \end{cases} \tag{3.12}$$

Then the conclusions of Theorem 2.1 hold for (1.1) where the minimum speed

$$c^* = 2\sqrt{(1-2\kappa)d_1},\ \lambda_1 := \lambda_1(c) = \tfrac{c-\sqrt{c^2-4d_1(1-2\kappa)}}{2d_1} > 0$$

and ν_{λ_1} is defined in (3.22). That is, the solution $(u_1(x,t), u_2(x,t)$ of (1.1) satisfies

(i.) If the functions $(u_1(x,0), u_2(x,0)) \leq (k_1, k_2)$ are nonnegative continuous and have compact support, then

$$\lim_{t\to\infty} \sup_{|x|\geq tc} (u_1(x,t), u_2(x,t)) = (0,0) \text{ for } c > c^*.$$

(ii.) If the functions $(u_1(x,0), u_2(x,0)) \leq (k_1, k_2)$ are nonnegative continuous and $u_1(x,0) \not\equiv 0$, then

$$(k_1^-, k_2^-) \leq \liminf_{t\to\infty} \inf_{|x|\leq tc} (u_1(x,t), u_2(x,t)) \leq (k_1^+, k_2^+), \text{ for } 0 < c < c^*.$$

(iii.) For each $c > c^*$ (1.1) admits a traveling wave solution $(\phi_1(\xi), \phi_2(\xi))$ such that $(0,0) \ll (\phi_1(\xi), \phi_2(\xi)) \leq (k_1^+, k_2^+)$, $\xi \in \mathbb{R}$,

$$(k_1^-, k_2^-) \leq \liminf_{\xi\to\infty} (\phi_1(\xi), \phi_2(\xi)) \leq \limsup_{\xi\to\infty} (\phi_1(\xi), \phi_2(\xi)) \leq (k_1^+, k_2^+)$$

and

$$\lim_{\xi\to-\infty} (\phi_1(\xi), \phi_2(\xi)) e^{-\lambda_1(c)\xi} = \nu_{\lambda_1}. \tag{3.13}$$

(iv.) For $c = c^*$ (2.3) admits a nonconstant traveling wave solution $(\phi_1(\xi), \phi_2(\xi))$ such that $(0,0) \leq (\phi_1(\xi), \phi_2(\xi)) \leq (k_1^+, k_2^+), \xi \in \mathbb{R}$.

(v.) For $0 < c < c^*$ (2.3) does not admit a traveling wave solution $(\phi_1(\xi), \phi_2(\xi))$ with $\liminf_{\xi\to\infty}(\phi_1(\xi), \phi_2(\xi)) \gg (0,0)$ and $(\phi_1(-\infty), \phi_2(-\infty)) = 0$.

(vi.) For any $l, m \in \mathbb{N} \cup \{0\}$, $h_1, \cdots, h_l, h_1', \cdots, h_m'$, $h \in \mathbb{R}$, $c_1, \cdots, c_l, c_1', \cdots, c_m'$ $> c_*$ and $\chi \in \{0,1\}$ with $l+m+\chi \geq 2$, (2.3) admits an entire solution $u_p(x,t)$, where $p := p_{l,m,\chi} = (c_1, h_1, \cdots, c_l, h_l, c_1', h_1', \cdots, c_m', h_m', \chi h)$. Moreover, the assertions (i)–(iii) *in Theorem 2.2 still hold for $u_p(\cdot,\cdot)$ as for $U_p(\cdot,\cdot)$.*

We now apply Theorems 2.1 and 2.2 to prove Theorem 3.1. Recall that

$$h(u_1) = \tfrac{u_1(1+\zeta^2)}{u_1^2+\zeta^2}.$$

It is easy to show that (1.1) has two equilibria $(0,0)$ and $(1,1)$. In fact, the following equalities hold at its non-trivial equilibrium

$$h(u_1) = \frac{\frac{1}{2-u_1} + \kappa - 1}{\kappa},\ u_2 = h(u_1). \tag{3.14}$$

Now it is clear that (3.14) has only one positive solution $(1,1)$. In fact, $(\frac{1}{2-u_1} + \kappa - 1)/\kappa$ in (3.14) is increasing and convex on $(0,\infty)$ and the first equation of (3.14) has only one solution $u_1 = 1$.

We shall define the two monotone systems. Note that $h(u_1)$ achieves its maximum value $(1+\zeta^2)/(2\zeta)$ when $u_1=\zeta$.

$$h^+(u_1)=\begin{cases} h(u_1), & 0\le u_1\le \zeta,\\ h(\zeta), & u_1\ge\zeta.\end{cases}$$

and the corresponding cooperative system is

$$\begin{aligned}\frac{\partial u_1}{\partial t}&=d_1\Delta u_1+s(u_2)u_1(2-u_1)-u_1\\ \frac{\partial u_2}{\partial t}&=d_2\Delta u_2+b(h^+(u_1)-u_2)\end{aligned}\tag{3.15}$$

In a similar manner, one can find (3.15) has two equilibria $(0,0)$ and (k_1^+,k_2^+) satisfying

$$h^+(k_1^+)=\frac{\frac{1}{2-k_1^+}+\kappa-1}{\kappa},\ k_2^+=h^+(k_1^+).\tag{3.16}$$

Since $h^+=h$ for $u_1\le\zeta$, then $k_1^+>\zeta$ (if $k_1^+\le\zeta$, then $k_1^+=1$ and $\zeta\ge 1$) and $h^+(k_1^+)=\frac{1+\zeta^2}{2\zeta}$. Solving k_1^+ directly from (3.16) gives that

$$k_1^+=2-\frac{1}{1+(\frac{1+\zeta^2}{2\zeta}-1)\kappa}>1>\zeta.$$

It follows that $k_2^+=h^+(k_1^+)=\frac{1+\zeta^2}{2\zeta}>1$.

Now there is a $h_0\in(0,\zeta]$ such that $h(h_0)<\min\{1,h(k_1^+)\}$ and define

$$h^-(u_1)=\begin{cases} h(u_1), & 0\le u_1\le h_0,\\ h(h_0), & u_1>h_0.\end{cases}$$

It is clear that

$$0<h^-(u_1)\le h(u_1)\le h^+(u_1)\le h'(0)u_1, u_1\in(0,k_1^+]$$

and $h^-(u_1)<1$ for $u_1\ge 0$.

The corresponding cooperative system for h^- is

$$\begin{aligned}\frac{\partial u_1}{\partial t}&=d_1\Delta u_1+s(u_2)u_1(2-u_1)-u_1\\ \frac{\partial u_2}{\partial t}&=d_2\Delta u_2+b(h^-(u_1)-u_2)\end{aligned}\tag{3.17}$$

In a similar manner, one can find (3.17) has two equilibria $(0,0)$ and (k_1^-,k_2^-) satisfying

$$h^-(k_1^-)=\frac{\frac{1}{2-k_1^-}+\kappa-1}{\kappa},\ k_2^-=h^-(k_1^-).\tag{3.18}$$

Since $h^-=h$ for $u_1\le h_0$, then $k_1^->h_0$ and $h^-(k_1^-)=h(h_0)$. Solving k_1^- directly from (3.18) gives that

$$k_1^-=2-\frac{1}{1+(h(h_0)-1)\kappa}<1 \text{ as } h(h_0)<1.$$

On the other hand, because $h(h_0)>0$, a simple calculation shows that $k_1^->\frac{1-2\kappa}{1-\kappa}>0$. As before we have $0<k_2^-=h^-(k_1^-)=h(h_0)<1$.

Thus,

$$(0,0)\ll(k_1^-,k_2^-)\le(1,1)\le(k_1^+,k_2^+).$$

We can always extend (3.15),(3.17) to be Liptschz continuous in $\mathbb{R}^2$ without changing the functions in the region $[0, k^+]$. Then the Comparison Principle [28, 33] implies that

$$0 \leq u(x,t) \leq k^+, x \in \mathbb{R}, t > 0.$$

Thus we are only interested in the invariant region. Now it is straightforward to check all other conditions of (H_1)(i)-(v).

We now need to check (H_2). The linearization of (1.1) at the origin is

$$\begin{aligned} \frac{\partial u_1}{\partial t} &= d_1 \Delta u_1 + (1-2\kappa) u_1 \\ \frac{\partial u_2}{\partial t} &= d_2 \Delta u_2 + b(h'(0) u_1 - u_2) \end{aligned} \tag{3.19}$$

where $h'(0) = \frac{1+\zeta^2}{\zeta^2}$. The matrix A_λ in (2.7) for (1.1) is

$$A_\lambda = (a_\lambda^{i,j}) = \begin{pmatrix} d_1\lambda^2 + 1 - 2\kappa & 0 \\ bh'(0) & d_2\lambda^2 - b \end{pmatrix}. \tag{3.20}$$

It is easy to see that

$$h^+(u_1) < h'(0) u_1, \;\; u_1 \in (0, \infty). \tag{3.21}$$

Now we shall verify (H_2) for (3.15). In fact, the principle eigenvalue of A_λ is $M(A_\lambda) = d_1\lambda^2 + 1 - 2\kappa$, which is a convex function of λ. Furthermore,

$$\Phi(\lambda) = \frac{M(A_\lambda)}{\lambda} = \frac{d_1\lambda^2 + 1 - 2\kappa}{\lambda}.$$

In fact $\Phi(\lambda)$ is also a strictly convex function of λ. The minimum of $\Phi(\lambda)$ is $c^* = 2\sqrt{(1-2\kappa)d_1}$ when $\lambda = \frac{\sqrt{1-2\kappa}}{\sqrt{d_1}}$. For each $c \geq c^*$,

$$\lambda_1(c) = \frac{c - \sqrt{c^2 - 4d_1(1-2\kappa)}}{2d_1}.$$

Let $\lambda_* = \frac{\sqrt{1-2\kappa}}{\sqrt{d_1}}$. For each $0 \leq \lambda \leq \lambda_*$, the positive eigenvector of A_λ corresponding to $M(A_\lambda)$ is

$$\nu_\lambda = \begin{pmatrix} \nu_\lambda^1 \\ \nu_\lambda^2 \end{pmatrix} = \begin{pmatrix} (d_1 - d_2)\lambda^2 + 1 - 2\kappa + b \\ bh'(0) \end{pmatrix} \tag{3.22}$$

Because of (3.11), ν_λ is a strictly positive vector for $\lambda \in [0, \lambda_*]$. This is clear when $d_1 \geq d_2$. If $d_1 < d_2$ and (3.11) holds, for $0 \leq \lambda \leq \lambda_*$, we have

$$(d_1 - d_2)\lambda^2 + 1 - 2\kappa + b \geq (d_1 - d_2)\lambda_*^2 + 1 - 2\kappa + b > 0.$$

Further from (3.22) we can see that

$$\frac{\nu_\lambda^2}{\nu_\lambda^1} = \frac{bh'(0)}{(d_1 - d_2)\lambda^2 + 1 - 2\kappa + b} = \frac{h'(0)}{\sigma}$$

where

$$\sigma = 1 + \frac{(d_1 - d_2)\lambda^2 + 1 - 2\kappa}{b}.$$

For $\lambda \in [0, \lambda_*]$, it is clear that

$$\sigma \geq \begin{cases} 1 + \frac{1-2\kappa}{b} > 0, & \text{if } d_1 \geq d_2, \\ (2 - \frac{d_2}{d_1})\frac{1-2\kappa}{b} + 1 > 0, & \text{if } d_1 < d_2. \end{cases}$$

Next, we verify the assumption $(\mathrm{H}_3)'$. For any $n \in \mathbb{Z}^+$, $\alpha_1, \cdots, \alpha_n > 0$ and $\lambda_1, \cdots, \lambda_n \in [0, \lambda_*]$, denote

$$(z_1, z_2) := \big(\alpha_1 v^1_{\lambda_1} + \cdots + \alpha_n v^1_{\lambda_n}, \alpha_1 v^2_{\lambda_1} + \cdots + \alpha_n v^2_{\lambda_n}\big) \gg (0,0).$$

Thus $(\mathrm{H}_3)'$ for (3.15) is equivalent to the following two inequalities

$$\begin{aligned} (\kappa z_2 + 1 - \kappa) z_1 (2 - z_1) - z_1 &\le (1 - 2\kappa) z_1 \\ b h^+(z_1) - b z_2 &\le b h'(0) z_1 - b z_2. \end{aligned} \tag{3.23}$$

Because $h^+(u_1) \le h'(0) u_1$, (3.23) is equivalent to the following inequality

$$(2 - z_1)\kappa \le (1 - \kappa)\frac{z_1}{z_2}. \tag{3.24}$$

Note that for any $\lambda \in [0, \lambda_*]$,

$$\frac{z_1}{z_2} \ge \begin{cases} (1 + \frac{1-2\kappa}{b})/h'(0), & \text{if } d_1 \ge d_2, \\ \big[(2 - \frac{d_2}{d_1})\frac{1-2\kappa}{b} + 1\big]/h'(0), & \text{if } d_1 < d_2. \end{cases}$$

In view of (3.12), it is easy to see that (3.24) holds.

It remains to show that the condition (ii) in Theorem 2.1 can be satisfied if $u_1(x, 0) \not\equiv 0$. The arguments here is the same as in Weinberger, Kawasaki and Shigesada [33]. We choose positive constants ρ, η so small that

$$-d_1 \rho^2 + (1 - 2\kappa) - (1 - \kappa)\eta > 0. \tag{3.25}$$

Since $u_2(x,t) \ge 0$, we have

$$\begin{aligned} \frac{\partial u_1}{\partial t} &\ge d_1 \Delta u_1 + (1 - \kappa) u_1 (2 - u_1) - u_1 \\ &= d_1 \Delta u_1 + u_1\big((1 - 2\kappa) - (1 - \kappa) u_1\big) \end{aligned} \tag{3.26}$$

By the strong maximum principle we have $u_1(x,t) > 0$ for $t > 0$. Thus we can require that $\eta \le u_1(x, t_1)$ for some $t_1 > 0$ and $|x| \le \frac{\pi}{2\rho}$ and some $t_1 > 0$ by choosing η small enough. If $(\hat{u_1}, \hat{u_2})$ is the solution of

$$\begin{aligned} \frac{\partial u_1}{\partial t} &= d_1 \Delta u_1 + u_1\big((1 - 2\kappa) - (1 - \kappa) u_1\big) \\ \frac{\partial u_2}{\partial t} &= d_2 \Delta u_2 + b(h^-(u_1) - u_2) \end{aligned} \tag{3.27}$$

with the initial values

$$u_1(x, t_1) = \begin{cases} \eta \cos(\rho x) & \text{for } |x| \le \frac{\pi}{2\rho} \\ 0 & \text{for } |x| \ge \frac{\pi}{2\rho} \end{cases}, \quad u_2(x, t_1) = 0. \tag{3.28}$$

It is clear that (3.27) has two equilibria

$$(0,0) \text{ and } (\tfrac{1-2\kappa}{1-\kappa}, h^-(\tfrac{1-2\kappa}{1-\kappa})) \gg 0.$$

Furthermore, there is no other stationary solution of (3.27) between the two equilibriums.

The comparison principle shows that the components of $(\hat{u_1}, \hat{u_2})$ are lower bounds for (u_1, u_2) when $t \ge t_1$. The inequality (3.25) shows that both $(\frac{\partial \hat{u_1}}{\partial t}, \frac{\partial \hat{u_2}}{\partial t})$ are nonnegative at $t = t_1$, and the comparison principle then implies that $(\hat{u_1}, \hat{u_2})$ are nondecreasing in t. It follows that $(\hat{u_1}, \hat{u_2})$ monotonically converges to $(\frac{1-2\kappa}{1-\kappa}, h^-(\frac{1-2\kappa}{1-\kappa}))$ uniformly in x on every bounded x-interval. Because $(u_1, u_2) \ge (\hat{u_1}, \hat{u_2})$, it follows that if we choose two positive constants (ω_1, ω_1) with

$$(\omega_1, \omega_1) < \Big(\frac{1 - 2\kappa}{1 - \kappa}, h^-(\frac{1 - 2\kappa}{1 - \kappa})\Big)$$

h

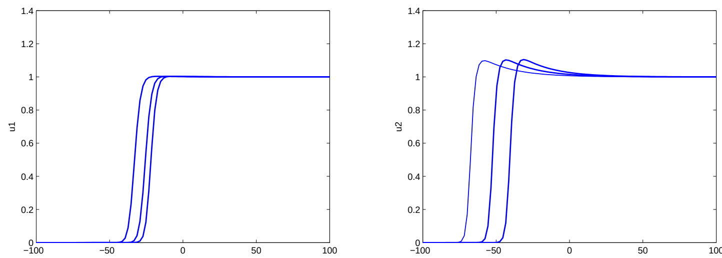

FIGURE 1. The simulations of the traveling wave solutions of (1.1). We choose $d_1 = d_2 = 1, \kappa = 0.05, \zeta = 0.1, b = 0.05$.

then for all sufficiently large t, the condition (ii) in Theorem 2.1 is automatically satisfied on the fixed interval $|x| \leq 2R_\omega$. We thus obtain the statement (4.21) without an extra condition.

4. **Discussion.** In this section, we first present two simulations for traveling wave solutions. Fig. 1 are the simulations of the traveling wave solutions of (1.1). We choose $d_1 = d_2 = 1, \kappa = 0.05, \zeta = 0.1, b = 0.05$, which satisfy the conditions of Theorem 3.1. Note that the traveling solutions are not monotone and the minimum speed $c^* = 2\sqrt{(1-2\kappa)d_1} = 1.89$. In general, it is often hard to simulate entire solutions. Nevertheless [39] produces a number of entire solutions for a discrete system.

Traveling solutions of reaction-diffusion equations are extensively used to describe biological invasions from one state to another state. The existence of traveling waves often indicates whether an invasion is successful. The minimum speed for a class of traveling solutions often reveals how fast the invasion spreads. For wound healing process, the existence of traveling waves of (1.1) indicates whether if the skin (or another organ-tissue) can repair itself after injury. The minimum speed of the traveling waves of (1.1) gives information on how long the healing process takes.

In general, epidermal migration, often start from differential locations from the wound edge. The dynamics of epidermal wound healing is better characterized by entire solutions which describe the interactions of travel waves (local repairing processes) with different speeds and originated from different locations. While our understanding of the wound healing process is limited, to the best of the knowledge of the authors, this is the first time that it is shown that there is an entire solution in the model for epidermal wound healing. We anticipate more research on the topics is forthcoming.

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