

## WAVEFRONT OF AN ANGIOGENESIS MODEL

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**ABSTRACT.** In this paper, we show the existence of traveling wave solutions to a chemotaxis model describing the initiation of angiogenesis. By a change of dependent variable, we transform the wave equation of the angiogenesis model to a Fisher type wave equation. Then we make use of the methods of analyzing the Fisher wave equation to obtain the existence of traveling wave solutions to the angiogenesis model. In virtue of the asymptotic behavior of the traveling wave solution at infinity, we find the explicit wave speed for cases of both zero and nonzero chemical diffusion. Finally based on the fact that the wave speed is convergent with respect to the chemical diffusion, we rigorously establish the zero chemical diffusion limit of traveling wave solutions by the energy estimates.

**1. Introduction.** Angiogenesis is a chemotactic process involving the generation of new blood vessels from pre-existing vessels. It is essential for the growth and development of solid tumors as well as the cancer metastasis. Tumor angiogenesis starts with cancerous tumor cells secreting some chemical substance (or signalling molecule), which is generally called angiogenesis growth factor, to induce neighboring endothelial cells to migrate toward the tumor in order to build its own capillary network and to supply nutrients and oxygen for its development (see an illustration in Fig. 1).

Full modeling of the complete tumor angiogenesis leads to very complex mathematical models [1, 2, 3, 5, 4]. However, the interaction between endothelial cells and angiogenesis growth factor can be described by the following chemotaxis model after simplification (see [12, 8, 26])

$$\begin{cases} u_t = (du_x - \chi uv^{-\alpha} v_x)_x, \\ v_t = \varepsilon v_{xx} - uv^m \end{cases} \quad (1.1)$$

with  $d, \chi, \alpha > 0, \varepsilon \geq 0$  and  $m \geq 1$ , where  $u(x, t)$  denotes the density of endothelial cells,  $v(x, t)$  stands for the concentration of the chemical substance (i.e., the endothelial angiogenesis growth factor), and the chemosensitivity function  $\phi(v) = \chi v^{-\alpha}$  reflects the fact that the chemosensitivity is lower for higher concentration of the chemical because of the saturation effect. In the case of haptotaxis where cancerous cells are directed to the substratum-bound attractants such as laminin or fibronectin, the model corresponds to (1.1) with  $\varepsilon = 0$  (see, e.g., [21]). The studies of system (1.1) hence have two categories:

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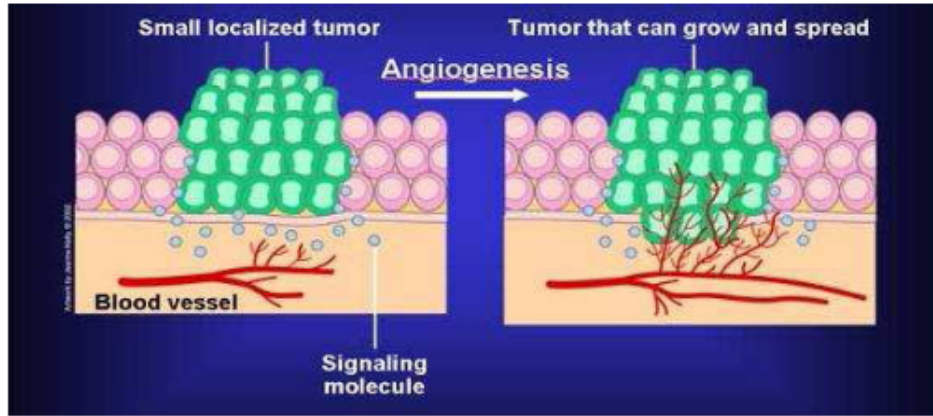


FIGURE 1. An illustration of tumor angiogenesis adopted from the website of National Cancer Institute. The initiation of angiogenesis involves the secretion of the signalling molecule (i.e. endothelial angiogenesis growth factor) by tumor cells, which diffuse and induce neighboring endothelial cells of the blood vessels to migrate toward the tumor in order to build its own capillary network as shown in the right picture of the figure.

*Zero chemical diffusion* ( $\varepsilon = 0$ ). The existence of global weak solutions of (1.1) was established by Corrias *et al* in [7, 6] with  $0 < \alpha < 1, m \geq 1$  in bounded domain with zero-flux boundary condition, and extended by Perthame [26] to unbounded domain. For a peculiar case:  $\alpha = 1, m = 1$ , the stability of solutions was established by Friedman and Tello [9], and the asymptotic behavior of solutions of (1.1) was given by Fontelos *et al* [8]. For the same parameter values, the existence of traveling wave solutions was shown in [30], and the nonlinear stability of traveling wave solutions was subsequently established in [15, 16]. Recently, the global existence and asymptotic behavior of solutions of the model with small and large initial data have been investigated in a series of papers [13, 14, 18].

*Non-zero chemical diffusion* ( $\varepsilon > 0$ ). In contrast to the case of zero diffusion, much less is the result for  $\varepsilon > 0$  except a recent work [17], whereby the existence and nonlinear stability of traveling wave solutions for a special case  $\alpha = 1, m = 1$  was established. However  $\varepsilon$  was required to be small in [17]. For  $m > 1$ , the non-existence of traveling wave solutions was proved by Schwetlick [29]. It is worthwhile to point out that the model (1.1) with  $0 \leq m < 1$  was previously proposed by Keller and Segel [10] to describe the chemotactic traveling band propagation of bacterial and a large amount of works followed to study the traveling wave solutions of such a model for both zero and nonzero chemical diffusion, for example see [27, 28, 25, 24, 23, 19, 20] and references therein. This indicates that the model (1.1) may interpret different biological phenomena depending upon the value of parameter  $m$ .

We will continue to discuss the traveling wave problem of model (1.1) with  $\varepsilon > 0$  for the case of  $\alpha = 1, m = 1$ , namely

$$\begin{cases} u_t = (du_x - \chi uv^{-1}v_x)_x, \\ v_t = \varepsilon v_{xx} - uv. \end{cases} \quad (1.2)$$

The existence of traveling wave solutions of (1.2) was established in [17] for  $\varepsilon > 0$  where  $\varepsilon$  was required to be small. The present paper will elaborate and develop results of [15, 17] by

- (1) removing the smallness assumption on  $\varepsilon$  prescribed in [17];
- (2) identifying the explicit traveling wave speed for both  $\varepsilon = 0$  and  $\varepsilon > 0$ ;
- (3) establishing the diffusion limit of traveling wave solutions as  $\varepsilon \rightarrow 0$ .

One considerable challenge of analyzing (1.2) stems from the singularity caused by term  $v^{-1}$  as  $v \rightarrow 0$ . In [17], a change of dependent variable  $v$  was used to remove the singularity by transforming the system (1.2) into a system of conservation laws. Then the theory of conservation laws was used to investigate the traveling wave solutions to the transformed system. But the smallness of  $\varepsilon$  was essentially assumed therein. In this paper, we shall employ another idea used in [23, 20] to study the traveling wave solutions of the system (1.2) by converting the wave equation of (1.2) to a Fisher type wave equation. Then we make use of the results of the Fisher wave equation to establish the existence of traveling wave solutions for (1.2) for arbitrary  $\varepsilon > 0$ . We apply the asymptotic behavior of traveling wave solutions to find the explicit wave speed and show the convergence of wave speed as  $\varepsilon \rightarrow 0$ . With the convergence of wave speed, we finally prove the convergence of traveling wave solutions as  $\varepsilon \rightarrow 0$ . It should be noted that the approach adopted in the present paper is fundamentally different from that in [15, 17] where the system (1.2) was first converted to a system of conservation laws by a change of variable, and then the analysis was performed toward the transformed system instead of the original model (1.2). In the present paper we deal with the model (1.2) directly.

The rest of paper is organized as follows. In section 2, we establish some preliminary results to set up the basic structure of analysis. In section 3, we derive the existence of traveling wave solutions of (1.2) for both  $\varepsilon = 0$  and  $\varepsilon > 0$ . In the subsequent section 4, we derive the explicit wave speeds for both  $\varepsilon = 0$  and  $\varepsilon > 0$ . Finally in section 5, the zero chemical diffusion limit of traveling wave solutions is rigorously derived by the energy estimates.

**2. Prior results.** A traveling wave solution of (1.2) for  $(x, t) \in \mathbb{R} \times [0, \infty)$  is a particular solution of the form

$$u(x, t) = U(z), \quad v(x, t) = V(z), \quad z = x - ct \quad (2.1)$$

satisfying boundary conditions

$$U(\pm\infty) = u_{\pm}, \quad V(\pm\infty) = v_{\pm}, \quad U'(\pm\infty) = V'(\pm\infty) = 0, \quad (2.2)$$

where  $c$  is the wave speed,  $z$  is the so-called wave variable, the prime  $'$  means the differentiation in  $z$ ,  $u_-/u_+$  and  $v_-/v_+$  are called left/right end states of  $u$  and  $s$ , respectively, describing the asymptotic behavior of traveling wave solutions as  $z \rightarrow -\infty/\infty$ .

Before embarking on the technical details, it is very helpful to first discuss some intuitive mathematical outcomes resulting from the biological relevance. The initiation of angiogenesis starts with the propagation of the endothelial angiogenesis growth factor to activate endothelial cells that line the interior surface of blood vessels to migrate out to form new capillary. So the migrating endothelial cell behaves as a ‘‘invasive’’ species and hence the pattern of propagation should be a wavefront. This indicates that  $u_- > 0, u_+ = 0$ . The propagation pattern of the endothelial

angiogenesis growth factor is other way around and thus  $v_- = 0, v_+ > 0$ . Therefore the biologically relevant boundary condition of traveling wave solutions are

$$\begin{aligned} U(-\infty) &= u_- > 0, \quad U(+\infty) = 0, \\ V(-\infty) &= 0, \quad V(+\infty) = v_+ > 0, \\ U'(\pm\infty) &= V'(\pm\infty) = 0. \end{aligned} \quad (2.3)$$

Therefore substituting the ansatz (2.1) into (1.2) and integrating the result subject to the boundary conditions (2.3) yield

$$\begin{cases} dU' + cU - \chi V^{-1} V' U = 0, \\ \varepsilon V'' + cV' - UV = 0. \end{cases} \quad (2.4)$$

If  $(U(z), V(z))$  is a solution of (2.4) with speed  $c$  fulfilling the boundary condition (2.2), then  $(U(-z), V(-z))$  is a solution of (2.4) with speed  $-c$  satisfying the boundary conditions  $U(\mp\infty) = u_{\pm}$ ,  $V(\mp\infty) = v_{\pm}$ ,  $U'(\pm\infty) = V'(\pm\infty) = 0$ . Hence for the proof of the existence of traveling wave solutions with speed  $c$ , it suffices to consider the case  $c \geq 0$ . Hereafter we assume that  $c \geq 0$ .

The conventional method of solving (2.4) subject to (2.3) was to convert (2.4) into a system of first order ordinary differential equations (ODEs). However the analysis of the corresponding first order ODE system of (2.4) confronts two considerable challenges: high dimensionality (i.e. there are three first order ODEs) and the singularity of  $V^{-1}$  as  $V \rightarrow 0$  (i.e. as  $z \rightarrow -\infty$ ). Luckily we can solve  $U$  in terms of  $V$  from the first equation of (2.4) and obtain

$$U(z) = C e^{-\frac{c}{\chi} z} V^{\frac{\chi}{d}}(z) = C \times F(z, V) \quad (2.5)$$

where  $C$  is a constant of integration and

$$F(z, V) = e^{-\frac{c}{\chi} z} V^{\frac{\chi}{d}}(z). \quad (2.6)$$

Substituting (2.5) back into the second equation of (2.4) yields a second order ordinary differential equation with variable coefficient

$$\varepsilon V'' + cV' - C e^{-\frac{c}{\chi} z} V^{\frac{\chi}{d}+1} = 0. \quad (2.7)$$

It is helpful to note that the traveling wave solution of (2.7) is translationally invariant in the independent variable  $z$  and the constant  $C$  represents a translation constant of the traveling wave. In fact, let  $V(z)$  be a solution of (2.7) and  $\tau$  satisfies  $e^{\frac{c}{\chi}\tau} = C$ . Then  $V(z + \tau)$  is also a solution of (2.7) corresponding to  $C = 1$ . Without loss of generality, we shall assume  $C = 1$  throughout the paper and consider the normalized traveling waves. Thus we have

$$U(z) = F(z, V) = e^{-\frac{c}{\chi} z} V^{\frac{\chi}{d}}(z). \quad (2.8)$$

In what follows, for the sake of convenience, we denote

$$k = \frac{c}{d}, \quad r = \frac{\chi}{d} + 1. \quad (2.9)$$

Then (2.7) with  $C = 1$  becomes

$$\varepsilon V'' + cV' - e^{-kz} V^r = 0. \quad (2.10)$$

We have two distinctive cases to consider: zero chemical diffusion  $\varepsilon = 0$  and nonzero chemical diffusion  $\varepsilon > 0$ .

3. Existence of T.W.S..

3.1. T.W.S. for zero chemical diffusion. With  $\varepsilon = 0$ , equation (2.10) becomes

$$cV' - e^{-kz}V^r = 0. \tag{3.1}$$

Then we have the following results.

**Theorem 3.1.** *The solution of (3.1) satisfying (2.3) exists if and only if  $c > 0$ . Hence the traveling wave solution  $(U, V)$  of (2.4), (2.3) exists if and only if  $c > 0$ . Furthermore if  $(U, V)$  exists, then  $U' < 0, V' > 0$ .*

*Proof.* If  $c = 0$ , then  $V^r = 0$ , which holds for all  $z$  if and only if  $V \equiv 0$ . But the boundary conditions (2.3) are violated. Hence  $V \equiv 0$  is not a traveling wave solution.

If  $c > 0$ , (3.1) is linear and can be explicitly solved to yield that

$$V(z) = \left( v_+^{-\frac{\chi}{d}} + \frac{\chi}{c^2} e^{-kz} \right)^{-\frac{d}{\chi}}. \tag{3.2}$$

Then it follows from (2.8) that

$$U(z) = \frac{1}{v_+^{-\frac{\chi}{d}} e^{kz} + \frac{\chi}{c^2}}. \tag{3.3}$$

It is trivial to check that  $V(-\infty) = 0, V(\infty) = v_+ > 0, U(-\infty) = \frac{c^2}{\chi} = u_-, U(\infty) = 0$ , satisfying the boundary condition (2.3). Therefore  $(U, V)$  given by (3.2)-(3.3) is a traveling wave solution of (1.2), (2.3). Lastly  $U' < 0$  and  $V' > 0$  can be verified by simple calculations. A numerical visualization of traveling wave solutions (3.2) and (3.3) is shown in Fig. 2. Then the proof is complete.  $\square$

3.2. T.W.S. for non-zero diffusion. In this section, we discuss the existence of traveling wave solutions of (2.4)-(2.3) for  $\varepsilon > 0$ . We first introduce a new parameter  $\mu$  with

$$\mu = -\frac{k}{r-1} = -\frac{c}{\chi} < 0 \tag{3.4}$$

and make a change of variable

$$V(z) = W(z)e^{-\mu z}. \tag{3.5}$$

Then substituting (3.5) into (2.7) and canceling  $e^{-\mu z}$ , we end up with

$$\varepsilon W'' + sW' + f(W) = 0, \quad f(W) = \eta W - W^r \tag{3.6}$$

where

$$s = c\left(1 + \frac{2\varepsilon}{\chi}\right), \quad \eta = \frac{c^2}{\chi^2}(\varepsilon + \chi). \tag{3.7}$$

Clearly equation (3.6) has two steady states: 0 and  $\rho = \eta^{1/(r-1)} = \eta^{\frac{d}{\chi}} > 0$ . Therefore  $f(0) = f(\rho) = 0$ . It is easy to verify that  $f'(0) > 0$  and  $f'(\rho) < 0$ . Now let's recall the well-known Fisher equation

$$w_t = w_{xx} + \tilde{f}(w) \tag{3.8}$$

where  $\tilde{f}(0) = \tilde{f}(\varrho) = 0$  and  $\tilde{f}'(0) > 0$  and  $\tilde{f}'(\varrho) < 0$ .

The equation for the traveling wave solution  $W(z) = w(x - st)$  of (3.8) is

$$\varepsilon W'' + sW' + \tilde{f}(W) = 0. \tag{3.9}$$

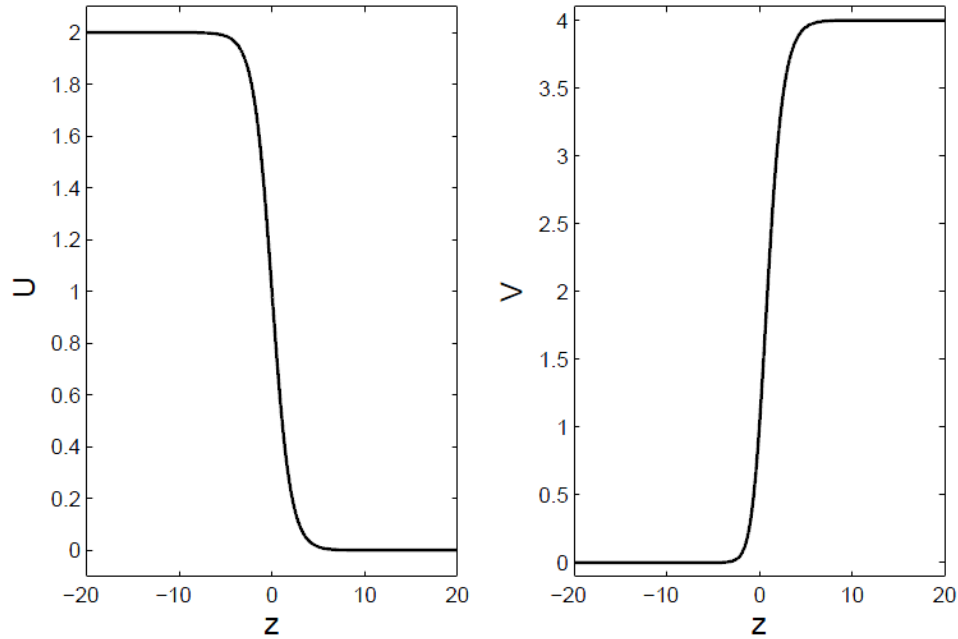


FIGURE 2. The plot of traveling wave solutions  $(U, V)$  of (3.2)-(3.3) for  $\varepsilon = 0$ , where  $v_+ = 4, d = 1, \chi = 1/2, c = 1, k = c/d, r = \chi/d + 1$ .

It is remarkable that equation (3.6) resembles the traveling wave equation of the Fisher equation with speed  $s$ . Then we perform phase plane analysis similar for the Fisher equation by rewriting (3.6) as a system of ordinary differential equation

$$\begin{cases} W' = \xi, \\ \xi' = -\frac{s}{\varepsilon}\xi - \frac{1}{\varepsilon}f(W). \end{cases} \tag{3.10}$$

For convenience, we first derive the results of the equation (3.6) based on the results for the Fisher equation. Then we translate the results back to  $U$  and  $V$  by the transformations of (3.5) and (2.8). It is well-known that Fisher wave equation (3.9) has a positive solution iff  $s \geq s_* = 2\sqrt{\varepsilon f'(0)}$ . We obtain the following theorem.

**Lemma 3.2.** *Let  $\varepsilon > 0$ . Then a nonnegative traveling wave solution  $W(z)$  of (3.6) exists if and only if*

$$s \geq s_* = 2\sqrt{\varepsilon f'(0)} = 2\sqrt{\varepsilon\eta}. \tag{3.11}$$

*If the traveling wave solution  $W(z)$  of (3.6) exists, it is a wavefront with  $W' < 0$  and satisfies the boundary conditions*

$$W(-\infty) = \eta^{\frac{d}{\chi}}, W(\infty) = 0.$$

*Moreover the traveling wavefront solution  $W(z)$  is unique up to a translation along the moving coordinate  $z$  for each given speed  $s$  satisfying (3.11) and has the following asymptotic behaviors:*

(a) *If  $s > s_* = 2\sqrt{\varepsilon f'(0)} = 2\sqrt{\varepsilon\eta}$ , then*

$$\begin{aligned} W(z) &\sim \eta^{\frac{d}{\chi}} + Ce^{\lambda_2^+ z}, \text{ as } z \rightarrow -\infty, \\ W(z) &\sim Ce^{\lambda_1^+ z}, \text{ as } z \rightarrow \infty \end{aligned} \tag{3.12}$$

where  $C$  is a positive generic constant and

$$\lambda_1^+ = \frac{-s + \sqrt{s^2 - 4\varepsilon\eta}}{2\varepsilon} = \mu, \quad \lambda_2^+ = \frac{-s + \sqrt{s^2 + 4\varepsilon\eta(r-1)}}{2\varepsilon}.$$

(b) If  $s = s_* = 2\sqrt{\varepsilon f'(0)} = 2\sqrt{\varepsilon\eta}$ , then

$$\begin{aligned} W(z) &\sim \eta^{\frac{d}{x}} - Ce^{-\sigma z} + O(e^{-2\sigma z}), \text{ as } z \rightarrow -\infty \\ W(z) &\sim (A - Bz)e^{-\frac{s_*}{2}z} + O(z^2e^{-s_*z}), \text{ as } z \rightarrow \infty \end{aligned} \tag{3.13}$$

where  $A, B, C$  are positive constants and

$$\sigma = \frac{s_* - \sqrt{s_*^2 + 4\varepsilon\eta(r-1)}}{2\varepsilon}.$$

*Proof.* Following the standard argument for the Fisher equation (or see results of [22, 31, 11]), the Lemma is proved with some simple calculations. We omit the details for brevity.  $\square$

**Theorem 3.3.** *The non-negative traveling wave solution  $(U, V)$  of model (2.4)-(2.3) exists if and only if*

$$c > c_* = 0.$$

Moreover solution  $(U, V)$  is monotone with  $U' < 0, V' > 0$ , and satisfies the following asymptotic behaviors as  $|z| \rightarrow \infty$ :

$$U(z) \sim \begin{cases} \left(\eta^{\frac{d}{x}} + Ce^{\lambda_2^+ z}\right)^{\frac{x}{d}}, & \text{as } z \rightarrow -\infty, \\ Ce^{-\frac{c}{d}z}, & \text{as } z \rightarrow \infty \end{cases} \tag{3.14}$$

and

$$V(z) \sim \begin{cases} \left(\eta^{\frac{d}{x}} + Ce^{\lambda_2^+ z}\right)e^{-\mu z}, & \text{as } z \rightarrow -\infty, \\ v_+ + Ce^{-\frac{c}{\varepsilon}z}, & \text{as } z \rightarrow \infty \end{cases} \tag{3.15}$$

where  $C$  is a generic constant and

$$\lambda_2^+ = \mu + \frac{-c + \sqrt{c^2 + 4\varepsilon\eta r}}{2\varepsilon} > 0. \tag{3.16}$$

*Proof.* First we notice that  $s \geq s_* = 2\sqrt{\varepsilon f'(0)}$  is equivalent to  $c \geq c_* = 0$  by simple calculations. When  $c = c_* = 0, \mu = 0$  from (3.4). Consequently  $s = s_* = 0$  and  $\eta = 0$ . So (3.6) becomes

$$\varepsilon W'' - W^r = 0$$

which gives that  $\int_{-\infty}^{\infty} W^r dz = 0$  and hence  $W \equiv 0$  since  $W \geq 0$ . This in turns means that  $V \equiv 0$  (3.5). Therefore  $V$  is not a traveling wave solution in this case.

When  $c > c_* = 0$ , the results of the Fisher waves given in Lemma 3.2 can be translated to  $V$  term by term. First applying (3.12) we can obtain the asymptotic behavior of  $V$  as  $z \rightarrow -\infty$  in (3.15). To derive the asymptotic decay rate of  $V$  as  $z \rightarrow \infty$ , we apply the asymptotic analysis. Note that as  $z \rightarrow \infty, e^{-kz}V(z) \rightarrow 0$ . Hence from (2.10), we know that the asymptotic behavior of  $V$  as  $z \rightarrow \infty$  is determined by the following problem

$$\varepsilon V'' + cV' = 0, V(\infty) = v_+$$

which yields  $V(z) = v_+ + Ce^{-\frac{c}{\varepsilon}z}$  where  $C$  is a constant. The proof of (3.15) is done. Combining (2.8) and (3.5) gives

$$U(z) = W^{\frac{\chi}{\alpha}}$$

since  $\chi\mu + c = 0$ . Then applying (3.12) into above equation, we obtain the asymptotic decay rate for  $U$ . It remains to prove the monotonicity of solution  $V$ , which can be shown by integrating the second equation of (2.4)

$$V' = \frac{1}{\varepsilon}e^{-\frac{c}{\varepsilon}z} \int_{-\infty}^z e^{\frac{c}{\varepsilon}\xi} UV d\xi > 0$$

since  $U, V > 0$  for all  $z \in (-\infty, \infty)$ . □

Fig. 3 gives a numerical traveling wave solution of angiogenesis model (1.2) for  $\varepsilon > 0$ . It is hard to numerically compute model (1.2) directly due to the singular term  $v^{-1}$ . Here we compute system (3.10) for  $W$  first and then use (3.5) and (2.8) to obtain  $V$  and  $U$ , respectively. From Theorem 3.3, we know that  $V(z) > 0$  for any  $z \in (-\infty, \infty)$  with  $V \rightarrow 0$  as  $z \rightarrow -\infty$ . Since there is a singular term  $V^{-1}$  in equation (2.4), one may be concerned with the asymptotic behavior of  $V'/V$  as  $z \rightarrow -\infty$  and see whether or not the singularity truly occurs. The following Lemma justifies that the singularity actually does not happen.

**Lemma 3.4.** *Let  $\varepsilon \geq 0$  and  $(U, V)$  be a traveling wave solution of the angiogenesis model (1.2), namely  $(U, V)$  fulfills (2.4)-(2.3). Then*

$$\frac{V'}{V} = \begin{cases} \frac{c}{\chi}, & z \rightarrow -\infty \\ 0, & z \rightarrow \infty. \end{cases}$$

*Proof.* The assertion can be proved by simple calculation using (3.2), (3.15) and boundary conditions (2.3). The details are omitted for brevity. □

**4. Wave speed.** In previous section, we already found that the model (1.2) has a traveling wave solution satisfying (2.3) for every wave speed  $c > c_* = 0$ . It seems that there is infinitely fast wave propagation and wave speed is not unique. In this section, we shall elucidate this ambiguity by finding the explicit wave speed in terms of model parameters.

**Theorem 4.1.** *Let the assumptions in Theorem 3.3 hold. Let  $c_0$  and  $c_\varepsilon$  be the wave speed for  $\varepsilon = 0$  and  $\varepsilon > 0$ , respectively. Then*

(i) *If  $\varepsilon = 0$ , the wave speed is uniquely determined by*

$$c_0 = \sqrt{\chi u_-}. \tag{4.1}$$

(ii) *If  $\varepsilon > 0$ , then the wave speed is given by*

$$c_\varepsilon = \chi \sqrt{\frac{u_-}{\varepsilon + \chi}}. \tag{4.2}$$

(iii)  $|c_\varepsilon - c_0| = \mathcal{O}(\varepsilon)$ .

*Proof.* (i) When  $\varepsilon = 0$ , the solution  $U(z)$  is given by (3.3) and satisfies

$$U(-\infty) = u_- = \frac{c_0^2}{\chi}.$$

This indicates (4.1).



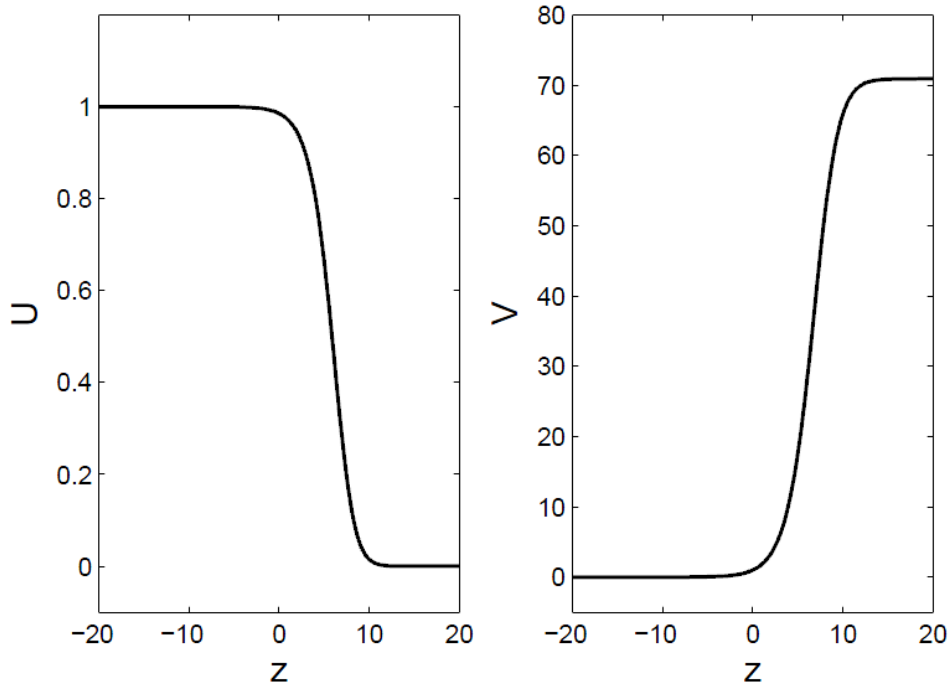


FIGURE 3. A numerical simulation of traveling wave profile of the model (1.2) for  $\varepsilon > 0$ . Parameter values:  $\varepsilon = 1, c = 1, d = 1, \chi = 2$  and  $r, \mu, s, \eta$  are obtained through  $r = \chi/d + 1, \mu = -\frac{c}{\chi}, s = c(1 + \frac{2\varepsilon}{\chi}), \eta = \frac{c^2}{\chi^2}(\varepsilon + \chi)$ .

(ii) For  $\varepsilon > 0$ , the asymptotic behavior of  $U$  is given by (3.14)

$$U(-\infty) = u_- = \eta = \frac{c_\varepsilon^2}{\chi^2}(\varepsilon + \chi)$$

which gives (4.2).

(iii) With the results in (i) and (ii), it follows that

$$c_\varepsilon - c_0 = -\frac{c_\varepsilon^2 \varepsilon}{\chi(c_\varepsilon + c_0)}.$$

Noticing that  $c_\varepsilon < c_0$ , we have

$$\left| \frac{c_\varepsilon^2}{\chi(c_\varepsilon + c_0)} \right| \leq \frac{c_\varepsilon}{2\chi} \leq \frac{c_0}{2\chi} = \frac{1}{2} \sqrt{\frac{u_-}{\chi}}.$$

The proof is complete. □

**Remark 1.** Theorem 4.1 says that the wave speed for both  $\varepsilon = 0$  and  $\varepsilon > 0$  is indeed bounded and unique if other parameters are fixed. It also indicates that both wave speeds  $c_0$  and  $c_\varepsilon$  are enhanced by the chemo-sensitivity coefficient  $\chi$ . The fact  $c_\varepsilon < c_0$  interprets that wave speed is diminished by the chemical diffusion  $\varepsilon$ . All these mathematical results are consistent with the biological intuitions.

**5. Diffusion limits of T.W.S.** From the preceding section, we have shown that  $|c_\varepsilon - c_0| \rightarrow 0$  as  $\varepsilon \rightarrow 0$ . Hence it is expected the traveling wave solutions are also convergent with respect to  $\varepsilon$ , which will be rigorously proved in this section. Precisely we have the following result.

**Theorem 5.1.** *Let traveling wave solutions of (1.2)-(2.3) be denoted by  $(U_\varepsilon, V_\varepsilon)$  for  $\varepsilon > 0$  and by  $(U_0, V_0)$  for  $\varepsilon = 0$ . Then*

$$|U_\varepsilon - U_0| = \mathcal{O}(\varepsilon), |V_\varepsilon - V_0| = \mathcal{O}(\varepsilon)$$

for every  $z \in (-\infty, \infty)$ .

*Proof.* By (2.10), we see that  $V_\varepsilon$  and  $V_0$  satisfy

$$\varepsilon V_\varepsilon'' + c_\varepsilon V_\varepsilon' - h(z, V_\varepsilon) = 0 \tag{5.1}$$

and

$$c_0 V_0' - h(z, V_0) = 0 \tag{5.2}$$

where  $h(z, V) = e^{-kz} V^r$ . Define

$$\mathbf{V} = V_\varepsilon - V_0.$$

Then we have from (5.1)-(5.2) that

$$\varepsilon \mathbf{V}'' + c_0 \mathbf{V}' + (c_\varepsilon - c_0) V_\varepsilon' + \varepsilon V_0'' = h(z, V_\varepsilon) - h(z, V_0). \tag{5.3}$$

By mean value theorem, it has that

$$h(z, V_\varepsilon) - h(z, V_0) = e^{-kz} (V_\varepsilon^r - V_0^r) = r e^{-kz} \xi^{r-1} (V_\varepsilon - V_0) = r e^{-kz} \xi^{r-1} \mathbf{V}$$

where  $\xi$  is a positive number between  $V_\varepsilon$  and  $V_0$ . Then multiplying (5.3) by  $\mathbf{V}$ , we have

$$\varepsilon \mathbf{V} \mathbf{V}'' + c_0 \mathbf{V} \mathbf{V}' + (c_\varepsilon - c_0) V_\varepsilon' \mathbf{V} + \varepsilon V_0'' \mathbf{V} = r e^{-kz} \xi^{r-1} \mathbf{V}^2 \geq 0 \tag{5.4}$$

since  $r e^{-kz} \xi^{r-1} \geq 0$ .

Hence integrating (5.4) on both sides yields

$$I = \int_z^\infty (\varepsilon \mathbf{V}'' + c_0 \mathbf{V}') \mathbf{V} dy + \varepsilon \int_z^\infty \mathbf{V} V_0'' dz + (c_\varepsilon - c_0) \int_z^\infty V_\varepsilon' \mathbf{V} dy \geq 0. \tag{5.5}$$

Note that  $\mathbf{V}(\infty) = \mathbf{V}'(\infty) = 0$ . Then

$$\begin{aligned} I &= -\varepsilon \mathbf{V}' \mathbf{V} - \frac{c_0}{2} \mathbf{V}^2 - \varepsilon \int_z^\infty |\mathbf{V}'|^2 dy + \varepsilon \int_z^\infty \mathbf{V} V_0'' dz + (c_\varepsilon - c_0) \int_z^\infty V_\varepsilon' \mathbf{V} dy \\ &\leq -\frac{\varepsilon}{2} (\mathbf{V}^2)' - \frac{c_0}{2} \mathbf{V}^2 + \varepsilon \int_z^\infty \mathbf{V} V_0'' dz + (c_\varepsilon - c_0) \int_z^\infty V_\varepsilon' \mathbf{V} dy. \end{aligned} \tag{5.6}$$

Using (5.5), we have

$$\frac{\varepsilon}{2} (\mathbf{V}^2)' + \frac{c_0}{2} \mathbf{V}^2 \leq \varepsilon \int_z^\infty \mathbf{V} V_0'' dz + (c_\varepsilon - c_0) \int_z^\infty V_\varepsilon' \mathbf{V} dy. \tag{5.7}$$

Let  $z_0$  be a point at which  $|\mathbf{V}(z)|$  attains its maximum on  $\mathbb{R}$ . Then  $(\mathbf{V}^2)'(z_0) = 2\mathbf{V}'(z_0)\mathbf{V}(z_0) = 0$  and hence

$$\begin{aligned} \mathbf{V}^2(z_0) &\leq \frac{2\varepsilon}{c_0} \int_z^\infty |\mathbf{V}(z_0)| |V_0''| dz + \frac{2}{c_0} |c_\varepsilon - c_0| \int_z^\infty |V_\varepsilon'| |\mathbf{V}(z_0)| dy \\ &\leq \frac{2}{c_0} |\mathbf{V}(z_0)| \left[ \varepsilon \int_z^\infty |V_0''| dy + |c_\varepsilon - c_0| \int_z^\infty |V_\varepsilon'| dy \right] \end{aligned} \tag{5.8}$$

which gives that

$$|\mathbf{V}| \leq \frac{2}{c_0} \left( \varepsilon \|V_0''\|_{L^1(\mathbb{R})} + |c_\varepsilon - c_0| \cdot \|V_\varepsilon'\|_{L^1(\mathbb{R})} \right). \tag{5.9}$$

Since  $V_\varepsilon' > 0$  by Theorem 3.3,  $\|V_\varepsilon'\|_{L^1(\mathbb{R})} = v_+ < \infty$ . With (3.2), by simple calculation, we can show that  $V_0'' \sim \left( e^{\frac{\chi kz}{d+\chi}} + e^{-\frac{dkz}{d+\chi}} \right)^{-(d/\chi+1)}$ . That is,  $V_0''$  exponentially decays with respect to  $z$  as  $|z| \rightarrow \infty$ . Hence  $\|V_0''\|_{L^1(\mathbb{R})} < \infty$ . In virtue of Theorem 4.1(iii), we have from (5.9) that

$$|\mathbf{V}| = |V_\varepsilon - V_0| = \mathcal{O}(\varepsilon). \tag{5.10}$$

Finally by (2.8) and mean value theorem, we deduce that

$$\begin{aligned} U_\varepsilon - U_0 &= e^{-\frac{c_\varepsilon}{d}z} V_\varepsilon^{\frac{\chi}{d}} - e^{-\frac{c_0}{d}z} V_0^{\frac{\chi}{d}} \\ &= e^{-\frac{c_\varepsilon}{d}z} (V_\varepsilon^{\frac{\chi}{d}} - V_0^{\frac{\chi}{d}}) + V_0^{\frac{\chi}{d}} (e^{-\frac{c_\varepsilon}{d}z} - e^{-\frac{c_0}{d}z}) \\ &= \frac{\chi}{d} e^{-\frac{c_\varepsilon}{d}z} \zeta_1^{\frac{\chi}{d}-1} (V_\varepsilon - V_0) - \frac{z}{d} e^{-\frac{z}{d}\zeta_2} (c_\varepsilon - c_0) \end{aligned}$$

where  $\zeta_1$  is between  $V_0$  and  $V_\varepsilon$  and  $c_\varepsilon < \zeta_2 < c_0$ .

Then the combination of Theorem 4.1(iii) and (5.10) concludes the proof.  $\square$

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