

A FREE BOUNDARY PROBLEM ARISING IN A MODEL OF WOUND HEALING

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Abstract. In this paper we consider a system of two semilinear parabolic reaction-diffusion equations with free boundary, which arises in a model of corneal epithelial wound healing. We prove that the initial-boundary value problem has a unique solution and that complete healing is achieved in finite time. We then proceed to consider travelling wave solutions of the same system, and establish the existence of such a solution.

Key words. free boundary, reaction-diffusion equations, travelling wave solutions, wound healing.

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0. Introduction.

The mathematical modeling of wound healing has received increased attention in recent years. One area of investigation is dermal wound healing, where complex biological processes are interacting [4, 7]. Two of these processes are the invasion of fibroblasts into the wound space and their alignment there [5], and the sprouting of blood vessel into the wound space (angiogenesis) [6]. Another area of investigation is corneal epithelial wound healing, which was modelled by Dale, Maini and Sheratt [1]. The model involves a system of two parabolic partial differential equations (semilinear reaction-diffusion equations) for the generic corneal stimulus concentration n , in the healed region, and the chemical stimulus concentration c (also called the epidermal growth factor), both in the healed and the wound regions. Their model is 1-dimensional and exhibits, after a short time, a travelling wave character. They computed the speed of the travelling wave to be approximately $20 \mu\text{mh}^{-1}$; the actual observed healing rate in corneal wounds is approximately $60 \mu\text{mh}^{-1}$.

This model was recently improved by Gaffney, Maini, McCaig, Zhao and Forrester [2] in two ways. First they include the presence of physiological electric field and, second, they introduce a free boundary into the model. The free boundary is the receding boundary of the wound region. Their computations show that the average speed of the free boundary varies linearly with the electric field over a large range, and that this linear relation is robust under variations of some parameters which are difficult to estimate precisely.

The purpose of this paper is to study the model introduced in [2] by rigorous mathematical analysis. In Part I we consider the semilinear reaction-diffusion system with free boundary and prove that the initial-boundary value problem has a unique solution for a time interval $0 \leq t < T_*$, where T_* , a finite number, is the time at which the wound becomes completely healed. In Part II we consider the travelling wave version of the model and prove that a travelling wave solution exists.

In order to make the paper more readable, we shall deal with a general system of reaction-diffusion equations, subject to some assumptions. In the concluding section of the paper we shall write down the explicit system developed in [2], and show how it satisfies the general assumptions made throughout Parts I and II.

Part I. The evolution problem

1. The model.

Consider the following system for $n(x, t)$, $c(x, t)$, $s(t)$:

$$\begin{aligned}
 (1.1) \quad & n_t = (d(n, c) n_x)_x + f(n, c), \quad 0 < x < s(t), \quad t > 0, \\
 (1.2) \quad & ac_t = c_{xx} + g(n, c), \quad 0 < x < 1, \quad t > 0, \quad (a \text{ a positive constant}) \\
 (1.3) \quad & n \equiv 0 \quad \text{if } s(t) < x < 1, \quad t > 0, \\
 (1.4) \quad & n(s(t), t) = n_*, \quad t > 0, \quad (n_* \text{ constant}) \\
 (1.5) \quad & \dot{s}(t) = -\frac{1}{n_*} d(n_*, c) n_x \quad \text{at } x = s(t), \quad t > 0,
 \end{aligned}$$

with boundary conditions

$$(1.6) \quad n_x(0, t) = 0 \quad c_x(0, t) = 0 \quad c_x(1, t) = 0 \quad \text{for } t > 0,$$

and initial conditions

$$\begin{aligned}
 (1.7) \quad & s(0) = s_0, \quad 0 < s_0 < 1, \\
 & n(x, 0) = n_0(x), \quad 0 < x < s_0, \\
 & c(x, t) = c_0(x), \quad 0 < x < 1.
 \end{aligned}$$

Here n represents the corneal stimulus cell density outside the wound, and c represents the chemical stimulus concentration in both the wounded and healed parts.

We assume that

$$(1.8) \quad 0 < n_* < 1,$$

and set

$$G = \{(n, c); \quad n_* \leq n \leq 2, \quad 0 \leq c \leq 1\}.$$

We also make the following assumptions:

$$\begin{aligned}
 (1.9) \quad & d(n, c) \text{ is in } C^1(G) \quad \text{and} \quad \partial d / \partial n \leq 0, \\
 & d(n, c) \geq d_0 > 0 \quad (d_0 \text{ constant});
 \end{aligned}$$

$$\begin{aligned}
 (1.10) \quad & f(n, c) \text{ is in } C^1(G) \text{ and} \\
 & f(n_*, c) > 0, \quad f(2, c) \leq 0 \quad \text{if } 0 \leq c \leq 1;
 \end{aligned}$$

$$\begin{aligned}
 (1.11) \quad & g(n, c) \text{ is in } C^1(G) \quad \text{and} \quad \partial g / \partial c < 0 \text{ in } G, \\
 & g(n, 0) \geq 0, \quad g(n, 1) \leq 0 \quad \text{for } n_* \leq n \leq 2;
 \end{aligned}$$

$$\begin{aligned}
 (1.12) \quad & n_0 \in C^2[0, s_0], \quad n_* < n_0(x) < 2 \quad \text{if } 0 \leq x < s_0, \\
 & n'_0(0) = 0, \quad n_0(s_0) = n_*, \quad n'_0(s_0) < 0;
 \end{aligned}$$

$$(1.13) \quad c_0 \in C^2[0, 1] \quad \text{and} \quad 0 \leq c_0(x) \leq 1.$$

We may clearly extend the definitions of the functions d, f, g in such a way that

$$\begin{aligned}
 (1.14) \quad & (1.9), (1.10), (1.11) \text{ hold for } -\infty < n, \quad c < \infty, \text{ and} \\
 & f(n, c) > 0 \quad \text{if } n \leq n_*, \quad f(n, c) \leq 0 \quad \text{if } n \geq 2, \quad \text{for all } c, \\
 & g(n, c) \geq 0 \quad \text{if } c \leq 0, \quad g(n, c) \leq 0 \quad \text{if } c \geq 1, \quad \text{for all } n.
 \end{aligned}$$

In the future we shall assume such an extension has already been made.

In Sections 2, 3 we shall prove the following theorem:

THEOREM 1.1. *Assume that (1.8)–(1.13) hold. Then there exists a unique solution (n, c, s) of (1.1)–(1.7) for $0 \leq t < T_*$, where $T_* < \infty$, and*

$$(1.15) \quad s'(t) > 0 \quad \text{if } 0 \leq t < T_* ,$$

$$(1.16) \quad s(t) \rightarrow 1 \quad \text{if } t \rightarrow T_* ;$$

furthermore,

$$(1.17) \quad n_* < n(x, t) \leq 2 \quad \text{if } 0 \leq x < s(t) , \quad 0 \leq t < T_* ,$$

$$(1.18) \quad 0 \leq c(x, t) \leq 1 \quad \text{if } 0 \leq x \leq 1 , \quad 0 \leq t < T_* .$$

Note that (1.16) means that the wound region $\{s(t) \leq x \leq 1\}$ disappears as $t \rightarrow T_*$.

In §2 we shall prove local existence and uniqueness. In §3 we shall derive a priori estimates which will enable us to complete the proof of Theorem 1.1.

2. Local existence and uniqueness. In this section we prove:

LEMMA 2.1. Under the assumptions of Theorem 1.1 there exists a unique solution of (1.1)–(1.7) for a small time interval $0 \leq t \leq T$ ($T > 0$).

Proof. Set

$$\delta = \min\{s_0, 1 - s_0\}$$

and let $\zeta(y)$ be a function in $C^3[0, 1]$ satisfying:

$$\zeta(y) = 1 \quad \text{if } |y - s_0| < \frac{\delta}{4} , \quad \zeta(y) = 0 \quad \text{if } |y - s_0| > \delta , \quad |\zeta'(y)| < \frac{2}{\delta} .$$

We introduce a transformation that will straighten the free boundary:

$$(2.1) \quad (x, t) \rightarrow (y, t) \quad \text{where} \quad x = y + \zeta(y)(s(t) - s_0) , \quad 0 \leq y \leq 1 .$$

Notice that as long as

$$(2.2) \quad |s(t) - s_0| < \frac{\delta}{4}$$

the transformation (2.1) is diffeomorphism from $[0, 1]$ onto $[0, 1]$ (since $\partial x / \partial y > \frac{1}{2}$), and

$$0 \leq x \leq s(t) \iff 0 \leq y \leq s_0 ,$$

$$s(t) \leq x \leq 1 \iff s_0 \leq y \leq 1 ,$$

$$x = s(t) \iff y = s_0 .$$

One easily computes that

$$\begin{aligned} \frac{\partial y}{\partial x} &= \frac{1}{1 + \zeta'(y)(s(t) - s_0)} \equiv \sqrt{A(s(t), y)} , \\ \frac{\partial^2 y}{\partial x^2} &= \frac{\zeta''(y)(s(t) - s_0)}{[1 + \zeta'(y)(s(t) - s_0)]^3} \equiv B(s(t), y) , \\ -\frac{1}{\dot{s}(t)} \frac{\partial y}{\partial t} &= \frac{\zeta(y)}{1 + \zeta'(y)(s(t) - s_0)} \equiv C(s(t), y) . \end{aligned}$$

Defining

$$\varphi(y, t) = n(x, t) , \quad \psi(y, t) = c(x, t)$$

and setting

$$D(\varphi, \psi) = d(n, c) , \quad F(\varphi, \psi) = f(n, c) , \quad G(\varphi, \psi) = g(n, c) ,$$

the system (1.1)–(1.7) takes the form

$$(2.3) \quad \varphi_t = AD(\varphi, \psi)\varphi_{yy} + (BD(\varphi, \psi) + \dot{s}C)\varphi_y + AD_\varphi\varphi_y^2 + AD_\psi\varphi_y\psi_y \quad \text{for } 0 < y < s_0 , \quad t > 0 ,$$

$$(2.4) \quad a\psi_t = A\psi_{yy} + (B + a\dot{s}C)\psi_y + G(\varphi, \psi) \quad \text{for } 0 < y < 1 , \quad t > 0 ,$$

$$(2.5) \quad \varphi \equiv 0 \quad \text{if } s_0 < y < 1 ,$$

with $A = A(s, y)$, $B = B(s, y)$, $C = C(s, y)$,

$$(2.6) \quad \varphi(s_0, t) = n_* ,$$

$$(2.7) \quad \dot{s}(t) = -\frac{1}{n_*} D(n_*, \psi(s_0, t)) \varphi_y(s_0, t) ,$$

and

$$(2.8) \quad \varphi_y(0, t) = \psi_y(0, t) = \psi_y(1, t) = 0 ,$$

$$(2.9) \quad \begin{cases} \varphi(y, 0) = \varphi_0(y) , & 0 \leq y < s_0 , \\ \psi(y, 0) = \psi_0(y) , & 0 \leq y \leq 1 , \end{cases}$$

where $\varphi_0(y) = n_0(x)$, $\psi_0(y) = c_0(x)$.

We introduce the quantity

$$(2.10) \quad s_1 = -\frac{1}{n_*} D(n_*, \psi_0(s_0)) \varphi_0'(s_0) \quad (s_1 > 0)$$

which should be the derivative $\dot{s}(0)$ if a solution exists.

We shall prove existence by invoking the Schauder fixed point theorem. Toward this purpose we introduce spaces

$$X_T = \{s \in C^1[0, T] , \quad s(0) = 0 , \quad \dot{s}(0) = s_1 , \quad |\dot{s}(t) - s_1| \leq 1 \quad \text{for } 0 \leq t \leq T\} ,$$

$$Y_T = \{\varphi \in C^0([0, s_0] \times [0, T]) , \quad \varphi(y, 0) = \varphi_0 , \quad |\varphi - \varphi_0|_{C^0([0, s_0] \times [0, T])} \leq 1\}$$

where T is such that

$$0 < T < \frac{\delta}{4(1 + s_1)} .$$

For any $(\tilde{s}, \tilde{\varphi}) \in X_T \times Y_T$ we then have

$$|\tilde{s}(t) - s_0| < \frac{\delta}{4} ,$$

so that the mapping $(x, y) \rightarrow (y, t)$ defined by

$$x = y + \zeta(y)(\tilde{s}(t) - s_0)$$

is a diffeomorphism, and we define ψ to be the solution of

$$a\psi_t = A(\tilde{s}, y)\psi_{yy} + (B(\tilde{s}, y) + a\dot{\tilde{s}}C(\tilde{s}, y))\psi_y + G(\tilde{\varphi}, \psi) \quad \text{for } 0 < y < 1, 0 < t < T$$

with $\tilde{\varphi} \equiv 0$ in $[s_0, 1] \times [0, T]$,

$$\begin{aligned} \psi_x(0, t) = \psi_x(1, t) = 0, \quad 0 < t < T, \\ \psi(y, 0) = \psi_0(y). \end{aligned}$$

Using L^p estimates for parabolic equations and Sobolev's inequalities, one can show that this system has a unique solution ψ with finite norm

$$(2.11) \quad \|\psi\|_{C^{1+\beta, (1+\beta)/2}([0,1] \times [0,T])} \leq K$$

for any $0 < \beta < 1$, where K will be used to denote constants depending only on s_0, s_1 , and on

$$|\varphi_0|_{C^2[0, s_0]}, \quad |\varphi_0|_{C^2[0,1]}.$$

In fact, results of this type, for more general nonlinear parabolic equations, are proved in [3].

Next we define a function φ as the solution of the parabolic problem:

$$\begin{aligned} \varphi_t = A(\tilde{s}, y)D(\tilde{\varphi}, \psi)\varphi_{yy} + [B(\tilde{s}, y)D(\tilde{\varphi}, \psi) + \dot{\tilde{s}}C(\tilde{s}, y)]\varphi_y + A(\tilde{s}, y)D_\varphi(\tilde{\varphi}, \psi)\varphi_y^2 \\ + A(\tilde{s}, y)D_\psi(\tilde{\varphi}, \psi)\varphi_y\psi_y + f(\varphi, \psi) \quad \text{for } 0 \leq y \leq s_0, 0 \leq t \leq T, \\ \varphi_y(0, t) = 0, \quad \varphi(s_0, t) = n_* \quad \text{for } 0 < t < T, \\ \varphi(y, 0) = \varphi_0(y) \quad \text{for } 0 < y < s_0. \end{aligned}$$

As before, this system has a unique solution φ with finite norm

$$(2.12) \quad \|\varphi\|_{C^{1+\beta, (1+\beta)/2}([0, s_0] \times [0, T])} \leq K.$$

Finally we define

$$(2.13) \quad s(t) = s_0 - \int_0^t \frac{1}{n_*} D(n_*, \psi(s_0, \tau))\varphi_y(s_0, \tau) d\tau$$

and introduce the mapping W by

$$(s, \varphi) = W(\tilde{s}, \tilde{\varphi}).$$

We want to show that W has a fixed point (s, φ) , which will then imply that, together with the corresponding ψ , it forms a solution to the system (2.3)–(2.9).

Observe that

$$\dot{s}(t) - s_1 = \frac{1}{n_*} \left\{ D(n_*, \psi_0(s_0)) \frac{\partial \varphi_0(s_0)}{\partial y} - D(n_*, \psi(s_0, t))\varphi_y(s_0, t) \right\}$$

and the right-hand side is in $C^{\beta/2}[0, T]$. Hence

$$(2.14) \quad \|\dot{s} - s_1\|_{C^{\beta/2}[0, T]} \leq K.$$

By (2.12) we also have

$$\|\varphi - \varphi_0\|_{C^{1+\beta, (1+\beta)/2}([0, s_0] \times [0, T])} \leq K.$$

Hence, if T is small enough,

$$\begin{aligned} \|\dot{s} - s_1\|_{C^0[0,T]} &\leq \|\dot{s} - s_1\|_{C^{\beta/2}[0,T]} T^{\beta/2} \leq 1, \\ \|\varphi - \varphi_0\|_{C^0[0,s_0]} &\leq \|\varphi - \varphi_0\|_{C^{0,(1+\beta)/2}([0,s_0] \times [0,T])} T^{\frac{1+\beta}{2}} \leq 1, \end{aligned}$$

so that W maps $X_T \times Y_T$ into itself.

From the estimates above it follows that the image of W lies in a compact subset of $X_T \times Y_T$, and a standard argument then also shows that W is continuous. Invoking the Schauder fixed point theorem we conclude that W has a fixed point in $X_T \times Y_T$.

We can further use the Schauder estimates to obtain additional regularity of the solution, such as the Hölder continuity of $\dot{s}(t)$, and of the second spatial derivatives of φ and ψ . It remains to prove uniqueness.

Let (s_i, φ_i, ψ_i) ($i = 1, 2$) be two solutions. Then

$$\|s_i\|_{C^{1+\beta/2}[0,T]} + \|\varphi_i\|_{C^{1+\beta,(1+\beta)/2}([0,s_0] \times [0,T])} + \|\psi_i\|_{C^{1+\beta,(1+\beta)/2}([0,1] \times [0,T])} \leq K.$$

Setting $\psi = \psi_1 - \psi_2$ and taking the difference of the equations for ψ_1, ψ_2 , we get

$$\begin{aligned} a\psi_t &= A(s_2, y)\psi_{yy} + [B(s_2, y) + a\dot{s}_2 C(s_2, y)]\psi_y + G_1\varphi + G_2\psi \\ &\quad + [A(s_1, y) - A(s_2, y)]\psi_{1,yy} + [B(s_1, y) - B(s_2, y)]\psi_{1,y} + a[\dot{s}_1 C(s_1, y) - \dot{s}_2 C(s_2, y)]\psi_{1,y} \end{aligned}$$

where G_1, G_2 are the partial derivatives of G with respect to the first and second variables evaluated at an intermediate point.

Using $W^{2,p}$ estimates for parabolic equations of the form $u_t - au_{yy} - bu_y + cu = g$ and Sobolev's imbedding, we get

$$(2.15) \quad \|\psi_1 - \psi_2\|_{C^{1+\beta,(1+\beta)/2}} \leq K\{\|\varphi_1 - \varphi_2\|_{C^0} + \|s_1 - s_2\|_{C^1}\}.$$

Similarly we derive the inequality

$$(2.16) \quad \|\varphi_1 - \varphi_2\|_{C^{1+\beta,(1+\beta)/2}} \leq K\{\|\psi_1 - \psi_2\|_{C^{1,0}} + \|s_1 - s_2\|_{C^1}\}.$$

Furthermore, taking the difference of the equations for s_1, s_2 in (2.7), we get

$$(2.17) \quad \|s_1 - s_2\|_{C^{1+\beta/2}} \leq K\|\psi_1 - \psi_2\|_{C^{0,\beta/2}} + \|\varphi_{1,y} - \varphi_{2,y}\|_{C^{0,\beta/2}}.$$

It then follows, upon using (2.16), (2.15), that

$$\begin{aligned} \|s_1 - s_2\|_{C^{1+\beta/2}} + \|\varphi_1 - \varphi_2\|_{C^{1+\beta,(1+\beta)/2}} + \|\psi_1 - \psi_2\|_{C^{1+\beta,(1+\beta)/2}} \\ \leq K\{\|\varphi_1 - \varphi_2\|_{C^0} + \|s_1 - s_2\|_{C^1}\} \leq KT^{\beta/2}\{\|\varphi_1 - \varphi_2\|_{C^{1+\beta,(1+\beta)/2}} + \|s_1 - s_2\|_{C^{1+\beta/2}}\}. \end{aligned}$$

Taking T such that also $KT^{\beta/2} < 1$, we conclude that $s_1 \equiv s_2$, $\varphi_1 \equiv \varphi_2$, $\psi_1 \equiv \psi_2$. \square

3. Completion of the proof of Theorem 1.1.

We first derive a priori estimates for any solution of (1.1)–(1.7), assuming that it exists in some interval $0 < t < T$; these bounds will be independent of T .

LEMMA 3.1. The solution satisfies:

$$(3.1) \quad n_* < n(x, t) < 2 \quad \text{if } 0 \leq x < s(t), \quad 0 \leq t \leq T,$$

$$(3.2) \quad 0 \leq c(x, t) \leq 1 \quad \text{if } 0 \leq x \leq 1, \quad 0 \leq t \leq T$$

and

$$(3.3) \quad n_x(s(t), t) < 0 \quad \text{if } 0 \leq t \leq T.$$

Proof. By (1.14)

$$n_t - (dn_x)_x \geq 0 \quad \text{if } n \leq n_* .$$

Hence the maximum principle yields the inequality $n > n_*$ if $0 < x < s(t)$, $0 < t < T$. Similarly we have from (1.14) that

$$n_t - (dn_x)_x \leq 0 \quad \text{if } n \geq 2$$

so that, by the maximum principle, $n < 2$ if $0 \leq x \leq s(t)$, $0 \leq t \leq T$. The proof of (3.2) is similar. Finally, noting that, since $f(n_*, c) > 0$,

$$n_t - (dn_x)_x = f(n, c) > 0$$

near the free boundary, the (strict) inequality (3.3) follows by the maximum principle. \square

From (3.3) and (1.5) we deduce that

$$(3.4) \quad \dot{s}(t) > 0 \quad \text{for } 0 \leq t \leq T ,$$

so that $s(t)$ is strictly monotone increasing.

Also, a standard parabolic estimate shows that c_x is bounded independent of T .

LEMMA 3.2. There exists a constant M independent of T such that

$$(3.5) \quad \dot{s}(t) \leq M \quad \text{for } 0 < t < T .$$

Proof. Let

$$Q = \{(x, t) ; \quad 0 < x < s(t) , \quad 0 < t < T\}$$

and introduce the operator

$$\mathcal{L}u = u_t - d(u, c)u_{xx} - d_u(u, c)u_x^2 - d_c(u, c)u_x c_x - f(u, c)$$

where c is the component of the solution (s, n, c) of (1.1)–(1.7). We shall construct a supersolution in the form

$$\bar{n}(x, t) = \begin{cases} 2 , & 0 < x < s(t) - \frac{1}{M} \\ n_* + (2 - n_*)\{2M(s(t) - x) - M^2(s(t) - x)^2\} , & s(t) - \frac{1}{M} < x < s(t) . \end{cases}$$

Notice that $\bar{n} \in W_\infty^{2,1}(Q)$ and

$$\bar{n}_x \leq 0 , \quad \bar{n}(s(t), t) = n_* .$$

In the interval $[0, s(t) - \frac{1}{M})$

$$\mathcal{L}\bar{n} = -f(2, c) \geq 0 .$$

In the interval $(s(t) - \frac{1}{M}, s(t))$

$$\begin{aligned}\bar{n}_t &= (2 - n_*)2M\dot{s}\{1 - M(s - x)\} \geq 0 \quad \text{since } \dot{s}(t) > 0, \\ -d(\bar{n}, c)\bar{n}_{xx} &= (2 - n_*)2M^2d(\bar{n}, c) \geq c_0M^2\end{aligned}$$

where $c_0 = (2 - n_*)2d_0 > 0$ (see (1.9)),

$$\begin{aligned}-d_n(\bar{n}, c)\bar{n}_x^2 &\geq 0 \quad (\text{by (1.9)}) , \\ | -d_c(\bar{n}, c)c_x\bar{n}_x | &\leq c_1M ,\end{aligned}$$

and

$$|f(\bar{n}, c)| \leq c_2$$

where c_1, c_2 are constants independent of M and T . It follows that

$$\mathcal{L}\bar{n} \geq c_0M^2 - c_1M - c_2 > 0$$

if M is large enough. Furthermore,

$$\bar{n}_x = 0 = n_x \quad \text{at } x = 0, \quad \bar{n} = n_* = n \quad \text{at } x = s(t)$$

and $\bar{n}(x, 0) \geq n_0(x)$ for large M . Hence, by comparison, $n(x, t) \leq \bar{n}(x, t)$ in Q and, consequently,

$$n_x(s(t), t) \geq \bar{n}_x(s(t), t) = -2M(2 - n_*) .$$

The assertion (3.5) (with another M) now follows by recalling (1.5).

From (3.5) and (3.4) we get

$$(3.6) \quad |\dot{s}(t)| \leq M .$$

□

LEMMA 3.3. *The solution to (1.1)–(1.7) exists and is unique, and it can be extended up to a time T^* satisfying $\lim_{t \nearrow T^*} s(t) = 1$.*

Proof. The assertion means that if the solution exists for $0 < t < T_0$, and if $s(T_0) < 1$, then the solution can be continued, uniquely, to a larger interval $0 < t < T_0 + \tau$ ($\tau > 0$). To prove this we observe that in the proof of Lemma 2.1 the size T of the time interval depends on a lower bound on $\min\{s, 1 - s\}$ at the initial time, and on the L^∞ bound of the first two derivatives of the initial data. From (3.6) and L^p estimates applied to the system with “straightened” free boundary, (2.3)–(2.9), we deduce a priori bounds on the first two derivatives of $n(x, t)$, $c(x, t)$ at $t = T_0$ (in fact, even $C^{2+\alpha}$ bounds, if we use a bootstrap argument and Schauder’s estimate). Since, further, $0 < 1 - s(T_0) < 1$, we can extend the solution, and uniquely so, to a larger interval $0 < t < T_0 + \tau$, as claimed. □

We next improve the inequality (3.4):

LEMMA 3.4. There exists a positive constant γ independent of T such that

$$(3.7) \quad \dot{s}(t) \geq \gamma \quad \text{for } 0 \leq t < T .$$

Proof. We shall construct a subsolution in the form

$$\underline{n}(x, t) = n_* + \begin{cases} \frac{\gamma}{2} s_0^2, & 0 < x < s(t) - s_0 \\ \gamma \left[s_0(s(t) - x) - \frac{1}{2}(x - s(t))^2 \right], & s(t) - s_0 < x < s(t). \end{cases}$$

Notice that $\underline{n} \in W_\infty^{2,1}(G)$.

In the interval $(0, s(t) - s_0)$

$$\mathcal{L}\underline{n} = -f(n_* + \frac{\gamma}{2} s_0^2, c) < 0$$

by (1.10), if γ is sufficiently small. In the interval $(s(t) - s_0, s(t))$,

$$\begin{aligned} \underline{n}_t &= \gamma[s_0 - (s(t) - x)]\dot{s}(t) \leq \gamma M && \text{by (3.6),} \\ f(\underline{n}, c) &\geq f(n_*, c) - C_1\gamma \end{aligned}$$

and all the other terms in $\mathcal{L}\underline{n}$ are bounded by $C_2\gamma$, where C_1, C_2 are positive constants independent of γ and T . Since, by (1.10), $f(n_*, c) \geq \mu > 0$ for all c , we conclude that

$$\mathcal{L}\underline{n} \leq -\mu + \gamma(M + C_1 + C_2) < 0$$

if γ is sufficiently small. We also have

$$\underline{n}_x = 0 = n_* \quad \text{at } x = 0, \quad \underline{n} = n_* = n \quad \text{at } x = s(t)$$

and $\underline{n}(x, 0) < n_0(x)$ if $0 \leq x < s_0$ provided γ is small enough; here we used the assumption $n'_0(s_0) < 0$.

By comparison we then have $\underline{n} \leq n$ in G and

$$n_x(s(t), t) \leq \underline{n}_x(s(t), t) = -\gamma s_0,$$

so that (3.7) holds (with another γ).

Combining Lemma 3.3 with 3.4 we see that there exists a finite number T_* such that the solution exists for all $0 < t < T_*$, and $s(T_*) = 1$. This completes the proof of Theorem 1.1. \square

Part II. Travelling wave solutions

4. Setting up the problem.

We seek a solution to (1.1)–(1.5) in the form of a travelling wave with constant speed c ($c > 0$):

$$n(x, t) = u(z), \quad c(x, t) = v(z) \quad z = ct - x \in \mathbb{R}^1.$$

The free boundary is given by $x = ct$, i.e., $z = 0$. Then

$$(4.1) \quad (d(u, v)u')' - cu' + f(u, v) = 0, \quad z > 0,$$

$$(4.2) \quad v'' - acv' + g(u, v) = 0, \quad -\infty < z < \infty,$$

$$(4.3) \quad u(z) \equiv 0, \quad z < 0.$$

Motivated by numerical results from [2], we wish to consider only solutions such that

$$(4.4) \quad u'(z) > 0, \quad z > 0.$$

We impose the boundary conditions

$$(4.5) \quad u(0) = u_* \quad (u_* = n_*) ,$$

$$(4.6) \quad d(u(0), v(0)) u'(0) = cu_* ,$$

$$(4.7) \quad u(\infty) = 1 ,$$

and

$$(4.8) \quad v(-\infty) = 1 ,$$

$$(4.9) \quad v(+\infty) = 0 .$$

As a first step we shall simplify the problem by reducing it to a system in the interval $\{z > 0\}$ only.

Set

$$(4.10) \quad g_0(v) = g(0, v) , \quad \beta = ac$$

so that

$$(4.11) \quad v'' - \beta v' + g_0(v) = 0 \quad \text{for} \quad -\infty < z < 0 .$$

LEMMA 4.1. *Assume that $g_0(v)$ satisfies:*

$$g_0(1) = 0 , \quad \frac{d}{dv} g_0(v) < 0 \quad \text{for all} \quad v \in \mathbb{R}^1 .$$

Then there exists a smooth function $\Psi(\beta, v)$ such that, for every $\beta \in (0, \infty)$, the problem

$$(4.12) \quad v'' - \beta v' + g_0(v) = 0 \quad \text{in} \quad (-\infty, 0) , \quad v(0) = v_0 , \quad v'(0) = v_1$$

has a bounded solution if and only if

$$(4.13) \quad v_1 = \Psi(\beta, v_0) ;$$

furthermore, the bounded solution satisfies: $\lim_{z \rightarrow -\infty} v(z) = 1$. The function $\Psi(\beta, v)$ has the following properties:

$$(4.14) \quad \frac{d\Psi}{dv} = \beta - \frac{g_0(v)}{\Psi} \quad \text{in} \quad \mathbb{R}^1 \setminus \{1\} ,$$

$$\Psi(\beta, 1) = 0 ,$$

and

$$(4.15) \quad \Psi_v > 0 \quad \text{in} \quad \mathbb{R}^1 .$$

Proof. We write (4.11) as an autonomous system

$$v' = p , \quad p' = \beta p - g_0(v) .$$

In the $v - p$ phase plane there is only one stationary point, namely, $(1, 0)$. It is a saddle point since the characteristic equation

$$\lambda^2 - \beta\lambda + g_0'(1) = 0$$

has two real roots, one positive and one negative. Hence there are only two trajectories leaving $(1, 0)$, which we shall denote by γ^+ and γ^- . The velocity field of the autonomous system is

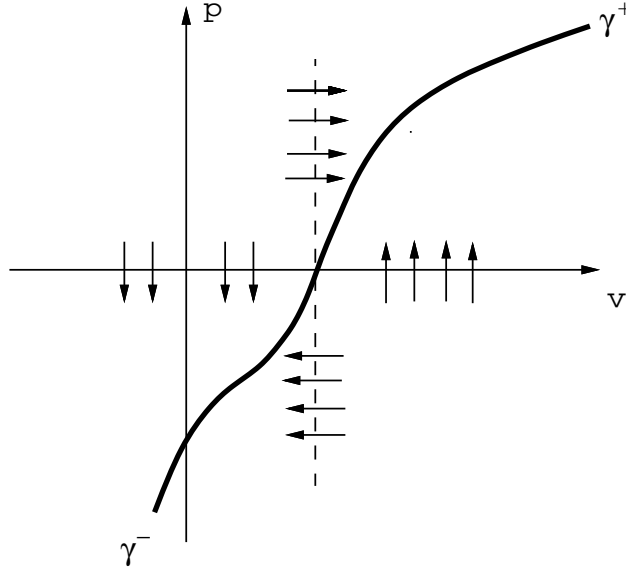


FIG. 1.

shown in Figure 1. Note that every trajectory can intersect the v -axis at most once. Hence $p = v'$ can change sign at most once and, consequently, $v(-\infty)$ exists. Since there is only one stationary point, we conclude that either $|v(-\infty)| = \infty$ or $v(-\infty) = 0$. Hence a solution is bounded if and only if (v_0, v_1) lies on the curve $\gamma^+ \cup \{(1, 0)\} \cup \gamma^- \equiv \Gamma$.

Along γ^+ , $p > 0$ and $v > 1$ so that $p' = \beta p - g_0(v) > 0$, whereas along γ^- , $p < 0$ and $v < 1$ so that $p' < 0$. It follows that Γ can be written as a curve $p = \Psi(\beta, v)$ and, then, a solution is bounded if and only if $v_1 = \Psi(\beta, v_0)$. It is clear that $\Psi(\beta, 1) = 0$, and the equation in (4.14) follows from

$$\frac{dp}{dv} = \beta - \frac{g_0}{p}.$$

From the last equation we get

$$(4.16) \quad \frac{d}{dv} \left(p \frac{dp}{dv} \right) = \beta \frac{dp}{dv} - \frac{dg_0}{dv} > \beta \frac{dp}{dv}.$$

To prove (4.15) notice that the inequality holds in a neighborhood of the origin. If the inequality does not hold for all $v \neq 0$ then there is a smallest positive v^* (or a largest negative value v^{**}) at which $\Psi_v(\beta, v)$ vanishes. It follows that $\Psi_{vv} \leq 0$ at v^* (or $\Psi_{vv} \geq 0$ at v^{**}). But we also have $p = p(v^*) > 0$ ($p = p(v^{**}) < 0$); cf. Figure 1. Therefore the left-hand side of (4.16) (with $p = \Psi(\beta, v)$) is negative, whereas the right-hand side vanishes at v^* (or v^{**}), which is a contradiction. \square

REMARK 4.1. In the special case $g_0(v) = k(1 - v)$ for some $k > 0$,

$$v = 1 - C e^{\lambda z}$$

where

$$\lambda = \frac{1}{2} (\beta + \sqrt{\beta^2 + 4k}),$$

and $\Psi(\beta, v) = \lambda(v - 1)$.

Lemma 4.1 allows us to reformulate problem (4.1)–(4.9) as follows:

Problem (P_0). Find (c, u, v) with $c > 0$ such that

$$(4.17) \quad (d(u, v)u')' - cu' + f(u, v) = 0, \quad z > 0,$$

$$(4.18) \quad v'' - acv' + g(u, v) = 0, \quad z > 0,$$

$$(4.19) \quad u(0) = u_*, \quad d(u_*, v(0))u'(0) = cu_*, \quad u(\infty) = 1,$$

$$(4.20) \quad -v'(0) + \Psi(ac, v(0)) = 0, \quad v(\infty) = 0,$$

$$(4.21) \quad u'(z) > 0, \quad z > 0.$$

From (4.21) and (4.19) we see that as z varies from 0 to ∞ , $u = u(z)$ varies from u_* to 1. We can therefore try to use u as an independent variable, i.e., set $z = z(u)$ as the inverse function of $u = u(z)$; u will vary in the interval

$$\Omega = \{u_* < u < 1\}.$$

We introduce new dependent functions by

$$(4.22) \quad Q(u) = d(u, v)u'(z)|_{z=z(u)}, \quad V(u) = v(z)|_{z=z(u)}.$$

Using the rule

$$\frac{d}{dz} = u' \frac{d}{du} = \frac{Q(u)}{d(u, v)} \frac{d}{du}$$

we can transform problem (P_0) into the following problem:

Problem (P_1). Find (c, Q, V) with $c > 0$ such that

$$(4.23) \quad QQ_u - cQ + d(u, V)f(u, V) = 0 \quad \text{in } \Omega,$$

$$(4.24) \quad \frac{Q}{d(u, V)} \left(\frac{Q}{d(u, V)} V_u \right)_u - ac \frac{Q}{d(u, V)} V_u + g(u, V) = 0 \quad \text{in } \Omega,$$

$$(4.25) \quad Q(u_*) = cu_*, \quad Q(1) = 0,$$

$$(4.26) \quad -\frac{Q(u_*)}{d(u_*, V(u_*))} V_u + \Psi(ac, V(u_*)) = 0, \quad V(1) = 0,$$

$$(4.27) \quad Q > 0 \quad \text{in } \Omega,$$

$$(4.28) \quad \int_{u_*}^1 \frac{d(s, V(s))}{Q(s)} ds = \infty.$$

Indeed we have:

LEMMA 4.2. *Problems (P_0) and (P_1) are equivalent.*

Proof. Given a solution to problem (P_0), define $z = z(u)$ as the inverse of $u = u(z)$ and define Q, V by (4.22). Then (4.23), (4.24), (4.26), (4.27) and the first boundary condition in (4.25) hold, and it remains to prove that $Q(1) = 0$. Since

$$(4.29) \quad z = \int_{u_*}^u \frac{d(s, V(s))}{Q(s)} ds$$

and $u(\infty) = 1$, we also have (4.28). Finally, note that the existence of $u(\infty)$ and $v(\infty)$ implies by standard ODE theory that u'', v'' are bounded, and then, by a simple argument in real analysis, $u'(\infty), v'(\infty)$ must exist and equal to zero. Taking $u \rightarrow 1$ in the first relation of (4.22) we then deduce that $Q(1) = 0$.

Conversely consider a solution to problem (P_1) and define $u = u(z)$ by

$$(4.30) \quad u'(z) = \frac{Q(u)}{d(u, V(u))}, \quad u(0) = u_*$$

and $v(z) = V(u(z))$. Then (4.29) holds, and one can easily show that all the equations in problem (P_0) are satisfied. \square

5. Statement of the main result.

In the sequel we shall work primarily (but not exclusively) with problem (P_1) . We shall need some assumptions that include all those made in (1.9)–(1.11) (except for the condition $f(2, c) \leq 0$, which will not be needed). Using the variables (u, v) instead (n, c) , we introduce the set (which coincides with G)

$$S = \{(u, v); \quad u_* \leq u \leq 1, \quad 0 \leq v \leq 1\}.$$

We assume:

$$(5.1) \quad \begin{aligned} &\text{the function } d(u, v) \text{ is in } C^1(S), \text{ and} \\ &0 < d_0 \leq d(u, v) \leq d_1 < \infty, \quad d_u \leq 0, \quad d_v \geq 0, \quad ad \leq 1 \end{aligned}$$

where a is the constant appearing in (4.2) and (4.18);

$$(5.2) \quad \begin{aligned} &\text{the function } f(u, v) \text{ is in } C^1(S) \text{ and} \\ &f(1, 0) = 0, \quad f_u(1, 0) < 0, \quad f(u, 0) > 0 \text{ for } u_* \leq u < 1, \\ &f_v(u, v) > 0 \text{ in } S; \end{aligned}$$

$$(5.3) \quad \begin{aligned} &\text{the function } g(u, v) \text{ is in } C^1(S) \text{ and} \\ &g(0, 1) = 0, \quad g(u, 0) \geq 0 \text{ and } g(u, 1) \leq 0 \text{ for } u_* \leq u \leq 1, \\ &g_u(u, v) < 0, \quad g_v(u, v) < 0 \text{ in } S; \end{aligned}$$

$$(5.4) \quad \begin{aligned} &\text{there exists a positive number } \ell \text{ such that } \ell(1 - u_*) > 1 \text{ and} \\ &\max_{0 \leq v \leq \ell(1-u)} \frac{f(u, v)}{d(u, v)} + \frac{1}{\ell} g(u, \ell(1-u)) \leq 0 \text{ for } 1 - \frac{1}{\ell} \leq u \leq 1. \end{aligned}$$

Note that $1 - \frac{1}{\ell} > u_*$.

THEOREM 5.1. *If the conditions (5.1)–(5.4) hold then problem (P_0) has at least one solution (c, u, v) and $v'(z) < 0$ for $0 < z < \infty$.*

The proof is given in the next three sections. In Section 6 we solve, for a given $V = V(u)$, the equation (4.23) for (c, Q) under the conditions $Q(u_*) = cu_*$, $Q(1) = 0$. Substituting this solution into equation (4.24), we solve the resulting equation, in Section 7, and denote the solution by W ; this defines a mapping $T : V \rightarrow W$. For technical reasons we shall actually consider the V -equation only in the interval $u_* \leq u < 1 - \varepsilon$ ($\varepsilon > 0$), in order to avoid the degeneracy of the leading coefficient at $u = 1$. Thus the mapping T depends on ε (and will be denoted by T_ε), and we shall prove that it has at least one fixed point. In Section 8 we let $\varepsilon \rightarrow 0$ and, invoking the equivalence established in Lemma 4.2, prove that the solution $(c_\varepsilon, Q_\varepsilon, V_\varepsilon)$ of the fixed point of T_ε converges to a solution of problem (P_1) .

6. Solution for (c, Q) , given $V(u)$. For any small $\varepsilon > 0$ we introduce the space

$$X_\varepsilon = \{V \in C^0[u_*, 1], \quad 0 \leq V \leq 1, \quad V \equiv 0 \quad \text{on} \quad [1 - \varepsilon, 1]\}.$$

Given $V(u)$ in X_ε , consider the problem:

Problem (P_2) . Find (c, Q) with $c > 0$ such that

$$(6.1) \quad QQ_u - cQ + d(u, V(u)) f(u, V(u)) = 0 \quad \text{in } \Omega,$$

$$(6.2) \quad Q(u_*) = cu_*, \quad Q(1) = 0, \quad Q > 0 \quad \text{in } \Omega.$$

THEOREM 6.1. *Under the assumptions (5.1), (5.2) there exists a unique solution to (6.1), (6.2); furthermore, the following estimates hold:*

$c_1 \leq c \leq c_2$ where

$$(6.3) \quad c_1 = \sqrt{d_0} \max_{\Omega} \left\{ \frac{1}{u} \int_{u_*}^u \frac{f(s, 0)}{s} ds \right\}^{1/2}, \quad c_2 = 2\sqrt{d_1} \max_{\Omega} \left\{ \frac{1}{u} \int_{u_*}^u \frac{f(s, 1)}{s} ds \right\}^{1/2},$$

$c_3(1 - u) \leq Q(u) \leq c_2u$ in Ω where

$$(6.4) \quad c_3 = \frac{1}{2} \left\{ -c_2 + \left[c_2^2 + 4d_0 \min_{\Omega} \frac{f(s, 0)}{1-s} \right]^{1/2} \right\},$$

and

$$(6.5) \quad Q(u) \leq \sqrt{2d_1} \left[\int_u^1 f(s, V(s)) ds \right]^{1/2} \leq \sqrt{2d_1} \|f\|_{L^\infty} \sqrt{1-u}.$$

Note, by (5.2), that $0 < c_1 < c_2$ and $c_3 > 0$.

To prove the theorem we consider first the more general

Problem (P_3) . Find (c, Q) with $c > 0$ such that

$$(6.6) \quad QQ_u - cQ + F(u) = 0 \quad \text{in } \Omega = (u_*, 1),$$

$$(6.7) \quad Q(u_*) = cu_*, \quad Q(1) = 0, \quad Q(u) > 0 \quad \text{in } \Omega$$

where

$$(6.8) \quad F \in C^0[u_*, 1], \quad F(1) = 0, \quad F(u) > 0 \quad \text{in } (u_*, 1).$$

LEMMA 6.2. *Problem (P_3) admits a unique solution (c, Q) . The solution has the following properties:*

$$(6.9) \quad c_F < c < 2c_F \quad \text{where} \quad c_F = \max_{\Omega} \left\{ \frac{1}{u} \int_{u_*}^u \frac{F(s)}{s} ds \right\}^{1/2},$$

$$(6.10) \quad 0 < Q(u) < cu \quad \text{in } \Omega,$$

$$(6.11) \quad \lambda(u)(1 - u) \leq Q(u) \leq \Lambda(u)(1 - u) \quad \text{in } \Omega$$

where

$$\lambda(u) = \frac{1}{2} \left\{ -c + \left[c^2 + 4 \min_{[u, 1]} \frac{F(s)}{1-s} \right]^{1/2} \right\} \in (0, \infty),$$

$$\Lambda(u) = \frac{1}{2} \left\{ -c + \left[c^2 + 4 \max_{[u, 1]} \frac{F(s)}{1-s} \right]^{1/2} \right\} \in (0, \infty) \cup \{\infty\},$$

$$(6.12) \quad Q(u) < \left\{ 2 \int_u^1 F(s) ds \right\}^{1/2} \leq \left\{ 2|F|_{L^\infty(\Omega)} \right\}^{1/2} (1-u)^{1/2} \quad \text{in } \Omega$$

and

$$(6.13) \quad c = \int_{u_*}^1 \frac{F(s)}{Q(s)} ds > 0 .$$

Note that if $F_u(1, 0) = -\infty$ then $\Lambda(u) = \infty$.

Proof. We first prove uniqueness. Suppose (c_1, Q_1) and (c_2, Q_2) are two solutions. It suffices to show that $c_1 = c_2$. We proceed by contradiction, assuming that $c_1 > c_2$. Then $Q_1(u_*) > Q_2(u_*)$, and we introduce

$$\bar{u} = \sup\{u \in [u_*, 1] , \quad Q_1 > Q_2 \quad \text{in } [u_*, u]\} .$$

If $\bar{u} < 1$ then $Q_1(\bar{u}) = Q_2(\bar{u})$ and $\frac{d}{du}(Q_1 - Q_2) \leq 0$ at \bar{u} . However from (6.6) we get

$$\frac{d}{du}(Q_1 - Q_2)|_{u=\bar{u}} = c_1 - c_2 - F(\bar{u}) \left[\frac{1}{Q_1(\bar{u})} - \frac{1}{Q_2(\bar{u})} \right] = c_1 - c_2 > 0 ,$$

a contradiction. We conclude that $\bar{u} = 1$, i.e., $Q_1 > Q_2$ in $[u_*, 1)$. Integrating (6.6) over $[u_*, 1]$ for (c_1, Q_1) and (c_2, Q_2) and taking the difference, we get, after using (6.7),

$$\begin{aligned} 0 > \frac{1}{2} (c_2^2 - c_1^2) u_*^2 &= \left[\frac{1}{2} Q_1^2 - \frac{1}{2} Q_2^2 \right]_{u=u_*}^{u=1} = \int_{u_*}^1 \left(Q_1 \frac{\partial Q_1}{\partial u} - Q_2 \frac{\partial Q_2}{\partial u} \right) du \\ &= \int_{u_*}^1 (c_1 Q_1 - c_2 Q_2) du > 0 , \end{aligned}$$

a contradiction.

To prove existence we extend $F(u)$ by 0 to $u > 1$. Denote by $Q(c, u)$ ($c > 0$) the solution to

$$(6.14) \quad Q_u = c - \frac{F}{Q} , \quad Q(u_*) = cu_*$$

and denote by $[u_*, \gamma(c))$ the maximal existence interval where $Q > 0$. The set

$$\mathcal{A} = \{c > 0 ; \quad \gamma(c) > 1\}$$

is clearly an open set. We claim that

$$(6.15) \quad [0, c_F) \cap \mathcal{A} = \emptyset .$$

Indeed, since $F > 0$ in Ω , (6.14) gives $Q_u < c$ so that, by integration, $Q < cu$ and, consequently,

$$Q_u < c - \frac{F}{cu} .$$

Again, by integration,

$$Q < cu - \int_{u_*}^u \frac{F(s)}{cs} ds = \frac{u}{c} \left\{ c^2 - \frac{1}{u} \int_{u_*}^u \frac{F(s)}{s} ds \right\} .$$

It follows that if $c < c_F$ then $\gamma(c) < 1$, i.e., (6.15) holds.

We next prove that

$$(6.16) \quad [2c_F, \infty) \subset \mathcal{A} .$$

Indeed, denote by $\gamma_1(c)$ the smallest value of u in $[u_*, \gamma(c)]$ such that $Q = \frac{1}{2}cu$, i.e.,

$$\gamma_1(c) = \sup \left\{ s \leq \gamma(c) , \quad Q(u) > \frac{1}{2}cu \quad \text{in } [u_*, s] \right\} .$$

If $\gamma_1 = \gamma_1(c) \leq 1$ then, integrating (6.14) over $[u_*, \gamma_1(c)]$, we obtain

$$\begin{aligned} Q(\gamma_1(c)) &= c\gamma_1 - \int_{u_*}^{\gamma_1} \frac{F}{Q} > c\gamma_1 - \int_{u_*}^{\gamma_1} \frac{2F(s)}{cs} ds \\ &= \frac{c\gamma_1}{2} \left\{ 2 - \frac{4}{c^2} \frac{1}{\gamma_1} \int_{u_*}^{\gamma_1} \frac{F(s)}{s} ds \right\} \geq \frac{c\gamma_1}{2} \quad \text{if } c \geq 2c_F , \end{aligned}$$

which is a contradiction. Hence $\gamma(c) \geq \gamma_1(c) > 1$ if $c \geq 2c_F$ and (6.16) is proved.

Now define $c_0 = \inf\{c; c \in \mathcal{A}\}$. By continuity, $\gamma(c_0) \geq 1$ and, from (6.16) and the proof of (6.15), $c_F < c_0 < 2c_F$. If $Q(c_0, 1) > 0$ then, as \mathcal{A} is open, there are values of c smaller than c_0 (and near c_0) for which $Q(c, u) > 0$ if $u_* \leq u \leq 1$, which contradicts the definition of c_0 . We conclude that $Q(c_0, 1) = 0$ and thus $(c_0, Q(c_0, u))$ is a solution to problem (P_3) . For simplicity we shall denote this solution by (c, Q) .

Integrating (6.6) over $[u, 1]$ we have

$$\frac{1}{2} [Q^2]_u^1 > - \int_u^1 F(s) ds$$

so that

$$Q^2(u) < 2 \int_u^1 F(s) ds ,$$

and (6.12) follows. Integrating (6.14) over $[u_*, 1]$ and using (6.7), the relation (6.13) also follows.

It remains to prove (6.11). We first derive the upper bound on Q . If we define

$$\delta = \inf\{\tilde{s} > 0 ; \quad Q(u) < \tilde{s} + \Lambda(u)(1 - u) \quad \text{in } [u_*, 1]\}$$

then it suffices to show that $\delta = 0$. Without loss of generality here we may assume that $\Lambda(1-) < \infty$. Then $\Lambda(u)$ is continuous and, if $\delta > 0$, there exists a point $u_1 \in [u_*, 1)$ such that $Q(u_1) = \delta + \Lambda(u_1)(1 - u_1)$ and

$$\left. \frac{dQ}{du} \right|_{u=u_1} \leq \left. \frac{d}{du} [\Lambda(u)(1 - u)] \right|_{u=u_1} \leq -\Lambda(u_1) ,$$

since $\Lambda(u)$ is monotone decreasing; the first inequality is actually an equality if $u^* < u_1 < 1$. Using (6.14) we get

$$-\Lambda(u_1) \geq c - \frac{F(u_1)}{\delta + \Lambda(u_1)(1 - u_1)} \geq c - \frac{F(u_1)}{\Lambda(u_1)(1 - u_1)} ,$$

that is

$$-\Lambda^2(u_1) > c\Lambda(u_1) - \frac{F(u_1)}{1 - u_1} \geq c\Lambda(u_1) - \max_{[u_1, 1]} \frac{F(s)}{1 - s} .$$

However, by definition of $\Lambda(u)$,

$$\Lambda^2(u) + c\Lambda(u) - \max_{[u,1]} \frac{F(s)}{1-s} = 0$$

which is a contradiction.

Similarly we define

$$\delta = \inf\{s > 0 ; \quad Q(u) > \lambda(u)(1-u) - s\}$$

and show that $\delta = 0$. □

Proof of Theorem 6.1. Applying Lemma 6.2 with $F(u) = d(u, V(u)) f(u, V(u))$ and using (5.1), (5.2) and the fact that $V(u)$ is in X_ε , the assertions of Theorem 6.1 immediately follow. (The assumptions $d_u \leq 0$, $d_v \geq 0$, $ad \leq 1$ are not needed for Theorem 6.1).

7. A fixed point $(c_\varepsilon, Q_\varepsilon, V_\varepsilon)$.

Given $V \in X_\varepsilon$, let (c, Q) denote the solution of (6.1), (6.2) and consider the problem:
Problem (P_4) . Find $W(u)$ such that

$$(7.1) \quad \frac{Q}{d} \left(\frac{Q}{d} W_u \right)_u - ac \frac{Q}{d} W_u + g(u, W) = 0 \quad \text{in } \Omega_\varepsilon = [u_*, 1 - \varepsilon] ,$$

$$(7.2) \quad -\frac{Q}{d} W_u + \Psi(ac, W) = 0 \quad \text{at } u = u_* ,$$

$$(7.3) \quad W(u) = 0 \quad \text{in } [1 - \varepsilon, 1]$$

where $d = d(u, V(u))$.

LEMMA 7.1. *Under the assumptions (5.1)–(5.3) there exists a unique solution W to problem (P_4) , and the following inequalities hold:*

$$(7.4) \quad 0 \leq W \leq 1 \quad \text{in } \Omega_\varepsilon ,$$

$$(7.5) \quad -M_\varepsilon \leq W_u \leq 0 \quad \text{in } \Omega_\varepsilon ,$$

$$(7.6) \quad |W_u(u_*)| \leq c_4$$

where M_ε is a constant which depends on ε but not on $V \in X_\varepsilon$, and c_4 is independent of ε and V .

Proof. Extend the definition of $g(u, w)$ to all $w \in \mathbb{R}^1$ such that $g_w < 0$. By Theorem 6.1

$$(7.7) \quad c_3\varepsilon \leq Q < c_2 \quad \text{in } [u_*, 1 - \varepsilon] ,$$

so that the differential equation (7.1) is non-degenerate in Ω_ε . The inequalities $g_w < 0$ and $\Psi_w > 0$ will enable us to use the comparison principle for the system (7.1)–(7.3). For any function $\tilde{W}(u)$ satisfying $0 \leq \tilde{W}(u) \leq 1$, we set $g = g(u, \tilde{W}(u))$, $\Psi = \Psi(ac, \tilde{W}(u))$ and denote the corresponding solution of (7.1)–(7.3) by $W(u)$. Since

$$\begin{aligned} g(u, 0) &\geq g(u, \tilde{W}(u)) \geq g(u, 1) , \\ \Psi(ac, 0) &\leq \Psi(ac, \tilde{W}(u)) \leq \Psi(ac, 1) , \end{aligned}$$

the comparison principle shows that $0 \leq W(u) \leq 1$. We can therefore apply the Schauder fixed point argument to the mapping $\tilde{W} \rightarrow W$ to deduce the existence of a solution to (7.1)–(7.3). Uniqueness of the solution of (7.1)–(7.3) follows again by a comparison argument.

Next, differentiating (7.1) and setting $Z = \frac{Q}{d} W_u$, we get

$$\left(\frac{Q}{d} Z_u \right)_u - acZ_u + g_v \frac{d}{Q} Z + g_u = 0 .$$

Also

$$Z|_{u=u_*} = \Psi(ac, W(u_*)) < 0 , \quad Z|_{u=1-\varepsilon} \leq 0 .$$

Since $g_v < 0$ and $g_u < 0$, the maximum principle yields $Z \leq 0$, i.e., $W_u \leq 0$. Finally, (7.6) and the first inequality in (7.5) follow from the fact that the equation (7.1) is non-degenerate (i.e., from (7.7)). \square

We shall now combine Lemma 7.1 with Theorem 6.1. For every $V \in X_\varepsilon$ we define (c, Q) by Theorem 6.1 and W by Lemma 7.1, and introduce the mapping T_ε by

$$T_\varepsilon V = W .$$

Clearly T_ε maps X_ε into itself, and its image lies in a compact subset of X_ε (since $|W_u| \leq M_\varepsilon$). By the uniqueness parts of Theorem 6.1 and Lemma 7.1 it also easily follows that T_ε is continuous. Invoking the Schauder fixed point theorem, we conclude that there exists at least one fixed point for T_ε . We shall denote it by $(c_\varepsilon, Q_\varepsilon, V_\varepsilon)$.

We define a function $u_\varepsilon(z)$ by

$$(7.8) \quad z = \int_{u_*}^{u_\varepsilon(z)} \frac{d(s, V_\varepsilon(s))}{Q_\varepsilon(s)} ds , \quad z \in [0, Z_\varepsilon]$$

where

$$(7.9) \quad Z_\varepsilon = \int_{u_*}^{1-\varepsilon} \frac{d(s, V_\varepsilon(s))}{Q_\varepsilon(s)} ds ,$$

and introduce also the function

$$v_\varepsilon(z) = V_\varepsilon(u_\varepsilon(z)) .$$

Then $(c_\varepsilon, u_\varepsilon(z), v_\varepsilon(z))$ form a solution of the system (4.17)–(4.21) in $[0, Z_\varepsilon]$, but without the conditions $u(\infty) = 1$, $v(\infty) = 0$.

By (6.9)–(6.11), the functions $Q_\varepsilon(u)$ are uniformly bounded from above and below by two positive constants, for $u_* \leq u \leq 1 - \delta$ (for any $\delta > 0$), and the same is true for the constants c_ε . Using also the estimates of Lemma 7.1, we deduce that $u_\varepsilon(0), u'_\varepsilon(0), v_\varepsilon(0), v'_\varepsilon(0)$, are uniformly bounded. Hence, we can choose a subsequence $\varepsilon \downarrow 0$ such that

$$(7.10) \quad (c_\varepsilon, u_\varepsilon, v_\varepsilon) \rightarrow (c, u, v)$$

where (c, u, v) is a solution of (4.17)–(4.21) for $0 < z < z_0$, where

$$(7.11) \quad z_0 = \lim_{\varepsilon \downarrow 0} Z_\varepsilon .$$

The corresponding limits (Q, V) of $(Q_\varepsilon, V_\varepsilon)$ also exist, and $Q(u) > 0$ if $u_* < u < 1$, $Q(1) = 0$.

LEMMA 7.2. *If $z_0 = \infty$ then (c, u, v) is a solution to problem (P_0) .*

Proof. The only assertions that still need to be proved are:

$$(7.12) \quad u(\infty) = 1 , \quad v(\infty) = 0 .$$

We know that $u(\infty)$, $v(\infty)$ exist. Consequently (by ODE theory) u'' and v'' are bounded and then $u'(\infty)$, $v'(\infty)$ must exist and be equal to zero. The relation (4.30) holds for $0 < z < \infty$, and taking $z \rightarrow \infty$ we get $Q(u(\infty)) = 0$, so that $u(\infty) = 1$. Finally, from (4.17) we deduce that

$$d(1, v(\infty))u'' + f(1, v(\infty)) \rightarrow 0 \quad \text{if } z \rightarrow \infty .$$

From this it follows that $f(1, v(\infty)) = 0$ (otherwise $u'(z)$ will not converge to zero as $z \rightarrow \infty$), so that, by (5.2), $v(\infty) = 0$. \square

8. Proof of Theorem 5.1.

In Section 7 we established the existence of a fixed point $(c_\varepsilon, u_\varepsilon, v_\varepsilon)$, or $(c_\varepsilon, Q_\varepsilon, V_\varepsilon)$, for the mapping $T_\varepsilon : X_\varepsilon \rightarrow X_\varepsilon$, and also proved that $\partial V_\varepsilon / \partial u \leq 0$. In this section we shall replace X_ε by the subset

$$(8.1) \quad Y_\varepsilon = \left\{ V \in C^0[u_*, 1] ; \quad 0 \leq V \leq 1, \quad V_u \leq 0, \right. \\ \left. V \equiv 0 \quad \text{on } [1 - \varepsilon, 1], \quad \text{and } V(u) \leq \ell(1 - u) \quad \text{in } \left[1 - \frac{1}{\ell}, 1\right] \right\}$$

where ℓ is the positive number appearing in the condition (5.4).

LEMMA 8.1. *Under the assumptions (5.1)–(5.4), T_ε has a fixed point in Y_ε .*

Proof. We only need to show that T_ε maps Y_ε into itself; the rest of the analysis is as before. If we set $T_\varepsilon V = W$ then, as before, $W_u \leq 0$, and so all we need to show is that

$$(8.2) \quad W(u) \leq \ell(1 - u) \quad \text{in } \left[1 - \frac{1}{\ell}, 1 - \varepsilon\right] .$$

Consider the function $\bar{W}(u) = \ell(1 - u)$ in $\left[1 - \frac{1}{\ell}, 1 - \varepsilon\right]$. It satisfies:

$$\bar{W}\left(1 - \frac{1}{\ell}\right) = 1 \geq W\left(1 - \frac{1}{\ell}\right), \quad \bar{W}(1 - \varepsilon) = \ell\varepsilon > 0 = W(1 - \varepsilon) .$$

Also

$$\begin{aligned} \mathcal{L}W &\equiv \frac{Q}{d} \left(\frac{Q}{d} \bar{W}_u \right)_u - \alpha c \frac{Q}{d} \bar{W}_u + g(u, \bar{W}) \\ &= -\ell \left\{ \frac{Q}{d} \frac{Q_u}{d} - \frac{Q^2}{d} \frac{d_u + d_v V_u}{d^2} \right\} + \ell \alpha c \frac{Q}{d} + g(u, \bar{W}) \\ &= -\frac{\ell}{d^2} \left\{ (c - acd)Q - df \right\} + \frac{Q^2 \ell}{d^3} (d_u + d_v V_u) + g(u, \bar{W}) \quad \text{by (6.1).} \end{aligned}$$

Since $d_u \leq 0$, $d_v \geq 0$, $V_u \leq 0$, $1 - ad \geq 0$, $Q > 0$, we get

$$\mathcal{L}W \leq \ell \left\{ \frac{f(u, V(u))}{d(u, V(u))} + \frac{1}{\ell} g(u, \ell(1 - u)) \right\} \leq 0 \quad \text{in } \left[1 - \frac{1}{\ell}, 1 - \varepsilon\right] ,$$

by (5.4); here we used the inequality $V(u) \leq \ell(1 - u)$ in $\left[1 - \frac{1}{\ell}, 1\right]$. Thus \bar{W} is a supersolution, and (8.2) follows by comparison. \square

We shall henceforth work with the solution $(c_\varepsilon, u_\varepsilon, v_\varepsilon)$, or $(c_\varepsilon, Q_\varepsilon, V_\varepsilon)$, corresponding to the space Y_ε and with the corresponding limits (c, u, v) (see (7.10)) and (c, Q, V) . We shall prove

that (c, u, v) is a solution to problem (P_0) . In view of Lemma 7.2, all we need to prove is the following:

LEMMA 8.2. *Under the assumptions (5.1)–(5.4) the following relations hold:*

$$(8.3) \quad z_0 = \int_{u_*}^1 \frac{d(s, V(s))}{Q(s)} ds = \infty .$$

Proof. Recalling that $f(1, 0) = 0$ and using Lemma 8.1 we have

$$f(u, V_\varepsilon(u)) \leq \|f_u\|_{L^\infty}(1-u) + \|f_v\|_{L^\infty}V_\varepsilon(u) \leq M(1-u) ,$$

for $u \in \left[1 - \frac{1}{\ell}, 1 - \varepsilon\right]$. Using this in (6.5) we get $Q_\varepsilon(u) \leq M(1-u)$ with another constant M , independent of ε . It follows that

$$Q(u) \leq M(1-u) \quad \text{in} \quad \left[1 - \frac{1}{\ell}, 1\right]$$

and, since $d(u, V(u)) \geq d_0 > 0$, the assertion (8.3) follows. \square

9. Application to corneal epithelial wound healing.

In the model that appears in [2] (see also [1]), after non-dimensionalization,

$$(9.1) \quad \frac{\partial N}{\partial t} = \frac{\partial}{\partial X} \left[(\alpha + 0.1\alpha C) \frac{\partial N}{\partial X} \right] + \frac{\partial}{\partial X} (e(X, t)N) + F(N, C),$$

$$(9.2) \quad \frac{\partial C}{\partial t} = D_C \frac{\partial^2 C}{\partial X^2} + G(N, C)$$

where

$$F(N, C) = +(0.9 + 0.1C)(2N - N^2) - N,$$

$$G(N, C) = A + B(N) - \mu N h(C) - \delta C,$$

$$h(C) = \frac{C}{\hat{C} + C}, \quad \delta = 242 ,$$

$$B(N) = B(0)\chi_{\{N=0\}} , \quad B(0) > 0 , \quad \alpha = 0.012 , \quad D_C = 6 , \quad \mu = 2 \times 10^4 .$$

Here $e(X, t)N$ accounts for the physiological electric field and it thus depends on the proximity of X to the free boundary. It seems, however, more natural to replace $e(X, t)N$ by a function $k(N)N_X$ where $k(n_*) > 0$, $k'(N) \leq 0$ if $N > n_*$, and $k(N) = 0$ if $N > n_* + \varepsilon_0$ for some $\varepsilon_0 > 0$. We shall take

$$k(N) = e_0 E(N) , \quad e_0 > 0$$

so that $E'(N) \leq 0$; it will be convenient to set $e_0 = \alpha e$, $e > 0$.

Let $X = \sqrt{\alpha x}$, $N = n(x, t)$, $C = 1 + C^*c(x, t)$ where, by [2], $C^* \sim 5-50$. Writing the system (9.1), (9.2) (with $e(X, t)N$ replaced by $\alpha e E(N)$) in the form (1.1), (1.2), we then have

$$(9.3) \quad d(n, c) = 1.1 + bc + eE(n)$$

where $a = \alpha/D_C = 2 \times 10^{-3}$, $b = 0.1C^*$,

$$(9.4) \quad f(n, c) = (1 + bc)n(1 - n) + bnc$$

and

$$g(n, c) = \frac{a}{C^*} G(n, 1 + C^*c) .$$

It is easily seen that all the assumptions made in Theorem 1.1 are satisfied.

In order to verify the assumptions of Theorem 5.1, we observe that the numerical results obtained in [1, 2], which exhibit a travelling wave solution, imply that

$$G(1, 1) = 0 \quad G(0, 1 + C^*) = 0 ,$$

so that

$$(9.5) \quad A = \delta + \mu h(1) , \quad C^* = \frac{1}{\delta} (\mu h(1) + B(0)) .$$

Setting

$$\theta = \frac{\mu h(1)}{\mu h(1) + B(0)} , \quad 0 < \theta < 1 ,$$

we get

$$(9.6) \quad g(n, c) = a\delta \left\{ -c + \theta(1 - n) + \theta n \left(1 - \frac{h(1 + C^*c)}{h(1)} \right) + (1 - \theta)\chi_{\{n=0\}} \right\} .$$

We easily check that the functions d, f, g then satisfy all the assumptions in (5.1)–(5.3). Thus it remains to show that condition (5.4) also holds; this is more delicate. We note that whereas in [1] (and also in [2]) \hat{C} is taken as 3, so that $h(1) = \frac{1}{4}$, the numerical graph in Figure 2 in [1] shows that actually $1 + C^* = 5$ in case $B(0) = 0$, so that, from the second relation in (9.5),

$$h(1) = \frac{\delta C^*}{\mu} \sim \frac{1}{20} .$$

We shall take an intermediate value, $h(1) = \frac{1}{10}$, so that $\hat{C} = 9$. Then

$$g(u, v) = 0.4 \left\{ -v + \theta(1 - u) - \theta C^* \frac{uv}{1 + bv} \right\}$$

in the healed region. Clearly

$$\max_{0 \leq v \leq w} \frac{f(u, v)}{d(u, v)} \leq u(1 - u) + \frac{buw}{1 + bw}$$

and, with $v = \ell(1 - u)$,

$$\frac{g(u, v)}{\ell} \Big|_{v=\ell(1-u)} \leq -4\theta b \frac{u(1-u)}{1+bw} \quad \text{if } \ell > 1 \geq \theta .$$

Hence the condition (5.4) holds if

$$(9.7) \quad 1 + \frac{\ell b}{1 + bw} - \frac{4\theta b}{1 + bw} \leq 0 \quad \text{for } 0 \leq w \leq 1 .$$

This inequality is satisfied for some ℓ, θ near 1 provided $2b > 1$, which is indeed the case since $b = 0.1C^*$ and $C^* > 8$ by (9.5).

We conclude that for the relevant range of parameters that occur in [1, 2] the functions d, f, g satisfy all the assumptions made in Theorem 1.1 and all the assumptions (5.1)–(5.3) made in Theorem 5.1. As for the last assumption (5.4) made in Theorem 5.1, it does hold for *some* range of relevant parameters.

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